The 5-Minute Urology Consult

3RD EDITION

Editor-in-Chief
Leonard G. Gomella, MD, FACS
The Bernard W. Godwin Professor of Prostate Cancer
Chairman
Department of Urology
Sidney Kimmel Medical College
Associate Director, Jefferson Sidney Kimmel Cancer Center
Clinical Director, Jefferson Sidney Kimmel Cancer Network
Thomas Jefferson University
Philadelphia, Pennsylvania

Associate Editors
Gerald L. Andriole, MD, FACS
Arthur L. Burnett, II, MD, MBA, FACS
Robert C. Flanigan, MD, FACS
Thomas E. Keane, MB, ChB, FRCSI, FACS
Harry P. Koo, MD, FAAP, FACS
Judd W. Moul, MD, FACS
Raju Thomas, MD, MHA, FACS
To Tricia, Leonard, Patrick, Andrew, and
Michael, for their understanding and
encouragement, and with appreciation
for their individual accomplishments.

"En tierra de los ciegos el tuerto es rey."

SPANISH PROVERB
I am very pleased to present the third edition of The 5-Minute Urology Consult. The first edition was released almost 15 years ago, with the second edition published in 2010. The continuing advances in urology lead to this much-needed 2015 update. The goal of this book is to provide the reader with useful information in a quick reference format to help with the everyday care of patients with urologic problems. This third edition has undergone extensive editing and updating to reflect the most current data possible at the time of publication.

Urologic diseases and conditions are common problems seen by all health care providers. Almost one-third of all genitourinary disorders involve the genitourinary system, and the urinary tract accounts for almost 25% of all solid tumors in adults. While this book is written primarily for urologists, any health care practitioner who deals with urologic complaints and conditions should find the book a useful resource. Students of urology, residents and fellows preparing for oral and written in-service examination, and practicing urologists preparing for certification examinations will find the book a useful study aid. While primarily written for practitioners in the United States, the table of contents has been reviewed by our international editorial board, which represent more than three dozen countries, in an attempt to capture as many diseases and conditions as possible for international readers.

The broad array of topics addressed in this book is based on reviews of published literature, major textbooks, grand rounds case presentations, validated Internet resources, and actual patient consultations. Topics are meant to represent “real-world” clinical questions from very broad to very specific topics. Some of the topics may appear redundant, such as Section I topics “Scrotum and testicle, masses” and “Scrotum, tumor and mass, adult, general considerations.” There is a deliberate reason for this, namely, to frame the thought process to differentiate scrotal masses from testicular masses when the presenting problem is not clear. If it is clearly a testicular mass, then the one topic deals effectively with that setting. If it is not a clear mass in the testicle, the reader can approach the problem more broadly in terms of a mass within the scrotum that may or may not involve the testicle. Coverage includes adult and pediatric urologic, as well as subspecialty areas of urology such as urologic oncology, endourology, female urology, neurourology, andrology, infectious diseases, and renal transplantation. It represents a core of essential “must-know” and practical information specifically written for the field of urology. While some surgical techniques are discussed, this is not meant to be a comprehensive urologic surgical text. Numerous high-quality publications address the finer points of urologic surgery. This book addresses pre and post operative care as well as some intra-operative techniques; however the focus is on more global patient management issues.

I am often surprised when asked why medical books such as this are even necessary as a reference in the modern world because there is so much information readily available on devices such as smartphones via the Internet. While the reality is that virtually any topic can be searched for on the Internet, the ability to sort through the information presented, confirm the validity, and rapidly find the specific information needed is often very time-consuming and can be prone to error. Multiple studies have shown that many websites can contain erroneous, misleading, or out-of-date information. Readers of this book can be assured that the information presented is held to the highest standards possible, as it is written, reviewed, and further edited primarily by academic urologists and other academic specialists. Every effort is made to present the most up-to-date standards of care at the time of publication.

This book, a member of the popular “5-Minute Consult” series published by Wolters Kluwer Health, generally follows the organizational formatting of the other books in the series. However, there are notable exceptions, as this book is focused on a primarily surgical subspecialty. Section I: Urologic Diseases and Conditions provides information on more than 300 major topics in the field of urology. The style of this section, while similar to the other books in the series, focuses more attention on the surgical management, where appropriate. Furthermore, evidence-based medicine references, standard fare in the “5-Minute Consult” series, are included in this urology edition. This is representative of the trend in the field of medicine to assign “levels of evidence” to treatment recommendations (see page ix for a further discussion). A challenge with any surgical discipline is that, when reviewing published literature, this type of information is not as well represented as in other medical disciplines. The reader will note that in this edition, the use of evidence-based medicine is identified in chapters as appropriate.

Many topics are further supported by algorithms and the enhanced image library available in the ebook version provided along with the print version. Both ICD-9 and preliminary high level ICD-10 codes have been incorporated in preparation for the rollout of ICD-10 in late 2015.

Section II: Short Topics: A to Z consists of more than 1,300 diseases, conditions, presenting complaints, or key concepts in the field that the practitioner must be aware of but may not be worthy of a complete 2-page chapter. Section III has been greatly expanded and now features nearly 90 visual algorithms to enhance many more clinically relevant topics. Section IV is dedicated exclusively to a core discipline in our field: Urinalysis and Urine Studies. Section V: Alternative and Complementary Urologic Therapies is a focused review that is of interest to both patients and caregivers alike. Section VI: Urologic Drug Reference is a very unique collection of information on hundreds of drugs used in urologic practice in the United States as well as some traditionally nonurologic medications that are clinically significant to the urologic practitioner. Additional urologic applications not often found on the package insert for “off-label” use in daily care are included for many medications. These “off-label” applications are noted on the basis of published literature with additional input and the personal observations of the authors and editors. Finally, Section VII: Reference Tables is a collection of useful reference information and forms. A media and image collection is available in this edition.
the ebook version of this book. Please see information inside front cover on how to access this content.

In any project of this magnitude, there are numerous individuals responsible for its success. I would like to thank the following individuals who provided the initial guidance in 1996 to develop the first urology version of the 5-Minute Consult: Lippincott Williams & Wilkins editors Carroll Cann and Craig Percy, and an early pioneer of the 5-Minute Consult concept, Dr. Mark Dambro. Thanks to my administrative assistants Denise Tropea and Barbara Devine, who provided key support to keep the contributors and this edition organized. A special thanks to the more than 370 authors and editors who took the time to contribute to this edition and the numerous contributors to the previous editions that laid a strong foundation for this third update. To my colleagues who served as Associate, Consulting, Specialty and International Editors, my most sincere gratitude and appreciation for the time you took to recruit authors, create and review content. It is also with great sadness that one of our international editors and an icon in the field of Urology, Professor John Fitzpatrick passed away during the completion of this book. He will be missed by all but his numerous contributions to our field will live on.

Residents from the Department of Urology of Thomas Jefferson University and from the University of West Virginia deserve special acknowledgement. They supported the content of both Section II "Short Topics" and Section III "Algorithms." Their names appear in the contributor listing as having been authors but are not specifically recognized for their work in these sections. Now however, they are.

The editorial and production staff at Wolters Kluwer Health have distinguished themselves as the best publishing team I have had the opportunity to work with. My personal interactions with the company and their willingness to discuss any and all issues relating to the book are testimony to their corporate philosophy in respecting the authors’ opinions to develop the best educational products possible in the field of medicine. Brian Brown, Keith Donnellan, and Brendan Huffman are the best partners a medical author could hope to work with. In the final production stages, David Saltzberg and Harish Kumar kept everything moving to stay on schedule. Special thanks to Philadelphia-based friend and professional photographer Robert Neroni, who captured the spirit of urology in our cover photo.

Our children, Leonard, Patrick, Andrew, and Michael, deserve credit for their encouragement and patience over the many years of my time spent working on this project. In this edition, I am very proud that a few of the boys were actually able to make tangible professional contributions.

Most importantly, I would like to thank my wife, Tricia, with the usual and customary accolades that authors share about their spouses in acknowledging the love and support provided. However, her attention to detail as a behind-the-scenes editorial partner and skilled reviewer for final content of this book added a degree of accuracy that I could never have accomplished alone.

Please contact me if you have corrections or suggestions on ways to improve future editions of the book. I hope that The 5-Minute Urology Consult will provide useful information to allow all of us to care for our urology patients in the best way possible.

Leonard G. Gomella, MD
leonard.gomella@jefferson.edu
www.urologyquestion.com
Evidence-based medicine (EBM) is generally defined as the use of current best medical evidence to aid in making decisions about the care of an individual patient. While the ultimate decision-making process for or against a given treatment must be made between the patient and the health care provider, EBM seeks to assess the quality of evidence that a specific course of action is based on. The underlying principle is the evaluation of medical interventions and the literature that supports these interventions in a systematic and organized fashion. Since its introduction as a concept in the modern medicine over 30 years ago, there has been increased emphasis on this concept in daily patient care. While there are currently many different systems of EBM, we have adopted the 5-Minute Clinical Consult standard of the “SORT Taxonomy” from the American Academy of Family Physicians. The key components are summarized later. A full review of this article can be viewed at http://www.aafp.org/afp/20040201/548.html. Throughout this edition of The 5-Minute Urology Consult, these evidence-based recommendations can be found. However, we recognize that in a primarily surgical-based specialty such as urology, this area is not yet as well defined as in more general areas of medical practice.

As an illustrative example in a chapter on hypertension, the EBM recommendation might read:

“Use thiazide diuretics as a first-line agent for the treatment of essential hypertension, as it has the greatest efficacy in preventing the vascular complications of hypertension (5A).”

The A designation, as noted in the algorithm later, implies this recommendation is based on the highest-quality, patient-oriented evidence, and should be followed. The number 5 refers to the source, which would be listed under the “References” heading as reference #5. Recommendations that are level A evidence are shaded blue in the text.

Strength of recommendation Definition

A Recommendation based on consistent and good-quality patient-oriented evidence.

- Highest-quality resource, such as a systematic review. This is a summary of the medical literature on a given topic that uses strict, explicit methods to perform a thorough search of the literature and then provides a critical appraisal of the individual studies concluding in a recommendation. The Cochrane reviews are considered by many to be the most prestigious collection of systematic reviews (www.cochrane.org).

B Recommendation based on inconsistent or limited-quality patient-oriented evidence.

- This implies that the data referenced are derived from high-quality randomized controlled trials that were performed to minimize bias in their outcome. Bias is anything that may interfere with the truth; in the medical literature, it is often unintentional but is more common than we appreciate. In short, always assume that some degree of bias exists in any research endeavor.

C Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening.

- This implies that the reference used does not meet the “A” or “B” requirements; these are often treatments recommended by consensus groups (such as the American Cancer Society). In some cases, they may be the standard of care. But implicit in a group’s recommendations is the bias of the group or author that supports the reference.

EDITORS

EDITOR-IN-CHIEF
Leonard G. Gomella, MD, FACS
The Bernard W. Godwin Professor of Prostate Cancer
Chairman
Department of Urology
Sidney Kimmel Medical College
Associate Director, Jefferson Sidney Kimmel Cancer
Center
Clinical Director Jefferson Sidney Kimmel Cancer Network
Thomas Jefferson University
Philadelphia, Pennsylvania

ASSOCIATE EDITORS
Gerald L. Andriole, MD, FACS
Robert K. Royce Distinguished Professor
Chief of Urologic Surgery
Division of Urologic Surgery
Washington University
St. Louis, Missouri

Arthur L. Burnett, II, MD, MBA, FACS
Patrick C. Walsh Professor of Urology
Department of Urology
The James Buchanan Brady Urological Institute
Baltimore, Maryland

Robert C. Flanigan, MD, FACS
Albert J. Jr. and Claire R. Sneath Professor
Chair, Department of Urology
Loyola University Stritch School of Medicine
Chicago (Maywood), Illinois

Thomas E. Keane, MB, ChB,
FRCSI, FACS
Professor and Chairman
Department of Urology
The Medical University of South Carolina
Charleston, South Carolina

Harry P. Koo, MD, FAAP, FACS
Chief of Pediatric Medicine
Department of Urology
Joseph M. Sanzari Children’s Hospital
Hackensack University Medical Center
Hackensack, New Jersey

Judd W. Moul, MD, FACS
James H. Semans, MD Professor of Surgery
Division of Urologic Surgery
Duke University Medical Center
Durham, North Carolina

Raju Thomas, MD, MHA, FACS
Professor and Chairman
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana

SECTION EDITORS
T. Ernesto Figueroa, MD, FAAP, FACS
Clinical Associate Professor
Sidney Kimmel Medical College
Chief, Division of Pediatric Urology
Nemours/Alfred I. DuPont Hospital for Children
Wilmington, Delaware

Deborah Tova Glassman, MD
Clinical Assistant Professor
Department of Urology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania

Kevin R. Loughlin, MD, MBA, FACS
Professor of Surgery (Urology)
Division of Urology
Brigham & Women's Hospital
Boston, Massachusetts

Franklin C. Lowe, MD, MPH
Professor of Clinical Urology
Columbia University College of Physicians & Surgeons
New York, New York

J. Ryan Mark, MD
Chief
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Video Editor
Editors

Alana M. Murphy, MD
Assistant Professor
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Jack H. Mydlo, MD
Professor and Chairman
Department of Urology
Temple University
Philadelphia, Pennsylvania

Andrew A. Gomella, BS
Class of 2018
Sidney Kimmel Medical College
Philadelphia, Pennsylvania

Sven Wenske, MD
Assistant Professor
Department of Urology
Columbia University College of Physicians & Surgeons
New York, New York

Stanley Zaslau, MD, MBA, FACS
Urology Residency Program Director
Division of Urology
West Virginia University
Morgantown, West Virginia

Michael L. Blute, Sr., MD, FACS
Walter S. Kerr, Jr. Professor of Surgery
Chief
Department of Urology
Massachusetts General Hospital
Boston, Massachusetts

Culley C. Carson, III, MD, FACS
Rhodes Distinguished Professor
Department of Urology
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

E. David Crawford, MD, FACS
Professor of Surgery/Urology/Radiation Oncology
University of Colorado, Denver
Denver, Colorado

James F. Donovan, Jr., MD
Professor of Surgery (Urology)
Director
Division of Urology
Department of Surgery
University of Cincinnati College of Medicine
Cincinnati, Ohio

Michael J. Droller, MD
Katherine and Clifford Goldsmith Professor of Urology
Professor of Oncology
The Mount Sinai Medical Center
Pelham, New York

Michael J. Erhard, MD
Medical Director
Division of Pediatric Urology
Nemours Children's Clinic
Jacksonville, Florida

Gabriel P. Haas, MD, FACS
Medical Director
Astellas Pharma Global Development
Deerfield, Illinois

Ethan J. Halpern, MD
Professor of Radiology and Urology
Vice Chairman of Radiology Research
Department of Radiology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania

CONSULTING EDITORS

Arie Belldegrun, MD, FACS
Professor & Chief of Urologic Oncology
Roy & Carol Dourman Chair in Urologic Oncology
Department of Urology
David Geffen School of Medicine at UCLA
Los Angeles, California

David A. Bloom, MD, FACS
The Jack Lapides Professor and Chair
Department of Urology
University of Michigan Medical School
Ann Arbor, Michigan
Editors
Editors

John Patrick Mulhall, MBBCh, FACS, FECSM
Director
Sexual and Reproductive Medicine Program
Division of Urology
Memorial Sloan Kettering Cancer Center
New York, New York
Erectile Dysfunction

Stephen Nakada, MD, FACS
The David T. Uehling Professor and Chairman
Department of Urology
University of Wisconsin
Madison, Wisconsin
Endourology & Urolithiasis

Craig S. Niederberger, MD, FACS
Professor and Department Head
Department of Urology
University of Illinois at Chicago
Chicago, Illinois
Infertility

David F. Penson, MD, MPH
Hamilton and Hawd Chair in Urologic Oncology
Chair, Department of Urologic Surgery
Professor of Urologic Surgery, Medicine and Health Policy
Vanderbilt University Medical Center
Nashville, Tennessee
Epidemiology and Health Related Quality of Life

Michael A. Pontari, MD
Professor of Urology
Department of Urology
Temple University
Philadelphia, Pennsylvania
Sexually Transmitted Infections

Ganesh V. Raj, MD, PhD, FACS
Associate Professor of Urology
Department of Urology
University of Texas Southwestern Medical Center
Dallas, Texas
Precision Medicine

Patrick J. Shenot, MD, FACS
Associate Professor
Deputy Chair and Residency Program Director
Department of Urology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania
Neurology

Philippe E. Spiess, MD
Associate Member
Department of Genitourinary Oncology
Moffitt Cancer Center
Tampa, Florida
Urologic Oncology/Penile Cancer

Edouard J. Trabulsi, MD, FACS
Associate Professor
Department of Urology
Sidney Kimmel Medical College
Sidney Kimmel Cancer Center
Thomas Jefferson University
Philadelphia, Pennsylvania
Urology

Robert G. Uzzo, MD, FACS
Professor and Chairman
Department of Surgical Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania
Urologic Oncology/Kidney Cancer

Richard Valicenti, MA, MD
Professor and Chair
Department of Radiation Oncology
UC Davis School of Medicine
Sacramento, California
Radiation Oncology

Sandip P. Vasavada, MD, FACS
Urologic Director
Center for Female Pelvic Medicine & Reconstructive Surgery
Cleveland Clinic Lerner College of Medicine
Cleveland, Ohio
Female Urology

Hunter Wessels, MD, FACS
Professor and Nelson Chair in Urology
Department of Urology
University of Washington
Seattle, Washington
Reconstructive Urology

INTERNATIONAL EDITORIAL BOARD

Taha Abo-Almagd Abdel-Meguid, MD
Professor
Department of Urology
King Abdulaziz University Hospital
Jeddah, Saudi Arabia
Editors

Atsushi Mizokami, MD, PhD
Lecturer
Department of Integrative Cancer Therapy & Urology
Kanazawa University Graduate School of Medical Sciences
Kanazawa, Japan

Francesco Montorsi, MD
Professor and Chairman
Director, Urological Research Institute
Department of Urology
Università Vita Salute San Raffaele
Milan, Italy

Guillermo Montoya, MD
Professor of Urology
Department of Urology
Hospital de Especialidades
Mexico City, Mexico

Alejandro Ramon Nolazco, MD
Especialista Consultor En Urologia
Hospital Britanico De Buenos Aires and
Hospital Universitario Austral
Buenos Aires, Argentina

Juliano Z. K. Panganiban, MD, FPCS, FPUA, MBAH
Urologic Surgeon/Consultant Urologist
Institute of Urology
St. Luke's Medical Center
Quezon City, Philippines

Dmitry Pushkar, MD
Professor and Chairman
General Scientific Secretary, Russian Society of Urology
Urologist General of Urology
Department of Urology
Moscow State University of Medicine & Dentistry
Moscow, Russia

Jacob Ramon, MD
Professor and Chairman
Department of Urology
Sheba Medical Center
Tel-Hashomer, Tel Aviv University
Tel Aviv, Israel

Arnulf Stenzl, MD
Professor and Chairman
Department of Urology
Eberhard-Karls University
Tübingen, Germany

Teuvo L.J. Tammela, MD, PhD
Professor of Urology and Chairman
Department of Surgery
Tampere University Hospital
Tampere, Finland

Claudio Teloken, MD, PhD
Professor of Urology
Chairman, Residency Program of Urology at
UFCSPA
Department of Urology
UFCSPA-Federal University of Medical Sciences
Porto Alegre, Brazil

Olivier Traxer, MD, PhD
Professor of Urology
Director of the Minimally Invasive Surgery
Department of Urology
University of Pierre et Marie Curie
Paris, France

Levent N. Türkeri, MD, PhD
Professor of Urology
Department of Urology
Marmara University School of Medicine
İstanbul, Turkey

Hendrik Van Poppel, MD, PhD
Chairman, Department of Urology
University Hospitals Leuven
Leuven, Belgium

Dr. Huberto Villavicencio
Director del servicio de Urología
Fundación Puigvert
Barcelona, Spain
CONTRIBUTORS

Divya Ajay, MD
Resident
Department of Urology
Duke University Medical Center
Durham, North Carolina

Osama Al-Omar, MD
Assistant Professor
Director Pediatric Urology
Division of Urology
West Virginia University
Morgantown, West Virginia

Michael J. Amirian, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Christopher Amling, MD, FACS
Professor and Chair
Department of Urology
Oregon Health & Science University
Portland, Oregon

Mark R. Anderson, MD, MSc
Resident in Urology
Division of Urology
Duke University Medical Center
Apex, North Carolina

Gerald L. Andriole, MD, FACS
Robert K. Royce Distinguished Professor
Chief of Urologic Surgery
Washington University in St. Louis
Barnes-Jewish Hospital and Siteman Cancer Center
St. Louis, Missouri

James B. Angel, MD
Resident
Division of Urology
Department of Surgery
University of Kentucky
Lexington, Kentucky

Jodi A. Antonelli, MD
Endourology Fellow
Department of Urology
UT Southwestern Medical Center
Dallas, Texas

Margarita M. Aponte, MD
Fellow
New York University Langone Medical Center
New York, New York

Angela M. Arlen, MD
Fellow
Department of Urology
Emory University School of Medicine
Atlanta, Georgia

Anthony Atala, MD, FACS
W.H. Boyce Professor
Chair-Department of Urology
Department of Urology
Wake Forest Institute for Regenerative Medicine
Wake Forest School of Medicine
Winston-Salem, North Carolina

Timothy D. Averch, MD, FACS
Professor and Vice Chair for Quality
Department of Endourology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Luigi Arollo, MD
Department of Pediatric Surgery
IRCCS Policlinico San Matteo Foundation
University of Pavia
Pavia, Italy

Demetrius H. Bagley, MD, FACS
The Nathan Lewis Hatfield Professor of Urology and Professor of Radiology
Department of Urology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania

Sonia Bahmani, MD
Fellow
Department of Urology
The Arthur Smith Institute for Urology
North Shore LIJ Healthcare System
New York, New York

Mark W. Ball, MD
Resident
James Buchanan Brady Urologic Institute
Johns Hopkins Medical Institutions
Baltimore, Maryland

Ahmad H. Bani-Hani, MD, FAAP
Assistant Professor, Department of Urology
Sidney Kimmel Medical College
Division of Urology
Nemours/Alfred I. duPont Hospital for Children
Wilmington, Delaware

Nima Baradaran, MD
Urology Resident
Department of Urology
Medical University of South Carolina
Charleston, South Carolina

John M. Barry, MD, FACS
Director
Living Donor Kidney Transplantation
Professor of Urology
Professor Emeritus of Surgery
Department of Urology
Oregon Health & Science University
Portland, Oregon

Julie S. Barthold, MD, FAAP
Professor of Urology and Pediatrics
Sidney Kimmel Medical College
Associate Chief, Nemours Division of Urology
Nemours/Alfred DuPont Hospital for Children
Wilmington, Delaware

Laurence S. Baskin, MD, FACS, FAAP
Chief Pediatric Urology
Children’s Hospital and Research Center, Oakland
Professor of Urology
University of California, San Francisco
San Francisco, California

Nelson Bennett, Jr., MD
Director of Sexual Medicine and Surgery
Institute of Urology
Lahey Hospital and Medical Center
Burlington, Massachusetts

Brian M. Benway, MD
Assistant Professor of Urologic Surgery
Washington University in St. Louis
St. Louis, Missouri

Boback M. Berookhim, MD, MBA
Fellow
Male Sexual and Reproductive Medicine
Urology Service
Department of Surgery
Memorial Sloan-Kettering Cancer Center
New York, New York

Fernando J. Blanco, Jr., MD
Assistant Professor of Urology
Columbia University
CEO
Urological Research Network
Miami, Florida

xvii
Contributors

Megan T. Bing, MD
Resident
Department of Urology
University of Iowa Hospitals and Clinics
Iowa City, Iowa

Trinity J. Bivalacqua, MD, PhD
Associate Professor of Urology and Oncology
James Buchanan Brady Urologic Institute
Johns Hopkins Medical Institutions
Baltimore, Maryland

Robert H. Blackwell, MD
Resident
Department of Urology
Loyola University Health System
Brookfield, Illinois

Aaron G. Boonjindasup, MD, MPH
Resident
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana

Daniel Box, MD
Resident
Department of Surgery
University of Cincinnati College of Medicine
Cincinnati, Ohio

Sam J. Brancato, MD
Urologic Oncology Fellow
National Cancer Institute
North Bethesda, Maryland

Gennady Bratslavsky, MD
Professor and Chair
Department of Urology
SUNY Upstate Medical University
Syracuse, New York

James A. Brown, MD, FACS
Professor
Department of Urology
University of Iowa
Iowa City, Iowa

Timothy E. Bunchman, MD
Professor & Director, Pediatric Nephrology
Virginia Commonwealth University
Richmond, Virginia

Arthur L. Burnett, II, MD, MBA, FACS
Patrick C. Walsh Professor of Urology
Department of Urology
The James Buchanan Brady Urological Institute
Baltimore, Maryland

Erin M. Burns, MD
Resident
Medical University of South Carolina
Charleston, South Carolina

Lysanne Campeau, MD, CM, PhD, FRCSC
Clinical Fellow
Department of Urology
New York University Langone Medical Center
New York, New York

Douglas A. Canning, MD, FACS
Professor of Urology in Surgery
University of Pennsylvania
Director, Pediatric Urology
The Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

Daniel J. Center, MD
Associate Member
Fox Chase Cancer Center
Vice Chairman
Urologic Institute of Southeastern Pennsylvania
Philadelphia, Pennsylvania

Christina Carpenter, MD
Resident
Department of Surgery
Division of Urology
Rutgers University–New Jersey Medical School
Newark, New Jersey

Brett S. Carver, MD
Assistant Attending
Department of Surgery
Memorial Sloan-Kettering Cancer Center
New York, New York

Pasquale Casale, MD, FACS
Joan and Irene Givens Professor of Urology
Columbia University
New York, New York

Kai-Wen Chuang, MD
Chief Resident
Arthur Smith Institute for Urology
North Shore-Long Island Jewish Health System
Manhattan, New York

Ryan Christopher Cleary, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Jonathan Cloutier, MD
Fellow in Endourology
Department of Urology
Tenon Hospital
University of Pierre et Marie Curie
Paris, France

Michael S. Cookson, MD
Chairman and Professor
Donald D. Albers Endowed Chair
Department of Surgery
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma

Christopher S. Cooper, MD, FAAP, FACS
Professor of Pediatric Urology
Associate Dean
Student Affairs & Curriculum
University of Iowa Carver College of Medicine
Iowa City, Iowa

Anthony T. Corcoran, MD
Fellow in Urologic Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Nicholas G. Cost, MD
Assistant Professor
Department of Surgery
University of Colorado School of Medicine
Aurora, Colorado

Nicholas Cowan, MD
Resident
Department of Urology
Oregon Health & Science University
Portland, Oregon

Nick Cowan, MD
Department of Urology
Oregon Health & Science University
Portland, Oregon

Brian Cox, MD
Chief Resident
Department of Urology
Oregon Health & Science University
Portland, Oregon
Bic N. Cung, MD  
Resident  
Department of Urology  
Temple University School of Medicine  
Philadelphia, Pennsylvania

Akhil Das, MD, FACS  
Assistant Professor of Urology  
Department of Urology  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Michel Daudon, PhD  
Service des Explorations Fonctionnelles  
Tetno Hospital  
University of Pierre et Marie Curie  
Paris, France

Ross M. Decker, MD, FRCS  
Professor and Chief  
Division of Urology  
MS Hershey Medical Center  
The Pennsylvania State University  
College of Medicine  
Hershey, Pennsylvania

Jessica M. DeLong, MD  
Fellow, Adult & Pediatric Reconstructive Urology  
Eastern Virginia Medical School  
Virginia Beach, Virginia

Joan C. Delia, MD  
Urology Resident  
Mount Sinai Medical Center  
Miami Beach, Florida

Robert B. Den, MD  
Assistant Professor of Radiation Oncology and Cancer Biology  
Radiation Oncology  
Kimmel Cancer Center  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Adam P. Dicker, MD, PhD  
Professor and Chair  
Radiation Oncology  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Roger R. Dmochowski, MD, MMHC, FACS  
Professor of Urology  
Vice Chair, Section of Surgical Sciences  
Department of Urology  
Vanderbilt University Medical Center  
Nashville, Tennessee

Mary Ellen T. Dolat, MD  
Resident  
Division of Urology in the Department of Surgery  
Virginia Commonwealth University  
Richmond, Virginia

Steve Dong, MD  
Clinical Instructor  
Department of Urology  
University of Southern California  
West Hollywood, California

Philip J. Dorsey, Jr., MD, MPH  
Resident  
Department of Urology  
Tulane University School of Medicine  
New Orleans, Louisiana

Elizabeth V. Dray, MD  
Resident  
Department of Urology  
Loyola University Medical Center  
Maywood, Illinois

Daniel Dug, III, MD  
Assistant Professor  
Department of Urology  
Oregon Health & Science University  
Portland, Oregon

John B. Effer, MD  
Clinical Instructor  
Department of Urologic Surgery  
Vanderbilt University Medical Center  
Nashville, Tennessee

Justin D. Etlett, MD, PhD  
Resident  
Medical University of South Carolina  
Charleston, South Carolina

Chandy Ellimoottil, MD  
Resident  
Department of Urology  
Loyola University Medical Center  
Maywood, Illinois

Leigh Mark Ettinger, MD, MS  
Clinical Assistant at the Hackensack University Medical Center  
Assistant Professor of Pediatrics at the University of Medicine & Dentistry of New Jersey  
Department of Pediatrics  
Hackensack University Medical Center  
Hackensack, New Jersey

Thomas M. Facelle, MD  
Resident  
Division of Urology  
Rutgers New Jersey Medical School  
Newark, New Jersey

Ahmer V. Farooq, DO  
Assistant Professor  
Department of Urology  
Loyola University Medical Center and Stritch School of Medicine  
Maywood, Illinois

Brad Figler, MD  
Assistant Professor of Urology  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

T. Ernesto Figueroa, MD, FAAP, FACS  
Clinical Associate Professor  
Sidney Kimmel Medical College  
Chief, Division of Pediatric Urology  
Nemours/Alfred I. DuPont Hospital for Children  
Wilmington, Delaware

Jason C. Fisher, MD  
Assistant Professor of Surgery  
Division of Pediatric Surgery  
Joseph M. Sarasani Children's Hospital  
Hackensack, New Jersey

Sallyanne M. Fisher, MSN, FNP-BC, CUNP  
Urology Nurse Practitioner  
Department of Veteran's Affairs Medical Center  
Wilmington, Delaware

Carrie L. Fitzgerald, DO, MPH  
Fellow  
Department of Urology  
University of Iowa Hospitals and Clinics  
Iowa City, Iowa

Robert C. Flanigan, MD, FACS  
Albert J. Jr. and Claire R. Speh Professor and Chair  
Department of Urology  
Loyola University Chicago (Maywood), Illinois

Drew A. Freilich, MD  
Resident  
Department of Urology  
New York Medical College  
White Plains, New York

Debra L. Fromer, MD  
Chief  
Female Pelvic Medicine & Reconstructive Medicine  
Department of Urology  
Hackensack University Medical Center  
Hackensack, New Jersey
Contributors

Chandan R. Kundavaram, MD  
Chief Resident  
Department of Urology  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Nicholas J. Kuntz, MD  
Resident in Urologic Surgery  
Division of Urology  
Duke University Medical Center  
Durham, North Carolina

Adonteng A. Kwakye, MD  
Resident  
Medical University of South Carolina  
Charleston, South Carolina

Lydia T. Laboccetta, MD  
Resident  
Medical University of South Carolina  
Charleston, South Carolina

John M. Lacy, MD  
Resident  
Department of Surgery  
Division of Urology  
University of Kentucky College of Medicine  
Lexington, Kentucky

H. Henry Lai, MD, FACS  
Assistant Professor of Urologic Surgery  
Washington University in St. Louis  
St. Louis, Missouri

Costas D. Lallas, MD, FACS  
Associate Professor  
Director, Robotic Surgery  
Department of Urology  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Sarah M. Lambert, MD  
Assistant Professor  
Division of Pediatric Urology  
Columbia University Medical Center  
Morgan Stanley Children’s Hospital of New York  
Presbyterian, New York, New York

Eric Langewisch, MD  
Assistant Professor  
Division of Nephrology  
Oregon Health & Science University  
Portland, Oregon

Dewud Lenkford, MD, MPH  
Resident  
Department of Urology  
New York Medical College  
Valhalla, New York

Michael C. Large, MD  
Fellow  
Urologic Oncology  
Department of Urology  
University of Chicago  
Chicago, Illinois

Benjamin R. Lee, MD, FACS  
Professor of Urology & Medicine (Oncology)  
Department of Urology  
Tulane University School of Medicine  
New Orleans, Louisiana

Hyeyoung Lee, MD, MS  
Clinical Assistant Professor of Urology  
Department of Urology  
Yonsei University College of Medicine  
Seodaemungu, Seoul, Korea

Yong Seung Lee, MD  
Clinical Research Assistant Professor  
Department of Urology  
Yonsei University College of Medicine  
Seodaemungu, Seoul, Korea

Ryan S. Levey, MD  
Resident  
Medical University of South Carolina  
Charleston, South Carolina

Garjoe Levien, MD  
Resident  
Division of Urology  
Department of Surgery  
University of Maryland School of Medicine  
Baltimore, Maryland

Patricia Lewandoski, MD  
Resident  
Department of Urology  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Kenneth Lieberman, MD  
Chief  
Section of Pediatric Nephrology  
Professor, Pediatrics  
Department of Pediatrics  
Hackensack University Medical Center  
Hackensack, New Jersey

Jianqing Lin, MD  
Assistant Professor  
Department of Medical Oncology  
Sidney Kimmel Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Mark C. Lindgren, MD  
Resident  
Department of Urology  
University of Illinois at Chicago  
Chicago, Illinois

Xiaolong Shawn Liu, MD  
Chief Resident  
Department of Urology  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Megan M. Lo, MD  
Assistant Professor  
Children’s Hospital of Richmond at VCU  
Richmond, Virginia

Christopher J. Long, MD  
Pediatric Urology  
Fellow Surgery  
Division of Urology  
The Children’s Hospital of Philadelphia  
Philadelphia, Pennsylvania

Franklin C. Lowe, MD, MPH, FACS  
Professor of Clinical Urology  
Department of Urology  
Columbia University, College of Physicians & Surgeons  
New York, New York

Adam M. Luxey, MD  
Resident  
Division of Urology  
West Virginia University  
Morgantown, West Virginia

Alosh Madala, MD  
Resident  
Department of Urology  
Upstate Medical University  
Syracuse, New York

Ramiro J. Madden-Fuentes, MD  
Resident  
Duke University Medical Center  
Durham, North Carolina

S. Bruce Malkowicz, MD, FACS  
Associate Professor of Surgery and Urology  
Co-Director  
Urologic Oncology  
Division of Urology  
University of Pennsylvania  
Philadelphia, Pennsylvania

J. Ryan Mark, MD  
Chief Resident  
Department of Urology  
Thomas Jefferson University  
Philadelphia, Pennsylvania

Viraj A. Master, MD, PhD, FACS  
Associate Professor  
Associate Chair of Clinical Affairs and Quality  
Department of Urology  
Emory University School of Medicine  
Atlanta, Georgia
Surena F. Matin, MD, FACS  
Associate Professor  
Director  
Minimally Invasive New Technology in Oncologic Surgery  
Department of Urology  
The University of Texas MD Anderson Cancer Center  
Houston, Texas  
Derek Matoka, MD  
Assistant Professor  
Department of Urology  
Loyola University Medical Center  
Stritch School of Medicine  
Maywood, Illinois  
Kurt A. McCammon, MD, FACS  
Associate Professor  
Urology  
Eastern Virginia Medical School  
Virginia Beach, Virginia  
Monica M. Metzdorf, MD  
Pediatric Urologist  
Kaiser Permanente  
Los Angeles, California  
Reza Mehrazin, MD  
Fellow  
Fellow, Urologic Oncology  
Fox Chase Cancer Center  
Philadelphia, Pennsylvania  
Matthew A. Meissner, MD  
Resident  
Department of Urology  
UT Southwestern Medical Center  
Dallas, Texas  
Van S. Menon, MD  
Resident  
Department of Urology  
Loyola University Medical Center  
Maywood, Illinois  
Megan M. Merrill, DO  
Urologic Oncology Fellow  
Department of Urology  
The University of Texas MD Anderson Cancer Center  
Houston, Texas  
Robert M. Moldwin, MD, FACS  
Professor of Urology  
North Shore-LIJ Hofstra University School of Medicine  
Director, Pelvic Pain Center, North Shore-LIJ Healthcare System  
Arthur Smith Institute for Urology  
Long Island Jewish Medical Center  
New Hyde Park, New York  
Allen F. Morey, MD, FACS  
Paul C. Peters Chair in Urology  
Professor  
Department of Urology  
UT Southwestern Medical Center  
Dallas, Texas  
Judd W. Moul, MD, FACS  
James H. Semans, MD Professor of Surgery  
Division of Urologic Surgery  
Duke University Medical Center  
Durham, North Carolina  
John Patrick Mulhall, MBChB, FACS, FECSM  
Director  
Sexual and Reproductive Medicine Program  
Division of Urology  
Memorial Sloan Kettering Cancer Center  
New York, New York  
Alana M. Murphy, MD  
Assistant Professor  
Department of Urology  
The University of Kansas  
Kansas City, Kansas  
Jack H. Mydlo, MD  
Professor and Chair  
Department of Urology  
Temple University School of Medicine  
Philadelphia, Pennsylvania  
Stephen Y. Nakada, MD, FACS  
The David T. Uehling Professor and Chairman  
Department of Urology  
University of Wisconsin  
Madison, Wisconsin  
Michael J. Naslund, MD  
Professor and Chief  
Division of Urology  
Department of Surgery  
Maryland Prostate Center  
University of Maryland School of Medicine  
Baltimore, Maryland  
Frank M. Nezu, MD  
Urology Division Chief  
Howard County General Hospital  
Clarksville, Maryland  
Samuel Walker Nickles, MD  
Resident  
Medical University of South Carolina  
Charleston, South Carolina  
Craig S. Niederberger, MD, FACS  
Professor and Department Head  
Department of Urology  
University of Illinois at Chicago  
Chicago, Illinois  
Dmitry Nikolovskiy, MD  
Assistant Professor  
Department of Urology  
SUNY Upstate Medical University  
Syracuse, New York  
Victor W. Nitti, MD, FACS  
Professor of Urology and Obstetrics & Gynecology  
Vice Chair  
Department of Urology  
Director  
Female Pelvic Medicine and Reconstructive Surgery  
Department of Urology  
New York University Langone Medical Center  
New York, New York  
Paul H. Noh, MD, FACS, FAAP  
Director of Minimally Invasive Surgery  
Associate Professor  
Division of Urology  
Cincinnati Children's Hospital Medical Center  
Cincinnati, Ohio  
Samuel Ohlander, MD  
Urology Resident  
Department of Urology  
University of Illinois at Chicago  
Chicago, Illinois  
Tara K. Ortiz, MD  
Urology Resident  
Department of Surgery  
Duke University Medical Center  
Durham, North Carolina  
John J. Pahira, MD  
Professor of Urology  
Department of Urology  
Georgetown University Hospital  
Washington DC  
Daniel C. Parker, MD  
Resident in Urology  
Department of Urology  
Temple University  
Philadelphia, Pennsylvania
Contributors

Neal Patel, MD
Resident
Division of Urology
Department of Surgery
Rutgers-Robert Wood Johnson Medical School
New Brunswick, New Jersey

Elizabeth K. Peacock, MD
Chief Resident
Medical University of South Carolina
Charleston, South Carolina

Margaret S. Pearle, MD, PhD, FACS
Professor of Urology
Professor of Internal Medicine
Department of Urology
UT Southwestern Medical Center
Dallas, Texas

David F. Penso, MD, MPH
Hamilton and Howd Chair in Urologic Oncology
Professor of Urologic Surgery
Department of Medicine
Vanderbilt University Medical Center
Nashville, Tennessee

Michael Perrotti, MD
Albany Urologic Oncology
Albany, New York

John L. Phillips, MD, FACS
Urology Program Director
Department of Urology
New York Medical College
Stony Brook, New York

Michael A. Poch, MD
Assistant Professor
Genitourinary Oncology
Moffitt Cancer Center
University of South Florida
Tampa, Florida

Dana Point, MD
Resident
Division of Urology
West Virginia University
Morgantown, West Virginia

Michael A. Pontari, MD
Professor and Vice-Chairperson
Department of Urology
Temple University School of Medicine
Philadelphia, Pennsylvania

Mary K. Powers, MD
Resident
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana

Sandip M. Prasad, MD, MPhil
Assistant Professor of Urology and Associate Director of the Urology Residency Program
Medical University of South Carolina
Charleston, South Carolina

Raj S. Pruthi, MD, FACS
Professor and Chief of Urology
Department of Surgery
University of North Carolina School of Medicine
Chapel Hill, North Carolina

Marcus L. Quek, MD, FACS
Assistant Professor
Department of Urology
Loyola University Medical Center
Maywood, Illinois

Ganesh V. Raj, MD, FACS
Associate Professor of Urology
Department of Urology
UT Southwestern Medical Center
Dallas, Texas

Pravin Rao, MD
Assistant Professor of Urology
Director of Reproductive Medicine and Surgery
Johns Hopkins University
Baltimore, Maryland

Amar J. Ravai, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Mathew C. Raynor, MD
Assistant Professor
Division of Urologic Surgery
The University of North Carolina School of Medicine
Chapel Hill, North Carolina

Nathaniel Readal, MD
Urology Resident
James Buchanan Brady Urological Institute
Baltimore, Maryland

Jeremy N. Reese, MD, MPH
Resident
Department of Urology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Matthew J. Resnick, MD
Assistant Professor of Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee

W. Stuart Reynolds, MD, MPH
Assistant Professor
Department of Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee

Kyle A. Richards, MD
Urologic Oncology Fellow
Surgery
The University of Chicago Medical Center
Chicago, Illinois

Julie M. Riley, MD
Assistant Professor
Department of Urology
University of New Mexico
Albuquerque, New Mexico

Chad R. Ritch, MD, MBA
Clinical Instructor
Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee

Nathan R. Roberts, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

James S. Ross, MD
Assistant Professor
Department of Urology
Yale School of Medicine
New Haven, Connecticut

Sherry S. Ross, MD
Assistant Professor of Surgery and Pediatrics
Department of Surgery
Duke University Medical Center
Durham, North Carolina

Joshua D. Roth, MD
Resident
Department of Urology
Indiana University School of Medicine
Indianapolis, Indiana

Eric S. Rovner, MD, FACS
Professor of Urology
Medical University of South Carolina
Charleston, South Carolina

Edmund S. Sabanegh, Jr., MD
Chairman
Department of Urology
Vanderbilt University Medical Center
Nashville, Tennessee

Lerner College of Medicine at Case Western Reserve University
Cleveland, Ohio
Contributors

Daniel D. Sackett, MD
Chief Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Gurdarshan S. Sandhu, MD
Urologic Oncology Fellow
Surgery
Washington University School of Medicine
St. Louis, Missouri

Bruce J. Schlimmer, MD
Assistant Professor of Pediatric Urology
Baylor College of Medicine and Texas Children's Hospital
Houston, Texas

Kymora Scotland, MD, PhD
Resident
Department of Urology
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania

Allen D. Seftel, MD, FACS
Professor of Urology
Cooper Medical School of Rowan University
Chief, Division of Urology
Cooper University Medical Center
Camden, New Jersey

Robert L. Segal, MD, FRCS (c)
Fellow
Sexual Medicine
Urology
James Buchanan Brady Urological Institute
Johns Hopkins Medical Institutions
Pikesville, Maryland

Casey Allison Seideman, MD
Resident
Department of Urology
UT Southwestern Medical Center
Dallas, Texas

Ahmad Shabsigh, MD, FACS
Assistant Professor of Urology
The Ohio State University Wexner Medical Center
Columbus, Ohio

Anish K. Shah, MD
Chief Resident
Department of Surgery
Division of Urology
University of Cincinnati College of Medicine
Cincinnati, Ohio

Arpeet Shah, MD
Resident
Department of Urology
Loyola University Medical Center
Chicago, Illinois

Ellen Shapiro, MD, FACS
Professor of Urology
Director
Pediatric Urology
Department of Urology
New York University School of Medicine
New York, New York

Oleg Shapiro, MD, FACS
Assistant Professor
Department of Urology
Upstate Medical University
Syracuse, New York

Patrick J. Shenot, MD, FACS
Associate Professor and Deputy Chair
Department of Urology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania

Yeniv Shilo, MD
Resident
Department of Urology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Avinav Sidana, MD
Resident
Department of Surgery
Division of Urology
University of Cincinnati College of Medicine
Cincinnati, Ohio

Jay Simhan, MD
Chief Resident
Department of Urology
Temple University
Philadelphia, Pennsylvania

Angela B. Smith, MD
Assistant Professor
Department of Urology
UNC School of Medicine
Chapel Hill, North Carolina

Paul H. Smith III, MD
Resident
Division of Urology
Penn State Milton S. Hershey Medical Center
Hershey, Pennsylvania

Grahame H.H. Smith, MBBS
Head of Urology
Department of Urology
The Sydney Children's Hospital Network
(Westmead)
Westmead, New South Wales, Australia

Zachary L. Smith, MD
Resident
Division of Urology
University of Pennsylvania
Philadelphia, Pennsylvania

Philippe E. Spiess, MD
Associate Member
Department of Genitourinary Oncology
Moffitt Cancer Center
Tampa, Florida

Christopher L. Starks, MD
Fellow
Center for Male Fertility
Department of Urology
Glickman Urological and Kidney Institute
The Cleveland Clinic Foundation
Shaker Heights, Ohio

Gillian Stearns, MD
Resident
Department of Urology
Upstate Medical University
Syracuse, New York

Douglas W. Storm, MD, FAAP, FACS
Assistant Professor of Pediatric Urology
Department of Urology
University of Iowa
Caver College of Medicine
Iowa City, Iowa

Andrew D. Strine, MD
Resident
Department of Urology
Indiana University School of Medicine
Indianapolis, Indiana

Stephen E. Strup, MD, FACS
James F. Glenn Professor and Chief of Urology
Department of Surgery
University of Kentucky College of Medicine
Lexington, Kentucky

Debasish Sundi, MD
Chief Resident
Brady Institute of Urology
Johns Hopkins Medical Institutions
Baltimore, Maryland

Gregory E. Tassign, MD, MSc
Staff Urologist
Clinical Instructor of Urology in Surgery
Surgery, Division of Urology
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Paul H. Smith II, MD
Resident
Division of Urology
University of Iowa
Caver College of Medicine
Iowa City, Iowa

Stephen E. Strup, MD, FACS
James F. Glenn Professor and Chief of Urology
Department of Surgery
University of Kentucky College of Medicine
Lexington, Kentucky

Debasish Sundi, MD
Chief Resident
Brady Institute of Urology
Johns Hopkins Medical Institutions
Baltimore, Maryland

Gregory E. Tassign, MD, MSc
Staff Urologist
Clinical Instructor of Urology in Surgery
Surgery, Division of Urology
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania
Contributors

Raju Thomas, MD, MHA, FACS
Professor and Chairman
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana

Adeep B. Thumar, MD
Chief Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Jeffrey J. Tomaszewski, MD
Fellow
Urologic Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Edouard J. Trabulsi, MD, FACS
Associate Professor
Department of Urology
Sidney Kimmel Medical College
Thomas Jefferson University
Philadelphia, Pennsylvania

Anthony J. Tracey, MD, MPH
Resident
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana

Matthew A. Uhlan, MD, MBA
Resident
Department of Urology
University of Iowa Hospitals and Clinics
Iowa City, Iowa

Robert G. Uzzo, MD, FACS
Chairman
Department of Surgical Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Vladimir A. Valera, MD, PhD
Resident
Department of Urology
New York Medical College
Valhalla, New York

Sandip P. Vasavada, MD, FACS
Urologic Director
Center for Female Pelvic Medicine & Reconstructive Surgery
Cleveland Clinic Lerner College of Medicine
Glickman Urological Institute
Cleveland, Ohio

Evelyn Vasquez, MD, MBA
Resident
Department of Urology
Loyola University Medical Center
Maywood, Illinois

Taylor B. Vaughan, MD
Department of Urology
Medical University of South Carolina
Charleston, South Carolina

Bryan Voelzke, MD, MS
Assistant Professor
Department of Urology
Harborview Medical Center at the University of Washington
Seattle, Washington

Srinivas Vourganti, MD
Clinical Fellow National Institutes of Health
National Cancer Institute
Urologic Oncology Branch
Washington, DC

Nikhil Waingankar, MD
Resident
The Arthur Smith Institute for Urology
North Shore-Long Island Jewish Health System
Long Island City, New York

Dana A. Weiss, MD
Pediatric Urology Fellow
Surgery, Division of Urology
The Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

Sven Wenske, MD
Assistant Professor
Department of Urology
Columbia University College of Physicians & Surgeons
New York, New York

Hunter Wessells, MD, FACS
Professor and Nelson Chair in Urology
Department of Urology
University of Washington
Seattle, Washington

Jessica Wetterlin, MD
Resident
Department of Urology
Loyola University Medical Center
Maywood, Illinois

Daniel A. Wolin, MD
Resident
Department of Urology
New York University
New York, New York

Michael E. Woods, MD
Associate Professor of Urology
Department of Urology
University of North Carolina School of Medicine
Chapel Hill, North Carolina

Christopher Wright, MD
Urology Resident
Rutgers-New Jersey Medical School
Newark, New Jersey

Blake A. Wynia, MD, MPH
Resident
Department of Urology
New York University
New York, New York

Rafael E. Yanes, MD
Resident
Department of Urology
Mount Sinai Medical Center
Bay Harbor Island, Florida

Shilo Yaniv, MD
Clinical Instructor in Urology
Department of Urology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Matthew A. Young, MD
Resident
Medical University of South Carolina
Charleston, South Carolina

Austin R. Younger, MD
Resident
Medical University of South Carolina
Charleston, South Carolina

Lee C. Zhao, MD, MS
Assistant Instructor
UT Southwestern Medical Center
Dallas, Texas

Philip T. Zhao, MD
Chief Resident
Division of Urology, Department of Surgery
Rutgers-Robert Wood Johnson Medical School
New Brunswick, New Jersey

Jack Matthew Zuckerman, MD
Resident
Department of Urology
Eastern Virginia Medical School
Norfolk, Virginia
## CONTENTS

<table>
<thead>
<tr>
<th>Section/I: Urologic Diseases and Conditions</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain, Lower</td>
<td>822</td>
</tr>
<tr>
<td>Acid Phosphatase Elevation</td>
<td>823</td>
</tr>
<tr>
<td>Acute Scrotum</td>
<td>824</td>
</tr>
<tr>
<td>Addison Disease (Adrenocortical Insufficiency)</td>
<td>825</td>
</tr>
<tr>
<td>Adrenal Mass, Solid</td>
<td>826</td>
</tr>
<tr>
<td>Alkaline Phosphatase Elevation</td>
<td>827</td>
</tr>
<tr>
<td>Anuria or Oliguria</td>
<td>828</td>
</tr>
<tr>
<td>Bladder Trauma</td>
<td>829</td>
</tr>
<tr>
<td>Bladder Tumor</td>
<td>830</td>
</tr>
<tr>
<td>Candiduria</td>
<td>831</td>
</tr>
<tr>
<td>Cushing Syndrome</td>
<td>832</td>
</tr>
<tr>
<td>Cystocele and/or Enterocoele</td>
<td>833</td>
</tr>
<tr>
<td>Delayed Puberty</td>
<td>834</td>
</tr>
<tr>
<td>Disorders of Sexual Development (DSD)</td>
<td>835</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>836</td>
</tr>
<tr>
<td>Dysuria</td>
<td>837</td>
</tr>
<tr>
<td>Ejaculation, Premature</td>
<td>838</td>
</tr>
<tr>
<td>Enuresis</td>
<td>839</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>840</td>
</tr>
<tr>
<td>Fecal Incontinence</td>
<td>841</td>
</tr>
<tr>
<td>Foley Catheter Problem (Difficult Placement, Male)</td>
<td>842</td>
</tr>
<tr>
<td>Genital Ulcers</td>
<td>843</td>
</tr>
<tr>
<td>Groin and Hip Pain</td>
<td>844</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>845</td>
</tr>
<tr>
<td>Hematuria, Adult</td>
<td>846</td>
</tr>
<tr>
<td>Hematuria, Macroscopic (Gross) Pediatric</td>
<td>847</td>
</tr>
<tr>
<td>Hematuria, Pediatric Microscopic Isolated</td>
<td>848</td>
</tr>
<tr>
<td>Hematuria, Traumatic</td>
<td>849</td>
</tr>
<tr>
<td>Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome)</td>
<td>850</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>851</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>852</td>
</tr>
<tr>
<td>Hypermagnesemia</td>
<td>853</td>
</tr>
<tr>
<td>Hypertension and Elevated Blood Pressure, Treatment</td>
<td>854</td>
</tr>
<tr>
<td>Hypovolemia</td>
<td>855</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>856</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>857</td>
</tr>
<tr>
<td>Hypoosmolar Urine Osmotic Cell Syndrome</td>
<td>858</td>
</tr>
<tr>
<td>Incontinence, Female</td>
<td>859</td>
</tr>
<tr>
<td>Incontinence, Male</td>
<td>860</td>
</tr>
<tr>
<td>Incontinence, Pediatric</td>
<td>861</td>
</tr>
<tr>
<td>Infertility</td>
<td>862</td>
</tr>
<tr>
<td>Infertility, Male Abnormal Semen</td>
<td>863</td>
</tr>
<tr>
<td>Infertility, Male, Low Semen Volume</td>
<td>864</td>
</tr>
<tr>
<td>Lower Urinary Tract Symptoms (LUTS), Male</td>
<td>865</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>866</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>867</td>
</tr>
<tr>
<td>Metabolic Acidosis</td>
<td>868</td>
</tr>
<tr>
<td>Metabolic Syndrome, Treatment</td>
<td>869</td>
</tr>
<tr>
<td>Nephrotic Syndrome</td>
<td>870</td>
</tr>
<tr>
<td>Nocturia</td>
<td>871</td>
</tr>
<tr>
<td>Parathyroid Hormone, Elevated Serum</td>
<td>872</td>
</tr>
<tr>
<td>Pelvic Pain, Female</td>
<td>873</td>
</tr>
<tr>
<td>Penile Squamous Cell Carcinoma</td>
<td>874</td>
</tr>
<tr>
<td>Penis, Trauma</td>
<td>875</td>
</tr>
<tr>
<td>Polyuria</td>
<td>876</td>
</tr>
<tr>
<td>Precocious Puberty</td>
<td>877</td>
</tr>
<tr>
<td>Priapism</td>
<td>878</td>
</tr>
<tr>
<td>Prostate Cancer, Castration Resistant</td>
<td>879</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>880</td>
</tr>
</tbody>
</table>

Alphabetical Topic Index xxvii
## Contents

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>881</td>
</tr>
<tr>
<td>PSA</td>
<td>882</td>
</tr>
<tr>
<td>Pulmonary Embolism, Diagnosis</td>
<td>883</td>
</tr>
<tr>
<td>Pulmonary Embolism, Treatment</td>
<td>884</td>
</tr>
<tr>
<td>Pyuria</td>
<td>885</td>
</tr>
<tr>
<td>Rectal Injury</td>
<td>886</td>
</tr>
<tr>
<td>Rectocele and Enterocele</td>
<td>887</td>
</tr>
<tr>
<td>Renal Colic Management</td>
<td>888</td>
</tr>
<tr>
<td>Renal Failure, Acute</td>
<td>889</td>
</tr>
<tr>
<td>Renal Mass</td>
<td>890</td>
</tr>
<tr>
<td>Renal Mass, Intraoperative Consult</td>
<td>891</td>
</tr>
<tr>
<td>Renal Trauma, Hemodynamically Stable</td>
<td>892</td>
</tr>
<tr>
<td>Scrotum and Testicle, Mass</td>
<td>893</td>
</tr>
<tr>
<td>Scrotum and Testicle, Trauma</td>
<td>894</td>
</tr>
<tr>
<td>Testis Cancer, Nonseminoma</td>
<td>895</td>
</tr>
<tr>
<td>Testis Cancer, Seminoma</td>
<td>896</td>
</tr>
<tr>
<td>Testosterone Deficiency (Hypogonadism)</td>
<td>897</td>
</tr>
<tr>
<td>Undescended Testicle (Cryptorchidism)</td>
<td>898</td>
</tr>
<tr>
<td>Uremia</td>
<td>899</td>
</tr>
<tr>
<td>Urethral Discharge</td>
<td>900</td>
</tr>
<tr>
<td>Urinary Retention, Male</td>
<td>901</td>
</tr>
<tr>
<td>Urine Leak From Vagina</td>
<td>902</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>903</td>
</tr>
<tr>
<td>Urolithiasis, Ureteral Calculi</td>
<td>904</td>
</tr>
<tr>
<td>UTI, Adult Female</td>
<td>905</td>
</tr>
<tr>
<td>UTI, Pediatric</td>
<td>906</td>
</tr>
<tr>
<td>Vaginal Bleeding, Abnormal</td>
<td>907</td>
</tr>
<tr>
<td>Vaginal Discharge</td>
<td>908</td>
</tr>
<tr>
<td>Vas Deferens, Congenital Absence</td>
<td>909</td>
</tr>
<tr>
<td>Vitamin D Deficiency</td>
<td>910</td>
</tr>
<tr>
<td>SECTION IV: Urinalysis and Urine Studies</td>
<td>911</td>
</tr>
<tr>
<td>I. Urine Analysis</td>
<td>912</td>
</tr>
<tr>
<td>II. Spot or Random Urine Studies</td>
<td>913</td>
</tr>
<tr>
<td>III. Creatinine Clearance and Glomemular Filtration Rate</td>
<td>913</td>
</tr>
<tr>
<td>IV. 24-hr Urine Studies</td>
<td>914</td>
</tr>
<tr>
<td>SECTION V: Alternative and Complementary Urologic Therapies</td>
<td>915</td>
</tr>
<tr>
<td>SECTION VI: Urologic Drug Reference</td>
<td>921</td>
</tr>
<tr>
<td>SECTION VII: Reference Tables</td>
<td>977</td>
</tr>
<tr>
<td>Aging Male Survey (AMS)</td>
<td>978</td>
</tr>
<tr>
<td>Antibiotic Prophylaxis: AUA Guidelines</td>
<td>979</td>
</tr>
<tr>
<td>Anticoagulation and Antiplatelet Therapy in Urologic Practice</td>
<td>982</td>
</tr>
<tr>
<td>AUA Symptom Index/International Prostate Symptom Score (I-PSG)</td>
<td>984</td>
</tr>
<tr>
<td>Catheter Guide</td>
<td>985</td>
</tr>
<tr>
<td>Contrast Agents, Genitourinary</td>
<td>986</td>
</tr>
<tr>
<td>International Index of Erectile Function (IEF)</td>
<td>987</td>
</tr>
<tr>
<td>Male Sexual Health Questionnaire (MSHQ) Short Form</td>
<td>989</td>
</tr>
<tr>
<td>National Institutes of Health (NIH) Chronic Prostatitis Symptom Index (CPSI)</td>
<td>990</td>
</tr>
<tr>
<td>Prostate Cancer Screening Guidelines</td>
<td>991</td>
</tr>
<tr>
<td>Sexual Health Inventory for Men IIEF-5</td>
<td>992</td>
</tr>
<tr>
<td>TMM Classification: Cervix Cancer</td>
<td>993</td>
</tr>
<tr>
<td>TMM Classification: Colon Cancer</td>
<td>994</td>
</tr>
<tr>
<td>TMM Classification: Kidney Cancer</td>
<td>995</td>
</tr>
<tr>
<td>TMM Classification: Penis Cancer</td>
<td>996</td>
</tr>
<tr>
<td>TMM Classification: Prostate Cancer</td>
<td>997</td>
</tr>
<tr>
<td>TMM Classification: Rectal Cancer</td>
<td>998</td>
</tr>
<tr>
<td>TMM Classification: Renal Pelvis and Ureter Cancer</td>
<td>999</td>
</tr>
<tr>
<td>TMM Classification: Testis Cancer</td>
<td>1000</td>
</tr>
<tr>
<td>TMM Classification: Urethral Cancer</td>
<td>1001</td>
</tr>
<tr>
<td>TMM Classification: Urinary Bladder Cancer</td>
<td>1002</td>
</tr>
<tr>
<td>Uroradiology Signs (See also Section II: &quot;Uroradiology Signs&quot;)</td>
<td>1003</td>
</tr>
<tr>
<td>Voiding Diary</td>
<td>1006</td>
</tr>
<tr>
<td>Alphabetical Topical Index (Section I and II)</td>
<td>1007</td>
</tr>
</tbody>
</table>

### Alphabetical Topical Index (Section I and II)

- 11-β-Hydroxylase (CYP1B1) Deficiency  
  - Page 642
- 2,8-Dihydroxyadenine (2,8-DHA) Urolithiasis  
  - Page 642
- 21-Hydroxylase (CYP21A2) Deficiency  
  - Page 642
- 5α-Reductase Deficiency  
  - Page 642
- Aarskog Syndrome (Faciodigitiogenital Syndrome)  
  - Page 642
- Abdominal Mass, Adult, Urologic Considerations  
  - Page 2
- Abdominal Mass, Newborn/Child, Urologic Considerations  
  - Page 4
- Abdominoperineal Resection (APR), Urologic Considerations  
  - Page 642
- Abrams–Griffiths Nomogram  
  - Page 642
- Acetaminophen Abuse, Urologic Considerations  
  - Page 642
- Acquired Renal Cystic Disease  
  - Page 643
- Acrosome Reaction Assay  
  - Page 643
- Acute Kidney Injury (AKI), Definitions  
  - Page 643
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Kidney Injury, Adult (Renal Failure, Acute)</td>
<td>6</td>
</tr>
<tr>
<td>Acute Kidney Injury, Pediatric (Renal Failure, Acute)</td>
<td>8</td>
</tr>
<tr>
<td>Acute Scrotum</td>
<td>10</td>
</tr>
<tr>
<td>Acute Tubular Necrosis</td>
<td>12</td>
</tr>
<tr>
<td>Addison Disease</td>
<td>14</td>
</tr>
<tr>
<td>Adenofibroma, Metanephric, Pediatric</td>
<td>643</td>
</tr>
<tr>
<td>Adenomatoid Tumors, Testicular and Paratesticular</td>
<td>16</td>
</tr>
<tr>
<td>Adrenal Adenoma</td>
<td>18</td>
</tr>
<tr>
<td>Adrenal Angiomyolipoma</td>
<td>643</td>
</tr>
<tr>
<td>Adrenal Calcifications</td>
<td>643</td>
</tr>
<tr>
<td>Adrenal Cortical Carcinoma</td>
<td>20</td>
</tr>
<tr>
<td>Adrenal Cysts and Pseudocysts</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Cytomegaly</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Hemorrhage</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Hypoplasia</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Incidentalomas</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Insufficiency, Acute (Adrenal Crisis)</td>
<td>22</td>
</tr>
<tr>
<td>Adrenal Mass</td>
<td>24</td>
</tr>
<tr>
<td>Adrenal Metastases</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Myelolipoma (Adrenal Myolipoma)</td>
<td>644</td>
</tr>
<tr>
<td>Adrenal Oncocytoma</td>
<td>644</td>
</tr>
<tr>
<td>Adrenalin</td>
<td>645</td>
</tr>
<tr>
<td>Adrenocortical Disease, Primary Pigmented Nodular</td>
<td>645</td>
</tr>
<tr>
<td>Adrenogenital Syndrome</td>
<td>645</td>
</tr>
<tr>
<td>Adrenoleukodystrophy</td>
<td>645</td>
</tr>
<tr>
<td>Aging Male Survey</td>
<td>645</td>
</tr>
<tr>
<td>Al Ghorab Corporal Shunt with Burnett &quot;Snake&quot; Maneuver</td>
<td>645</td>
</tr>
<tr>
<td>Al Ghorab Corporal Shunt with Burnett &quot;Snake&quot; Maneuver</td>
<td>645</td>
</tr>
<tr>
<td>Algestose</td>
<td>646</td>
</tr>
<tr>
<td>Alkaline Phosphatase, Urologic Considerations</td>
<td>646</td>
</tr>
<tr>
<td>Alkaptonuria</td>
<td>646</td>
</tr>
<tr>
<td>Allalporiol Hyperosensitivity Syndrome (AHS)</td>
<td>646</td>
</tr>
<tr>
<td>Aplastic Genitalium</td>
<td>646</td>
</tr>
<tr>
<td>α-(Alpha) Fetoprotein</td>
<td>646</td>
</tr>
<tr>
<td>Alport Disease/Syndrome</td>
<td>646</td>
</tr>
<tr>
<td>Alström–Edwards Syndrome</td>
<td>646</td>
</tr>
<tr>
<td>Alzheimer Disease, Urologic Considerations</td>
<td>646</td>
</tr>
<tr>
<td>Ambiguous Genitalia</td>
<td>646</td>
</tr>
<tr>
<td>American Association for the Surgery of Trauma (AASST) Organ Severity Scales: Genitourinary Injuries</td>
<td>647</td>
</tr>
<tr>
<td>Aminoaciduria</td>
<td>647</td>
</tr>
<tr>
<td>Ammonium Chloride Loading Test</td>
<td>647</td>
</tr>
<tr>
<td>Ammonium Urate Urolithias</td>
<td>647</td>
</tr>
<tr>
<td>Amsterdam and Bethesda Criteria for Lynch Syndrome</td>
<td>647</td>
</tr>
<tr>
<td>Amyloidosis, Genitourinary</td>
<td>26</td>
</tr>
<tr>
<td>Anal Sphincter Tone and Sensation, Urologic Considerations</td>
<td>647</td>
</tr>
<tr>
<td>Anderson-Hynes Pyeloplasty</td>
<td>647</td>
</tr>
<tr>
<td>Andrews Procedure (Hydrocele)</td>
<td>648</td>
</tr>
<tr>
<td>Androgen Deficiency in the Aging Male (ADAM) and ADAM Questionnaire</td>
<td>648</td>
</tr>
<tr>
<td>Androgen Deprivation Syndrome (ADS)/Metabolic Syndrome</td>
<td>648</td>
</tr>
<tr>
<td>Androgen Insensitivity Syndrome (AIS; or Androgen Resistance Syndrome), Complete (CAIS) and Partial (PAIS)</td>
<td>648</td>
</tr>
<tr>
<td>Androgen/Anabolic Steroid Abuse</td>
<td>649</td>
</tr>
<tr>
<td>Andropause (Late-Onset Hypogonadism)</td>
<td>28</td>
</tr>
<tr>
<td>Angiokeratoma of Fordyce (Penile and Scrotal Angiokeratomas)</td>
<td>649</td>
</tr>
<tr>
<td>Angioglyphoma, Penile</td>
<td>649</td>
</tr>
<tr>
<td>Angiomyxoma, Perineal</td>
<td>649</td>
</tr>
<tr>
<td>Angiosarcoma, Genitourinary</td>
<td>649</td>
</tr>
<tr>
<td>Anogenital Intraepithelial Neoplasia</td>
<td>649</td>
</tr>
<tr>
<td>Anorectal Malformations: Imperforate Anus, Cloaca, and Urogenital Sin Anomalies</td>
<td>30</td>
</tr>
<tr>
<td>Anorgasmusia, Female</td>
<td>649</td>
</tr>
<tr>
<td>Anorgasmusia, Male</td>
<td>32</td>
</tr>
<tr>
<td>Anterior Urethral Valves</td>
<td>649</td>
</tr>
<tr>
<td>Antiandrogen Withdrawal Syndrome (Flutamide Withdrawal Syndrome)</td>
<td>649</td>
</tr>
<tr>
<td>Antiserum Antibodies</td>
<td>650</td>
</tr>
<tr>
<td>Anuria and Oliguria, Adult</td>
<td>34</td>
</tr>
<tr>
<td>Anuria and Oliguria, Pediatric</td>
<td>36</td>
</tr>
<tr>
<td>Aphthous Ulcer, External Genitalia</td>
<td>650</td>
</tr>
<tr>
<td>Appendix Testis and Appendix Epithydymis, Torsion</td>
<td>650</td>
</tr>
<tr>
<td>Aristolotic Acid (Fang Chi)</td>
<td>650</td>
</tr>
<tr>
<td>Artrovenous Fistula (AVF), Renal (or Arteriovenous Malformation (AVM))</td>
<td>650</td>
</tr>
<tr>
<td>Artificial Insemination (AI)</td>
<td>651</td>
</tr>
<tr>
<td>Aask-Upmark Kidney</td>
<td>651</td>
</tr>
<tr>
<td>Asosia Hypospadas Repair</td>
<td>651</td>
</tr>
<tr>
<td>Aspergilosis, Genitourinary</td>
<td>651</td>
</tr>
<tr>
<td>Aspermia</td>
<td>651</td>
</tr>
<tr>
<td>Assisted Reproductive Technology (ART)</td>
<td>651</td>
</tr>
<tr>
<td>Asthenospermia</td>
<td>651</td>
</tr>
</tbody>
</table>
Bladder, Pheochromocytoma 659
Bladder Sarcoma (Leiomyosarcoma/Rhabdomyosarcoma) 659
Bladder Small Cell Carcinoma (Oat Cell, Signet Ring) 660
Bladder, Teardrop 660
Bladder Trabeculation andCells 660
Bladder Trauma 70
Bladder Tumors, Benign and Malignant, General Considerations 72
Bladder, Villous Adenoma 660
Bladder Wall Calcification, Differential Diagnosis 660
Bladder Wall Thickening, Differential Diagnosis 660
Blastomyces, Genitourinary 660
Bleomycin Toxicity 661
Blue Diaper Syndrome 661
Blue Dot Sign 661
Blue Nevus (Melanosis), Urologic Considerations 661
Boyarsky Guidelines for BPH 663
Boyce Nephrotomy (Anatrophic Nephrotomotomy) 663
Brachytherapy Seed Embolus 663
Brain Metastasis, Urologic Considerations 663
Brenner Tumors 663
Bricker Ureteral Anastomosis 663
Brigham Sling (Urethropexy) 663
Brink Score 663
British Testicular Tumor Classification 663
Bronchogenic Cyst, Retropitoneal 663
Brunn Buds and Nests (von Brunn Nests) 663
Brushite (Calcium Monohydrogen Phosphate) 664
BTA Testing (BTA and BTA Stat Urine Test) 664
Bulbocavernous Reflex 664
Bulking Agents, Injectable 664
Bullous Pemphigoid 664
BUN (Blood Urea Nitrogen), Increased/Decreased 665
Burk Coeponsusption 665
Burns, External Genitalia and Perineum 76
Buschke-Lowenstein Tumor 665
Byar Flaps 665
Calcifications, Abdominal and Pelvic 665
Calcifications, Bladder 665
Calcifications, Prostate 665
Calcifications, Renal 665
Calcinyin, Idiopathic Scrotal 665
Calciphylaxis 665
Calcium Load and Fast Studies 666
Calcium Supplementation and Urolithiasis 666
Calycal Diverticula 78
Camey I and II Orthotopic Urinary Diversion 666
Canal of Nuck Hydrocele and Cyst (Female Hydrocele) 666
Candidiasis—Cutaneous, External Genitalia 666
Captopril Test 666
Carcinoid Tumors, Genitourinary 666
Carcinosarcoma, Bladder 666
Carcinosarcoma, Prostate 667
Carney Syndrome (Carney Complex) 667
Carney Triad 667
Caruncle, Urethral 667
Casale Procedure 667
Cat-Eye Syndrome 667
Catheterizable Stoma Problems 80
Cauda Equina Syndrome 667
Caudal Regression Syndrome 667
Cavernosography 667
Cavernosometry 668
Cecil Urethral Stricture Repair 668
Cecouretrocule 668
Cello Scrotum 668
Cerebral Palsy, Urologic Considerations 668
Cervical Cancer, Urologic Considerations 668
Charcot-Boeckler Crystals and Filaments 668
Charge Association 668
## Contents

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy Toxicity, Urologic Considerations</td>
<td>668</td>
</tr>
<tr>
<td>Chlamydia Sexually Transmitted Disease</td>
<td>669</td>
</tr>
<tr>
<td>Chordee</td>
<td>82</td>
</tr>
<tr>
<td>Christmas Tree Bladder</td>
<td>669</td>
</tr>
<tr>
<td>Chronic Kidney Disease (CKD)</td>
<td>669</td>
</tr>
<tr>
<td>Chronic Kidney Disease, Adult (Renal Failure, Chronic)</td>
<td>84</td>
</tr>
<tr>
<td>Chronic Kidney Disease, Pediatric (Renal Failure, Chronic)</td>
<td>86</td>
</tr>
<tr>
<td>Chronic Pelvic Pain Syndrome/Chronic Prostatitis (CPPS/CP) in Males</td>
<td>669</td>
</tr>
<tr>
<td>Chronic Pelvic Pain Syndrome (CPPS) in Females</td>
<td>669</td>
</tr>
<tr>
<td>Chronic Prostatitis Symptom Index (CPSI)/NIH-CPSI (National Institutes of Health CPSI)</td>
<td>670</td>
</tr>
<tr>
<td>Churg-Strauss Syndrome</td>
<td>670</td>
</tr>
<tr>
<td>Chylocele</td>
<td>670</td>
</tr>
<tr>
<td>Chylous Ascites</td>
<td>88</td>
</tr>
<tr>
<td>Chyluria</td>
<td>90</td>
</tr>
<tr>
<td>Circumcision, Adult Considerations</td>
<td>92</td>
</tr>
<tr>
<td>Circumcision, Female</td>
<td>670</td>
</tr>
<tr>
<td>Circumcision, Pediatric Considerations</td>
<td>94</td>
</tr>
<tr>
<td>Ciplatin Toxicity</td>
<td>670</td>
</tr>
<tr>
<td>Clitoral Length</td>
<td>671</td>
</tr>
<tr>
<td>Clitoral Priapism</td>
<td>671</td>
</tr>
<tr>
<td>Clitoromegaly</td>
<td>671</td>
</tr>
<tr>
<td>Clonidine Suppression Test</td>
<td>671</td>
</tr>
<tr>
<td>Clostridium Difficile Collis, Urologic Considerations</td>
<td>671</td>
</tr>
<tr>
<td>Cloi Retention</td>
<td>671</td>
</tr>
<tr>
<td>Cob Collar</td>
<td>671</td>
</tr>
<tr>
<td>Cobra Head Sign</td>
<td>671</td>
</tr>
<tr>
<td>Cocccidiomycosis, Genitourinary</td>
<td>671</td>
</tr>
<tr>
<td>Cohen (“Cross-Trigonal”) Ureteral Reimplantation</td>
<td>672</td>
</tr>
<tr>
<td>Coital Incontinence (Coital leakage/Intercourse Incontinence)</td>
<td>672</td>
</tr>
<tr>
<td>Collecting System Duplication, Complete</td>
<td>672</td>
</tr>
<tr>
<td>Colon and Rectal Cancer, Urologic Considerations</td>
<td>672</td>
</tr>
<tr>
<td>Column of Berlin, Hypertrophied</td>
<td>672</td>
</tr>
<tr>
<td>Compartment Syndrome, Urologic Considerations</td>
<td>672</td>
</tr>
<tr>
<td>Compulsive Masturbation</td>
<td>672</td>
</tr>
<tr>
<td>Condyloma Acuminata (Veneral Warts)</td>
<td>96</td>
</tr>
<tr>
<td>Condylomata Lata</td>
<td>672</td>
</tr>
<tr>
<td>Congenital Adrenal Hyperplasia (CAH)</td>
<td>672</td>
</tr>
<tr>
<td>Congenital Nephrosis/Nephrotic Syndrome</td>
<td>673</td>
</tr>
<tr>
<td>Constipation, Urologic Considerations</td>
<td>673</td>
</tr>
<tr>
<td>Contact Dermatitis, Urologic Considerations</td>
<td>673</td>
</tr>
<tr>
<td>Contrast Allergy and Reactions</td>
<td>98</td>
</tr>
<tr>
<td>Contrast-Induced Nephropathy (CIN)</td>
<td>674</td>
</tr>
<tr>
<td>Cordonnier and Nestt Ureteral Anastomosis</td>
<td>674</td>
</tr>
<tr>
<td>Corpora Amylacea (CA)</td>
<td>674</td>
</tr>
<tr>
<td>Cortical Necrosis, Acute (Renal Cortical Necrosis)</td>
<td>674</td>
</tr>
<tr>
<td>Costovertebral Angle Tenderness</td>
<td>674</td>
</tr>
<tr>
<td>Cough Stress Test</td>
<td>674</td>
</tr>
<tr>
<td>Cowper Duct Cyst</td>
<td>674</td>
</tr>
<tr>
<td>Cowper Gland Carcinoma</td>
<td>675</td>
</tr>
<tr>
<td>Cowperitis (Inflammation of Bulbourethral Gland)</td>
<td>675</td>
</tr>
<tr>
<td>Creatine, Serum, Increased/Decreased</td>
<td>675</td>
</tr>
<tr>
<td>Credé Maneuver</td>
<td>675</td>
</tr>
<tr>
<td>Cremasteric Reflex</td>
<td>675</td>
</tr>
<tr>
<td>Cryptiform Clear Cell Hyperplasia of the Prostate</td>
<td>675</td>
</tr>
<tr>
<td>Cryptococcus, Genitourinary</td>
<td>675</td>
</tr>
<tr>
<td>Crystal-Induced Acute Kidney Injury (Acute Renal Failure)</td>
<td>675</td>
</tr>
<tr>
<td>CT Scan, Urologic Considerations</td>
<td>675</td>
</tr>
<tr>
<td>Culp-Deweed Pyeloplasty</td>
<td>676</td>
</tr>
<tr>
<td>Cunningham Clamp</td>
<td>676</td>
</tr>
<tr>
<td>Cushing Disease and Syndrome</td>
<td>100</td>
</tr>
<tr>
<td>Cyclophosphamide (Cytoxan) Toxicity</td>
<td>676</td>
</tr>
<tr>
<td>Cystadenocarcinoma, Genitourinary</td>
<td>676</td>
</tr>
<tr>
<td>Cystadenoma, Genitourinary</td>
<td>676</td>
</tr>
<tr>
<td>Cystadenoma/Cystadenocarcinoma, Retroperitoneal</td>
<td>676</td>
</tr>
<tr>
<td>Cystatin C</td>
<td>676</td>
</tr>
<tr>
<td>Cystic Fibrosis, Urologic Considerations</td>
<td>676</td>
</tr>
<tr>
<td>Cystinosis</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis Cynica</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, Emphysematous</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, Eosinophilic</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis Follicularis</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis Glandularis and Cystitis Glandularis of Intestinal Type</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, General Considerations</td>
<td>102</td>
</tr>
<tr>
<td>Cystitis, Granulomatous</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)</td>
<td>104</td>
</tr>
<tr>
<td>Cystitis, Polypoid and Papillary</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, Radiation</td>
<td>677</td>
</tr>
<tr>
<td>Cystitis, Viral</td>
<td>678</td>
</tr>
<tr>
<td>Cystocele Grading: Baden–Walker, Pelvic Organ Prostate Quantification (POP-Q)</td>
<td>678</td>
</tr>
</tbody>
</table>
xxxiv

Contents

Epididymis, Obstruction 686
Epididymitis 138
Epididymas 140
Epitheliod Hemangioma, Penis and Scrotum 686
Erectile Dysfunction Inventory of Treatment Survey (EDITs) 686
Erectile Dysfunction, Following Pelvic Surgery or Radiation 142
Erectile Dysfunction/Impotence, General Considerations 144
Erection Hardness Score (EHS) for ED 686
Erysipelas, External Genitalia 686
Erythema Multiforme (EM), External Genitalia 686
Erythrasma 686
Excretory Urogram, Intraoperative (“On Table IVP”/“Single-Shot IVP”) 686
Expressed Prostatic Secretions (EPS) 686
Exstrophy, Bladder (Classic Exstrophy) 146
Exstrophy, Cloacal 148
Exstrophy–Epispadias Complex (EEC) 687
Extragonadal Germ Cell Tumors (EGCT) 687
Extramammary Paget Disease, Urologic Considerations 687
Extramedullary Hematopoesis, Renal 687
Extravasation During Urologic Surgery 687
Fabry Disease/Syndrome 687
Familial Testotoxicosis 687
Fanconi Syndrome 687
Fatty Casts 688
Fecal Incontinence, Urologic Considerations 688
Fecaluria 688
Female Hypoactive Sexual Desire Disorder 688
Female Sex Function Index (FSFI) 688
Fenestrated Enucleation Disease/Syndrome 688
Fenestrated Urethral Disease/Syndrome 688
Fertility and Cancer Therapy, Urologic Considerations 150
Fibroepithelial Polyp, Genitourinary 688
Fibroepithelial Polyp, Penis 689
Fibrous Hamartoma of Infancy 689
Fibrous Pseudotumor of Testicular Tunic 689
Fiducial Markers 689
Filarialis, Urologic Considerations 689
Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter) 152
Fine-Needle Aspiration (FNA) of Prostate 689
FISH: Urinary Fluorescent In Situ Hybridization (UroVysion Test) 689
Fistula, Enterovesical 690
Fistula, Rectourethral 690
Fistula, Ureterocystic 690
Fistula, Vesicocutaneous 690
Fistula, Vesicouretic 690
Fistula, Vesicovaginal and Ureterovaginal 690
Fitz–Hugh–Curtis Syndrome 691
Flank Hernia Following Nephrectomy 691
Flank Pain, General 154
Fluorescent (Blue Light) Cystoscopy 691
Foley Catheter Problems (Insertion and Removal) 156
Foley Y-V Pyeloplasty 691
Fordyce Spots (Ectopic Sebaceous Glands), Penis 691
Foreign Body, Bladder and Urethra 691
Formalin Instillation, Indications and Technique 691
Fossa Navicularis Diverculum 691
Fournier Gangrene 158
Fowler Syndrome (Primary Disorder of Urthral Sphincter Relaxation) 692
Fowler–Stephens Orchiopexy 692
Fracture Risk Associated with Prostate Cancer and Androgen Deprivation Therapy 692
Frail X Syndrome 692
Fraya Syndrome 692
French Catheter Scale 692, 985
Frequency, Urinary 692
Frequency–Dysuria Syndrome 692
Fuhrman Nuclear Grading Classification, Renal Cell Carcinoma (RCC) 693
Fungal Infections, Genitourinary 160
Funguria 693
Funiculitis 693
Game of Intrafallopian Transfer (GIFT) 693
Ganglioneuromatous Adenoma, Adrenal 693
Ganglioneuroma, Adrenal 693
Gartner Duct Cyst 693
Genital Arousal Disorder (Persistent) 693
Genital Piercing, Urologic Considerations 694
Genital Skin Loss 694
Genital Ulcers 694
Genitourinary Pain Index (GUPI) 694
Contents

Hodgson Types I, II, III Hypospadias Repair 702
Honeymoon Cystitis 702
Horseshoe Kidney 702
Horton-Devine “Flip-Flap” Hypospadias Repair 702
Hot Flushes/Vasomotor Instability in Males 188
Hounsfield Units 702
HPC-1 (Hereditary Prostate Cancer 1 Locus) 703
HPV (Human Papilloma Virus), Urologic Considerations 703
Human Growth Hormone (hGH), Urologic Considerations 703
Hunner Ulcer 703
Hutch Diverticulum 703
Hydatid Cyst (Hydatid Disease) 703
Hydrocalycosis 703
Hydrocele of the Spermatic Cord 703
Hydrocele, Adult & Pediatric 190
Hydrocele and Hydrometrocolpos, Pediatric 192
Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Adult 194
Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Pediatric 196
Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Prenatal 198
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Adult Female 210
Incontinence, Urinary, Following Radical Prostatectomy 214
Incontinence, Urinary, Pediatric 216
Indevus Urgency Severity Scale (IUSS) 710
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome) 200
Hyperbaric Oxygen, Urologic Considerations 703
Hypercalcemia, Urologic Considerations 704
Hypercalcium (Absorptive, Renal, and Resorptive) 704
Hypercarbia During Laparoscopy 704
Hypercarnitine 705
Hyperkalemia, Urologic Considerations 705
Hypermagnesemia, Urologic Considerations 705
Hypernatremia, Urologic Considerations 705
Hyponatremia, Urologic Considerations 705
Incontinence, Urinary, Adult Male 212
Incontinence, Urinary, Following Radical Prostatectomy 214
Hymenal Skin Tags 703
Contents

Intermittent Hormonal Therapy (IHT)/Intermittent Androgen Deprivation (IAD) 711
International Children's Continence Society (ICCS), Terminology 711
International Germ Cell Cancer Collaborative Group (IGCCCG) 711
International Prostate Symptom Score (I-PSS) 712, 984
Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS) 712
Interstitial Nephritis 712
Intracytoplasmic Sperm Injection (ICSI) 712
Intraoperative Floppy Iris Syndrome (IFIS) 712
Intrauterine Insemination (IUI) 712
Intrinsic Sphincter Deficiency (ISD) 712
Inverted Papilloma, Bladder 712
Inverted Papilloma, Ureter and Renal Pelvis 712
IRS (Intergroup Rhabdomyosarcoma Study) Clinical Classification 713
Jaboulay/Winkelman Procedure (Hydrocelectomy) 713
Jack Stones 713
Jarisch–Herxheimer Reaction 713
Jejunal–Ileal Bypass, Urologic Considerations 713
Jeune Syndrome (Asphyxiating Thoracic Dysplasia) 713
Joint Replacement, Urologic Considerations 713
Juvenile Gangrenous Vasculitis, Scrotal (Pyoderma Gangrenosum) 714
Juxtaglomerular Cell Tumor, Kidney 714
Kallmann Syndrome 714
Kaposi Sarcoma, Urologic Considerations 714
Kartagener Syndrome (Immotile Cilia Syndrome) 714
Kegel Exercises 714
Kelami Classification System (Modified) 714
Kelly Plication 714
Kerr Kirks 714
Ketamine Abuse, Urologic Considerations 714
Kibric Test 715
Kidney, Metastasis To 715
Kidney, Supernumerary 715
Klinefelter Syndrome 715
Klippel–Trenaunay–Weber Syndrome 716
Kock Pouch and Hemi–Kock Neobladder 716
Koyler Stent 716
Kruger Strict Sperm Morphology 716
Labal Adhesions and Fusion 716
Lactate Dehydrogenase (LDH), Urologic Considerations 716
Lapides Classification of Voiding Dysfunction 716
Laser Technologies and Urologic Applications 716
Latex Allergy, Urologic Considerations 717
Leaurence–Moon–Bardet–Biedell Syndrome 716
Lazy Bladder Syndrome (Nurse's Bladder) 716
Leadbetter–Clarke Ureteral Anastomosis 717
Leadbetter–Politano Ureteroneocystostomy 717
Leak Point Pressure (LPP)/Abdominal Leak Point Pressure (ALPP) 717
LeBag Neobladder 717
LeDuc Ureteral Anastomosis 717
Leiomyomatosis, Hereditary 717
Leopard Syndrome 717
Lesch–Nyhan Syndrome 717
Leukemia, Urologic Considerations 717
Leukoplakia, Penis 718
Leukorrhea 718
Libido, Diminished, Female 718
Libido, Diminished, Male 718
Lichen Nitidus, Penis 718
Lichen Planus, Penis 718
Lichen Sclerosis Et Atrophicus 718
Lichen Simplex Chronicus (Lichen Simplex Complex) 718
Lich–Gregoir Ureteral Reimplantation 718
Liddle's Syndrome 718
Lipoma, Bladder 719
Lipoma, Spermatic Cord 719
Lipomatosis, Pelvic 719
Lipomeningocele, Urologic Considerations 719
Liver Metastasis, Urologic Considerations 719
Lobar Nephronia 719
Lobar Nephronia 719
Lord Procedure (Hydrocelectomy) 719
Lowe Syndrome 720
Lower Urinary Tract Symptoms 720
Lub Syndrome 720
Lyme Disease, Urologic Considerations 720
Lymphadenopathy, Inguinal 720
Lymphadexopathy, Pelvic and Retroperitoneal 720
Lymphangiogram, Pedal 720
Lymphangiomia, Bladder 720
## Contents

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphangioma, Renal</td>
<td>720</td>
</tr>
<tr>
<td>Lymphangioma, Retroperitoneal</td>
<td>720</td>
</tr>
<tr>
<td>Lymphangioma, Scrotal</td>
<td>720</td>
</tr>
<tr>
<td>Lymphatic Asciises</td>
<td>724</td>
</tr>
<tr>
<td>Lymphcele, Pelvic</td>
<td>720</td>
</tr>
<tr>
<td>Lymphogranuloma Venereum</td>
<td>720</td>
</tr>
<tr>
<td>Lymphoma, Urologic Considerations</td>
<td>721</td>
</tr>
<tr>
<td>Lymphoreticular Malignant Neoplasm, Penile</td>
<td>721</td>
</tr>
<tr>
<td>Lymphovascular Invasion (LVI), Urologic Considerations</td>
<td>721</td>
</tr>
<tr>
<td>Lynch Syndrome</td>
<td>721</td>
</tr>
<tr>
<td>MACE (Malone Antegrade Continent Enema)</td>
<td>721</td>
</tr>
<tr>
<td>Macro-Orchidism (MO)</td>
<td>721</td>
</tr>
<tr>
<td>MAG 3 Renal Scan</td>
<td>721</td>
</tr>
<tr>
<td>MAGPI Hypospadias Repair</td>
<td>721</td>
</tr>
<tr>
<td>Mainz I, II, III Pouch Urinary Diversion</td>
<td>722</td>
</tr>
<tr>
<td>Malacoplakia, Genitourinary</td>
<td>722</td>
</tr>
<tr>
<td>Malaria (Black Water Fever), Urologic Considerations</td>
<td>722</td>
</tr>
<tr>
<td>Male Sexual Function Scale</td>
<td>722</td>
</tr>
<tr>
<td>Male Sexual Health Questionnaire (MSHQ) and the MSHQ Short Form</td>
<td>722</td>
</tr>
<tr>
<td>Malrotated Kidney/Renal Malrotation</td>
<td>722</td>
</tr>
<tr>
<td>Marshall–Marchetti–Krantz (MMK) Cystourethropexy</td>
<td>722</td>
</tr>
<tr>
<td>Marlius Graft</td>
<td>722</td>
</tr>
<tr>
<td>Mathieu Hypospadias Repair</td>
<td>722</td>
</tr>
<tr>
<td>Maturation Arrest</td>
<td>722</td>
</tr>
<tr>
<td>Maximum Androgen Blockade (MAB)/Combined Hormonal Therapy (CHT)</td>
<td>723</td>
</tr>
<tr>
<td>Meyer–Rokitansky–Kuster–Hauser Syndrome (Rokitansky–Kuster–Hauser Syndrome)</td>
<td>723</td>
</tr>
<tr>
<td>Mayo Clinic Grading System for Prostate Cancer</td>
<td>723</td>
</tr>
<tr>
<td>McCune–Albright Syndrome</td>
<td>723</td>
</tr>
<tr>
<td>McGuire Urinal</td>
<td>723</td>
</tr>
<tr>
<td>Meatal Stenosis, Urethral, Female</td>
<td>723</td>
</tr>
<tr>
<td>Meatal Stenosis, Urethral, Male</td>
<td>723</td>
</tr>
<tr>
<td>Meckel–Gruber Syndrome (Meckel Syndrome)</td>
<td>723</td>
</tr>
<tr>
<td>Median Bar</td>
<td>723</td>
</tr>
<tr>
<td>Median Raphe Cyst</td>
<td>723</td>
</tr>
<tr>
<td>Medications That Can Impact Voiding Function</td>
<td>723</td>
</tr>
<tr>
<td>Medullary Cystic Kidney</td>
<td>724</td>
</tr>
<tr>
<td>Medullary Cystic Kidney Disease (MCKD)</td>
<td>724</td>
</tr>
<tr>
<td>Medullary Sponge Kidney (MSK)</td>
<td>724</td>
</tr>
<tr>
<td>Megacystis, Congenital</td>
<td>724</td>
</tr>
<tr>
<td>Megacystis-Megaureter Syndrome</td>
<td>725</td>
</tr>
<tr>
<td>Megalourethra</td>
<td>725</td>
</tr>
<tr>
<td>Megaureter, Congenital</td>
<td>725</td>
</tr>
<tr>
<td>Melanoma, Adrenal</td>
<td>725</td>
</tr>
<tr>
<td>Melanoma, Genitourinary</td>
<td>725</td>
</tr>
<tr>
<td>Melanoma, Urethral</td>
<td>725</td>
</tr>
<tr>
<td>Menkes Syndrome (Menkes Kinky Hair Disease)</td>
<td>725</td>
</tr>
<tr>
<td>Menopause, Urologic Considerations</td>
<td>725</td>
</tr>
<tr>
<td>Metabolic Stone Evaluation (24-hr Urine Studies)</td>
<td>725</td>
</tr>
<tr>
<td>Metabolic Syndrome, Urologic Considerations</td>
<td>725</td>
</tr>
<tr>
<td>Metanephrin Adenofibroma, Kidney (Nephrogenic Adenofibroma)</td>
<td>725</td>
</tr>
<tr>
<td>Metanephrin Adenoma</td>
<td>727</td>
</tr>
<tr>
<td>Metapyrone Test</td>
<td>727</td>
</tr>
<tr>
<td>Meyer-Weigert Law</td>
<td>727</td>
</tr>
<tr>
<td>MIBG Scan</td>
<td>727</td>
</tr>
<tr>
<td>Michaelis–Gutmann Bodies</td>
<td>727</td>
</tr>
<tr>
<td>Microcystic/Nested Variant Urothelial Carcinoma</td>
<td>727</td>
</tr>
<tr>
<td>Microthiasis, Testis</td>
<td>727</td>
</tr>
<tr>
<td>Micropapillary Bladder Cancer</td>
<td>727</td>
</tr>
<tr>
<td>Microphallic (Microphallic)</td>
<td>727</td>
</tr>
<tr>
<td>Micturation Syncope</td>
<td>728</td>
</tr>
<tr>
<td>Milk of Calcium, Urinary Tract</td>
<td>728</td>
</tr>
<tr>
<td>Milk–Alkali Syndrome</td>
<td>728</td>
</tr>
<tr>
<td>Mitrofanoff Principle</td>
<td>728</td>
</tr>
<tr>
<td>Mixed Epithelial Stromal Tumor of the Kidney (MESTK)</td>
<td>728</td>
</tr>
<tr>
<td>Molluscum Contagiosus</td>
<td>728</td>
</tr>
<tr>
<td>Mondor Disease</td>
<td>728</td>
</tr>
<tr>
<td>Monfort Technique</td>
<td>728</td>
</tr>
<tr>
<td>Monti Procedure</td>
<td>728</td>
</tr>
<tr>
<td>Morris Syndrome</td>
<td>729</td>
</tr>
<tr>
<td>Moskowitz Vaginal Prolapse Repair</td>
<td>729</td>
</tr>
<tr>
<td>Mostofi (WHO) Grading System, Prostate Cancer</td>
<td>729</td>
</tr>
<tr>
<td>Mowat–Wilson Syndrome</td>
<td>729</td>
</tr>
<tr>
<td>Mucormycosis, Genitourinary</td>
<td>729</td>
</tr>
<tr>
<td>Mucourea (Mucourea)</td>
<td>729</td>
</tr>
<tr>
<td>Mui–Torre Syndrome</td>
<td>729</td>
</tr>
<tr>
<td>Mulberry Stones</td>
<td>729</td>
</tr>
</tbody>
</table>
Mulcahy Protocol 729
Müllerian Duct Remnants and Syndrome (PMDS) 730
Multicystic Dysplastic Kidney 246
Multilocular Cystic Nephroma (Cystic Nephroma, Multilocular Cyst) 730
Multiple Endocrine Neoplasia (MEN I, MEN II) 730
Multiple Myeloma, Urologic Considerations 730
Multiple Sclerosis, Urologic Considerations 248
Mumps Orchitis 730
MURCS Association (Müllerian Duct, Renal, and Cervical Vertebral Defects) 730
Muscle Flap Types, Urologic Considerations 730
Mustardé Hypospadias Repair 730
Myasthenia Gravis, Urologic Considerations 250
Mycoplasma Genitalium Infection 731
Mycoplasma Hominis, Urinary Tract Infection 731
Myelodysplasia (Spinal Dysraphism), Urologic Considerations 252
Myocutaneous Flaps 731
Myofascial Pain, Urologic Considerations 731
Myofascial Pelvic Pain Syndrome (MPPS) 731
Myoglobin Nephrotoxicity 731
Myoglobinuria 731
Nagamatsu Incision 731
National Comprehensive Cancer Network (NCCN) Guidelines 732
National Institutes of Health (NIH) Chronic Prostatitis Symptom Index (CPSI) 732, 990
Necrospermia 732
Nelson Syndrome 732
Nephritis, Radiation 732
Nephrocalcinosis, Adult 254
Nephrocalcinosis, Neonatal 732
Nephrogenic Adenoma (NA) and Metaplasia 732
Nephrogenic Syndrome of Inappropriate Antidiuresis 732
Nephrogenic Systemic Fibrosis/Fibrosing Dermopathy (NSF/NFD) 732
Nephrometry Scoring Systems (PADUA, C-Index, RENAL) 732
Nephropathis (Juvenile, Infantile, and Adolescent) 733
Nephropathy, Analgesic 733
Nephropathy, Ischemic 733
Nephropathy, Membranous 733
Nephropathy, Minimal Change 733
Nephropathy, Obstructive 733
Nephropathy, Urate (Urate Nephropathy) 733
Nephroptosis 734
Nephrotic Syndrome 256
Nesbit Chordee Repair 734
Neuroblastoma 258
Neuroendocrine Tumors, Genitourinary 734
Neurofibromatosis, Urologic Considerations 734
Neurogenic Bladder, General Considerations 260
Neurogenic Detrusor Overactivity (NDO) 734
Neuromodulation, Urologic Considerations 734
Nevus–Zincke Classification 734
NMP-22 Testing 735
Nocturia 262
Nocturnal Erections, Normal and Abnormal 735
Nocturnal Penile Tumescence (NPT) Testing 735
Nocturnal Polyuria (NP) 735
Nomograms, Urologic 735
Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) 735
Nonsacral Neuromodulation 735
Noonan Syndrome 735
N-Telopeptide, Urinary (NTX) 735
Nutcracker Syndrome 735
Obesity, Urologic Considerations 736
Oblurator Nerve Injury, Intraoperative 736
Oblurator Reflex, Urologic Considerations 736
O’Leary–Sant Scores (O’Leary–Sant Interstitial Cystitis Symptom Index [ICSI]) 736
Oligoasthenoteratospermia 736
Oligospermia 736
Omphalolecele-Exstrophy of the Bladder—Imperforate Anus-Spina Bifida Defects (OEIS) Complex 736
Opioid-Induced Hypogonadism 736
Opitz–Frias Syndrome 737
Ovar–Facial–Digital (OFD) Syndrome 737
Orchitis, General Considerations 264
Orchitis, Granulomatous 737
Ostentis Pubis, Urologic Considerations 266
Osteonecrosis of the Jaw (ONJ), Urologic Considerations 737
Contents

Osteoporosis and Osteopenia, Urologic Considerations 737
Osteotomy, Urologic Considerations 738
Ovarian Cancer, Urologic Considerations 738
Ovarian Remnant Syndrome 738
Ovarian Vein Syndrome 738
Overactive Bladder (OAB) 738
Oxalate-Associated Renal Disease 738
Oxalate, Dietary 738
p53, Urologic Considerations 738
Pad Testing 738
Pagano Ureteral Anastomosis 739
Page Kidney 739
Paget Disease, Anogenital/Extramammary 739
Paget Disease, Bone 739
Painful Bladder Syndrome (PBS) 739
Palliative Radiation, Urologic Considerations 739
Pancreatitis, Autoimmune Urologic Considerations 739
Paneth Cell-Like Change, Prostate 739
Papillary Necrosis, Renal 270
Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP) 740
Papilloma, Bladder 740
Papilloma, Renal Pelvis 740
Papillomatosis, Renal 740
Paquin Ureteral Reimplantation 740
Paraphilias, Urologic Considerations 740
Parastomal Hernia 740
Paratesticular Rhabdomyosarcoma 741
Paratesticular Tumors 741
Pararectal and Vaginal Wall Masses 741
Parkinson Disease, Urologic Considerations 741
Parin Table 741
Patel Syndrome 741
Patient Perception of Bladder Condition (PPBC) 741
Patient Perception of Intensity of Urgency Scale (PPIUS) 741
PCA3 (Prostate Cancer Gene 3 Urine Assay) 741
Pearly Papules of Penis 742
Pediatric-Modified Risk Injury Failure Loss End-Stage Renal Disease (PRIFLE) 742
Pediculosis Pubis (Crab Lice/Pubic Lice) 742
Peliosis Hepatis 742
Pelvic Floor Dysfunction 742
Pelvic Fracture, Urologic Considerations 742
Pelvic Liposarcoma 742
Pelvic Organ Prolapse (Cystocele and Enterocele) 276
Pelvic Organ Prolapse Quantification System (POP-Q) 743
Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom Scale 743
Pelvic Pain, Female 278
Pelvic Pain, Male 743
Pelvis, Blid, Renal 743
Pelvis, Extrarenal 743
Pemphigus Foliacetus and Vulgaris 743
Penile and Corporal Body Mass 743
Penile Brachial Pressure Index (PBI) 743
Penile Doppler Ultrasound Indications and Parameters 743
Penile Enhancement and Lengthening 743
Penile Intraepithelial Neoplasia 744
Penile Necrosis (Gangrene) Non-Fournier Gangrene 744
Penile Pain Syndrome 744
Penile Prosthesis Problems (Infection/Extrusion/Malfunction) 280
Penile Prosthesis, Models and Descriptions 744
Penile Rehabilitation 744
Penile Shortening 744
Penile Skin Bridges (Penile Bands) 745
Penile, Mass (Noncunaneous) 745
Penis, Agenesis (Aphallia) 745
Penis, Angiosarcoma 745
Penis, Artificial Nodules (Tacho Nodules, Bulletus, Fang Muk, Chagan Balls) 745
Penis, Basal Cell Carcinoma 745
Penis, Bowenoid Papulosis 745
Penis, Buried (Concealed/Hidden/Trapped) 745
Penis, Cancer, General Considerations 282
Penis, Cancer, Lymphadenopathy 284
Penis, Curvature, and/or Pain 286
Penis, Cutaneous Horn 745
Penis, Cutaneous Lesion 288
Penis, Cysts 746
Penis, Duplication (Diphallus) 746
Penis, Fixed Drug Eruptions 746
Penis, Hemangioma (Cavernous Hemangioma) 746
Contents

Pregnancy, Bacteriuria, Pyuria, and Urinary Tract Infection 754
Pregnancy, Hematuria 754
Pregnancy, Radiologic Considerations 754
Pregnancy, Renal Transplantation 754
Pregnancy, Urinary Diversion 755
Pregnancy, Urinary Tract Obstruction 755
Pregnancy, Urolithiasis 314
Pregnancy, Urologic Malignancy 755
Pregnancy, Urologic Medications 755
Prehn Sign 755
Prentiss Maneuver 755
Preputial Stones 755
Pressure–Flow Studies 755
Priapism, Stuttering (Intermittent Priapism) 755
Priapism 316
Primitive Neuroectodermal Tumors (PNET) (Extraskeletal Ewing Sarcoma) 756
Princeton III Consensus Recommendations: Erectile Dysfunction (ED) and Cardiovascular Disease 756
Prolactin, Serum Level 756
Prolapse, Staging Systems 756
Propantheline Stimulation Test 756
Prophylactic Antibiotics, AUA Guidelines 756, 979
Prostascint Scan 756
Prostate Biopsy, Infections and Complications 318
Prostate Cancer Screening Guidelines 756, 991
Prostate Cancer, Active Surveillance and Watchful Wailing 757
Prostate Cancer, Basal Cell Carcinoma 757
Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Cryotherapy 320
Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radiation Therapy 322
Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy 324
Prostate Cancer, Circulating Tumor Cells (CTC's) 757
Prostate Cancer, Ductal Adenocarcinoma 757
Prostate Cancer, Familial 758
Prostate Cancer, General 326
Prostate Cancer, Leiomyosarcoma, and Other Uncommon Sarcomas 758
Prostate Cancer, Localized (T1, T2) 328
Prostate Cancer, Locally Advanced (Clinical T3, T4) 330
Prostate Cancer, Locally Advanced (Pathologic T3, T4) 332
Prostate Cancer, Metastatic (Clinical and Pathologic N+, M+) 334
Prostate Cancer, Mucocele Adenocarcinoma 758
Prostate Cancer, Positive Margin Following Radical Prostatectomy 336
Prostate Cancer, Prevention (Chemoprevention) 758
Prostate Cancer, Rising PSA Following Androgen Ablation (Castration-Resistant Prostate Cancer, CRPC and mCRPC) 338
Prostate Cancer Risk Calculators 758
Prostate Cancer, Risk Stratification (D'Amico Classification) 759
Prostate Cancer, Secondary Hormonal Therapy 759
Prostate Cancer, Small Cell (Neuroendocrine) 759
Prostate Cancer, Squamous and Adenosquamous 759
Prostate Cancer, Urothelial 340
Prostate Cancer, Very Low Risk and Active Surveillance 342
Prostate Health Index (PHI) and [-2] proPSA 759
Prostate Urethral Angle 760
Prostate, Abscess 344
Prostate, Basal Cell Hyperplasia 760
Prostate, Benign Enlargement (Benign Prostate Enlargement [BPE]) 760
Prostate, Benign Hyperplasia/Hypertrophy (BPH) 346
Prostate, Benign Obstruction (Benign Prostatic Obstruction [BPO]) 760
Prostate, Calculi 348, 760
Prostate, Female 760
Prostate, Hematuria 760
Prostate, Infarction 760
Prostate, Massage 760
Prostate, Nodule 350
Prostate Stents (Urolume and Spanner) 761
Prostatic Acid Phosphatase (PAP) 761
Prostatic Intraepithelial Neoplasia (PIN) 352
Prostatic Urethral Polyps 761
Prostatic Utricle Anomalies 761
Prostatic Utricle Calcification 761
Prostatitis, Amebic Bacterial (NIH 1) 354
Prostatitis, Asymptomatic Inflammatory (NIH IV) 761
Prostatitis, Chronic Nonbacterial, Inflammatory and Noninflammatory (NIH CP/CPPS III A and B) 356
<table>
<thead>
<tr>
<th></th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostatitis, Chronic, Bacterial (NIH II)</td>
<td>358</td>
</tr>
<tr>
<td>Prostatitis, General</td>
<td>360</td>
</tr>
<tr>
<td>Prostatitis, Granulomatous</td>
<td>362</td>
</tr>
<tr>
<td>Prostatitis, Mycotic (Fungal Prostatitis)</td>
<td>761</td>
</tr>
<tr>
<td>Prostatitis, NIH Classification System</td>
<td>762</td>
</tr>
<tr>
<td>Prostatitis, Stress</td>
<td>762</td>
</tr>
<tr>
<td>Prostatitis, Tuberculous</td>
<td>762</td>
</tr>
<tr>
<td>Prostatodynia</td>
<td>762</td>
</tr>
<tr>
<td>Prosthesis, Infected Penile</td>
<td>762</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>364</td>
</tr>
<tr>
<td>Prune Belly (Eagle–Barrett or Triad) Syndrome</td>
<td>366</td>
</tr>
<tr>
<td>Pruritus, External Genitalia, Male</td>
<td>762</td>
</tr>
<tr>
<td>PSA, Age-Adjusted (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA Bounce (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA Complexed (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA Density (PSAD) (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA Elevation Following Negative Prostate Biopsy</td>
<td>368</td>
</tr>
<tr>
<td>PSA Elevation, General Considerations</td>
<td>370</td>
</tr>
<tr>
<td>PSA Failure, ASTRO and Phoenix Definitions (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA, Free and Total (See Section II &quot;PSA, General Considerations&quot;)</td>
<td>763</td>
</tr>
<tr>
<td>PSA, General Considerations and PSA Derivatives</td>
<td>763</td>
</tr>
<tr>
<td>PSA, Race-Adjusted (See Section II &quot;PSA, General Considerations and PSA Derivatives&quot;)</td>
<td>765</td>
</tr>
<tr>
<td>PSA, RT-PCR</td>
<td>765</td>
</tr>
<tr>
<td>PSA Velocity (PSAV) and PSA Doubling Time (PSADT) (See Section II &quot;PSA, General Considerations and PSA Derivatives&quot;)</td>
<td>765</td>
</tr>
<tr>
<td>Pseudodysynergia (Hinman Syndrome)</td>
<td>765</td>
</tr>
<tr>
<td>Pseudohormaphroditism, Male (XY DSD) and Female (XX DSD)</td>
<td>372</td>
</tr>
<tr>
<td>Pseudomyxoma Ovarii-Like Posttherapeutic Alteration in Prostate Adenocarcinoma</td>
<td>765</td>
</tr>
<tr>
<td>PSMA (Prostate-Specific Membrane Antigen)</td>
<td>765</td>
</tr>
<tr>
<td>Psosas Abscess, Urologic Considerations</td>
<td>765</td>
</tr>
<tr>
<td>Psosas Hitch Procedure</td>
<td>766</td>
</tr>
<tr>
<td>Psoriasis, External Genitalia</td>
<td>766</td>
</tr>
<tr>
<td>Psychogenic Polydipsia</td>
<td>766</td>
</tr>
<tr>
<td>Pudendal Nerve Entrapment/Pudendal Neuropathy</td>
<td>766</td>
</tr>
<tr>
<td>Pulmonary Metastasis, Urologic Considerations</td>
<td>766</td>
</tr>
<tr>
<td>Purple Urine Bag Syndrome</td>
<td>766</td>
</tr>
<tr>
<td>Pyelitis Cystica</td>
<td>766</td>
</tr>
<tr>
<td>Pyelitis Glandularis</td>
<td>766</td>
</tr>
<tr>
<td>Pyelogenic Cyst</td>
<td>767</td>
</tr>
<tr>
<td>Pyelonephritis, Acute</td>
<td>374</td>
</tr>
<tr>
<td>Pyelonephritis, Acute, Pediatric</td>
<td>376</td>
</tr>
<tr>
<td>Pyelonephritis, Chronic</td>
<td>378</td>
</tr>
<tr>
<td>Pyelonephritis, Enzymeatherosus</td>
<td>380</td>
</tr>
<tr>
<td>Pyelonephritis, Xanthogranulomatosis</td>
<td>382</td>
</tr>
<tr>
<td>Pyycycosis</td>
<td>767</td>
</tr>
<tr>
<td>Pyonephrosis</td>
<td>767</td>
</tr>
<tr>
<td>Pyospermia</td>
<td>767</td>
</tr>
<tr>
<td>Pyuria</td>
<td>386</td>
</tr>
<tr>
<td>Q-Tip Test</td>
<td>767</td>
</tr>
<tr>
<td>Quakel Corporal Shunt</td>
<td>767</td>
</tr>
<tr>
<td>Radiation Exposure Guidelines</td>
<td>767</td>
</tr>
<tr>
<td>Radiation, Pelvic, Urologic Considerations</td>
<td>767</td>
</tr>
<tr>
<td>Radiation Proctis, Urologic Considerations</td>
<td>768</td>
</tr>
<tr>
<td>Radiation, Renal and Retroperitoneal, Urologic Considerations</td>
<td>768</td>
</tr>
<tr>
<td>Radiopharmaceuticals, Urologic Considerations (Strontium89, Samarium153, Radium223)</td>
<td>768</td>
</tr>
<tr>
<td>Rapid Plasma Reagin (RPR) Blood Test</td>
<td>768</td>
</tr>
<tr>
<td>Raz Bladder Neck Suspension (Urethropexy)</td>
<td>768</td>
</tr>
<tr>
<td>Raz Vaginal Wall Sling</td>
<td>768</td>
</tr>
<tr>
<td>Reactive Arthritis/Reactive Arthritis Triad (Formerly Reiter Syndrome)</td>
<td>768</td>
</tr>
<tr>
<td>Rectal Injury During Radical Prostatectomy or Radical Cystectomy</td>
<td>388</td>
</tr>
<tr>
<td>Recocete, Urologic Considerations</td>
<td>769</td>
</tr>
<tr>
<td>Red Scrotum Syndrome</td>
<td>769</td>
</tr>
<tr>
<td>Reed Syndrome</td>
<td>769</td>
</tr>
<tr>
<td>Reflux Nephropathy</td>
<td>769</td>
</tr>
<tr>
<td>Reifenstein Syndrome</td>
<td>769</td>
</tr>
<tr>
<td>Reinke Crystals</td>
<td>769</td>
</tr>
<tr>
<td>Renal Adenoma (Papillary Adenoma)</td>
<td>769</td>
</tr>
<tr>
<td>Renal Agenesis (Bilateral and Unilateral)</td>
<td>769</td>
</tr>
<tr>
<td>Renal Anatomy, Normal Radiographic Findings (Sizes, Calyces)</td>
<td>769</td>
</tr>
<tr>
<td>Renal and Perirenal Abscess</td>
<td>390</td>
</tr>
<tr>
<td>Renal Angiomydipoma</td>
<td>392</td>
</tr>
<tr>
<td>Renal Artery Anerym</td>
<td>770</td>
</tr>
<tr>
<td>Renal Artery Fibromuscular Dysplasia</td>
<td>770</td>
</tr>
<tr>
<td>Renal Artery Stenosis/Renovascular Hypertension</td>
<td>394</td>
</tr>
<tr>
<td>Renal Capsular Neoplasms</td>
<td>396</td>
</tr>
<tr>
<td>Renal Carcinoid Tumor</td>
<td>770</td>
</tr>
<tr>
<td>Renal Cell Carcinoma with Tumor Thrombus</td>
<td>398</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Chromophobe</td>
<td>770</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Clear Cell</td>
<td>770</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Familial</td>
<td>770</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, General</td>
<td>400</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Localized (T1–T2)</td>
<td>402</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Locally Advanced (T3–T4)</td>
<td>404</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Metastatic (N+, M+)</td>
<td>406</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Papillary Types 1 and 2</td>
<td>771</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Pediatric</td>
<td>408</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Sarcomatoid</td>
<td>771</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Tubulocystic</td>
<td>771</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Unclassified</td>
<td>771</td>
</tr>
<tr>
<td>Renal Cell Carcinoma, Xp11.2;TFE3 Translocations</td>
<td>771</td>
</tr>
<tr>
<td>Renal Cortical Adenoma</td>
<td>772</td>
</tr>
<tr>
<td>Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)</td>
<td>412</td>
</tr>
<tr>
<td>Renal Dysplasia, Hypodysplasia, and Hypoplasia</td>
<td>414</td>
</tr>
<tr>
<td>Renal Ectopia</td>
<td>416</td>
</tr>
<tr>
<td>Renal Fusion Anomalies</td>
<td>418</td>
</tr>
<tr>
<td>Renal Hemangioma</td>
<td>772</td>
</tr>
<tr>
<td>Renal Hemangioendothelioma</td>
<td>772</td>
</tr>
<tr>
<td>Renal Infarction</td>
<td>420</td>
</tr>
<tr>
<td>Renal Leiomysarcoma</td>
<td>772</td>
</tr>
<tr>
<td>Renal Leiomysarcoma</td>
<td>772</td>
</tr>
<tr>
<td>Renal Lymphangiectasia</td>
<td>772</td>
</tr>
<tr>
<td>Renal Malrotation</td>
<td>772</td>
</tr>
<tr>
<td>Renal Mass</td>
<td>422</td>
</tr>
<tr>
<td>Renal Mass, Indeterminate</td>
<td>772</td>
</tr>
<tr>
<td>Renal Mass, Intraoperative Consultation</td>
<td>424</td>
</tr>
<tr>
<td>Renal Medullary Carcinoma</td>
<td>773</td>
</tr>
<tr>
<td>Renal Oncocytoma</td>
<td>426</td>
</tr>
<tr>
<td>Renal Osteodystrophy</td>
<td>773</td>
</tr>
<tr>
<td>Renal Pseudotumor</td>
<td>773</td>
</tr>
<tr>
<td>Renal Sarcoma, Adult and Pediatric</td>
<td>428</td>
</tr>
<tr>
<td>Renal Sinus Abnormalities</td>
<td>773</td>
</tr>
<tr>
<td>Renal Transplant Types (Standard/Extended/Donor After Death)</td>
<td>773</td>
</tr>
<tr>
<td>Renal Transplantation and Neoplasia</td>
<td>773</td>
</tr>
<tr>
<td>Renal Trauma, Adult</td>
<td>430</td>
</tr>
<tr>
<td>Renal Trauma, Pediatric</td>
<td>432</td>
</tr>
<tr>
<td>Renal Tubular Acidosis</td>
<td>434</td>
</tr>
<tr>
<td>Renal Tumors, WHO 2004 Classification</td>
<td>774</td>
</tr>
<tr>
<td>Renal Vein Thrombosis, Adult and Pediatric</td>
<td>436</td>
</tr>
<tr>
<td>Renal Vein, Leiomyosarcoma</td>
<td>774</td>
</tr>
<tr>
<td>Renal–Retinal Syndrome</td>
<td>774</td>
</tr>
<tr>
<td>Renin, Plasma and Renal Vein</td>
<td>774</td>
</tr>
<tr>
<td>Reninoma (Renin-Secreting Juxtaglomerular Cell Tumor)</td>
<td>775</td>
</tr>
<tr>
<td>Reno-Alimentary Fistula</td>
<td>775</td>
</tr>
<tr>
<td>Reno-Bronchial Fistula</td>
<td>775</td>
</tr>
<tr>
<td>Renomedullary Interstitial Cell Tumor (Medullary Fibroma, Renal Hamartoma)</td>
<td>775</td>
</tr>
<tr>
<td>Reperfusion Injury, Renal (Renal Ischemia and Reperfusion Injury)</td>
<td>775</td>
</tr>
<tr>
<td>Residual Urine (Postvoid Residual [PVR])</td>
<td>775</td>
</tr>
<tr>
<td>Resistive Indices (RI)</td>
<td>775</td>
</tr>
<tr>
<td>Retr Estis, Adenocarcinoma</td>
<td>775</td>
</tr>
<tr>
<td>Retr Estis, Tubular Ectasia and Cystic Dysplasia</td>
<td>776</td>
</tr>
<tr>
<td>Retrocaval/Circumcaval Ureter</td>
<td>776</td>
</tr>
<tr>
<td>Retrograde Ejaculation</td>
<td>438</td>
</tr>
<tr>
<td>Retrograde Urethrogram (RUG), Technique</td>
<td>776</td>
</tr>
<tr>
<td>Retropéritoeneal Abscess</td>
<td>440</td>
</tr>
<tr>
<td>Retropéritoeneal Fibrosis (RPF, Ormond Disease)</td>
<td>442</td>
</tr>
<tr>
<td>Retropéritoeneal Hematoma</td>
<td>776</td>
</tr>
<tr>
<td>Retropéritoeneal Liposarcoma</td>
<td>776</td>
</tr>
<tr>
<td>Retropéritoeneal Lymphoma</td>
<td>776</td>
</tr>
<tr>
<td>Retropéritoeneal Masses, Fluid, and Cysts</td>
<td>444</td>
</tr>
<tr>
<td>Retropéritoeneal Rheumatoid Nodules</td>
<td>776</td>
</tr>
<tr>
<td>Retropéritoeneal Sarcoma</td>
<td>777</td>
</tr>
<tr>
<td>Retropéritoeneum, Fat Necrosis</td>
<td>777</td>
</tr>
<tr>
<td>Rhabdoid Tumor, Malignant</td>
<td>777</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>446</td>
</tr>
<tr>
<td>Rhabdomyosarcoma, Pediatric (Sarcoma Botryoides)</td>
<td>448</td>
</tr>
<tr>
<td>Rieger Syndrome</td>
<td>777</td>
</tr>
<tr>
<td>Rifle Criterion for Acute Renal Injury</td>
<td>777</td>
</tr>
<tr>
<td>Rim Sign (Rim Nephrogram)</td>
<td>777</td>
</tr>
<tr>
<td>Robinow Syndrome</td>
<td>777</td>
</tr>
<tr>
<td>Robson Staging System</td>
<td>777</td>
</tr>
<tr>
<td>Rokitansky-Kuster-Hauser Syndrome</td>
<td>778</td>
</tr>
<tr>
<td>Rosewater Syndrome</td>
<td>778</td>
</tr>
<tr>
<td>Rovsing Polycystic Kidney Operation</td>
<td>778</td>
</tr>
<tr>
<td>Rovsing Syndrome</td>
<td>778</td>
</tr>
<tr>
<td>Sacral Agenesis, Urologic Consideration</td>
<td>450</td>
</tr>
<tr>
<td>Topic</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Sacral Neuromodulation</td>
<td>778</td>
</tr>
<tr>
<td>SANI Score</td>
<td>778</td>
</tr>
<tr>
<td>Sarcoidosis, Urologic Considerations</td>
<td>452</td>
</tr>
<tr>
<td>Sarcoma, Clear Cell of the Kidney</td>
<td>778</td>
</tr>
<tr>
<td>Saw Palmetto</td>
<td>778</td>
</tr>
<tr>
<td>Scalp, Urologic Considerations</td>
<td>778</td>
</tr>
<tr>
<td>Scardino-Prince Pyeloplasty</td>
<td>779</td>
</tr>
<tr>
<td>Schaefer Obstruction Grading System</td>
<td>779</td>
</tr>
<tr>
<td>Schiller-Duval Bodies</td>
<td>779</td>
</tr>
<tr>
<td>Schistosomiasis, Urologic Considerations</td>
<td>779</td>
</tr>
<tr>
<td>Schwannoma, Renal</td>
<td>779</td>
</tr>
<tr>
<td>Scleroderma, Urologic Considerations</td>
<td>779</td>
</tr>
<tr>
<td>Sclerosing Adenosis of the Prostate</td>
<td>779</td>
</tr>
<tr>
<td>Scrotal Pain Syndrome (Chronic Scrotal Pain Syndrome)</td>
<td>779</td>
</tr>
<tr>
<td>Scrotal Pearls (Scrotoliths)</td>
<td>779</td>
</tr>
<tr>
<td>Scrotal Skin Lesions</td>
<td>779</td>
</tr>
<tr>
<td>Scrotal Tongue</td>
<td>780</td>
</tr>
<tr>
<td>Scrotal Varices</td>
<td>780</td>
</tr>
<tr>
<td>Scrotum and Testicle, Mass</td>
<td>454</td>
</tr>
<tr>
<td>Scrotum and Testicle, Trauma</td>
<td>456</td>
</tr>
<tr>
<td>Scrotum, Accessory and Ectopic</td>
<td>780</td>
</tr>
<tr>
<td>Scrotum, Blifid</td>
<td>780</td>
</tr>
<tr>
<td>Scrotum, Engulfment (Penoscrotal Transposition)</td>
<td>780</td>
</tr>
<tr>
<td>Scrotum, Epidermal Inclusion Cyst</td>
<td>780</td>
</tr>
<tr>
<td>Scrotum, Fat Necrosis</td>
<td>781</td>
</tr>
<tr>
<td>Scrotum, Giant Neurolemmoma</td>
<td>781</td>
</tr>
<tr>
<td>Scrotum, Hemangioma</td>
<td>781</td>
</tr>
<tr>
<td>Scrotum, Hyoplasia</td>
<td>781</td>
</tr>
<tr>
<td>Scrotum, Idiopathic Calcinosis</td>
<td>781</td>
</tr>
<tr>
<td>Scrotum, Squamous Cell Carcinoma</td>
<td>458</td>
</tr>
<tr>
<td>SEAPI Incontinence Classification System</td>
<td>781</td>
</tr>
<tr>
<td>Seborheic Dermatitis</td>
<td>781</td>
</tr>
<tr>
<td>Semen Analysis, Abnormal Findings and Terminology</td>
<td>781</td>
</tr>
<tr>
<td>Semen Analysis, Technique, Normal Values</td>
<td>782</td>
</tr>
<tr>
<td>Semen Leukocytes</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Plasma Hypersensitivity (Seminal Plasma Allergy) and Hypersensitivity to Human Semen (HHS)</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Vesicle Agenesis</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Vesicle Amyloidosis</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Vesicle Calcui and Calcifications</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Vesicle, Carcinoma</td>
<td>782</td>
</tr>
<tr>
<td>Seminal Vesicle, Cysts and Massals</td>
<td>460</td>
</tr>
<tr>
<td>Seminal Vesicle, Cysts</td>
<td>783</td>
</tr>
<tr>
<td>Seminal Vesiculitis</td>
<td>783</td>
</tr>
<tr>
<td>Seminoma with High Mitotic Rate (Seminoma, Anaplastic)</td>
<td>783</td>
</tr>
<tr>
<td>Seminoma, Classic</td>
<td>783</td>
</tr>
<tr>
<td>Seminoma, Spermatocytic</td>
<td>783</td>
</tr>
<tr>
<td>Sex Reversal Syndrome (XX Male)</td>
<td>783</td>
</tr>
<tr>
<td>Sex-Hormone Binding Globulin (SHBG)</td>
<td>783</td>
</tr>
<tr>
<td>Sexsomia</td>
<td>783</td>
</tr>
<tr>
<td>Sexual Abuse, Pediatric</td>
<td>462</td>
</tr>
<tr>
<td>Sexual Anhedonia/Ejaculatory Anhedonia</td>
<td>783</td>
</tr>
<tr>
<td>Sexual Dysfunction, Female</td>
<td>464</td>
</tr>
<tr>
<td>Sexual Function Survey (SFS) (International Index of Erectile Function [IEF])</td>
<td>784, 988</td>
</tr>
<tr>
<td>Sexual Health Inventory for Men (SHIM) Score</td>
<td>784, 992</td>
</tr>
<tr>
<td>Sexually Transmitted Infections (STIs)</td>
<td>466</td>
</tr>
<tr>
<td>Shy Drager Syndrome, Urologic Considerations</td>
<td>784</td>
</tr>
<tr>
<td>Sickle Cell Disease, Urologic Considerations</td>
<td>468</td>
</tr>
<tr>
<td>Signet Ring Carcinoma, Prostate</td>
<td>784</td>
</tr>
<tr>
<td>Silber Vasoxidepidermosotomy</td>
<td>784</td>
</tr>
<tr>
<td>Skene (Paraurethral) Gland Adenocarcinoma</td>
<td>784</td>
</tr>
<tr>
<td>Skene (Paraurethral) Gland, Inflammation/Adenitis</td>
<td>784</td>
</tr>
<tr>
<td>Skin Tags, External Genitalia (Acrochordon, Pedunculated Papilloma)</td>
<td>784</td>
</tr>
<tr>
<td>Sleep Apnea, Urologic Considerations</td>
<td>784</td>
</tr>
<tr>
<td>Sling Materials</td>
<td>785</td>
</tr>
<tr>
<td>Smeagma</td>
<td>785</td>
</tr>
<tr>
<td>Smith–Lemi–Opitz Syndrome</td>
<td>785</td>
</tr>
<tr>
<td>Smoking, Urologic Considerations</td>
<td>785</td>
</tr>
<tr>
<td>Snodgrass Hypospadias Repair</td>
<td>785</td>
</tr>
<tr>
<td>Soap-Bubble Nephrogram</td>
<td>785</td>
</tr>
<tr>
<td>Sodium Cyanide Nitroprusside Test</td>
<td>785</td>
</tr>
<tr>
<td>Solitary Fibrous Tumor, Renal</td>
<td>785</td>
</tr>
<tr>
<td>Sperm Granuloma</td>
<td>785</td>
</tr>
<tr>
<td>Sperm Penetration Asssay (SPA, Hamster Test)</td>
<td>786</td>
</tr>
<tr>
<td>Sperm Vitality</td>
<td>786</td>
</tr>
<tr>
<td>Spermatic Cord Mass and Tumors</td>
<td>470</td>
</tr>
<tr>
<td>Spermatic Cord, Liposarcoma</td>
<td>786</td>
</tr>
<tr>
<td>Spermatocele</td>
<td>472</td>
</tr>
<tr>
<td>Spina Bifida/Spina Bifida Occulta, Urologic Considerations</td>
<td>786</td>
</tr>
<tr>
<td>Topic</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Spinal Cord Compression, Urologic Considerations</td>
<td>786</td>
</tr>
<tr>
<td>Spinal Cord Injury, Urologic Considerations</td>
<td>474</td>
</tr>
<tr>
<td>Spinal Shock</td>
<td>786</td>
</tr>
<tr>
<td>Spindle Cell Neoplasm, Urologic Considerations</td>
<td>786</td>
</tr>
<tr>
<td>Spinning Top Urethra</td>
<td>787</td>
</tr>
<tr>
<td>Splenic Injury During Radical Nephrectomy</td>
<td>787</td>
</tr>
<tr>
<td>Splenorenal Fusion</td>
<td>787</td>
</tr>
<tr>
<td>Splenic/Splenosis, Urologic Considerations</td>
<td>787</td>
</tr>
<tr>
<td>Sports Hernia (Athletic Pubalgia, Sportman's Hernia)</td>
<td>787</td>
</tr>
<tr>
<td>Squamous Metaplasia, Genitourinary</td>
<td>787</td>
</tr>
<tr>
<td>Stamey Procedure (Urethropexy)</td>
<td>787</td>
</tr>
<tr>
<td>Stamey Test (3-Glass Test, 4-Glass Test, Meares–Stamey Test)</td>
<td>788</td>
</tr>
<tr>
<td>Stauffer Syndrome</td>
<td>788</td>
</tr>
<tr>
<td>Steinstrasse</td>
<td>788</td>
</tr>
<tr>
<td>STING Procedure</td>
<td>788</td>
</tr>
<tr>
<td>Stranguria</td>
<td>788</td>
</tr>
<tr>
<td>Strek Gonad</td>
<td>788</td>
</tr>
<tr>
<td>Stress Urinary Incontinence, Female</td>
<td>476</td>
</tr>
<tr>
<td>Stress Urinary Incontinence, Male</td>
<td>478</td>
</tr>
<tr>
<td>Stricker Ureteral Anastomosis</td>
<td>788</td>
</tr>
<tr>
<td>Stroke (CVA), Urologic Considerations</td>
<td>480</td>
</tr>
<tr>
<td>Struvite</td>
<td>788</td>
</tr>
<tr>
<td>Studer Pouch</td>
<td>789</td>
</tr>
<tr>
<td>Superficial Inguinal Pouch of Denis-Browne</td>
<td>789</td>
</tr>
<tr>
<td>Supernumerary Kidney</td>
<td>789</td>
</tr>
<tr>
<td>Supine Stress Test</td>
<td>789</td>
</tr>
<tr>
<td>Suprapubic Pain, General Considerations</td>
<td>482</td>
</tr>
<tr>
<td>Swyer Syndrome (XY Sex Reversal)</td>
<td>789</td>
</tr>
<tr>
<td>Syndrome of Inappropriate Antidiuretic Hormone (SIADH)</td>
<td>789</td>
</tr>
<tr>
<td>Syphilis</td>
<td>484</td>
</tr>
<tr>
<td>Systemic Lupus, Urologic Considerations</td>
<td>789</td>
</tr>
<tr>
<td>Tabes Dorsalis</td>
<td>789</td>
</tr>
<tr>
<td>Taghaandan</td>
<td>790</td>
</tr>
<tr>
<td>Takayasu Arteritis, Urologic Considerations</td>
<td>790</td>
</tr>
<tr>
<td>Tanner Stages/Classification of Sexual Maturity</td>
<td>790</td>
</tr>
<tr>
<td>Teratoma, Sacrococcygeal, Urologic Considerations</td>
<td>790</td>
</tr>
<tr>
<td>Testicular Feminization Syndrome</td>
<td>790</td>
</tr>
<tr>
<td>Testicular Prosthesis</td>
<td>790</td>
</tr>
<tr>
<td>Testis Biopsy, Indications</td>
<td>790</td>
</tr>
<tr>
<td>Testis Cancer, Adult General Considerations</td>
<td>486</td>
</tr>
<tr>
<td>Testis Cancer, Choriocarcinoma</td>
<td>488</td>
</tr>
<tr>
<td>Testis Cancer, Embryonal Carcinoma</td>
<td>490</td>
</tr>
<tr>
<td>Testis Cancer, Endodermal Sinus Tumors (Yolk Sac Tumors)</td>
<td>492</td>
</tr>
<tr>
<td>Testis Cancer, Nonseminomatous Germ Cell Tumor, General</td>
<td>494</td>
</tr>
<tr>
<td>Testis Cancer, Pediatric, General Considerations</td>
<td>496</td>
</tr>
<tr>
<td>Testis Cancer, Seminoma</td>
<td>498</td>
</tr>
<tr>
<td>Testis, Carcinoid</td>
<td>790</td>
</tr>
<tr>
<td>Testis, Carcinoma In Situ (CIS)/Intratubular Germ Cell Neoplasia (ITGCN)</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Cystic Lymphangiomas</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Cysts</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Dermoid Cyst</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Hemangioma</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Leukemia</td>
<td>791</td>
</tr>
<tr>
<td>Testis, Leydig Cell Tumor</td>
<td>500</td>
</tr>
<tr>
<td>Testis, Lymphoma</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Metastasis To</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Microlithias</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Normal Size</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Pain (Orchalgia)</td>
<td>502</td>
</tr>
<tr>
<td>Testis, Retractile</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Sertoli Cell Tumor</td>
<td>504</td>
</tr>
<tr>
<td>Testis, Sex Cord Stromal Tumors</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Teratoma, Extragonalal</td>
<td>792</td>
</tr>
<tr>
<td>Testis, Teratoma, Mature and Immature</td>
<td>506</td>
</tr>
<tr>
<td>Testis, Tumor and Mass, Adult, General Considerations</td>
<td>508</td>
</tr>
<tr>
<td>Testis, Tumor and Mass, Pediatric, General Considerations</td>
<td>510</td>
</tr>
<tr>
<td>Testis, Vasocongestion From Sexual Arousal Without Ejaculation (&quot;Blue Balls&quot;)</td>
<td>792</td>
</tr>
<tr>
<td>Testosterone (Free and Total) Serum</td>
<td>792</td>
</tr>
<tr>
<td>Testosterone Replacement Following Localized Prostate Cancer Therapy</td>
<td>793</td>
</tr>
<tr>
<td>Testosterone Replacement Therapy, General Principles</td>
<td>512</td>
</tr>
<tr>
<td>Testosterone Replacement Therapy, Prostate Cancer Risk</td>
<td>793</td>
</tr>
<tr>
<td>Testosterone, Decreased (Hypogonadism)</td>
<td>514</td>
</tr>
<tr>
<td>Tethered Cord</td>
<td>793</td>
</tr>
<tr>
<td>Tethered Cord Syndrome</td>
<td>793</td>
</tr>
<tr>
<td>Thiersch-Duplay Hypospadias Repair</td>
<td>793</td>
</tr>
<tr>
<td>Thompson Pyeloplasty</td>
<td>793</td>
</tr>
<tr>
<td>Thoracic Kidney</td>
<td>794</td>
</tr>
</tbody>
</table>
Tinea Crucis (Jock Itch) 794
TMPRSS2-ERG Gene Fusion, Prostate Cancer 794
Toileting Programs 794
Torsion, Testis or Testicular/Epididymal Appendages 518
Transesophageal Echocardiogram (TEE), Urologic Considerations 794
Transureteroureterostomy, Technique and Indications 794
Transplant Rejection, Renal 520
Transsexualism, Urologic Considerations 794
Transurethral Resection (TUR) Syndrome 522
Tri-Mix 794
Trichomoniasis 795
Trichotemnomania, Pubic 795
Trichotillomania, Pubic 795
Trigonitis 795
Trisomy 4 P 795
Trisomy 8 795
Trisomy 9 795
Trisomy 9 P 795
Trisomy 10 Q 795
Trisomy 11 Q 795
Trisomy 13 795
Trisomy 18 (Edwards Syndrome) 795
Trisomy 20 P 796
Trisomy 21 796
Trisomy 22 796
Trisomy Syndrome 796
Trocare Injury During Laparoscopy 524
True Hermaphroditism (OVO-Testicular Disorder of Sexual Differentiation [OVO-DSD]) 796
Tuberculosis, Bladder and Urethra 796
Tuberculosis, Genitourinary, General Considerations 526
Tuberculosis, Kidney and Ureter 528
Tuberculosis, Male External Genitalia 796
Tuberculosis, Prostate and Epididymis 796
Tuberous Sclerosis 796
Tumor Lysis Syndrome (TLS) 796
Tunica Albuginea/Paratesticular Tumors and Cysts 530
Tunica Vaginalis Tumors 797
Turner Syndrome (XO Syndrome) 797
Turner–Warwick Inlay Urethroplasty 797
UISS-UCLA International Kidney Cancer Staging System 797
Umbilical Abnormalities, Urologic Considerations 532
Underactive Bladder (Detrusor Underactivity) 534
Undervirilized Male Syndrome (Mild Androgen Insensitivity) 797
Undescended Testes (Cryptorchidism) 536
Uninhibited Detrusor Contraction 797
Urachal Abnormalities 797
Urachal Carcinoma 538
Urachal Carcinoma Staging Systems 798
Uralt, Dietary 798
Ureaplasma Urealyticum 798
Ureter and Renal Pelvic Tumors, General Considerations 540
Ureter and Renal Pelvis, Squamous Cell Carcinoma 542
Ureter and Renal Pelvis, Urothelial Carcinoma 544
Ureter, Agenesis/Atresia 798
Ureter, Deviation 798
Ureter, Diverticulum 798
Ureter, Duplicated and Blifid 798
Ureter, Ectopic (Ureteral Ectopia) 799
Ureter, Fibroepithelial Polyps 799
Ureter, Fish Hook (Reverse J) 799
Ureter, Hamangiomatosis 799
Ureter, Intraoperative Injury 546
Ureter, J Hooking 799
Ureter, Leiomyoma 799
Ureter, Leiomyosarcoma 799
Ureter, Metastasis To 799
Ureter, Nephrogenic Adenoma (NA) 799
Ureter, Neurofibroma 799
Ureter, Obstruction 548
Ureter, Pipe-Stem 800
Ureter, Radiation Injury To 800
Ureter, Retrocaval (Circumcaval, Postcaval) 800
Ureter, Shepherd’s Crook 800
Ureter, Spiral (Corkscrew) 800
Ureter, Stone Passage Statistics 800
Ureter, Stricture 800
Ureter, Trauma 550
Ureter, Valves 800
Ureteral Jets 801
Ureteral Stricture Following Urinary Diversion 801
Ureteritis 801
Contents

Ureteritis Cystica 801
Ureterocelectomy 552
Ureteroureteric Anastomotic Stricture 554
Ureteroneocystostomy, Techniques and Indications 801
Ureteropelvic Junction Obstruction 556
Urethra, Abscess (Periurethral Abscess) 558
Urethra, Adenocarcinoma of Accessory Glands 801
Urethra, Adenomatous Polyps 801
Urethra, Bleeding (Blood at Meatus) 801
Urethra, Calculus 802
Urethra, Condyloma (Warts) 802
Urethra, Diverticular Carcinoma 802
Urethra, Diverticulum, Male 802
Urethra, Duplication 802
Urethra, Foreign Body 802
Urethra, Hemangioma 802
Urethra, Leiomyoma 802
Urethra, Leiomyosarcoma 803
Urethra, Leukoplakia 803
Urethra, Lymphoma 803
Urethra, Malacoplakia 803
Urethra, Malignant Melanoma 803
Urethra, Meatus, Normal Caliber 803
Urethra, Metastasis To 803
Urethra, Nephrogenic Metaplasia (Adenoma) 803
Urethra, Obstruction 803
Urethra, Polyps (Fibroepithelial, Adenomatous, Inflammatory) 804
Urethra, Prolapse (Female) 804
Urethra, Villosus Adenoma 804
Urethral Carcinoma, General Considerations 560
Urethral Caruncle 562
Urethral Discharge 564
Urethral Diverticula, Female 566
Urethral Hypermobility 804
Urethral Mass 566
Urethral Pressure Profile (UPP) 804
Urethral Sling, Indications and Anatomic Positions 804
Urethral Squamous-cell Carcinoma 570
Urethra, Stenosis/Stricture, Female 804
Urethral Stricture, Male 572
Urethral Syndrome 804
Urethral Trauma (Anterior and Posterior) 574
Urethritis, Acute 805
Urethritis, Chronic, Female 805
Urethritis, Gonococcal and Nongonococcal 576
Urethritis, Polypoid 805
Urethritis, Serine 805
Urethrocystocele 805
Urethrovaginitis, Diabetic 805
Urge Incontinence/Urge Urinary Incontinence (UII) 805
Urinary Incontinence Score (UPS) 806
Urinary Incontinence, Female 806
Urinary Incontinence, Risk of Malignancy 806
Urinary Incontinence, Postoperative 807
Urinary Incontinence, Stresses 807
Urinary Retention after Stress Urinary Incontinence Surgery in Females 580
Urinary Retention Following Brachytherapy 807
Urinary Retention, Adult Female 582
Urinary Retention, Adult Male 584
Urinary Retention, Pediatric 586
Urinary Retention, Postoperative 587
Urinary Tract Infection (UTI), Adult Female 588
Urinary Tract Infection (UTI), Adult Male 590
Urinary Tract Infection (UTI), Catheter-Associated (CAUTI, CA-UTI) 592, 807
Urinary Tract Infection (UTI), Complicated, Adult 594
Urinary Tract Infection (UTI) Complicated, Pediatric 596
Urinary Tract Infection (UTI), Pediatric 598
Urinary Tract Infection (UTI), Pediatric 807
Urinary, Abnormal Color 807
Urinary, Abnormal Cytology 807
Urinary, Foaming 807
Urinary, Odor 808
Urinary, Particles In 808
Urinoma (Perinephric Pseudocyst) 808
Urinolotraphy 808
Urodynamics, Indications and Normal Values 808
Urogenital Distress Inventory (UDI-6) 809
Urolithiasis, Adult, General 600
Urolithiasis, Calcium Oxalate/Phosphate 602
<table>
<thead>
<tr>
<th>Syndrome/Condition</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-linked Spinal and Bulbar Atrophy Syndrome (Kennedy Syndrome)</td>
<td>817</td>
</tr>
<tr>
<td>XX Gonadal Dysgenesis (46, XX)</td>
<td>817</td>
</tr>
<tr>
<td>XX Male Reversal Syndrome (XX Male)</td>
<td>817</td>
</tr>
<tr>
<td>XXX Syndrome (Triple X Syndrome, Triplo-X)</td>
<td>817</td>
</tr>
<tr>
<td>XXXY Syndrome</td>
<td>818</td>
</tr>
<tr>
<td>XXY Syndrome (Klinefelter Syndrome)</td>
<td>818</td>
</tr>
<tr>
<td>Yolk Sac Tumor, Bladder</td>
<td>818</td>
</tr>
<tr>
<td>Yolk Sac Tumor, Prostate</td>
<td>818</td>
</tr>
<tr>
<td>Young Classification of Posterior Urethral Valves</td>
<td>818</td>
</tr>
<tr>
<td>Young-Dees-Leadbetter Bladder Reconstruction</td>
<td>818</td>
</tr>
<tr>
<td>Young Syndrome</td>
<td>818</td>
</tr>
<tr>
<td>Zellweger Syndrome (Cerebrohepatorenal Syndrome)</td>
<td>818</td>
</tr>
<tr>
<td>Zinner Syndrome</td>
<td>818</td>
</tr>
<tr>
<td>Zipper Entrapment</td>
<td>818</td>
</tr>
<tr>
<td>Zona Pellucida Binding Assay</td>
<td>819</td>
</tr>
</tbody>
</table>
ABDOMINAL MASS, ADULT, UROLOGIC CONSIDERATIONS

Brian M. Benway, MD
Gerald L. Andriole, MD, FACS

BASICS

DESCRIPTION
Urologic masses are usually retroperitoneal in adults
May arise from several sites
- Renal (malignant and benign)
- Adrenal
- Germ cell (intraperitoneal lymphadenopathy)
- Neoplastic
- Other (intraperitoneal fibrosis [RPF], hematoma, abscess, lymphocele, lymphoma, urinary retention)

EPIDEMIOLOGY
Incidence
- Renal cell carcinoma: 55,000 new cases per year
- Incidence is rising (1)
- Testicular cancer: 8,000 new cases per year
- Renal cell carcinoma: 55,000 new cases per year

Prevalence
Varies with disease type

RISK FACTORS
- Cancer (renal, adrenal, testis)
- Prior surgery (lymphocele)
- Trauma (hematoma, urinoma)
- Infection (abscess, RPF)
- Prior surgery (lymphocele)
- Cancer (renal, adrenal, testis)

PATHOPHYSIOLOGY
- Various urologic pathologic conditions may present with a mass:
  - Primary renal neoplasms:
    - Wilms tumor, renal cell carcinoma, lymphoma
  - Benign:
    - Renal cortical adenoma, renal oncocytoma, renal hamartoma (angiomylipoma) fibroma
  - Primary adrenal neoplasms:
    - Adrenal cortical carcinoma, pheochromocytoma, adrenal adenoma, paraganglioma
  - Hydroptosis
  - Primary and metastatic germ cell tumor (GCT): Are composed of seminoma, embryonal cell carcinoma, yolk sac tumor, teratoma, and choriocarcinoma
  - Primary intraperitoneal GCTs can occur intraperitoneally
  - Metastatic GCTs are associated with retroperitoneal lymphadenopathy

- Renal abscesses: Usually follow insufficient treatment of tubular nephritis; s raw aspiration may be needed to make a diagnosis
- TB can cause calcified abscess formation; Pus developing from a renal source may track alongside psoas muscle and appear in the groin, where it must be distinguished from hernia
- Periphe...
DIFFERENTIAL DIAGNOSIS

- Adrenal mass: See Section I “Adrenal Mass”
- Distended bladder
- Gynecologic:
  - Pregnancy, uterine fibroids, ovarian cysts, malignancy
  - Hydro nephrosis
- Other: Retroperitoneal masses, fluid, and cysts
- Ruptured abdominal aortic aneurysm
- Urachal abnormality

TREATMENT

GENERAL MEASURES

- Varies by underlying ailment
  - Renal malignancy: radical or partial nephrectomy, ablation, observation (3)
  - Adrenal malignancy: adrenalectomy
  - Adrenal adenoma: excision or observation
  - Testis cancer: retroperitoneal lymph node dissection, chemotherapy, radiation
  - Renal abscess, xanthogranulomatous pyelonephritis: antibiotics, drainage, nephrectomy
  - Cysts: excision, decortication, drainage and sclerosis
  - Retention: placement of Foley catheter
  - Hydro nephrosis: double J stent placement or percutaneous nephrostomy tube placement

MEDICATION

First Line
- Antibiotics for abscess or obstruction
  - Corticosteroids, tamoxifen for RPF

Second Line
- Mycophenolate mofetil, azathioprine for RPF

ADDITIONAL TREATMENT

- Radiation Therapy: limited utility for renalcell carcinoma
- Used for seminomatous germ cell tumors

Ongoing Care

PROGNOSIS

Prognosis depends upon clinical diagnosis and staging

COMPLICATIONS

See associated chapters regarding disease-specific interventions

FOLLOW-UP

Patient Monitoring
Depends upon clinical diagnosis and management.

Patient Resources
N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)
- Abdominal Mass, Adult, Urologic Considerations
- Abdominal Mass, Newborn, Child, Urologic Considerations
- Hydro nephrosis
- Renal Masses
- Renal Cell Carcinoma
- Retroperitoneal Masses, Fluid, and Cysts
- Retroperitoneal Fibrosis
- Testis Cancer

CODES

ICD9
- 189.0 Malignant neoplasm of kidney, except pelvis
- 194.0 Malignant neoplasm of adrenal gland
- 789.30 Abdominal or pelvic swelling, mass, or lump, unspecified site

ICD10
- C64.9 Malignant neoplasm of unsp kidney, except renal pelvis
- C74.90 Malignant neoplasm of unsp part of unspecified adrenal gland
- R19.00 Intra-abd and pelvic swelling, mass and lump, unspecified site

CLINICAL/SURGICAL PEARLS

- Abdominal masses in the adult can arise from several different processes.
- Radiographic information is often essential to diagnosis.
- Management varies upon disease type.
ABDOMINAL MASS, NEWBORN/CHILD, UROLOGIC CONSIDERATIONS

Sang Won Han, MD

Yong Seung Lee, MD

**DIAGNOSIS**

**HISTORY**

- Prenatal ultrasound (1):
  - Glycosuria: Associated with PKD, bilateral UPI, neural tube defects, polyhydramnios, nephrotic syndrome, polyhydramnios, multiple congenital anomalies.
  - Polyhydramnios: Associated with high GI obstruction.
- Postnatal history:
  - Initial diagnosis:
  - Duration from detection of mass:
  - Rapidity of growth:
  - Constitutional symptoms:
  - Fever, pain, weight loss, UFI, diarrhea, hematuria, melena, anorexia, bilious vomiting.

**PHYSICAL EXAM**

- Perform thorough abdominal exam (2):
  - Size and location:
  - Nontender or tender:
  - Solid or cystic:
  - Size and location:
  - Constitutional symptoms:
  - Fever, pain, weight loss, UFI, diarrhea, hematuria, melena, anorexia, bilious vomiting.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- CBC:
  - Leukocytosis suggests possible infection.
  - Anemia, neutropenia, thrombocytopenia may suggest bone marrow involvement.
- Urinalysis:
  - Hematuria seen in Wilms tumor, renal vein thrombosis.
- BUN/creatinine/electrolytes:
  - Elevated BUN/creatinine suggests renal compromise, dehydration.
  - Leukocytosis in boys.

**Imaging**

- Plain abdominal x-rays:
  - Check for obstruction, fluid levels, air-liquid levels, presence of air in rectum.
  - Calcifications suggest nephroblastoma, teratoma, hepatoblastoma, meconium peritonitis, urinary, or biliary stones.
- Ultrasonography & CT:
  - Used to enhance findings on US or solid mass on CT.
  - Used to rule out lower urinary tract pathology.

**DIFFERENTIAL DIAGNOSIS**

- Hydrocystoma: Most common cause of neonatal abdominal mass (70%)
  - UPI obstruction: Most common cause of hydrocystic abdominal mass.
  - Other causes: UVI obstruction, PUV, VUR, megaloureter, and ureteroceles.
  - Unilateral flank mass; more common on left, and boys.
- Nephroblastoma:
  - Wilms tumor: Most common cause of neonatal abdominal masses.
  - Unilateral flank mass; more common on left, and boys.

**RISK FACTORS**

- Variability with disease type.
- Prevalence:
  - Abdominal mass in 1 per 1,000 live births.
- Incidence:
  - Almost 2/3 of infantile abdominal masses arise from kidneys.
  - Most masses are nonsurgical; 87% of surgical masses are renal.

**DESCRIPTION**

- Disease specific.
- Related to organ of origin.

**PATHOPHYSIOLOGY**

- Disease specific.
- Organ of origin.

**GENERAL PREVENTION**

- N/A

**DIAGNOSTIC PROCEDURES/SURGERY**

**PATHOLOGIC FINDINGS**

**DIFFERENTIAL DIAGNOSIS**

- Hydrocystoma: Most common cause of neonatal abdominal mass (70%)
  - UPI obstruction: Most common cause of hydrocystic abdominal mass.
  - Other causes: UVI obstruction, PUV, VUR, megaloureter, and ureteroceles.
  - Unilateral flank mass; male.

**RISK FACTORS**

- Variability with disease type.
- Prevalence:
  - Abdominal mass in 1 per 1,000 live births.
- Incidence:
  - Almost 2/3 of infantile abdominal masses arise from kidneys.
  - Most masses are nonsurgical; 87% of surgical masses are renal.
**Genital mass – RMS:**
- Primary five tumors are 3rd most common solid abdominal mass in childhood (15% total).
- Average lesions: 1/3 Hemangioendothelioma, mesenchymal hamartoma, adenoma, focal nodular hyperplasia, conglomeral cyst.
- Malignant: D1 (Neuroblastoma most common <5 yr; hepatocellular carcinoma present ages 12–15).

**Sphincter mass:**
- Congenital splenic cyst.
- Congenital mesenteric lymphatic malformation.

**Hypertrophic pyloric stenosis**
- 2 major subtypes: Embryonal (most common), 15–20% arise from genitourinary system.
- Presents as large mobile midabdominal mass.
- 1:3,000 girls.
- Pelvic midline mass; US shows fluid-filled mass.
- Due to obstruction from vaginal atresia or Hydrometrocolpos: Gross distension of the vaginal pouch.
- 90% have catecholamine excess.
- Fever, malaise, weight loss; ill-appearing newborn.
- Most common malignancy of newborn.
- Combination surgery, chemotherapy, and radiation therapy are used. Mean age 3.5 mo.
- Most common renal neoplasm of infancy.
- Most common renal tumor diagnosed on antenatal US.
- Fixed, painless, irregular mass that often crosses midline.
- Occasionally rapidly enlarging.
- Differential: Neuroblastoma, Rhabdomyosarcoma (most common in children), benign lesions.

**Surgical approach:**
- Abdominal hysterectomy.
- Adrenal hemangioma.
- Congenital mesoblastic nephroma.

**Radiation therapy**
- Chemotherapy is 1st line prior to radiation or surgery.
- Treatment schema based on INSS stage, age, histopathology.
- MYC amplification, DNA ploidy, and Shimada histopathology.
- RMS: Chemotherapy + surgery is the current treatment of choice.
- Neuroblastoma.
- Polycystic Kidney Disease.
- Multicystic Dysplastic Kidney.
- Wilms Tumor (Nephroblastoma).

**Neuroblastoma**
- Multidisciplinary approach may involve surgery, chemotherapeutic agents, and radiation.
- Chemotherapy is 1st line, followed by surgery and radiation in higher stages.
- Radiation Therapy: Local control is likely by age 1 yr.
- Additional Therapies: Neuroblastoma: Multidisciplinary approach may include bone or stem cell transplantation.

**Lymphoma**
- Common in children.
- Most common malignancy in children.
- 60% non-Hodgkin; 1/3 involve abdomen; can present as intussusception.

**Radiation Therapy**
- Chemotherapy is 1st line prior to radiation or surgery.
- Treatment schema based on INSS stage, age, histopathology.
- MYC amplification, DNA ploidy, and Shimada histopathology.
- RMS: Chemotherapy + surgery is the current treatment of choice.
- Neuroblastoma.
- Polycystic Kidney Disease.
- Multicystic Dysplastic Kidney.
- Wilms Tumor (Nephroblastoma).

**Hemangiomas:**
- Most common congenital vascular anomalies.
- Congenital hemolytic anemias.
- Congenital splenic cysts.
- 12–15% of hepatocellular carcinoma.

**Hepatobiliary masses:**
- Benign lesions: 1/3 (hemangioendothelioma, mesenchymal hamartoma, adenoma, focal nodular hyperplasia, conglomeral cyst).
- Malignant: D1 (Neuroblastoma most common <5 yr; hepatocellular carcinoma present ages 12–15).

**ABDOMINAL MASS, NEWBORN/CHILD, UROLOGIC CONSIDERATIONS**

**Medical Management**
- Stabilize patient as necessary. Treatment is based on diagnosis.

**Surgery/Older Procedures**
- Surgery is specific to disease process. In general, tumors, obstructive/infection problems will need surgery.

**Additional Treatment**
- Radiation Therapy: RMS: Part of a multidisciplinary approach to create therapy including surgical excision and chemotherapy.
- Wilms tumor: For higher stage favorable histology.
- Chemotherapy is 1st line prior to radiation or surgery.
- Treatment schema based on INSS stage, age, histopathology.
- MYC amplification, DNA ploidy, and Shimada histopathology.

**Clinical/Surgical Pearls**
- Determining the age (neonates vs. children) can differentiate between likely etiologies. In general, older children are more at risk for developing malignant masses compared with neonates and young children.
- Two most common entities causing neonatal abdominal mass (U/P): obstruction and MCDF.
- Surgery is usually done in the hydroureteric kidney and nonfunction MCDF.
- Concerning malignant masses, neuroblastoma, and hepatoblastoma are more likely in children <2; older children are more susceptible to Wilms, hepatocellular carcinoma, genitourinary tract tumors, and germ line tumors.

**Follow-up**
- Patient Monitoring: Disease specific.

**Patient Resources**

**ADDITONAL READING**

**PubMed**
- Urogynecologic Syndromes: Review of recent literature.
- Urogenital anomalies.
- Beckwith-Wiedemann, and Denys–Drash.
- Wilms Tumor (Nephroblastoma).
- Wilms Tumor (Nephroblastoma).
ACUTE KIDNEY INJURY, ADULT (RENAL FAILURE, ACUTE)
Fernando J. Bianco, Jr., MD
Joan C. Delto, MD

ASSOCIATED CONDITIONS
- Dehydration
- Trauma
- Burns
- Sepsis
- Urinary tract infection
- Chronic renal insufficiency
- Hypertension
- Congestive heart failure
- Liver disease, cirrhosis
- Nephrolithiasis
- BPH
- Advanced prostate or bladder cancer, malignancy
- Malignant hypotension

GENERAL PREVENTION
- Hydration
- Proper renal dosing of medication; daily dosing of antibiotics
- Avoidance of nephrotoxic agents
- Adequate voiding (timed, double voiding)
- Risk of contrast reduced AKI may be reduced by N-acetylcysteine 600 mg PO BID on day prior to and day of contrast and sodium NaCl(Cr): 3 mL/kg/h × 1 hr before and 1 mL/kg/h × 6 hr after contrast administration

DIAGNOSIS
- History
  - Urine: Hematuria, proteinuria, casts, crystals
  - Transient renal hypoperfusion (reversible)
  - Urine output, drain output
  - Volume status, body weight
  - Vital signs: Blood pressure, heart rate, orthostatic changes

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - CBC, BUN, creatinine, electrolytes (including Ca/Mg/Phos), consider arterial blood gases (ABGs)
  - AKI
    - Serum cystatin C (SCr) at least 0.3 mg/dl, over a 48-hr period
    - Over 2.5 times the baseline SCr value within the 7 previous days
  - Common lab abnormalities in AKI:
    - Decrease in Na, phosphate, Mg, uric acid
    - NephroCheckTM detects the presence of insulin-like growth-factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases (TIMP-2) in the urine (both AKI associated); the test provides a risk score of developing AKI within 12 hrs
    - Creatinine kinase (rhabdomyolysis)
  - Urine
    - Urinalysis: Blood, protein, casts, crystals
    - Transient renal hypoperfusion (reversible)
    - Hematuria (hemoglobinuria, hemoglobinuria, hemoglobinuria, hemoglobinuria)
    - Proteinuria: Without proteinuria, with proteinuria, with proteinuria, with proteinuria
    - Urinalysis: Blood, protein, casts, crystals
    - Increased: Hematuria, proteinuria, casts, crystals
    - Decreased: Hematuria, proteinuria, casts, crystals
    - Nephrotoxicity: Investigate the presence of insulin-like growth-factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases (TIMP-2) in the urine (both AKI associated); the test provides a risk score of developing AKI within 12 hrs
    - Creatinine kinase (rhabdomyolysis)
    - Hematuria (hemoglobinuria, hemoglobinuria, hemoglobinuria, hemoglobinuria)
    - Proteinuria: Without proteinuria, with proteinuria, with proteinuria, with proteinuria
    - Urinalysis: Blood, protein, casts, crystals
    - Increased: Hematuria, proteinuria, casts, crystals
    - Decreased: Hematuria, proteinuria, casts, crystals
    - Nephrotoxicity: Investigate the presence of insulin-like growth-factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases (TIMP-2) in the urine (both AKI associated); the test provides a risk score of developing AKI within 12 hrs
    - Creatinine kinase (rhabdomyolysis)
  - Urine
    - Urinalysis: Blood, protein, casts, crystals
    - Hematuria (hemoglobinuria, hemoglobinuria, hemoglobinuria, hemoglobinuria)
    - Proteinuria: Without proteinuria, with proteinuria, with proteinuria, with proteinuria
    - Urinalysis: Blood, protein, casts, crystals
    - Increased: Hematuria, proteinuria, casts, crystals
    - Decreased: Hematuria, proteinuria, casts, crystals
    - Nephrotoxicity: Investigate the presence of insulin-like growth-factor binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases (TIMP-2) in the urine (both AKI associated); the test provides a risk score of developing AKI within 12 hrs
    - Creatinine kinase (rhabdomyolysis)

PHYSICAL EXAM
- Vital signs: Blood pressure, heart rate, orthostatic changes
- Volume status, body weight
- Urinary output, drain output

PHYSICAL EXAM
- Vital signs: Blood pressure, heart rate, orthostatic changes
- Volume status, body weight
- Urinary output, drain output
Diagnostic Procedures/Surgery

- Cystoscopy with retrograde pyelography
- Renal biopsy (acute glomerular nephritis)

Pathologic Findings

- Acute glomerular nephritis
  - Interstitial edema, marked interstitial infiltrate of T cells and monocytes
  - Eosinophils, plasma cells
  - PMN cells
  - Granulomas

DIFFERENTIAL DIAGNOSIS (4)

- Prerenal (≈55%): Hypovolemia, volume depletion (iv fluids, excessive sweating, dehydration, hemorrhage), renal artery stenosis/embolism, burns, heart failure, liver failure
- Intravascular (≈40%): ATN (from prolonged prerenal insufficiency, radiographic contrast material, aminoglycosides, NSAIDs, or other nephrotic substances); glomerulonephritis, acute interstitial nephritis (drug-induced); arteriolar insult; nephritis (drug-induced); arteriolar insults; vasculitis; glomerular substances; glomerulonephritis; acute interstitial nephritis
- Postrenal (≈5%): Extravascular compression (eg, BPH, carcinoma, pregnancy), intrinsic obstruction (eg, calculus, tumor, clot, stricture, sloughed papilla); decreased function (eg, neoplastic bladder)
- Paused AHT: Exogenous chromogens (eg, bilirubin, ascorbic acid, uric acid) and exogenous chromogens (eg, cephalosporins, trimethoprim, cimetidine) may interfere with the creatinine assay and cause falsely elevated results.

TREATMENT

GENERAL MEASURES

- All require close management of fluid, acid-base, and electrolyte balance and the removal of urinary toxins
- Captopril, a dopamine agonist, may decrease AKI
- Furosemide is ineffective in preventing and treating AKI
- Prerenal
  - Renal perfusion; isotonic fluid replacement
- Postrenal
  - Foley or suprapubic tube drainage
- Ensure proper placement within bladder
  - urine present within bladder
  - Rule out catheter obstruction (musca, clot)
- Peritoneal nephrostomy tube
- Treatment of hyperkalemia
  - Monitor EKG when K+ > 6 mEq/L
  - iv calcium
  - Sodium bicarbonate (pH adjust)
  - Insulin and glucose
  - Kayexalate
  - Hemodialysis for severe hyperkalemia or refractory to treatment
- Control of urinary extravasation
- Dietary considerations
  - Maintain carbohydrate and protein intake
  - Restrict: Phosphorus, potassium, sodium
  - Monitor of creatinine, potassium, calcium, and phosphorus
  - Repeat imaging (US) to re-evaluate hydronephrosis
  - If question of stent migration, obtain KUB or US
  - Urinary stents will need to eventually be exchanged or removed
- Consideration of internalization of percutaneous nephrostomy tubes

Patient Resources

- National Kidney Foundation: www.kidney.org
- dialysis.org

REFERENCE


ADDITIONAL READING

- Duty RC, Kauduri DR. Assessment and Management of Incidentally Detected Urineless Hydronephrosis in Adults. AJU. (Update Series). 2012;71(5).
- See Also (Topic, Algorithm, Media)
  - Acute Kidney Injury (AKI), Pediatric (Renal Failure, Acute)
  - Acute Glomerulonephritis
  - Acute Tubular Necrosis
  - Contrast-Induced Nephropathy (CIN)
  - Postobstructive Diuresis

ICD9

- 584.3 Acute kidney failure with lesion of tubular nephrons
- 584.9 Acute kidney failure, unspecified
- 593.81 Vascular disorders of kidney

ICD10

- N17.0 Acute kidney failure with tubular necrosis
- N17.9 Acute kidney failure, unspecified
- N28.0 Ischemia and infarction of kidney

CLINICAL/SURGICAL PEARLS

- Maximize urinary drainage.
- Avoid nephrotoxic agents.
- Upper tract obstructive uropathy should be acutely managed by stent vs. percutaneous nephrostomy.
ACUTE KIDNEY INJURY, PEDIATRIC (RENAL FAILURE, ACUTE)
Leigh Mark Etinger, MD, MS
Kenneth Lieberman, MD

PATHOPHYSIOLOGY
- Prerenal and intrinsic renal injury disrupt the regional perfusion of, and subsequent oxygen delivery to, the kidney(s).
- The renal arterial gradient of oxygen tension from comes to medulla makes the kidney highly susceptible to hypoxic and oxidative injury during ischemia and reperfusion.
- Prion-like perforated glomerular endothelial cells release vasoactive substances, proteases, reactive oxygen species, and nitric oxide and activate the coagulation cascade and complement pathways.
- Even well-perfused kidneys can develop AKI during sepsis from circulating cytokines, lymphocytes, T cells, and other factors.
- When faced with the presence of cardiac, pulmonary, or hepatic failure it is likely due to endothelial activation or circulatory abnormalities.
- Nephrotoxic agents such as their own mechanism of damage, eg, by forming crystals in the microcirculations of the kidney.
- Rhabdomyolysis causes intravascular vasodilatation, direct ischemic tubular injury, and tubular obstruction in acidic urine.
- Prerenal injury is due to intraglomerular flow disruption from the kidney.
- Must be bilateral to cause PRFLE findings but can be unilateral if only one kidney is present due to congenital absence, prior nephrectomy, or kidney transplant.
- AKI is multifactorial, especially in the ICU setting.

ASSOCIATED CONDITIONS
CKD increases the risk for AKI.

GENERAL PREVENTION
- Prerenal:
  - Maintain cardiac output and oxygenation with vasopressors and blood transfusions as needed.
  - Intrinsic renin:
  - Careful dosing and therapeutic drug level monitoring of antihypertensives or avoidance altogether.
  - Use lipid formulation of angiotensin II or another antifibrinolytic alternative.
  - Contrast-induced AKI
  - Avoid the use of contrast.
  - Use either iso- or low-osmolar iodinated contrast media.
  - Intravenous fluid expansion for those patients at risk.
  - Acute NSAIDs
  - Animal models have shown the potential benefit of vasodilators, growth factors, antioxidants, and anti-inflammatory drugs in preventing AKI.
  - A single dose of theophylline given to neonates with severe perinatal asphyxia has been shown to significantly reduce the risk of AKI.

DIAGNOSIS

HISTORY
- Evaluate for shock, sepsis, bleeding, dehydration, gastrointestinal losses.
- Assess recent medication exposure, including natural products.
- History of urologic surgery, anatomic problems, or kidney transplantation.
- Family history of ESRD, HUS.
- Recent trauma, crush injury.
- Seek signs of CKD, such as growth delay.
- Review recent blood tests to determine baseline serum creatinine (SCr) and onset of AKI.

PHYSICAL EXAM
- Assess hydration status, blood pressure, heart rate, and temperature.
- Lungs for rales.
- Abdomen for masses.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- SCr and blood urea nitrogen will be elevated.
- May have hyperkalemia, acidosis.
- Hemoglobin will be low if bleeding.
- HUS causes thrombocytopenia, increased lactate dehydrogenase.
- Muscle damage is the cause creatinine kinase will be elevated and urinary myoglobin will be positive.
- Unlikely to detect red blood cells, proteinuria.
- Urine eosinophils indicate interstitial nephritis.
- Store UOP monitoring to assess AKI stage and progression.

Imaging
- Renal ultrasound with Doppler analysis of the renal artery and veins.
- Hypoechoic indicates obstruction.
- Increase echogenicity consistent with medical renal disease.
- Thrombosis of renal artery or vein.
- Small echogenic kidneys, cystic kidneys indicate CKD.

- Bladder ultrasound
- Thrombosed, thick-walled bladder may indicate lower urinary tract abnormality such as a neurogenic bladder or obstruction.

- Technetium-99m MAG3 renal scan can be used in prolonged AKI to differentiate prolonged ATN from permanent cortical necrosis.

BASICS

DESCRIPTION
- A system or recently acquired functional impairment of the kidney relative to physiologic demands with or without actual kidney injury.
- Causes: Red to potentially life-threatening alterations in fluid, electrolyte, acid-base and hormonal homeostasis.
- Terminology: acute tubular necrosis (ATN) to acute renal failure (ARF) to acute kidney injury (AKI) of varying grades to standardize reporting, clinical care, and research.
- Diagnosis: the Pediatric Modified Risk Injury (pRIFLE) criteria on the estimated creatinine clearance (eCrCl), based on Schwartz formula) and urine output (UOP) (I):
  - Risk: eCrCl decrease by 25% and/or UOP <0.5 mL/kg/h for 8 hr.
  - Injury: eCrCl decrease by 50% and/or UOP <0.5 mL/kg/h for 16 hr.
  - Failure: eCrCl decrease by 75% or eCrCl <35 mL/min/1.73 m2 and/or UOP <0.3 mL/kg/h for 24 hr or anuria for 12 hr.
  - Loss: Persistent failure in AKI.
- Postrenal injury is due to antegrade urine flow disruption from the kidney.
  - Must be bilateral to cause pRIFLE findings but can be unilateral if only one kidney is present due to congenital absence, prior nephrectomy, or kidney transplant.
  - AKI is multifactorial, especially in the ICU setting.

ASSOCIATED CONDITIONS
CKD increases the risk for AKI.

GENERAL PREVENTION
- Prerenal:
  - Maintain cardiac output and oxygenation with vasopressors and blood transfusions as needed.
  - Intrinsic renin:
  - Careful dosing and therapeutic drug level monitoring of antihypertensives or avoidance altogether.
  - Use lipid formulation of angiotensin II or another antifibrinolytic alternative.
  - Contrast-induced AKI
  - Avoid the use of contrast.
  - Use either iso- or low-osmolar iodinated contrast media.
  - Intravenous fluid expansion for those patients at risk.
  - Acute NSAIDs
  - Animal models have shown the potential benefit of vasodilators, growth factors, antioxidants, and anti-inflammatory drugs in preventing AKI.
  - A single dose of theophylline given to neonates with severe perinatal asphyxia has been shown to significantly reduce the risk of AKI.

DIAGNOSIS

HISTORY
- Evaluate for shock, sepsis, bleeding, dehydration, gastrointestinal losses.
- Assess recent medication exposure, including natural products.
- History of urologic surgery, anatomic problems, or kidney transplantation.
- Family history of ESRD, HUS.
- Recent trauma, crush injury.
- Seek signs of CKD, such as growth delay.
- Review recent blood tests to determine baseline serum creatinine (SCr) and onset of AKI.

PHYSICAL EXAM
- Assess hydration status, blood pressure, heart rate, and temperature.
- Lungs for rales.
- Abdomen for masses.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- SCr and blood urea nitrogen will be elevated.
- May have hyperkalemia, acidosis.
- Hemoglobin will be low if bleeding.
- HUS causes thrombocytopenia, increased lactate dehydrogenase.
- Muscle damage is the cause creatinine kinase will be elevated and urinary myoglobin will be positive.
- Unlikely to detect red blood cells, proteinuria.
- Urine eosinophils indicate interstitial nephritis.
- Store UOP monitoring to assess AKI stage and progression.

Imaging
- Renal ultrasound with Doppler analysis of the renal artery and veins.
- Hypoechoic indicates obstruction.
- Increase echogenicity consistent with medical renal disease.
- Thrombosis of renal artery or vein.
- Small echogenic kidneys, cystic kidneys indicate CKD.

- Bladder ultrasound
- Thrombosed, thick-walled bladder may indicate lower urinary tract abnormality such as a neurogenic bladder or obstruction.

- Technetium-99m MAG3 renal scan can be used in prolonged AKI to differentiate prolonged ATN from permanent cortical necrosis.
Differential Diagnosis
Kidney biopsy may reveal ATN, interstitial disease, or glomerulonephritis.

Pathologic Findings
Prolonged AKI without a clear etiology may require prolonged dialysis or need for surgical intervention.

Diagnostic Procedures/Surgery
- Hemodialysis or peritoneal dialysis may play a role in supportive care.
- Continuous renal replacement therapy (CRRT) has been shown to improve pediatric AKI.

Surgical Intervention
- Bilateral nephrolithiasis due to cystinuria may be managed with extracorporeal shock wave lithotripsy, endoscopic surgery, or surgery.

Medication
- Avoid potentially nephrotoxic drugs and gadolinium.
- Nephrogenic systemic fibrosis (NSF) is a rare but potentially lethal fibrosing disorder of the skin, liver, and heart.

Prognosis
- Mortality may be increased in pediatric AKI.
- The Pediatric Modified Risk Injury Failure Loss End Stage (Pediatric M-RIFLE) is used to assess outcomes.

Additional Reading
See also (Topic, Algorithm, Media): Acute Kidney Injury, Adult; Acute Kidney Injury, Pediatric; Chronic Kidney Disease, Pediatric; Radiation Therapy.

Clinical/Surgical Pearls
- AKI is multifactorial.
- Seek prompt medical attention when AKI is present.
- Avoid potential nephrotoxic drugs and gadolinium.

Follow-Up
- Patient Monitoring: Monitor I&O, blood pressure, somatic growth, urinalysis for signs of CKD after resolution of AKI.
- Patient Resources:
  - American Society of Pediatric Nephrology: www.aspneph.com/parentpatient.asp
  - Kidney & Urology Foundation of America: www.kidney.org/patients/index.cfn
  - National Kidney Foundation: www.kidney.org/patients/index.cfn
ACUTE SCROTUM

Patrick T. Gomella, MD, MPH
Leonard G. Gomella, MD, FACS

BASICS

DESCRIPTION
- Acute pain and swelling in the scrotum is typically related to testicular pathology and is usually referred to as “acute scrotum”. In the absence of obvious trauma.
- Occasionally pain from urinary colic can be referred to the testicle but swelling is usually absent.
- Chronic testicular pain is referred to orchalgia.
- Testicular torsion is a major cause of the acute scrotum particularly in children and requires timely diagnosis and treatment to avoid testicular loss.
- In adults acute epididymitis-orchitis is the most common cause of an acute scrotum.
- In children torsion of a testicular appendix or testicle are most common causes.

EPIDEMIOLOGY

Incidence
- Testicular torsion occurs most commonly in neonates and postpubertal boys and is more common on the left.
- However in 1 series 39% of patients were reported to be in men >21 yr of age (1).
- Torsion of an appendix more common in prepubertal boys.
- Approximately 600,000 cases of epididymitis/in US.

Prevalence
- Testicular torsion: 1:4,000 males.
- Testicular torsion reported in 10% of family members;

Genetics
- Testicular torsion reported in 10% of family members; may be autosomal or X-linked recessive; no specific genetic defects identified.

PATHOPHYSIOLOGY

- Testicular torsion can be either intravaginal or extravaginal.
- Intravaginal testicular torsion is twisting of the spermatic cord within the tunica vaginalis.
- Usually due to a so-called “bell clapper deformity.” A failure of normal posterior anchoring of the gubernaculum, epididymis, and testis.
- Leaves the testis free to rotate within the tunica vaginalis of the scrotum much like the clapper inside of a bell (present in 12% of males).
- Intravaginal testicular torsion is twisting of both the spermatic cord and tunica vaginalis.
- Perinatal: Extravaginal testicular torsion is usually the cause.

• Appendiceal torsion is a result of vascualr compromise may be related to pedunculated anatomy of the appendix.
• Appendicular testis 95% of appendiceal torsions.
• Appendix appendicus torsion is less common.
• Epididymitis
• Can present as acute or chronic epididymitis.
• Acute: Severe swelling, tenderness, rigors, high fevers
• Infectious causes
• In men >25 yr of age, Chlamydia trachomatis and Neisseria gonorrhoeae (sexually transmitted infections) are the most common pathogens.
• In men >35 yr of age colibactin most common
• Less common pathogens: Ureaplasma, TB, Brucella species; with HIV infection, Cytophaga/lymphogranulomatis, and Cryptococcus.
• Less frequent causes include autoimmune diseases, sarcoid, trauma.
• In a prepubertal boy epididymitis is almost always associated with a urinary tract anomaly.

ASSOCIATED CONDITIONS
- Torsion:
  - Bell clapper deformity: 10–15% of males
  - Cryptorchidism
  - Other sexually transmitted infections
  - Prostatic hypertrophy

GENERAL PREVENTION
- Torsion: Reduce testicular loss risk by:
  - Early diagnosis and treatment
  - Community awareness about testes pain
  - Elective bilateral orchidopexy for intermittent pain
  - Community awareness about testis pain

DIAGNOSIS

HISTORY
- Rule out any traumatic insult to the genit area:
  - Some patients report minor trauma before presentation of torsion.
- Sexual practice history
  - Recent urinary tract instrumentation
- Testicular torsion:
  - The classic presentation is sudden hemiscrotal pain often awakening the patient from sleep
  - Pain can radiate to the groin
  - Nausea and/or vomiting can be present
  - Movement tends to worsen the pain
  - A history of intermittent testicular discomfort may be present suggesting past torsion and detorsion
- Appendiceal torsion:
  - Symptoms are similar to testicular torsion but not as severe.
  - Epididymitis
  - Can present with acute fever, chills, rigors, or as chronic testicular/appendix discomfort
  - More likely to be associated with voiding complaints than torsion.

PHYSICAL EXAM

- General:
  - Vital signs; low-grade fevers with torsion, fever with UTI
  - Presence of inguinal hernia
  - Abdominal and flank tenderness
- GI exam:
  - Ausis crematric reflex (2).
  - Assess crematric reflex:
  - Normal is contraction of the cremaster muscle with elevation of the testis.
  - Absent reflex may aid in differentiating testicular torsion from epididymitis/other causes of an acute scrotum where reflex is present.
  - Phren sign (pain relief with elevation of testicle)

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- “W subsidi:
  - White cells and positive leukocyte esterase
  - Signs of epididymitis or UTI
  - Red blood cells suggest renal or urethral source of pain (eg, stone)
  - In cases of torsion UA usually negative

URINE CULTURE:
- Possible if epididymitis or UTI suspected.
- Consider leukocyte esterase if leukocyte esterase is present.
- Culture and nuclear acid amplification testing for chlamydia and gonorrhea.

IMAGING
- Scrotal US with Doppler:
  - Intravaginal testicular torsion findings
  - Usually shows decreased or absent arterial flow but may be normal.
- Appendecial torsion findings:
  - Normal exam most common
  - Spermatic cord complex mass without vascular flow may be present.
- Epididymitis:
  - Enlarged epididymis reported as “epididymitis” often present
  - Doppler flow normal or increased.
ACUTE SCROTUM

Diagnostic Procedures/Surgery
In cases of testicular torsion, surgical exploration is usually diagnostic and therapeutic.

Pathologic Findings
N/A

Differential Diagnosis
- Abscess or other infection such as Furuncle gangrene
- Appendiceal torsion (appendiceal tests or epididymis: testo)
  - Most commonly seen in prepubertal boys
  - Most common cause of acute scrotum in this age group
- Epididymitis due to UTI or STD: Rare or uncommon
  - In pediatric age group, more likely in adult
  - Often associated with genitourinary trauma
- Henoch–Schönlein purpura
  - Rash usually present
  - Incorparated inguinal hernia
- Orchitis: With the exception of mumps orchitis, isolated orchitis without epididymitis in adults is rare
  - Referred pain: Urolithiasis or intra-abdominal process such as appendicitis
- Testicular infarction due to spermatic cord injury or thrombosis
  - Testicular torsion: Most common in peripubertal boys but can occur at any age, less common than appendiceal torsion
  - Testicular tumor: Usually painless but may have tenderness with trauma
  - Trauma and possible testicular rupture: History suggestive, hemorrhage usually present
  - Orchidectomy: Consider avoiding feminization

TREATMENT

ALERT
Testicular torsion is a surgical emergency because the likelihood of testicular salvage diminishes with the duration of torsion.

General Measures
- Clinical history, exam, and diagnostic studies (ultrasound, Color Doppler Ultrasonography) have a high degree of accuracy in making the diagnosis
- Emergency exploration indicated if evaluation suggests irreversible testicular torsion or diagnosis is equivocal
  - If torsion is present and surgery cannot be performed in a reasonable amount of time, manual detorsion should be considered
  - Most cases of epididymitis can be treated on an outpatient basis

Medication
First Line
Epididymitis: Acute
- Iox, scrotal elevation, and NSAIDs with antipyretics
- Younger males: Ceftriaxone (250 mg IM) along with doxycycline (100 mg PO BID x 10 days)
- Older males: Ceftriaxone (250 mg IM) along with a 10-day course of fluoroquinolones for enteric organisms (ciprofloxacin 500 mg PO BID or levofloxacin 500 mg PO BID)
- Epididymitis: Chronic
  - Scrotal elevation, avoid sexual and athletic activity, warm baths, and NSAIDs
  - Appendiceal torsion: bioptern to reduce inflammation and discomfort
  - Testis torsion: Pain control may require opioids

Second Line
N/A

Surgery/Other Procedures
- Urgent exploratory/ultrasound exploration for extravasational testicular torsion to avoid asymmetrical contralateral torsion
- Manual detorsion: Use only if surgery is delayed >2 hr
  - Testis most often rotates medially during torsion
  - Manual detorsion is accomplished by attempting to rotate the testicle laterally toward the thigh
  - The twisting can range from 180–720 degrees such that multiple detorsion twists may be required
  - However, if the testis is >1/3 of the testis, the torsion rotation can be lateral
  - Successful detorsion still requires operative intervention and orchidectomy

Hallmarks of successful manual detorsion include
- Pain relief, testicle assuming a lower position in the scrotum, reorientation of the testicle from transverse lie to vertical positioning, restoration of Doppler blood flow

Additional Treatment
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

Follow-Up

Patient Monitoring
Epididymitis due to culture proven C. orchitidis or N. gonorrhoeae: refer sex partners for evaluation and treatment disease

Patient Resources

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Acute Scrotum Algorithm
- Adult Scrotum Image
- Appendix: Tests and Appendiceal Epidiymis, Torsion
- Epididymitis
- Testis, Torsion, or Testicular/Epididymal Appendages

ICD
N/A

ICD9
- 609.90 Ochitis and epididymitis, unspecified
- N08.9 Unspecified disorder of male genital organs
- N08.2 Torsion of testes, unspecified

ICD10
- N44.00 Torsion of tests, unspecified
- N44.10 Testicular torsion and separation
- N50.9 Disorder of male genital organs, unspecified

Clinical/Surgical Pearls
- Color Doppler ultrasonography is the preferred imaging technique for evaluating the acute scrotum.
  - Cremasteric reflex is usually absent in testicular torsion.
ACUTE TUBULAR NECROSIS
Costas D. Lallas, MD, FACS

ASSOCIATED CONDITIONS
- Sepsis
- Hemorrhage (operative, obstetric, trauma)
- Pre-existing renal insufficiency (diabetes, hypertension)
- Edematous states such as CHF

GENERAL PREVENTION
- Avoid prolonged renal ischemia by timely management of hemorrhage, dehydration and other causes of renal hypoperfusion
- Avoidance of contract agents in the setting of renal insufficiency (contrast-induced nephropathy)
- Appropriate management of potentially nephrotoxic medications

DIAGNOSIS
HISTORY
- Specific attention to:
  - Hypertensive episode, blood transfusions, intravenous contrast exposure
- Meticulous listing of medications to include dosage
- Lab tests:
  - Rate of rise of plasma creatinine: Rise of <0.3–0.5 mg/dL in ATN vs. slower rise with ischemic or toxic insults
  - BUN/plasma creatinine ratio: The ratio is normal at 10 to 15:1 in ATN, but >20:1 in prerenal disease due to the increase in passive reabsorption of urea, the ratio may also be increased with GI bleed, muscle breakdown, and administration of corticosteroids or tamsulosine
  - Rate of rise of plasma creatinine: Rise of >0.3–0.5 mg/dL in ATN vs. slower rise with prenal disease
  - Urine tests:
    - Ureteral: Muddy brown granular and epithelial cell casts and free epithelial cells secondary to sloughing of the tubular epithelium vs. amorphous in prerenal disease
    - Urine sodium concentration: High (>40 mEq/L) due to tubular injury vs. <20 mEq/L in prerenal disease
    - Fractional excretion of sodium (FENa): Above 2% in ATN while <1% in prerenal disease, measured as urine Na divided by plasma Na times plasma Cr divided by urine Cr, although causes of ATN associated with a low FENa that are due to intravascular contrast material, rhabdomyolysis, sepsis, and multisystem organ failure
    - Urine osmolality: Urine osmolality <450 mOsm/kg in ATN secondary to loss of concentrating ability
    - 500 mOsm/kg in prerenal disease
    - Urine creatinine concentration divided by plasma creatinine concentration: Ratio <20:1 in ATN while >40:1 in prerenal disease, reflecting loss of tubular water reabsorption

IMAGING
- Renal ultrasonography:
  - Sensitivity test to determine obstruction, Doppler can detect gross blood flow in renal vein and artery
  - Plain abdominal film
    - Identifies the presence or location of renal calculi and is particularly helpful to discern the proper position of stents and drains
- Functional studies
  - Nuclear scans can determine perfusion or tubular secretion; MRI can give some functional information while providing anatomic information

Diagnostic Procedures/Surgery
N/A

Pathologic Findings
- Tubal cell injury (TUB): Tubal epithelial cells are particularly sensitive to ischemia and are also submitted to toxicants. The structural changes include those of reversible injury (such as cellular swelling, loss of brush border and polarity, bleeding, and cell detachment) and those associated with lethal injury (necrosis and apoptosis)
- Disturbances in blood flow:
  - Intrarenal reperfusion results in both reduced glomerular blood flow and reduced oxygen delivery to the functionally important tubules in the outer medulla (thick ascending limb and straight segment of the proximal tubule)

DIFFERENTIAL DIAGNOSIS
- Prerenal azotemia
- Postrenal azotemia
- Other forms of renal azotemia
- Glomerulonephritis, disseminated intravascular coagulopathy, arterial or venous obstruction, intravascular precipitation

PATHOPHYSIOLOGY (1)
- Acute tubular injury
  - Renal hypoperfusion and renal ischemia are the most common causes of ATN
  - The ischemic form is due to the reductions in glomerular filtration rate (GFR) secondary to vascular and tubular factors
  - Ischemia from reductions in GFR from decreased renal plasma flow or distal to the afferent arteriole. After return of normal blood flow, ATN persists secondary to tubular changes
  - In addition, both exogenous and endogenous nephrotoxic compounds exist
- Tubular factors: Backleak and tubular obstruction

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Serum tests (2):
  - BUN/plasma creatinine ratio: The ratio is normal at 10 to 15:1 in ATN, but >20:1 in prerenal disease due to the increase in passive reabsorption of urea, the ratio may also be increased with GI bleed, muscle breakdown, and administration of corticosteroids or tamsulosine
  - Rate of rise of plasma creatinine: Rise of >0.3–0.5 mg/dL in ATN vs. slower rise with prenal disease

RISK FACTORS
- Decreased renal perfusion from:
  - Prolonged hypotension, surgical interruption of blood supply to kidneys
  - Contraindications to nephrotoxic agents:
    - Nonsteroidal anti-inflammatory drugs (NSAIDs), and ACE inhibitors, cyclosporine
  - Nephrotoxic agents:
    - Radiocontrast media (low osmolality is possibly safer), amphotericin, amphotericin, tubular obstruction secondary to a sloughed brush border, cellular debris, Tamm-Horsfall protein, and decreased filtration pressure contribute to obstruction and maintenance of ATN
**TREATMENT**

**GENERAL MEASURES**
- Define and treat the underlying cause.
- Discontinue any nephrotoxic agents.
- Prophylaxis and treatment of complications of ARF.
- Early nephrology consultation.
- Management of fluid disturbances.
- Maintain a euvolemic state by restricting total fluids to no more than urine output plus insensible losses.

**MEDICATION**

**First Line**
- High-dose loop diuretics (1–3 g/d) may convert oliguric to nonoliguric ATN in some patients; it has not been determined that this conversion decreases the duration of ATN or mortality. Oliguria may increase urine output, but its benefit is in question.
- Studies suggest that patients who respond to mannitol, furosemide, or dopamine with an increased urine output have better outcomes than nonresponders.
- Management of electrolyte disturbances.
- Electrolyte disturbances can be minimized by prophylactic institution of a low-potassium, low-protein diet accompanied by fluid restriction and oral phosphate binders.
- Hyperkalemia is the most common and most dangerous abnormality and should be treated aggressively with calcium supplementation until potassium levels can be reduced with combinations of insulin and glucose or potassium-binding resins.

**Second Line**

**SURGERY/OTHER PROCEDURES**
- Metabolized urea, pentobarbital (PB), and continuous arteriovenous hemofiltration (CAVH) — CAVH: Need ICU, limited mobility, need anticoagulation, removes fluid but slow correction of electrolyte abnormalities
- PB: To artificial renal failure but slower correction of electrolyte abnormalities
- HD: Expensive, anticoagulation necessary, vascular access necessary but allow rapid correction of fluid and electrolyte abnormalities

**ADDITIONAL TREATMENT**

**Radiation Therapy**

N/A

**Additional Therapies**

N/A

**Complementary & Alternative Therapies**

N/A

**ONGOING CARE**

**PROGNOSIS**
- Slight improvements in survival in those patients with ATN requiring dialysis, in an ICU setting.
- The Mayo Clinic compared 1977–1979 with 1991–1992 showed high survival both in hospital (32% vs. 32%) and at 1 yr (30% vs. 21%)
- Higher mortality rates are seen in elderly patients and in patients with respiratory failure, multiple organ failure, pre-existing chronic diseases, and systemic hypertension
- Major causes of death are infection and underlying disease, not renal failure
- Patients at risk are generally very ill, with evidence of multiple organ dysfunction
- Of patients who survive ATN, nearly half will have a complete recovery of renal function and a majority of the remainder have an incomplete recovery. Only about 5% of all ARF patients require chronic maintenance dialysis

**COMPLICATIONS**
- Fluid overload, electrolyte disturbances, metabolic acidosis
- Hyperkalemia, edema, acute pulmonary edema, hypernatremia, hyperpercapnia, hyperglycemia, hyperuricemia, hyperkalemia
- Furosemide, dopamine
- GI: Nausea, vomiting, GI bleed; neurologic: Encephalopathy, coma, seizures, peripheral neuropathy; cardiac: Pericarditis, uremic pneumonitis; hematologic: Bleeding, anemia; immunologic: Impaired granulocyte/polyclonal function

**FOLLOW-UP**

**Patient Monitoring**
- Duration
  - Renal failure phase usually lasts 7–21 days if the primary insult (ischemia, nephrotoxin) can be corrected. Recovery is usually heralded by a progressive increase in urine output and a return of BUN and Cr to the previous baseline.
  - Recovery of renal function
  - Irreversible loss of renal function can occur if the combination of pre-existing renal disease and prolonged ARF secondary to repeat ischemic insults and/or nephrotoxic administration
  - If the patient survives, baseline Cr is usually only 1–2 mg/dL above baseline.
- Those patients that need dialysis and have bioincompatibility with the dialysis membrane or have repeat episodes of hyperkalemia have a worse prognosis.

**Patient Resources**

N/A

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

Acute Kidney Injury, Adult (Renal Failure, Acute) Acute Kidney Injury, Pediatric (Renal Failure, Acute) Contrast Induced Nephropathy (CIN)

**CODES**

ICD9 584.5 Acute kidney failure with lesion of tubular necrosis

ICD10 N17.0 Acute kidney failure with tubular necrosis

**CLINICAL/SURGICAL PEARLS**

- High-dose loop diuretics (1–3 g/d) may convert oliguric to nonoliguric ATN in some patients; it has not been determined that this conversion decreases the duration of ATN or mortality.
- Of patients who survive ATN, nearly half will have a complete recovery of renal function and a majority of the remainder have an incomplete recovery. Only about 5% of all ARF patients require chronic maintenance dialysis.
- A patient’s weight is helpful information, and its daily measurement is important in the diagnosis and management of ARF.
ADDISON DISEASE
Shaun G.S. Grewal, MD
Gerald L. Andriole, MD, FACS

**BASICS**

**DESCRIPTION**
- Primary adrenocortical insufficiency
- Inadequate production of glucocorticoid and mineralocorticoid
- Differentiated from secondary (pituitary) and tertiary (hypothalamic) causes of adrenal causes of adrenocortical insufficiency in which mineralocorticoids are normally spared

**RISK FACTORS**

**Prevalence**
- 93–140 per million (1)
- Females more frequently affected than males
- 4.7–6.2 per million in Western populations (1)

**Incidence**
- 50–140 per million (1)
- Mortality: 0.3 per 100,000

**GENERAL PREVENTION**
- No general prevention guidelines exist for prevention of primary hypoaldosteronism.

**PATHOPHYSIOLOGY**

**Autocrine disorders** are the most common cause in developed nations (90–90%)
- 90% of adrenal gland must be destroyed to cause insufficiency
- Decreased production of cortisol, aldosterone, and adrenal androgens
- Hyperpigmentation due to increased ACTH and proopiomelanocortin-related peptides
- Hypocalcemia due to increased PTHrP

**ACUTE ADRENAL INSUFFICIENCY**

- Classic triad: Hyponatremia, hyperkalemia, azotemia
- Acute adrenal insufficiency: Life-threatening hypotensive shock

**DIAGNOSTIC TESTS & INTERPRETATION**

**Screening test**
- Low cortisol (<165 nmol/L)
- Elevated ACTH (>45 pmol/L)

**Confirmation of abnormal screening test**
- Serum cortisol at 0, 30, and 60 min
- Peak cortisol >550 nmol/L diagnostic (2)

**ASSOCIATED CONDITIONS**
- Autoimmune endocrine disorders
- Thyroid disorder (17%)
- Diabetes mellitus (12%)
- Gonadal dysfunction (12%)

**GENERAL PREVENTION**
- No general prevention guidelines exist for prevention of primary hypoaldosteronism.
Diagnostic Procedures/Surgery
No specific diagnostic procedures
Pathologic Findings
Atrophic adrenals in autoimmune adrenalitis

DIFFERENTIAL DIAGNOSIS
Primary adrenal insufficiency (Addison disease)
Secondary adrenal insufficiency (pituitary failure)
No hyperpigmentation (lack of ACTH elevation)
Etiologies include chronic steroids, pancytopenia, infarction, struma ovarii, pituitary apoplexy, pituitary surgery
Tertiary adrenocortical insufficiency

TREATMENT
GENERAL MEASURES
Acute adrenal insufficiency (addisonian crisis)
5 S’s:
Salt
Sugar
Steroids
Support
Search for precipitating cause

MEDICATION
First Line
Cortisol replacement:
– Hydrocortisone 10–25 mg tid
– BID dosing: 20 mg, 10 mg
– TID dosing: 15 mg, 5 mg, 5 mg
– Monitor body weight and signs/symptoms of over/under replacement
Mineralocorticoid replacement:
– Fludrocortisone 0.05–0.20 mg/d
– Monitor blood pressure, peripheral edema, serum sodium, and potassium
Major stress: Surgery, Trauma, sepsis
– IV hydrocortisone 100–300 mg/TID dosing
then taper
– Monitor stress
– Increase steroid dose 2–3 fold then taper over several days
Second Line
Dehydroepiandrosterone (DHEA) replacement
– 25–50 mg/d
– Impacts mood/feeling of well-being (3)

SURGERY/OTHER PROCEDURES
Stress dose steroids: 25–150 mg hydrocortisone or 5–30 mg methylprednisolone IV day of the procedure in addition to maintenance therapy; taper to the usual dose over 1–2 days

ADDITIONAL TREATMENT
Radiation Therapy

Additional Therapies
Salt loading prior to major stress recommended by some
Future advances using long-acting hydrocortisone preparations to better mimic physiologic case

Complementary & Alternative Therapies
No established alternative therapies

ONGOING CARE
PROGNOSIS
Adrenal crisis may be lethal.
Recommended dosages for glucocorticoid and mineralocorticoid replacement rarely cause significant side effects; dose monitoring is essential to prevent excess treatment.

COMPLICATIONS
Side effects of excess steroid replacement:
– Weight gain, high BP, hyperglycemia, growth retardation, bruising, cardiovascular risks, gastric ulcers, poor wound healing, skin striae, osteoporosis
Side effects of excess mineralocorticoid:
– Hypertension, bradycardia, hyperkalemia, congestive heart failure, suppressed renin levels, growth retardation
– Acute withdrawal of chronic steroid replacement may precipitate acute adrenal crisis
Must rule out or treat glucocorticoid deficiency prior to initiation of thyroxine for hypothyroidism, as this may precipitate adrenal crisis

FOLLOW-UP
Patient Monitoring
– Medic-alert bracelet to be worn at all times
– Instruct patients on proper use of emergency hydrocortisone injections
– Monitor for signs of appropriate glucocorticoid and mineralocorticoid replacement

Patient Resources
– www.addisonsdisease.net
– www.addisonssupport.com

REFERENCES

ADDITIONAL READING
See Also (Topic, Algorithm, Media)
Addison Disease (Adrenocortical Insufficiency)
Algorithm
Waterhouse–Friderichsen Syndrome

CODES
ICD9 255.41 Glucocorticoid deficiency
ICD10 E27.1 Primary adrenocortical insufficiency

CLINICAL/SURGICAL PEARLS
Addisonian crisis: is acute, life-threatening shock.
– 5 S’s for treatment of Addisonian crisis
– Salt, Sugar, Steroids, Support for precipitating cause
– Classic triad: Hypotension, Hypertension, Azotemia
– Use “stress dose” steroids for patients with Addison disease undergoing surgical procedures.
ADENOMATOID TUMORS, TESTICULAR AND PARATESTICULAR

Ramiro J. Madden-Fuentes, MD
Judd W. Moul, MD, FACS

DIAGNOSIS

HISTORY
- Duration of lesion and size
- Interval growth
- Associated pain, dysuria, tenderness — epididymitis
- Prior malignancy or scrotal pathology
- Exposure to tuberculosis (TB)
- History of sarcoidosis, histoplasmosis
- History of urinary tract infection or sexually transmitted infection
- Recent GU manipulation — bacillus Calmette-Guérin (BCG) instillation

PHYSICAL EXAM
- Scrotal exam — Identify location of mass — single or multiple
  - Evaluate for varicocele or hydrocele
  - Compare with contralateral scrotal contents
  - Evaluate if fixed, mobile, indurated, or encroaching on other structures
  - Evaluate for spermatic cord involvement
- Inguinal exam — Evaluate for lymphadenopathy
  - Hernia

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Tumor markers if concern for testicular mass — α-fetoprotein (AFP), β-human chorionic gonadotropin (β-HCG)
- Lactate dehydrogenase (LDH)
  - Purified protein derivative (PPD) if TB suspected
  - No specific labs to diagnose adenomatoid tumors

Imaging
- Scrotal ultrasound
  - Solid vs. cystic
  - Location — testicular or paratesticular
  - If located in the tunica albuginea can grow into the testicular parenchyma and resemble a testicular malignancy
    - Vascular or avascular

DIFFERENTIAL DIAGNOSIS

Benign tumors of epididymis:
- Leiomyoma
- Papillary cystadenoma (associated with von Hippel-Lindau syndrome)
- Lipomas
- Hamartomas
- Adrenal cortical adenomas

Malignant tumors of the epididymis:
- Sarcoma (rhabdomyosarcoma, leiomyosarcoma, fibrosarcoma, liposarcoma)
- Melanotic neuroectodermal tumor of the epididymis
- Extension of primary testicular tumor
- Metastatic tumor to epididymis
  - Urologic (prostate, kidney)
  - GI (stomach, colon, carcinoid, pancreas)
- Other lesions of the epididymis
  - Granuloma (sperm, TB, sarcoidosis)
  - SpERMatocele
  - Epididymitis
  - Epidermoid inclusion cyst
  - Epididymal abscess
### Adenomatoid Tumors, Testicular and Paratesticular

**Treatment**

**General Measures**
- Excision via inguinal approach – for benign lesions
- Epididymitis – consider sexually transmitted infection as source in young men and treat accordingly (see Sexually Transmitted Infections section)

**Medication**
- First Line: N/A
- Second Line: N/A

**Surgery/Other Procedures**
- Excision of suspicious lesion via inguinal approach with proximal vascular control
- Frozen section
- If positive for malignancy, radical orchiectomy
- Further surgical therapy guided by pathology but may include retroperitoneal lymph node dissection if rhabdomyosarcoma

**Additional Treatment**
- Radiation Therapy: N/A
- Additional Therapies: N/A
- Complementary & Alternative Therapies: N/A

**Ongoing Care**

**Prognosis**
Adenomatoid tumors are uniformly benign with no well-documented cases of true invasion, metastasis, or recurrence after excision (3)[C]

**Complications**
Scrotal hematoma, pain, infection

**Follow-Up**
- Oncologic follow-up if malignant disease
- Patient testicular self-exam

**Patient Resources**

---

**References**

**Additional Reading**
- Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. MMWR. 2010;59 (No. RR-12)
- See Also (Topic, Algorithm, Media)
  - Adenomatoid Tumors, Testicular and Paratesticular Image of
  - Epididymis, Cystadenoma
  - Epididymis, Metastasis to
  - Epididymis
  - Paratesticular Tumors, General
  - Sexually Transmitted Infections

---

**Codes**
- ICD9: 222.0 Benign neoplasm of testis
- 222.3 Benign neoplasm of epididymis
- 222.8 Benign neoplasm of other specified sites of male genital organs
- ICD10: 229.8 Benign neoplasm of other specified male genital organs
  - 229.20 Benign neoplasm of unspecified testis
  - 229.30 Benign neoplasm of unspecified epididymis

**Clinical/Surgical Pearls**
- Adenomatoid tumors are benign with no reported metastasis.
- Excision via inguinal approach with proximal vascular control preferred.
- Treatment for epididymitis is guided by risk of sexually transmitted infections as a source.
- Ultrasound is important to delineate a testicular vs. paratesticular origin of the mass.
**ADRENAL ADENOMA**

Aaron G. Boonjindasup, MD, MPH
Raju Thomas, MD, MHA, FACS

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- Extent of endocrine evaluation in patients with adrenal adenoma is controversial. Basic screening consists of:
  - Basic metabolic panel (BMP)
  - If elevated K+ and patient also hypertensive may be aldosterone-secreting lesion
  - Plasma metanephrines: Most sensitive test for pheochromocytoma
  - 24-hr urine cortisol
  - Low-dose dexamethasone suppression test to rule out SCS if suspected clinically
- Complete endocrine evaluation should be performed if findings on examination and history suggest excess of specific hormone or if positive findings found on screening examination

**Primary hyperaldosteronism (Conn syndrome)**

- Basic metabolic profile
  - Hypokalemia, alkalosis, HTN
  - Aldosterone: Renin ratio
- Values that define a positive screen subject to lab variability: be < 30 suggested by NIH as cut-off for positive aldosteronemia to renin ratio and indicates need for confirmatory testing
- Confirmatory testing for hyperaldosteronism
  - 3-day oral sodium-loading test—high sodium diet for 3 days followed by 24-hr urine measurements of aldosterone, sodium, and creatinine
- + test = 24-hr aldosterone > 12 mg/d
  - Captopril suppression test may be used for patients with cardiac and renal disease which prohibit sodium loading
- Cushing syndrome
  - 24-hr urine cortisol > 100 mg
- If equivocal, perform low-dose dexamethasone suppression test
  - 1 mg dexamethasone at 11 pm
  - Plasma cortisol between 8 AM and 9 AM
- Normal: Cortisol ≤ 15 pg/mL – ACTH dependent
  - Loss of signal between in- and out-of-phase images (microscopic fat-sensitive sequence)
- If screening: Stop tricyclic antidepressants, in patients also on antidepressants
- Phenoxybenzamine for patients also on alpha-blocker
- Captopril suppression test may be used for patients with cardiac and renal disease which prohibit sodium loading

**DIAGNOSIS**

**History**

- Determine history of hypertension, obesity, and glucose intolerance
- Suggestive of Cushing syndrome or adenocortical carcinoma
- Hypertension and history of hypokalemia
- Aldosterone-producing adenoma
- History of malignancy
- Patient medications (“spoilage” for hypertension)

**Physical Exam**

- Blood pressure and heart rate
- Look for stigmata of Cushing syndrome
- Hirudin, oilogonemia, easy bruising, acne, muscle weakness, truncal obesity, buffalo hump, purple striae

**Alert**

- Subclinical Cushing syndrome (SCS) can occur where abnormalities of the hypothalamic–pituitary–adrenal axes exist in the absence of overt signs and symptoms of Cushing syndrome
- May occur in 5–24% of patients with incidentally discovered adenomas
- May not be clinically evident following standard screening for cortisol hypersecretion
- 1 mg overnight dexamethasone suppression test most sensitive for SCS
- Should be performed in ALL patients with adrenal mass and metabolic syndrome

**Imaging**

- Adrenal adenoma: Small, well-defined, homogeneous
- Size criteria important
  - ≤ 5 cm usually benign
  - ≥ 6 cm – 25% malignant
- May occur in 5–24% of patients with incidentally discovered adenomas

**Diagnostic Procedures/Surgery**

- Adrenal biopsy or fine needle aspiration may be performed in select cases
- Reserved for differentiation of metastatic disease and benign lesion
- May not be able to differentiate between benign from malignant adrenocortical tumor
- Rule out pheochromocytoma with plasma metanephrines screening before performing biopsy on an adrenal mass

**Pathologic Findings**

- Aldosterone-producing adenoma
- Spironolactone bodies – eosinophilic laminated collagenous inclusions
- Found after treatment with spironolactone
- Cortisol-producing adenoma
- Vacuolated neoplastic cells
- Metanephrine-positive
- Bilateral adenomas
- Fungal, TB, histoplasmosis
ADRENAL ADENOMA

Differential Diagnosis
- Adrenal cortical carcinoma (up to 80% functional)
- Adrenal hemorrhage
- Adrenal myelolipoma
- Adrenal myelolipoma
- Adrenal lymphoma
- Adrenal metastasis
- Neuroblastoma
- Pheochromocytoma
- TLE, or other infectious cause

Treatment

General Measures
- Based on functional status and size of lesion
- Correct hyperkalemia and electrolyte abnormalities.

Medication

First Line
- For hormonally active adenomas in patients who refuse surgery or have contraindications to surgery
  - Cortisone
  - Spironolactone, eplerenone
  - Aldosterone receptor antagonists in the distal convoluted tubule (DCT)
  - 2nd line – Amiloride, triamterene
  - Inhibitors of OCT aldosterone sensitive sodium channels
- Cushing syndrome
  - Amilorides
  - Blocks the 1st step in cortisol synthesis (Shatzl and preprenolone)
  - Metopronol
  - Blocks the final step in cortisol synthesis (11-deoxycortisol to cortisol)
- Adrenal hemorrhage
  - IV fluids
- Adrenal adenomas
  - 1st step in cortisol synthesis

Second Line

N/A

Surgery/Other Procedures

- Surgical indications
  - Hormonally active masses
  - Any masses > 5 cm (25% of masses > 6 cm are assumed to be adrenal cortical carcinoma)
  - Masses with suspicious imaging characteristics of carcinoma
  - Hemorrhage, irregular borders, HU > 20
  - Laparoscopic and robotic approaches are described, but may have limitations with larger lesions
  - Retrosurgical approach possible for both open and laparoscopic surgery may reduce ileus
- Postoperative stress dose steroids indicated during unilateral adrenalectomy for cortisol producing adenomas and may be indicated for patients with SCS
- Prophylactically: 50 mg hydrocortisone IV q8h postop day 1

Steroid supplementation will be needed after adrenalectomy for cortisol-producing tumors and suppressed HPA recover (median of 15 mo)
- Postoperatively (POD 2): Hydrocortisone 20 mg PO qAM, 10 mg qAM
- Hydrocortisone slowly tapered over 3 mo to 10 mg daily
- AM cortisol should be measured and repeated until > 10 ng/dL
- Confirm recovery of HPA with cosyntropin test
  - Monitor for electrolyte disturbances with BMP and postoperative AI in patients with hormonally active tumors and/or SCS
- Acute AI (-addison state)

Alert

This is a life-threatening condition often preceded by hypotension unresponsive to fluid resuscitation.
- May occur in the postoperative state in the setting of cortisol-secreting lesion with downregulated cortisone adrenocortical function, and in patients with previous contralateral adrenal resection or due to concurrent illness or infection
- Other non-specific symptoms may include abdominal pain, salt craving, nausea, vomiting, fatigue, and fever
- Electrolyte abnormalities such as hyperkalemia or hyperaldosteronism and other laboratory abnormalities such as anemia, leukocytosis, or eosinophilia may also be found
- Prolonged use of steroids may increase risk of postoperative adrenal insufficiency

May begin steroid replacement if high clinical index of suspicion
- Diagnosis Obtain AM serum cortisol and ACTH level:
  - Normal > 10 ng/dL, low-normal (3.4–10 ng/dL), AI < 3 ng/dL
  - Confirmatory testing with evaluation of response to ACTH stimulation (cosyntropin test)
  - Measure serum cortisol at baseline
    - Give cosyntropin 0.25 mg IV
    - Measure serum cortisol at 60 min after dose
  - Adequate response: Cortisol > 18 pg/dL
- If acute AI is highly suspected, don’t wait for result before treating:
  - Give 2–3 0.1 D5 NS quickly and 4 mg dexamethasone IV
  - Use dexamethasone because IV cortisol will interfere with the diagnosis later during hospitalization
- Maintenance therapy:
  - Hydrocortisone 30 mg/d
    - Fludrocortisone 0.05–0.1 mg/d

Complications

- Hypertension
- Diabetes mellitus
- Atherosclerosis
- Prior wound healing
- Nephrotic syndrome
  - 14% of patients with Cushing syndrome – due to hypertension
- Adrenal insufficiency (Addison disease)

Follow-up

Patient Monitoring
- Nonfunctioning benign adrenal mass can be followed with physical and radiologic examinations
  - > 20% show enlargement > 1 cm
- No guideline on growth velocity on surgical treatment

References


See Also (Topic, Algorithm, Media)
- Adrenal Adenoma Image
- Adrenal Cortical Carcinoma
- Adrenal Cyst and Pseudocyst
- Adrenal Hemorrhage
- Adrenal Incidentaloma
- Adrenal Mass
- Adrenal Mass, Algorithm
- Adrenal Mass Image
- Adrenal Metastasis
- Adrenal Myelolipoma
- Adrenal Myelolipoma

Codes

ICD9
- 115.1 Benign neoplasm of adrenal gland
- 253.0 Cushing’s syndrome
- 253.10 Cushing’s syndrome

ICD10
- D55.00 Benign neoplasms of unspecified adrenal gland
- E82.4 Pituitary-dependent Cushing’s disease
- E26.01 Cushing’s syndrome

Clinical/Surgical Pearls

- Adrenal lesions should be surgically treated if > 5 cm or if functional active.
- No guideline on normal growth velocity for adrenal lesions.
- Melanoma, lung, breast, colon, and renal cell cancers have metastatic predilection to adrenal gland.

ONGOING CARE
- Unilateral Cushing syndrome can be fatal due to cardiovascular, thromboembolic, or hypertensive complications or infection
- Surgical removal of hormonally active adenomas is usually curative

Prognosis

- Unilateral Cushing syndrome can be fatal due to cardiovascular, thromboembolic, or hypertensive complications or infection
- Surgical removal of hormonally active adenomas is usually curative
ADRENAL CORTICAL CARCINOMA
John M. Lacy, MD, FACS
Stephen E. Strup, MD, FACS

DIAGNOSIS

HISTORY
- Most common symptoms are related to excess cortisol production (Cushing’s syndrome) in 50–60%, then virilization (20%), or mixed syndromes (20–30%)
- History of onset of symptoms ≤ 12 mo is suspicious for ACC
- Constitutional symptoms: - Weight loss, melasma, weakness, nausea, or vomiting usually associated with poor prognosis
- In children, suggested by generalized weight gain and delayed linear growth
- Nonfunctional tumors may be larger and present with mass effect
- Painful or palpable mass
- Lower extremity edema
- Urinary obstruction
- Budd-Chiari syndrome
- GI symptoms
- Hyperaldosteronism (primary)
- Hypertension
- Hypercalcemia
- Renal failure
- Incidental finding during imaging workup for other malignancies
- Difficult to distinguish between benign and malignant tumors

PHYSICAL EXAM
- Palpable abdominal mass
- Palpable supraclavicular lymph nodes
- Constitutional symptoms:
  - Weight loss, malaise, weakness, nausea, or vomiting
  - Constitutional symptoms: - Weight loss, melasma, weakness, nausea, or vomiting

DIAGNOSTIC TESTS & INTERPRETATION
Lab Tests for glucocorticoid excess (minimum 3 out of 4 tests)
- Dexamethasone suppression test
- 24-hr urinary free cortisol
- Basal cortisol (serum)
- ACTH (plasma)

 Sexual steroids and steroid precursors:
- 17-OH-progesterone (serum)
- Testosterone (serum)
- 17-β-estradiol
- 24-hr urine steroid metabolite exam

Metabolic bone disease:
- Parathyroid hormone
- 25-hydroxyvitamin D
- Bone mineral density (BMD)
- Bone scan

DIAGNOSTIC PROCEDURES/SURGERY
- CT of abdomen is preferred initial study in patients with ACC
- Differentiation between benign and malignant tumors
- Imaging:
  - CT of abdomen is performed initial study in patients with ACC
  - Benign tumors
  - Homogeneous appearance with well-delineated margins
  - Generally < 4–6 cm, smooth and round or oval contour
  - < 10 HFU or rapid washout of contrast < 15 min
  - Primary ACC:
  - Nonhomogeneous internal architecture
  - Irregular contour, invasion of surrounding structures
  - > 10 HFU or delayed washout of contrast > 15 min
  - MRI not proven to be more sensitive in differentiating malignant from benign tumors
  - Preferential imaging modality for evaluation of vena caval involvement
- ACC, Cushing’s syndrome: to the liver on T1-weighted images; heterogeneous signal intensity (brighter white) on T2-weighted images
- FDG-PET potentially useful in radiologically indeterminate lesions
- Bone scan if suspicious of skeletal metastases.

Pathologic Findings
- Macroscopic:
  - Lobulated, orange tumor with necrotic areas, calcifications, mitral valve vegetations
- Microscopic:
  - Weiss criteria for malignancy includes: ≥ 3 of the following:
    - High nuclear grade
    - Mitotic rate > 5/50/hpf
    - Atypical mitotic figures
    - Stromal invasion
    - Diffuse architecture in >33% of tumor
    - Necrosis
    - Vascular invasion
    - Sinusoidal invasion
    - Capsular invasion
- Antigen Ki-67: a promising new immunohistochemical marker
- Marker of proliferative activity
- Low-risk ACC: expressed in >10% of cells
- High-risk ACC: expressed in >10% of cells

DIFFERENTIAL DIAGNOSIS
- Functioning adrenal mass:
  - Adenoma, aldosterone, pheochromocytoma
- Nonfunctioning adrenal masses:
  - Hemorrhage, cyst, metastatic tumor, neurinoma
- Other: Renal cell carcinoma
TREATMENT

GENERAL MEASURES

Complete surgical excision is treatment of choice in resectable stage I or II tumors and children.

MEDICATION

- resectable stage I or II tumors and children
- Complete surgical excision is treatment of choice in

GENERAL MEASURES

- Laparoscopy
- Open approaches

Indications for surgery

- Clinical trials underway for targeted therapies
- If failed initial polychemotherapy regimen, may try
- If failed mitotane monotherapy, add cytotoxic

TREATMENT

Rapid development of symptoms is key to
distinguishing ACC from Cushing’s syndrome.

ADDITIONAL TREATMENT

- Adrenal crisis in patients who undergo surgery for
- Hydrocortisone must be administered during surgery
- Adrenal Mass Algorithm

ADDITIONAL READING

- Carnaille B. Adrenocortical Carcinoma: Which

REFERENCES

- Carnaille B. Adrenocortical Carcinoma: Which
- 1. Carnaille B. Adrenocortical Carcinoma: Which
- Therapeutic Management of advanced
- Carnaille B. Adrenocortical carcinoma: Which surgical approach?
- Radiotherapy in adrenocortical carcinoma.
ADRENAL INSUFFICIENCY, ACUTE (ADRENAL CRISIS)

Debasish Sundi, MD
Misop Han, MD

BASICS

DESCRIPTION

• Acute adrenal insufficiency (Sometimes called Addisonian crisis) symptoms are attributable to mineralocorticoid deficiency—there are many etiologies (1).
• Adrenal crisis is a subtype of acute adrenal insufficiency, it is a rapid and intense process triggered by a stressor such as surgery or sepsis.
• Symptoms of the Addison disease (chronic adrenal insufficiency) are difficult to recognize when the diagnosis of Addison disease is made when patients present with an acute crisis.
• Patient may present in hemodynamic compromise secondary to sodium and plasma volume depletion.
• Addisonian crisis should be treated immediately; treatment should not be delayed pending diagnostic test results.
• The disease usually results from bilateral adrenal cortex destruction. Destruction of the adrenal cortex causes a combined deficiency of glucocorticoids, mineralocorticoids, and adrenal androgens.

ALERT

Hypoglycemia and shock refractory to resuscitation with fluids and vasopressors should be considered Addisonian crisis and treated with intravenous steroids.

EPIDEMIOLOGY

Incidence

• Addison disease incidence: 0.6/100,000 per year
• Up to 0.7% of patients undergoing major surgery may experience adrenal insufficiency.

Prevalence

• Addison disease prevalence: 4–11/100,000
• ~11% of patients with septic shock manifest adrenal insufficiency.

RISK FACTORS

• Maternal: Bilateral adrenal hemorrhage from birth trauma
• Children: Pseudonodular or meningococcal septicaemia leading to acute hemorrageic destruction of both adrenal glands (Waterhouse–Friedrichsen syndrome)
• Adults: Adrenal crisis after surgical or septic stress, bilateral adrenal hemorrhage from systemic anticoagulation or coagulopathy disorder
• Special at-risk populations: Pregnant women, patients with idiopathic adrenal vein thrombosis, patients who have undergone nephrectomy or vascular embolization of adrenal medullas.
• Most common cause: Ruptured withdrawal of steroids from patients with adrenal atrophy secondary to chronic steroid use
Medications: Ketoconazole, amitriptyline, dexamethasone, histidine, phenytoin, rifampin

Genetics

• Hereditary factors may influence development of autoimmune adrenal insufficiency.
• Familial glucocorticoid insufficiency may be associated with a relative gene pattern.
• Addison disease has been associated with a variety of autoimmune diseases.

PATHOPHYSIOLOGY

• The adrenal cortex produces 3 classes of steroid hormones: Mineralocorticoids (aldosterone), glucocorticoids (cortisol), and androgens.
• Cortisol deficiency is primarily responsible for the manifestations of the crisis.
• Primary adrenal insufficiency is due to failure of the adrenal cortex.
• Secondary adrenal insufficiency is caused by failure of ACTH stimulation of the adrenal cortex.
• Chronic steroid administrations result in suppression of ACTH production via feedback inhibition.

ASSOCIATED CONDITIONS

Nearly 50% of patients with adrenals have some form of autoimmune disease: Hyperparathyroidism, poralal collapse, diabetes mellitus type I, hypothyroidism (Hashimoto thyroiditis), or hyperthyroidism (Grave disease).

GENERAL PREVENTION

• Perioperative stress dose steroid replacement when indicated (68).
• Low threshold to intervene with IV glucocorticoid replacement at early signs of fluid refractory hypotension.

DIAGNOSIS

HISTORY

• Prior steroid use:
  – Risk increase with minimum 20 mg prednisone or equivalent for at least 5 days within the past 12 mo
  – Patients receiving normal physiologic levels require the equivalent of 20 mg/day within 1 mo to recover normal adrenal function.
• Patients receiving glucocorticoids who have symptoms of adrenal insufficiency and have no role in the acute management of adrenal crisis.

• Acute adrenal crisis usually presents acutely with hypotension or hypotensive shock:
  – Clinical picture is more complex as a result of a mixture of preceding slow-onset symptoms and signs including abdominal pain, sepsis, pituitary or adrenal hemorrhage, surgery, or trauma.
  – Acute adrenal insufficiency should be considered in patients presenting in the emergency room with abdominal pain, nausea, diarrhea, hypotension, and fever.
  – The etiologies of hypotension is profound hypovolemia.
  – Hypotension may be one of the last signs (granulomatous because mineralocorticoid secretion is usually somewhat preserved in patients on chronic glucocorticoid replacement.

PHYSICAL EXAM

• Check blood pressure: Extreme hypotension and/or shock refractory to fluids and vasopressors suggests acute adrenal crisis.
• Vittorio often coexists with Addison disease:
  – Hyperpigmentation along palmar creases, buccal mucosa, pressure points, perianal mucosa, and nipple areolae.
  – Check for signs of generalized weakness and specifically muscle weakness.
  – Check for loss of axillary hair in females.
  – In adrenal crisis, patients may be hyper- or hypo-

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• Plasma cortisol: Early AM levels <3 μg/dL
  – 90 mmol/L suggests diagnosis.
• Serum ACTH:
  – If low in the setting of low cortisol, patient has pituitary/hypothalamic disease.
  – If high in the setting of low cortisol, primary adrenal insufficiency exists.
• Electrolyte abnormalities: Decreased sodium and chloride levels, increased potassium levels, and an increased BUN/Cr ratio (reflecting hypovolemia)
  – Hypocalcaemia may be seen during adrenal crisis.
  – Hypocalcaemia may be seen with associated polyglandular failure and hypoparathyroidism.
• Exogenous glucocorticoids and melanocyte-stimulating hormone levels may be found.

ALERT

Labs are used only in the setting of nonemergent adrenal insufficiency and have no role in the acute management of adrenal crisis.

Imaging

• Abdominal x-rays may show adrenal calcifications if adrenal insufficiency is secondary to fungal or TB infection.
• Abdominal CT may show enlarged adrenal glands with TB infection or miliary mases.
• Adenals may be small secondary to idiopathic atrophy, autoimmune adrenalitis, or advanced TB.
• Adrenal gland hemorrhage or thrombosis may be seen.
ADRENAL INSUFFICIENCY, ACUTE (ADRENAL CRISIS)

Diagnostic Procedures/Surgery
- Rapid ACTH stimulation ( cosyntropin, a synthetic derivative of ACTH test)
  - Following injection of baseline serum cortisol, 250 μg of synthetic ACTH is administered IM or IV.
  - Plasma cortisol response is measured at 60 min.
  - Those with no response have primary adrenal failure. If the cortisol levels increase following synthetic ACTH injection, the adrenal insufficiency was secondary to pituitary dysfunction.

Pathologic Findings
- Autoimmune adrenal cortical infiltration
- Adrenal cortical infection/necrosis, with or without hemorrhage
- Metastatic carcinoma in adrenal gland
- Tuberculosis (transient of adrenal)
- Radiation effect

Differential Diagnosis
- Acute insufficiency (addisonian crisis) [1A]
  - Addison disease
  - Secondary adrenal insufficiency
  - Celiac disease
  - Syndrome of inappropriate ADH secretion
  - Severe nutritional deficiencies
  - Neuroblastoma
  - Pancoast-Taylor syndrome
  - Salt depletion nephritis
  - Bronchogenic carcinoma
  - Anorexia nervosa, depression

Treatment

General Measures
- In critically ill and decompensating patients, maintenance airway, and ensure adequate ventilation.
- Treatment instituted with IV fluid and maintenance dose of steroids, as needed
- In critically ill and decompensating patients, maintenance dose of steroids, as needed
- Stabilized.

Medication

First Line
- IV fluids: 0.9% NS or 5% dextrose in NS
- Hydrocortisone: 100 mg IV bolus immediately, followed by either 100 mg q8h or 10 mg/m2 continuous infusion for 2–3 days [25A].
- Dexamethasone: 2–8 mg as a single dose, this may be repeated as necessary

Second Line
- Pediatric considerations:
  - Hydrocortisone: 1–2 mg/kg/100 laser immediately, followed by 25–150 mg/d given in divided doses q8–q12h (infants and young children)
  - Gynecic considerations:
  - Start dosage on the low end of the dosing range due to greater frequency of impaired cardiac and renal function
  - Increased susceptibility to adverse effects such as glucocorticoids, diabetes, and osteoporosis with long-term therapy

Follow-up
- Patient Monitoring
  - Consider increase in steroid dosing when the patient has an episode of minor fever, infection, trauma, or physical stress.
  - Monitor blood pressure, weight, serum electrolytes, and blood glucose levels.
  - Monitor growth in pediatric patients.
  - Bone density, ophthalmologic exams.

Patient Resources

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Adrenal Cellulitis
- Addison Disease
- Addison Disease (Adrenocortical Insufficiency)
- Algorithm [2]
- Adrenal Hemorrhage
- Adrenal Hypoplasia

Ongoing Care

Prognosis
- There is a high risk of morbidity and mortality associated with uncorrected acute crisis. May result in cardiovascular collapse if not recognized.
- Excellent long-term prognosis following immediate management of acute crisis and long-term maintenance therapy.

Complications
- Abdominal distention, peritonitis
- Edema, glaucoma, increased intraocular pressure
- Hypertension, hyperammonemia
- Immunosuppression
- Mood changes, weight gain, hirsutism

Additional Treatment

Surgery/Other Procedures
- Perioperative management during routine urologic surgery.
- Consultation with the preoperative physician for medical clearance and the procedural anesthesiologist is advised.
- Many patients taking low-dose prednisone (such as for autoinflammatory disorders) are able to undergo major surgery without any endocrine instability even without administration of intravenous stress-dose steroids [1B]. Incident fluid refractory hypotension in this group should be promptly treated with IV hydrocortisone.
- Patients with chronic adrenal failure and complete physical steroid replacement do generally require pericellular stress-dose steroids.
- Individualization of stress-doses and postoperative taper regimen is recommended.

Additional Reading
- References
- Additional Reading
**ADRENAL MASS**

Kyle A. Richards, MD

**PATHOPHYSIOLOGY**

- Adrenal glands consist of an outer cortex and inner medulla and are part of the endocrine system
- Abnormal secretion of hormones = symptoms

**Adrenal cortex**
- Zona glomerulosa
  - Produces mineralocorticoid aldosterone
  - Regulates sodium and fluid homeostasis
  - Promotes exchange of potassium for sodium in distal tubules of kidney
  - Excess aldosterone = Cushing's syndrome
- Zona fasciculata
  - Produces glucocorticoid cortisol
  - Regulates cellular and glucose metabolism, immune processes, and other regulatory functions
  - Excess cortisol = Cushing's syndrome
- Zona reticularis
  - Produces adrenal androgens
  - Excess androgens = virilization
- Adrenal medulla
  - Produces catecholamines
  - Excess catecholamines = pheochromocytoma
- Addison's disease = adrenal insufficiency
- Usually not caused by adrenal masses

**ASSOCIATED CONDITIONS**

- See "Genetics"
- Hypertension (spontaneous or precipitated by postural change, anxiety, meds, and Valsalva
- Forceful heartbeat, pallor, tremor, headache, emotional and cognitive changes, proximal muscle weakness
- Facial rounding and plethora
- Central adiposity
- Thin skin, purple striae, and acne
- Hirsutism
- Gynecomastia or testicular atrophy

**DIAGNOSIS**

**HISTORY**

- Focus on symptoms suggestive of adrenal hyperfunction or malignant disease
- Cushing's syndrome
  - Weight gain
  - Easy bruising
  - Pervasive weakness
  - Emotional and cognitive changes
  - Opportunistic and fungal infections
  - Altered reproductive function
  - Pheochromocytoma
  - Episodic symptoms
  - Frustrated heartbeat, palpitations, tremors, headache, and diahrosis
  - Spontaneous or precipitated by postural change, anxiety, meds, and Valsalva
  - Primary hyperaldosteronism
  - Nocturia/polyuria (due to hypokalemia)
  - Muscle cramps and palpitations

**DIAGNOSTIC TESTS & INTERPRETATION**

- 24-hr urinary aldosterone excretion test while patient maintains high sodium diet
- Salt loading test

**BASICS**

**DESCRIPTION**

- An adrenal mass is generally considered to be an adrenal lesion > 1 cm
- Often found after abdominal imaging and often termed "adrenal incidentaloma"
- Rarely presents with acute or chronic symptoms

**INCIDENCE**

- Incidental adrenal mass (1,2,4)
  - Peak incidence at age 50–70
  - 2–6% bilateral
  - 1–2 per million persons per year
  - Bimodal age distribution: Age < 50–60% right side, 30–40% left side, 10–15% bilateral
  - Slightly higher incidence on left side
  - 2–6% bilateral
  - 1–2 per million persons per year
  - Bimodal age distribution: Age < 50–60% right side, 30–40% left side, 10–15% bilateral
  - Slightly higher incidence on left side
  - 1–2 per million persons per year
  - Bimodal age distribution: Age < 50–60% right side, 30–40% left side, 10–15% bilateral
  - Slightly higher incidence on left side

**GENETICS**

- Rare genetic syndromes may predispose to adrenal masses (1,4)
  - Beckwith–Weidemann syndrome
  -von Hippel–Lindau disease
  - McCune–Albright syndrome
  - Carney complex
  - Multiple endocrine neoplasia 2
  - Multiple endocrine neoplasia 1
  - Li–Fraumeni syndrome
  - Tuberous sclerosis
  - Von Hippel–Lindau syndrome

**PATHOLOGIES**

- 4% in patients undergoing CT scan
- 6% in autopsy series
- Increases with age (2,4)
  - 0.2% age 20–29, 7% age ≥ 70

**RISK FACTORS**

- Sex (1)
  - Malignant adrenal mass: Male > female (2:1)
  - Benign adrenal mass: Female > male (1.7:1)
- Aging
- Prior history of cancer especially melanoma, lung, breast, or kidney
- 50% of these adrenal masses are metastases

**DIAGNOSTIC TESTS & INTERPRETATION**

- 24-hr urinary free cortisol (5)
  - Aldosterone-to-renin ratio (morning)
  - 91–98% sensitivity and specificity
  - Serum cortisol > 5 μg/dL is diagnostic

**DIAGNOSTIC TESTS & INTERPRETATION**

- Cutoff for
  - 97% specificity
  - 95% specificity
  - 95%–99% specificity
  - 95%–99% sensitivity
  - 95%–99% specificity
  - 95%–99% sensitivity

**DIAGNOSTIC TESTS & INTERPRETATION**

- Confirmatory testing
- Saline infusion test
- 24-hr urinary aldosterone excretion test while patient maintains high sodium diet

**DIAGNOSTIC TESTS & INTERPRETATION**

- Cushing’s syndrome
  - Hypokalemia, hypoglycemic
  - 24-hr urinary cortisol (5)
  - 80 μg/24 h excludes diagnosis
  - Cortisol suppression testing
  - 1 mg dexamethasone at 11 pm and measure serum cortisol at 8 am the next day
  - Serum cortisol > 5 μg/dL is diagnostic

**DIAGNOSTIC TESTS & INTERPRETATION**

- Primary hyperaldosteronism
  - Nocturia/polyuria (due to hypokalemia)
  - Muscle cramps and palpitations
  - Adrenocortical carcinoma
  - Sporadic adrenal cancer
  - Cushing’s syndrome (see above)
  - Altered reproductive or sexual function
  - Hyperaldosteronism (see above)
  - Sex steroid-secreting tumor
  - Altered reproductive or sexual function
  - Metastatic cancer
  - History of intra-adrenal cancer
  - Medical history
  - Multiple endocrine syndromes
  - Medications such as exogenous steroids
  - Family history
  - See "Genetics"
**Adrenocortical carcinoma (CA)**
- Most commonly cortical origin
- Serum dehydroepiandrosterone (SHEA)
- Sex steroid-secreting tumor
- Serum testosterone and 17α-estradiol in women with uterine or men with feminization

**Pathologic Findings**
- Adrenal medullary tumors
- Adrenal cortical tumors (4)
- Adrenal insufficiency post adrenalectomy

**Diagnostic Procedures/Surgery**
- CT scan

**Hemorrhage**
- Cystic
- Hemorrhage
- Necrotic core
- Low density on T2-weighted imaging

**Concurrent adrenal hemorrhage**
- Hemorrhage
- Necrosis
- Calcification

**Differential Diagnosis**
- Cushing's Disease and Syndrome
- Adrenal Myelolipoma
- Adenal Adenoma and Cortical Carcinoma

**Pseudocyst**
- Cysts (pseudo)cyst, parasitic, epithelial- and endothelial (false cysts)

**Clinical Pearls**
- Assess all for biochemical function.
- Remove all adrenal masses > 5 cm.
- Do not biopsy pheochromocytoma.

**Radiation Therapy**
- Only for palliation of bone metastases from adrenal cortical carcinoma

**ADDITIONAL THERAPIES**
- N/A

**REFERENCES**

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
- Addison Disease
- Adrenal Adenoma and Cortical Carcinoma
- Adrenal Angiomyolipoma
- Adrenal Calcifications
- Adrenal Cysts and Pseudocysts
- Adrenal Hemorrhage
- Adrenal Incidentaloma
- Adrenal Mass Algorithm
- Adrenal Mass Image ID
- Adrenal Metastasis
- Adrenal Myelolipoma
- Adrenal Oncocytoma
- Cushing's Disease and Syndrome
- Phaeochromocytoma

**TREATMENT**

**General Measures**
- Observation, resection, or medical therapy
- Depends on size of lesion, functionality, malignant potential, and overall health of patient

**Medication**
- First Line
  - Cushing's syndrome (SC)
    - Amenoleptanide, metyrapone, ketoconazole
  - Phaeochromocytoma
    - Phenylephrine, propranolol
  - Primary hyperaldosteronism: Spironolactone
  - Adrenocortical carcinoma: Mitotane
- Second Line
  - Adrenocortical carcinoma
    - Etoposide, etoposide, 5-fluorouracil, doxorubicin, vincristine

**Surgery/Other Procedures**
- Should remove all functional adrenal masses
- Open surgery if large or locally advanced; evaluate for vein thrombus or adjacent organ invasion
- Minimally invasive surgery is now accepted
- Minimal invasive surgery is now accepted
- Remove masses > 5 cm; high malignancy risk
- Consider partial adrenalectomy for solitary adrenals, bilateral disease, familial syndromes

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- Only for palliation of bone metastases from adrenal cortical carcinoma

**ADDITIONAL THERAPIES**
- N/A

**Ongoing Care**

**Prognosis**
- Adrenocortical carcinoma: 33–72% of patients with primary hyperaldosteronism (PH)
- 10–15% recurrence rate after resection of phaeochromocytoma
- Adrenocortical carcinoma has poor prognosis
  - Mean survival 18 mo (418)
  - 3–yr survival 15–47%

**Complications**
- Adrenal insufficiency post adrenalectomy
- Unrecognized malignancy in phaeochromocytoma

**Follow-Up**

**Patient Monitoring**
- Conservative management principles (218)
  - Repeat imaging at 6, 12, and 24 mo
  - Repeat hormonal testing annually for 4 yr
  - If growth ≥ 1 cm or autonomous hormonal secretion, consider surgery

**Patient Resources**
- www.pheochromocytoma.org
- www.cancer.gov/cancertopics/types/adrenocortical
AMYLOIDOSIS, GENITOURINARY

Christopher Wright, MD
Mark L. Jordan, MD, FACS

DESCRIPTION

• Heterogeneous group of disorders with extracellular deposition of protein in aberrant fibrillar form:
  – Kidney, uterus, seminal vesicles, prostate, penis, and testicles can be involved
  – >50% of gentinourinary (GU) tract cases involve the bladder
  – Commonly forms “pseudotumors” in bladder, uterus, or renal pelvis
  • 25 structurally unrelated proteins known to cause amyloidosis
  • May be primary, secondary, or hereditary
  • May be organ limited or systemic

EPIDEMIOLOGY

Incidence

• Uncommon disorder and exact worldwide incidence is unknown
• In the United States appears to be stable at 6–10 cases per million person-years
• Age-specific incidence rates increase in each decade over age 40
  – Median age at diagnosis is 64 yr and <5% of patients are under age 40

RISK FACTORS

• Chronic and recurrent mucosal and submucosal inflammation
• Hemodialysis patients develop deposits in kidneys
• Chronic inflammatory disorders

Genetics

• Familial or hereditary amyloidosis exists
• Dozens of specific variations described
• Familial forms often do not present until adulthood
• Patients with immunoglobulin light chain (AL) amyloidosis frequently have chronic renal abnormalities but there is no single chromosome change that is diagnostic

PATHOPHYSIOLOGY

• More than 20 distinct low–molecular-weight proteins are recognized to form amyloid fibrils, the 2 most common being:
  – AA, formerly referred to as primary amyloidosis
  • Fibrils composed of fragments of monoclonal light chains
  • Aged patients may have amyloidosis alone or in association with other plasma cell dyscrasias (eg, multiple myeloma)
  – AL-amyloidosis
  • Fibrils composed of fragments of the acute phase reactant serum amyloid A
  • Usually reactive (secondary) to chronic inflammation
  • Thought to be a misleading event; misfolded variants are prone to self-aggregation
  – These become insoluble complexes that accumulate in tissues
  • Renal amyloid is often a glomerular deposition leading to nephrotic syndrome

ASSOCIATED CONDITIONS

• End-stage renal disease (ESRD) requiring dialysis
• Nephrotic syndrome
• Diabetes
• Multiple myeloma
• Familial Mediterranean fever (FMF)

• Hereditary inflammatory disorder characterized by severe attacks of abdominal pain in 95% of patients
• AA amyloidosis with renal failure is common

GENERAL PREVENTION

N/A

DIAGNOSIS

• Clinical presentation depends on the number and nature of the organs affected
• Even in patients with multiple-organ involvement, it is usually possible to identify 1 organ as the “dominant” site of involvement

HISTORY

• Non-specific symptoms such as fatigue and weight loss are common
• Patient on dialysis
• Family history of amyloidosis
• Chronic disease or inflammation
• Familial Mediterranean fever (FMF)

• Chronic disease or inflammation
• Cardiac:
  – 60% of patients
  – Signs/symptoms of heart failure
• Neurologic:
  – 20% with mixed sensory and peripheral neuropathy
  – Carpal tunnel syndrome
  – Liver:
  – 70% will have hepatomegaly
• Bladder:
  – Patients with amyloidosis in 75%
  – Nephrotic syndrome (rarely, frequency)
  – Clinically similar to bladder cancer
• Ureter:
  – Flank pain if obstruction
  – Anuria if bilateral amyloidosis
• Prostate:
  – Hematuria
  – Prostate:
  – Hematuria
  – Bladder outlet obstruction may be present

PHYSICAL EXAM

• Peripheral edema (nephrotic syndrome)
• Hepatosplenomegaly
• General medical no specific physical exam findings

DIAGNOSTIC TESTS & INTERPRETATION

• Proteinuria in 50–80%
• Renal failure in 50%
• Elevated liver function tests (cholestatic pattern)
• Diagnosis of AL amyloidosis requires evidence of a monoclonal proliferative disorder
• Serum or urine monoclonal (M) protein can be detected

Imaging

• CT or ultrasound (US) may demonstrate hydronephrosis secondary to obstruction (peripheral amyloidosis)
• Magnetic resonance imaging (MRI):
  – T2-weighted images are suggestive of amyloid deposition. Can be confused with prostate cancer invading into seminal vesicles or MRI for prostate biopsy

Diagnostic Procedures/Surgery

• Cystoscopy for hematuria
  – Lesions are difficult to distinguish from transitional cell carcinoma (TCC) without biopsy or resection
• Uroscopy or retrograde pyelogram for ureteral involvement
  – Bladder:
    – Abdominal fat pad aspirate or bone marrow biopsy have high success rates and are preferred sites of biopsy
    – Renal biopsy performed if former is negative with high suspicion
    – Will be positive in 90% of cases

Pathologic Findings

• Diagnosis requires histologic demonstration of amyloid deposits:
  – Congo red stain
  – Change under light microscope
  – Green birefringence under polarized light
  – Electron microscopy can be used to identify microfibrils
  – Immunohistochemical analysis aids in typing: Diagnosis of transthyretin type amyloidosis
  – If limits need for further evaluation as it identifies the amyloidosis as inherited
• Serum or urine monoclonal protein can be seen in radical prostatectomy specimen but the significance is unknown

DIFFERENTIAL DIAGNOSIS

• Bladder:
  – Difficult to distinguish from TCC without biopsy
• Ureter:
  – May be confused with stones or other causes of obstruction (eg, strictures)
• Nephrotic syndrome and glomerulonephritis
AMYLOIDOSIS, GENITOURINARY

TREATMENT

GENERAL MEASURES
- In AL amyloidosis treatment is aimed at reducing the production of monoclonal light chain precursor with chemotherapy or, occasional, radiotherapy or surgery of a localized amyloidogenic plasmacytoma
- In AA amyloidosis treatment is generally supportive with therapy directed at primary cause if identified

MEDICATION

First Line
- High-dose melphalan chemotherapy followed by autologous blood stem cell transplantation (2) – 25–67% complete hematologic response seen in single and multicenter trials
- Response far exceeds cyclic oral melphalan and prednisone (see 2nd line)
- Colchicine can be used in FMF to prevent proteinuria

Second Line
- Low-dose oral melphalan with prednisone in a cyclical fashion – Rarely results in complete hematologic response or reversal of amyloid-related organ dysfunction

SURGERY/OTHER PROCEDURES
- Renal transplant – Graft survival similar to matched controls without amyloidosis
- Recurs in graft in 20–33% due to continued activity of underlying disease
- TUR of bladder lesion with fulguration – Adjuvant intravesical DMSO has shown success in preventing recurrence (3)

ADDITIONAL TREATMENT

Radiation Therapy
Only rarely used for localized amyloidogenic plasmacytoma

Additional Therapies
- Supportive care
- Management of heart failure
- Salt restriction, diuretics, and treatment of secondary hyperlipidemia for nephrotic syndrome
- Analgesics for neuropathic pain

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Single institution experience of 421 patients who received high-dose melphalan with stem cell transplant shows event-free survival and overall survival of 2.6 and 6.3 yr, respectively (4)
- Long-term survival in those who develop renal failure remains poor – Ranges from 12–24 mo
- AA amyloidosis has better prognosis

COMPLICATIONS
See above

FOLLOW-UP

Patient Monitoring
- Bladder or urethra – Repeat periodic surveillance cystoscopies – Recurrence rates >50%
- Ureters – US or CT to monitor hydronephrosis

Patient Resources
Amyloidosis foundation (www.amyloidosis.org)

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Amyloidosis Imaging
- Bladder Tumors, Benign and Malignant, General Considerations
- Bladder Mass, Differential Diagnosis
- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)

ICD9
- 277.30 Amyloidosis, unspecified
- 277.39 Other amyloidosis

ICD10
- E85.3 Secondary systemic amyloidosis
- E85.8 Other amyloidosis
- N08 Glomerular disorders in diseases classified elsewhere

CLINICAL/SURGICAL PEARLS
- Both surgically and radiologically, genitourinary amyloidosis may mimic TCC in GU tract, therefore biopsy is needed.
- Additional far paper pad aspirate is preferred location to obtain biopsy, followed by bone marrow and finally kidney.
ANDROPause (Late-Onset Hypogonadism)

Katie S. Murray, DO
Tomas L. Griebling, MD, MPH, FACS

**DESCRIPTION**
- Hypogonadism is a reduction in serum testosterone and other circulating androgens.
- Primary hypogonadism: Arias directly from testicular causes
- Secondary hypogonadism is where changes occur in hypothalamic-pituitary-testicular axis
- Late-onset hypogonadism is a gradual reduction in serum testosterone levels in elderly men; often referred to as “andropause.”

**EPIDEMIOLOGY**
- Estimates suggest more than 4.5 million elderly American men may be affected.
- % of men report moderate or severe scores consistent with hypogonadism on surveys (1)
- Thought to be underreported and undiagnosed in elderly males.

**RISK FACTORS**
- Decreases in serum testosterone occur naturally as part of the aging process.
- Genetics

**PATHOPHYSIOLOGY**
- Testosterone age-related declines vary by reported study:
  - Testosterone declined approximately 100 ng/dL (3.5 nmol/L) from age 20–80 yr
  - Testosterone fell 1.3% from age 40–79 yr
  - As age increases, there is:
    - Decreased number of Leydig cells within the testicle (site of testosterone production)
  - Decreased testicular responsiveness to LH (controversial)
  - Diminished in the amplitude of circadian release of T
  - Increased serum sex hormone binding globulin (SHBG)
    - Levels 1, therefore less bioavailable (functionally active) T
  - Relationship with cardiovascular (CV) disease is thought to be multifactorial
    - Nitric oxide (NO) is an important mediator in both CV health and erectile function

**ASSOCIATED CONDITIONS**
- Metabolic syndrome
- Diabetes mellitus
- Hypertension
- Tobacco abuse
- Sleep apnea
- Psychological disorders
- Social stress

**GENERAL PREVENTION**
- None

**DIAGNOSIS**

**HISTORY**
- Patients often complain of:
  - Fruity decreased grip strength, diminished gait speed, easy fatigue and exhaustion, unintentional weight loss, and low levels for physical activity
  - Decreased energy
  - Decreased mentation
  - Decrease in muscle mass and strength
  - Decreased libido
  - Erectile dysfunction
  - Loss of morning mictions
  - Increased visceral fat
  - Decrease in bone mineral density (osteoporosis and osteopenia)
  - Sleep disturbances
  - Depression
  - Metabolic syndrome
  - Poor glycemic control and diabetes mellitus
  - Cognitive/other CV disease

**PHYSICAL EXAM**
- Overall energy, muscle mass, and disposition
- Psychological evaluation
- Screen for clinical depression
- Include complete GU exam
- Coronary/CV disease
- Poor glycemic control and diabetes mellitus
- Metabolic syndrome
- Depression
- Sleep disturbances
- Diminution in muscle mass and strength
- Decreased libido
- Decreased mentation
- Decreased energy
- Frailty—decreased grip strength, diminished gait speed, easy fatigue and exhaustion, unintentional weight loss, and low levels for physical activity

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- TT: Diurnal variations so most accurate specimens are obtained in the morning (prior to 10:00 AM)
- “Normal” ranges vary widely by lab and definition of hypogonadism
- General accepted values although there is no clear lab definition of hypogonadism
  - <150 ng/dL with symptoms
  - <200 ng/dL without symptoms
- PDA research trial definition: <300 ng/dL
- Free testosterone
  - <50 pg/mL
- SHBG (sex hormone binding globulin)
  - Increases with aging, which leaves a greater percentage of protein-bound testosterone and lower levels of circulating free testosterone
  - Estradiol: Increased aromatization of testosterone to estradiol in adipose tissue
  - If abnormal TT levels, then check LH and prolactin

- Blood glucose to screen for diabetes mellitus
- PSA for prostate cancer screening
- Monitoring while on testosterone replacement therapy (TRT)
  - CBC to monitor hematocrit (risk of polycythemia)
  - PSA
  - Liver function tests

**Imaging**
- Bone density scan to evaluate for osteoporosis or osteopenia

**Differential Diagnosis**
- Acute critical illness (surgery, head trauma)
- Age-related decline (“Andropause”)
- Alcoholism
- Chronic illness (liver failure, chronic renal failure, hypertension, hypothyroidism, diabetes, sleep apnea, obesity, anorexia nervosa, depression, HIV)
- Hematologic (leukemia, lymphoma)
- Hypoestrogenism of the pituitary, Leydig cells
- Hypothalamic (hypothyroidism)
- Kallmann syndrome (congenital absence of GnRH)
- Klinefelter syndrome
- Medications: LHRH analogs/antagonists, glucocorticoids, anesthetics, estrogen, progesterin (eg, megestrol), chronic opioids, marijuana (controversial)
- Nissenson syndrome
- Pituitary infections, infarction, trauma, radiation (decreased LHRH production)
- Pituitary tumors, macroadenomas, hypophysitis
- Prader–Willi syndrome
- Sertoli cell-only syndrome
- Testicular failure (primary): Congenital or acquired anorchia, cystorchidism, mumps orchitis, radiation therapy, chemotherapy
- Testicular tumors

**DIAGNOSTIC PROCEDURES/SURGERY**
- Prostate biopsy if PSA and DRE are suspicious for prostatic cancer

**Pathologic Findings**

**BASICS**
TREATMENT

GENERAL MEASURES
- Can treat ED with phosphodiesterase-5 inhibitors if no contraindications
  - Avanafil
  - Sildenafil
  - Tadalafil
  - Vardenafil
  - Start at lowest dose and titrate up for efficacy

MEDICATION

First Line
- TRT (3)[B]
  - Intramuscular, transdermal (patches and gels), and buccal preparations. See Section I “Testosterone Replacement Therapy, General Principles” for specifics on TRT agents
  - Selection is dependent on patient/physician preference and feasibility
  - Considerations in the older male: The American Geriatrics Society (AGS) lists testosterone in the Beers Criteria as a medication to generally avoid in older adults because of potential for cardiac problems and men with personal history of prostate cancer (4)[A]
  - The choice of TRT should be individualized on specific clinical needs
  - Absolute contraindications: Personal history of breast cancer or untreated prostate cancer
  - Relative contraindications: Polycythemia, BPH causing urinary retention, treated prostate cancer

Second Line
- N/A

SURGERY/OTHER PROCEDURES
Men with primary erectile dysfunction complaints can discuss surgical placement of penile prostheses, use of vacuum erection devices, or vasoactive intracavernosal injection therapy

ADDITIONAL TREATMENT
- Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- Weight loss
- Weight loss
- Phytotherapies: Limited research on safety and efficacy of herbal medications
- Limited data on ability of any OTC supplement to influence T levels

ONGOING CARE

PROGNOSIS
- TRT is associated with improved responses in many areas
  - Quality of life
  - Mood and affect
  - Sexual function and libido
  - Cognitive function
  - Glycemic control

COMPLICATIONS
- Prostate cancer diagnosis or progression of disease
- Polypharmacy
  - Potential for cardiac and cerebral vascular events

FOLLOW-UP
- Patient Monitoring
  - Hemoglobin and hematocrit
  - Bone mineral density
  - DRE and PSA for prostate cancer screening
  - Continued monitoring of testosterone levels
  - Overall men’s health issues
  - Blood glucose
  - Serum lipids
  - Overall cardiovascular health

Patient Resources
- Urology Care Foundation AUA www.urologyhealth.org/urology/index.cfm?article=132

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Beers Criteria
- Erectile Dysfunction/Impotence, General Considerations
- Hypogonadism, Society Definitions
- Tests, Normal Size
- Testosterone (Free and Total) Lab Testing
- Testosterone Replacement Following Localized Prostate Cancer Therapy
- Testosterone Replacement Therapy, General Principles
- Testosterone, Decreased (Hypogonadism)

CODES

ICD9
- 253.4 Other anterior pituitary disorders
- 257.2 Other testicular hypofunction

ICD10
- E23.0 Hypopituitarism
- E29.1 Testicular hypofunction

CLINICAL/SURGICAL PEARLS
Treatment is based upon symptomatology more than lab values.
ANORECTAL MALFORMATIONS: IMPERFORATE ANUS, CLOACA, AND UROGENITAL SINUS ANOMALIES

Youngae Im, MD
Sang Won Han, MD

BASICS

DESCRIPTION
- Anorectal malformations (ARMs) are a spectrum of congenital anomalies involving the anorectal and urogenital systems, such that the anus and distal rectum are often absent.
- Imperforate anus: Absence of an anus, typically with a fistula between the rectum and lower urinary tract.
- Persistent urogenital sinus (UGS) is seen in 4 entities: (1) Urogenital sinus anomalies (UGS); (2) Pure UGS. With normal external genitalia; (3) Cloaca: In females, a common channel between lower urinary tract, vagina, and rectum; (4) Female eunuchosity

EPIDEMIOLOGY
Incidence
- ARM: 1 in 5,000–5,000 live births
- Cloaca: 1 in 50,000–100,000 live births
- UGS: 1 in 500 live births
- Incidence of ARM in the setting of genetic disease is about 5–10%

Prevalence
N/A

RISK FACTORS
- Proposed association with in utero vascular accidents, maternal diabetes and obesity, maternal ingestion of thalidomide, phenytoin, and caffeine
- Some degree of heritability, as incidence of subsequent children having ARM is 1%

Genetics
- ARM found in certain congenital syndromes with associated genital abnormalities (2)
  - Trisomy 21: Imperforate anus without fistula
  - Microdeletion of chromosome 22q11.2
  - Familial inheritance pattern: ARM with a rectovesical or rectovestibular fistula, almost 15% had a positive family history for an ARM
  - Currarino Trio: ARM, sacral agenesis, presacral mass (or meningocele); autosomal dominant
  - Tessier-Blocks syndrome: ARM, external ear abnormalities, hearing loss, polydactyly, renal anomalies; autosomal dominant
  - Cat eye syndrome: ARM, coloboma, presacral tail, heart defects, urinary tract abnormalities, mental retardation

PATHOPHYSIOLOGY
- Classic theory: The anorectal septum (mesodermic) fails to grow caudally to meet the lateral fetal folds to divide the cloacal membrane (endoderm and ectoderm) into the anterior urogenital membrane and the posterior anal membrane.
- Alternative theory: A mesenchymal mass displaces the dorsal cloacal membrane anteriorly, preventing its joining with the field gut.

ASSOCIATED CONDITIONS
- About 50–67% of all ARM are associated with other anomalies
- In general, the higher the ARM, the more likely there are associated anomalies
- Can occur as an isolated abnormality or as part of a syndrome:
  - VACTERL: Vertebral, anorectal, cardiac, tracheoesophageal fistula, renal, limb anomalies
  - Spinal and bony anomalies are present in 33–50% of ARM:
    - Tethered cord in 20–30%
    - Scoliosis, the most common vertebral anomaly
- Genitourinary abnormalities are common in ARM, but must not be diagnosed until puberty or adulthood
  - Duplicated vagina with septum
  - Absent vagina, vaginal atresia
  - Retractile urethra
  - Hydrometrocolpos in UGS associated with CAH
- Cardiovascular abnormalities are present in 10–30% of ARM:
  - Atrial septal defects and ventricular septal defects are most common
- Tracheoesophageal fistula (TEF) and esophageal atresia (EA) occur in 5–10% with ARM
  - 15% had a positive family history for an ARM

GENERAL PREVENTION
- International Consortium on Anorectal Malformations aims to identify genetic and environmental risk factors in ARM.
- No prevention reduction strategies are currently available.

DIAGNOSIS

HISTORY
- Perianal diagnosis: Low sensitivity/specifcity
  - Dilated colon, oligohydramnios, and distended vagina on prenatal US may be signs of ARM
  - Antenatal findings suggestive of cloacal anomaly:
    - Transient fetal ascites with bilobed or trilobed pelvic cystic structures
    - Bilateral hydrocolonoscopy or oligohydramnios
  - Lower level ARM and UGS may go undiagnosed in newborn until later symptoms develop:
    - Constipation, abdominal distension in rectal atresia, anorectal stenosis
    - Urinary incontinence and/or incontinence in UGS

PHYSICAL EXAM
- Thoroughly examine the perineum to determine number and position of orifices:
  - Perineum flattened in higher level ARM
  - Assess the genitalia: rule out hypospadias, cryptorchidism, chordee
  - Assess vesicourethral: Look for scrotal anomalies
  - Rule out associated pathologies:
    - Cardiac auscultation for murmur
    - Urethrogram: Pull back catheter
  - It may take up to 24 hr for signs of fistula to be evident

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Urinalysis: Abnormal if fistula to urinary tract
  - 17-hydroxy-progesterone in UGS with virilization to rule out CAH
  - Karyotype if ambiguous genitalia

Imaging
- Studies to determine level of ARM:
  - Prone, cross table lateral plain film
  - Should be performed at 24 hr after birth to allow enteric gas to reach the most distal area of the colon
  - Distance between rectal gas shadow and perineal opening measured
- Abdominal US: Evaluate bilateral kidneys, bladder, and urogenital structures
- Voiding cystourethrogram (VCUG)/urogram: Evaluate presence of VUR as well as relation of urinary tract to rectum (and to urogenital structures)
- Cystoscopy: Distal to mucosal fistula and proximal to colostomy to evaluate colonic anal and its relation to other pelvic structures prior to definitive surgery
- Spinal imaging:
  - Spinal US prior to 6 mo of age
  - Spinal MRI after 6 mo of age

Diagnostic Procedures/Surgery
- ECMO: Extracorporeal memmbrane oxygenation
- In general, the higher the ARM, the more likely there are associated anomalies
- UGS: Urogenital sinus anomalies
  - Pure UGS: With normal external genitalia

Pathologic Findings
- Rule out associated pathologies:
  - Cardiac auscultation for murmur
  - Urethrogram: Pull back catheter
Differential Diagnosis
- Classification systems for ARM (5):
  - Wingpread classification: Traditional “low,” “intermediate,” or “high”-ARM
  - Penile classification: Based on the presence and position of the fistula
  - Krickenbeck anatomic classification: An anatomic description of ARM, type of surgical procedure performed, and postop assessment of bowel movements, constipation, and soiling
  - Lesions in the male: Classifying patients (a) into low-lying or higher lesions have important clinical implications with regard to their treatment and prognosis
  - Imperforate anus without fistula, rectal atresia, neorectal fistula
  - Recto posterior urethral fistula
  - Rectovestibular fistula
  - Lesions in the female:
    - In cases of urinary retention, cutaneous vesicostomy may be necessary as newborn
    - In cases of hydrometrocolpos, vaginotomy may be performed, and postop assessment of bowel movements, constipation, and soiling
    - Diverting colostomy with mucous fistula needed in cases of imperforate anus without fistula, rectal atresia, neorectal fistula

TREATMENT

General Measures
- Newborn should not be given any enteric intake and should have nasogastric suction
- Should follow through puberty and child-bearing issues

Medication
- Antibiotics are non-specific and perioperatively
- Prophylactic antibiotics continued at least until VUR IV antibiotics neonatally and perioperatively

Surgery/Other Procedures
- Newborn should have nasal gastric suction
- Should follow through puberty and child-bearing issues
- NGB in many ARM, but rarely due to surgery

Ongoing Care
- Close follow-up needed to manage long-term problems like fecal and urinary incontinence and associated urologic abnormalities
- Should follow through puberty and child-bearing age due to potential for hydrometrocolpos/chromatometra, infertility, ectopic pregnancy, delivery issues

Patient Resources
- http://www.pubmed.gov/anorectal-malformation-treatment

Anorectal Malformations: Imperforate Anus, Cloaca, and Urogenital Sinus Anomalies

References

Additional Reading
- See Also (Topic, Algorithm, Media)
  - Anorectal Malformations: Imperforate Anus, Cloaca and Urogenital Sinus Anomalies Images D
  - Disorders of Sexual Differentiation
  - Exstrophy, Cloacal

ICD-9
- E96.1 Congenital malformation of intestine, unspecified
- 751.5 Other anomalies of intestine

ICD-10
- E25.0 Congenital anorectal disorders associated with anorectal malformations
- Q42.3 Congenital absence, atresia and stenosis of anus without fistula
- Q43.9 Congenital malformation of intestine, unspecified

Clinical/Surgical Pearls
- ARM usually requires neonatal surgical interventions and follow-up to obtain and maintain fecal and urinary continence.
ANORGASMIA, MALE
Robert L. Segal, MD, FRCS(C)
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION
- Anorgasmia is defined as the complete inability to achieve an orgasm (the physical and emotional sensation experienced at the peak of sexual excitation) (1)
- In males, orgasm is typically associated with ejaculation (antegrade semen passage through the urethra)
- There is more robust literature in the female population with anorgasmia
- Also described in some references as orgasmic disorder, orgasmic dysfunction, or orgasmic inhibition
- Anorgasmia is often associated with delayed/inhibited ejaculation or anejaculation, although orgasm and ejaculation are separate phenomena
- Orgasm is a cerebrally mediated event, whereas ejaculation is localized to the genitourinary tract
- Must result in personal distress or interpersonal difficulty according to definitions by the DSM-IV-TR and the World Health Organization Second Consultation on Sexual Dysfunction (2)

EPIDEMIOLOGY
Incidence
- N/A

Prevalence
- Difficult to clearly report, as there is no clear definition of normal ejaculatory latency time
- In general, DE is reported at low rates in the literature, rarely exceeding 3% (3,4), but has been reported in up to 25% of clinical cohorts (2)

RISK FACTORS
- Advancing age
- Endocrinopathies (hypothyroidism, hypogonadism)
- Pelvic trauma/surgery (radical prostatectomy, retroperitoneal, bilateral sympatheticotomy)
- Pelvic radiation therapy
- Neuropathy (multiple sclerosis, diabetes mellitus, spinal cord injury)
- Secondary to medication (thiazide diuretics, tricyclic and selective serotonin reuptake inhibitor [SSRI] antidepressants, alcohol, gabapentin)

PATHOPHYSIOLOGY
- Unless a specific organic cause is noted (see Risk Factors), anorgasmia is associated with underlying psychological factors
- Fear, anxiety, hostility, and relationship difficulties
- It has been suggested to relate to orthodoxy of religious belief (ie, it is sinful to experience sexual pleasure)
- “Performance anxiety” may be a common cause
- May relate to men deriving greater arousal/enjoyment from masturbation than intercourse (2)
- Masturbatory frequency/style may be predisposing factors, as men with coital anorgasmia may report high levels of masturbation (2)
- Alcohol may transiently cause anorgasmia

ASSOCIATED CONDITIONS
- Anejaculation
- Delayed/inhibited ejaculation
- Depression
- Infertility

DIAGNOSIS

HISTORY
- Is the problem lifelong or acquired?
- Sexual history
- Establish the conditions (if any) where the patient is able to experience orgasm
- Assess the presence of life stressors or other psychological factors, the quality of the patient's nonssexual relationship with the partner

Medication use
- SSRIs and gabapentin have been implicated

PHYSICAL EXAM
- Genital exam to verify the presence and normality of testicles and epididymides bilaterally
- Secondary sexual characteristics and hair distribution
- Neurologic exam to assess genital sensation
- May not be contributory

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Serum morning testosterone level
- As indicated
  - Semen analysis
  - Semen culture
  - Urine culture
  - Urine cytology
  - Thyroid screen

Imaging
- Scrotal/transrectal ultrasound if indicated

Diagnostic Procedures/Surgery
- None

Pathologic Findings
- N/A

DIFFERENTIAL DIAGNOSIS
- Psychiatric distress (anxiety, depression)
- Retrograde ejaculation
- Anejaculation
- Delayed ejaculation
- Reduced ejaculation
- Penile hypoesthesia

Genetics
- N/A
ANORGASMIA, MALE

TREATMENT

GENERAL MEASURES
- Treatment should be etiology specific
- May include patient/couple psychoeducation and/or psychosexual therapy
- Pharmacologic treatment has met limited success

MEDICATION
First Line
- None currently FDA approved

Second Line
- No drugs are specifically approved for treatment of anorgasmia, so any treatment is off-label
  - Cyproheptadine (increases cerebral serotonin levels)
  - Amantadine (stimulant of dopaminergic nerves)
  - Bupropion, buspirone, and yohimbine have been anecdotally employed to reverse SSRI-induced anorgasmia

SURGERY/OTHER PROCEDURES
- None

ADDITIONAL TREATMENT
- Radiation Therapy
- None

ADDITIONAL TREATMENT: Radiation Therapy
- None

ADDITIONAL THERAPIES
- Psychotherapy
- Masturbation retraining
- Education on revised sexual techniques which maximize arousal

Complementary & Alternative Therapies
- Yohimbine has utility in anecdotal reports

ONGOING CARE

PROGNOSIS
- Continued support/psychotherapy may be required
- Anorgasmia related to trauma/surgery, radiation therapy, and neuropathies may not be reversible

COMPLICATIONS
- None

FOLLOW-UP
- Patient Monitoring
  - N/A

Patient Resources
- N/A

REFERENCES

ADDISIONAL READING

See Also (Topic, Algorithm, Media)
- Ejaculatory Disorders (Delayed, Decreased, or Absent)
- Erectile Dysfunction, Following Pelvic Surgery or Radiation

CODES
- ICD9
  - 302.74 Male orgasmic disorder
  - 608.89 Other specified disorders of male genital organs
- ICD10
  - P52.23 Male orgasmic disorder
  - N03.11 Retarded ejaculation

CLINICAL/SURGICAL PEARLS
- Anorgasmia is often associated with ejaculatory disorders.
- Unless a specific organic cause is noted, anorgasmia is associated with underlying psychological factors.
- Anorgasmia related to trauma/surgery, radiation therapy, and neuropathies may not be reversible.
- There are no approved pharmacologic treatments for anorgasmia.
Oligoanuria may result from 3 broad categories:
- Nephrotoxic medications
- Myeloma
- Hypertension
- Diabetes mellitus
- Congestive heart failure

Associated with a severe decrease in the glomerular filtration rate (GFR) compromising kidney’s main functions:
- Maintenance of body composition (such as fluid, acid-base, electrolyte content, and concentration)
- Excretion of metabolic end products and foreign substances (toxins, drugs, and diagnostic radiographic contrast)

**BASICS**

**DESCRIPTION**
- Anuria: urine output of < 0 mL/d
- Oliguria: urine output of 50 mL/d or < 50 mL/d
- Often the earliest sign of impaired renal function
- Associated with a severe decrease in the glomerular filtration rate (GFR) compromising kidney’s main functions:
  - Maintenance of body composition (such as fluid, acid-base, electrolyte content, and concentration)
  - Excretion of metabolic end products and foreign substances (toxins, drugs, and diagnostic radiographic contrast)

**Epidemiology**

**Incidence**
- Frequency depends on various clinical settings:
  - 1% at admission
  - 2–5% during hospitalization
  - 4–15% after cardiopulmonary bypass

**Prevalence**

**Risk Factors**
- Chronic kidney disease
- Congestive heart failure
- Diabetes mellitus
- Hypertension
- Myeloma
- Nephrotoxic medications

**GENETICS**

**Pathophysiology**
- Oliguria may result from 3 broad
- pathophysiologic processes: Prerenal, intrarenal, and postrenal causes

**Prevention**
- Pharmacologic responses that lead to decreased GFR:
  - Maintain GFR by afferent arterial dilatation and efferent arteriolar constriction (mediated by angiotensin II)

**Diagnosis**

**History**
- Age, gender
- Duration of symptoms
- Chronic kidney disease
- Diabetes mellitus
- Hypertension
- Cardiac disease
- Liver disease
- Organ transplantation

**Physical Exam**

**Diuretics**
- Burns, trauma, surgery

**Urinalysis**
- Normal, or hyaline casts
- Blood cell casts
- Tubular epithelial cells

**Lab**
- Serum electrolytes
  - Hyponatremia
  - Hyperkalemia
  - Hyperphosphatemia

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Sodium, potassium, bicarbonate, creatinine, blood urea nitrogen, uric acid, calcium, magnesium, phosphorus, protein, cholesterol, triglycerides, glucose, lipid profile, hepatitis panel, antinuclear antibody, rheumatoid factor, prostate-specific antigen, prostate-specific acid phosphatase, urinalysis
- Urine indices
  - Protein: Fractional excretion of sodium (FeNa):< 1%, serum BUN/Cr ratio: < 20:1
  - Intravenous: Nefia: > 1%, serum BUN/Cr ratio: < 20:1
  - Postrenal: Nefia: > 1%, serum BUN/Cr ratio: > 20:1
Imaging
- Renal/bladder ultrasonography: 1st line in imaging, noninvasive, no radiation exposure
  - Hydronephrosis and hydrothorax
- Kidney stones
- Pyelocalyceal system
- Intravenous urography: To evaluate vascular/renal
- Nuclear renal scans (such as technetium 99 m mercaptoacetyltriglycine [MAG3]): To assess the adequacy of renal perfusion and obstructive uropathy
- Intravenous pyelography or intravenous contrast dye generally does not indicate as it may exacerbate renal injury

Diagnostic Procedures/Surgery
- Foley catheter placement: To rule out lower urinary tract obstruction
- Retrograde pyelography with cystoscopy: To define the site and cause of obstruction
- Renal biopsy: To determine intrarenal etiology
- Urodynamic study: To evaluate functional abnormality of the bladder (neurogenic bladder)
- Nuclear renal scans (such as technetium 99 m mercaptoacetyltriglycine [MAG3]): To assess the adequacy of renal perfusion and obstructive uropathy
- Voiding cystourethrogram: To evaluate vesicoureteral reflux
- Duplex Doppler ultrasound: To evaluate the patency of renal artery and vein
- Renal/bladder ultrasonography: 1st line in imaging, noninvasive, no radiation exposure

-- Uremic pericarditis
-- Refractory acidosis
-- Refractory volume overload
-- Refractory hyperkalemia

MEDICATION
First Line
- Parenteral fluids: Usually rapidly reversed following restoring renal perfusion
- Replace fluid with intravenous hydration or blood product transfusion
- Diuretics and low-dose dopamine
- Discontinue the nephrotoxic medications (NSAIDs, ARBs, ACEIs)
- Optimize cardiac output and volume status
- Intravenous: ATN is the most common cause
  - There is no single or sequence of interventions that will significantly improve renal function after onset of ATN [1][A]
  - Use of diuretics and low-dose dopamine
  - Increasing urine output does not shorten the duration of renal failure, decrease the requirement for dialysis or improve survival in patients with established oliguric ARF [2][A]
  - Diuretics may be given for a short length of time for volume control
  - Low-dose dopamine (1–3 μg/kg/min, intravenously) does not reduce mortality or promote the recovery of renal function [4][A]

SURGERY/OTHER PROCEDURES
- Obstructive uropathy: Usually responds to release of obstruction
- There is no single or sequence of interventions that will significantly improve renal function after onset of ATN [1][A]
- Inability to manage electrolytes and fluid balance
- Requirement for renal replacement therapy
- Mortality rate depends on the underlying cause and associated medical condition
- Identification and timely treatment of reversible causes are crucial because the therapeutic window may be small
- In most clinical situations, acute oliguria is reversible and does not result in permanent renal impairment
- Mortality rate depends on the underlying cause and associated medical condition
- Identification and timely treatment of reversible causes are crucial because the therapeutic window may be small
- There is no single or sequence of interventions that will significantly improve renal function after onset of ATN [1][A]

ONGOING CARE
PROGNOSIS
- Mortality rates depend on the underlying cause and associated medical condition
- In most clinical situations, acute oliguria is reversible and does not result in permanent renal impairment
- In most clinical situations, acute oliguria is reversible and does not result in permanent renal impairment
- Identification and timely treatment of reversible causes are crucial because the therapeutic window may be small

COMPLICATIONS
- Nephrotoxic medications (NSAIDs, ARBs, ACEIs)
- Optimize cardiac output and volume status
- Intravenous: ATN is the most common cause
- There is no single or sequence of interventions that will significantly improve renal function after onset of ATN [1][A]
- Use of diuretics and low-dose dopamine
- Increasing urine output does not shorten the duration of renal failure, decrease the requirement for dialysis or improve survival in patients with established oliguric ARF [2][A]
- Diuretics may be given for a short length of time for volume control
- Low-dose dopamine (1–3 μg/kg/min, intravenously) does not reduce mortality or promote the recovery of renal function [4][A]

FOLLOW-UP
Patient Monitoring
- Serial renal function testing for resolution
- Subsequent renal imaging study to confirm the resolution of prerenal obstruction

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Acute Kidney Injury, Adult (Renal Failure, Acute)
- Acute Kidney Injury, Pediatric (Renal Failure, Acute)
- Acute Tubular Necrosis (ATN)
- Anuria or Oliguria Algorithm

CODES
ICD-10
- N19.8 Unspecified disorder of kidney and ureter
- N19.86 Urinary obstruction, unspecified
- N19.80 Oliguria and anuria
- N13.8 Obstructive and reflux uropathy, unspecified
- N12.9 Disorder of kidney and ureter, unspecified
- R34 Anuria and oliguria

ICD10
- N19.8 Unspecified disorder of kidney and ureter
- N19.86 Urinary obstruction, unspecified
- N19.80 Oliguria and anuria
- N13.8 Obstructive and reflux uropathy, unspecified
- N12.9 Disorder of kidney and ureter, unspecified
- R34 Anuria and oliguria

CLINICAL/SURGICAL PEARLS
- Oliguria is often the earliest sign of impaired renal function
- Prompt diagnosis and timely treatment of reversible causes are crucial because the therapeutic window may be small
- Diuretics and low-dose dopamine do not reduce mortality or promote the recovery of renal function

ANURIA AND Oliguria, ADULT
ANURIA AND OLIGURIA, PEDIATRIC
Jennifer A. Hagerty, DO

BASICS
DESCRIPTION
• Typically, 1st sign of impaired renal function
• Anuria: No urine output
• Oliguria: Significantly reduced urine volume
  – <1 mL/kg/h in infants
  – <0.5 mL/kg/h in children

EPIDEMIOLOGY
Incidence
• 10% of newborns in the NICU (1)[C]
• 2–5% of children in the ICU (1)[C]
• 10–30% of children undergoing cardiac surgery (1)[C]

Prevalence
N/A

RISK FACTORS
• Hypovolemia
• Intrinsic renal disease
• Urinary tract obstruction
• Glomerulonephritis
• Nephrotic medications

Genetics
Dependent on diagnosis

PATHOPHYSIOLOGY
Prerenal failure
• Most common cause of oliguria
• Hypoperfusion in otherwise normal kidneys
• Administration of nephrotoxic agents can precipitate oliguria when reduced renal perfusion is present

Intrinsic renal failure
• Associated with structural kidney damage including acute tubular necrosis (ischemia, drugs, or toxins), primary glomerular diseases, or vascular lesions
• Altered tubule cell metabolism leads to ischemia, then altered metabolism and subsequently cell death

Postrenal failure
• Obstructive uropathy
• Usually reversible with relief of the obstruction

ASSOCIATED CONDITIONS
• Pre-existing renal disease
• Obstructive uropathy

GENERAL PREVENTION
• Maintain adequate hydration
• Avoid nephrotoxic agents in children with underlying renal disease

DIAGNOSIS
HISTORY
• Age, sex
• Duration of symptoms
• Pre-existing renal disease
• Medications
• Symptoms of urinary tract obstruction
• Antecedent history
• Family history

PHYSICAL EXAM
• Signs of hypovolemia
  – Tachycardia
  – Hypotension
  – Decreased skin turgor
  – Dry mucous membranes
• Signs of hypervolemia
• Signs of obstructive uropathy
  – Palpable bladder or kidney
  – Urine leukocytosis

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Urinalysis
  – Protein, red cells, casts: Possible glomerulonephritis
  – Low specific gravity: Possible acute interstitial nephritis or intrinsic renal disease
  – High specific gravity: Possible prerenal cause
  – Nitrate: Suggests infection
• Basic metabolic panel
  – BUN/Cr ratio: >20 suggests prerenal cause
  – Evaluate renal function and electrolyte balance

Imaging
• Renal and bladder ultrasound for hydronephrosis and bladder distention and thickening of the wall
  • VCUG for suspected bladder outlet obstruction
  • Nuclear renal scan for function, diastasis, and drainage

Diagnostic Procedures/Surgery
Placement of a urethral catheter

Pathologic Findings
Dependent on diagnosis

DIFFERENTIAL DIAGNOSIS
• Prerenal
  – Burns
  – Dehydration
  – Drugs
  – GI losses
  – Heart disease
  – Hemorrhage
  – Respiratory distress syndrome
  – Shock/leaks
• Intrinsic renal disease
  – Acute tubular necrosis
  – Exposure to nephrotoxins (drugs, myoglobin, uric acid)
• Congenital kidney disease
• Renal vascular abnormalities
• Glomerulonephritis
• Urinary tract obstruction
• Neoplastic bladder
• Posterior urethral valves
• Meatal stenosis
• Bilateral UPJ or ureteral obstruction or unilateral in a solitary kidney
• Bilateral obstructing calculi

TREATMENT
GENERAL MEASURES
• Treatment of the underlying cause
• Appropriate medical management for acid-base disorder, fluid imbalance, electrolyte imbalance (such as hyperkalemia, hyperphosphatemia, hypocalcemia)
• Strict volume monitoring of input and output
• Avoidance of nephrotoxic agents (NSAIDs, ARBs (angiotensin receptor blockers), ACEIs (angiotensin-converting enzyme inhibitors))

MEDICATION
First Line
• Hydration to optimize cardiac output and volume status

Second Line
• Diuretics considered if adequate intravascular volume status and patient remains oliguric
• Hemodialysis or peritoneal dialysis to be considered if severe electrolyte abnormalities or volume overload
**SURGERY/OTHER PROCEDURES**
Relief of obstruction with urethral catheter, ureteral stenting, or nephrostomy tube

**ADDITIONAL TREATMENT**
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
None

**ONGOING CARE**

**PROGNOSIS**
- Acute oliguria is often completely reversible if recognized and treated promptly
- Small increases in serum creatinine can be indicative of worsening outcome [26]

**COMPLICATIONS**
- Progression to permanent renal injury
- Infections secondary to uremia leading to impaired defenses
- Cardiovascular complications secondary to fluid overload and electrolyte abnormalities
- Neurologic changes: Confusion, lethargy, and seizures
- Gastrointestinal effects: Anorexia, nausea, and vomiting

**FOLLOW-UP**

**Patient Monitoring**
- Serial renal function testing until resolution of anuria/oliguria
- Imaging based on diagnosis
  - Monitor renal/bladder ultrasound for obstructive uropathy

**Patient Resources**
- American Society of Pediatric Nephrology: www.aspneph.com
- National Kidney Foundation: www.kidney.org

**REFERENCES**

**ADDITIONAL READING**

**See Also** (Topic, Algorithm, Media)
- Acute Kidney Injury, Adult
- Acute Kidney Injury, Pediatric
- Chronic Kidney Disease, Pediatric
- Posterior Urethral Valves
- Ureteropelvic Junction Obstruction
- Urinary Retention, Pediatric

**CODES**

**ICD9**
- 276.52 Hypovolemia
- 599.60 Urinary obstruction, unspecified
- 788.5 Oliguria and anuria

**ICD10**
- E86.1 Hypovolemia
- N13.9 Obstructive and reflux uropathy, unspecified
- R34 Anuria and oliguria

**CLINICAL/SURGICAL PEARLS**
- Prerenal oliguria is typically reversible with complete return of renal function within 24–72 hr.
- Avoid nephrotoxic agents in patients with underlying intrinsic renal failure.
AUTONOMIC DYSREFLEXIA
Michael J. Amirian, MD
Patrick J. Shenot, MD, FACS

BASICS

DESCRIPTION
Autonomic dysreflexia (AD) occurs in patients with spinal cord lesions at and above the 6th thoracic level (T6).

– Potentially life-threatening condition in response to noxious stimuli.

– Spinal cord lesions at and above the 6th thoracic level (T6) are most common causes to trigger AD

– Rapid, external BP elevation, bradycardia, headache, diaphoresis, sweating, nausea, and piloerection

EPIDEMIOLOGY
Incidence
Unknown

Prevalence
• ~85% of quadriplegic and high paraplegic individuals prone to AD in response to noxious stimuli

• More common in men than women

• Due to increased bladder outlet resistance

RISK FACTORS

– Male

– High spinal cord injury (SCI)

Genetics
None

PATHOPHYSIOLOGY

– Activation of sympathetic neurones in lateral horn of spinal cord causing unopposed reflex sympathetic activity

– Stimulate bladder or bowel distention and pain

– Vasodilatation and subsequent hypertension (HTN)

– In response, vagal nerve triggers bradycardia

– Vagal nerve is able to vasodilate above injury (flushing in face), but vessels below injury remain vasoconstricted

– Other symptoms of sympathetic activation

– Diaphoresis and piloerection

ASSOCIATED CONDITIONS
SCI

GENERAL PREVENTION

– Avoid rapid or prolonged bladder distention

– Maintain regular schedule of bowel emptying

– Monitor for pressure sores

DIAGNOSIS

HISTORY

– SCI or transverse myelitis at T6 or above

– Known for urologic causes

– Bladder distention

– Recent instrumentation

– Indwelling urethral or suprapubic tube

– Urinary tract infection (UTI)

– Nerve, urethral, or bladder calcification

– Epididymitis or orchitis

– Fracture

– Bladder outlet obstruction

– Hypertension

– Pheochromocytoma

– Brain stem tumors

– Malignant hypertension

– Renal, ureteral, or bladder calculi

– Urinary tract infection

– Indwelling urethral or suprapubic tube

– Recent instrumentation

– Male

– Females

– Pregnancy and labor

– Sexual intercourse

– Ingrown toenails

– Tight clothing

– Pressure sores

– Bowel distention

– Urodynamic testing

– Bladder distention

– Pressure sores

– Tight clothing

– Inguinal hernia

– Sexual intercourse

– Pregnancy and labor

– Symptoms may include blurred vision, nasal congestion, anxiety, HTN in this patient population

PHYSICAL EXAM

– BP often severely elevated and often accompanied by diaphoresis and piloerection

– A normal BP of 120/80 may actually represent “Bite and swallow” technique

– A BP 20–40 mmHg above the patients baseline

– Consider that the resting BP is decreased after SCI

– Flushing and profuse sweating above level of injury

– Skin congestion, anxiety

DIAGNOSTIC TESTS & INTERPRETATION

Lab

– Urinalysis and urine culture

– Evaluate for infection

– UTI can be a trigger for AD

Imaging

– CT of abdomen and pelvis

– Evaluate for urolithiasis if cause not apparent

– Urodynamic tests

– Evaluate bladder compliance

– Risk out persistently elevated bladder pressures

Pathologic Findings

None

DIFFERENTIAL DIAGNOSIS

– Brain stem tumors

– Paracoccyeal HTN

– Pheochromocytoma

– Preeclampsia

TREATMENT

GENERAL MEASURES

– Removal of triggering stimulus is the 1st step

– MINIMIZE noxious stimuli below level of injury

– Bladder drainage or bowel decompression

– If present, consider gentle Foley catheter irrigation with no more than 10–20 mL saline to make sure that the catheter is patent

– Monitor BP closely during acute episodes

– BP >150 mmHg requires urgent management to avoid severe complications

– Siting the patient upright might reduce BP

– Tadalafil) for erectile dysfunction

– Nitrates: Sub lingual nitroglycerine, apply 1”, 2% nitro paste

– Nitrates should be avoided in patients who may be using PDE-5 inhibitors (sildenafil, vardenaft, tadalafil) for erectile dysfunction

– Nifedipine 10 mg PO immediate release form

– “Bite and swallow” technique

– Captavil 25 mg IV

– Hydralazine or Labetalol 10 mg IV

– Chronic treatment with α-blockers may improve some symptoms of AD (T6)

– Doxazosin 2–8 mg PO QD

– Terazosin 2–8 mg PO QD

– Salmeterol 6.4 mg PO QD

– Allopurinol 10 mg PO QD

– Appropriate antibiotics if UTI suspected

Second Line

– Phenylephrine 10 mg PO BD

– Botulinum toxin injection into the detrusor

– For patients on intermittent catheterization to decrease bladder pressure

– Botulinum toxin injection into external sphincter

– For patients who wish to relieve pain to decrease voiding pressures

ALERT

Left untreated consequences of autonomic dysreflexia can cause seizures, intracranial bleeds, hypertensive encephalopathy, and death.

MEDICATION

First Line

– Acute episodes managed with nitrites or arterial dilators under closely monitored conditions

Second Line

– Doxazosin 2–8 mg PO QD

– Terazosin 2–8 mg PO QD

– Salmeterol 6.4 mg PO QD

– Allopurinol 10 mg PO QD

– Appropriate antibiotics if UTI suspected

– Phenylephrine 10 mg PO BD

– Botulinum toxin injection into the detrusor

– For patients on intermittent catheterization to decrease bladder pressure

– Botulinum toxin injection into external sphincter

– For patients who wish to relieve pain to decrease voiding pressures

ACUTE PHASE

– Intramuscular injection of glyceryl trinitrate

– Labetalol 100 mg IV

– Sildenafil 50 mg PO

– Hydralazine 10 mg IV
A

SURGERY/OTHER PROCEDURES
- Sphincterotomy or sphincter-stent prosthesis
  - Allows reflex voiding with low-pressure bladder emptying into a condom catheter (2)(A).
- Bladder augmentation
  - Only in patients with ability to catheterize
- Sacral rhizotomy
  - For severe cases (3)(B)

ADDITIONAL TREATMENT
Radiation Therapy
N/A
Additional Therapies
N/A
Complementary & Alternative Therapies
N/A

ONGOING CARE
PROGNOSIS
Managed effectively will have little impact on patient

COMPLICATIONS
Intracerebral and subarachnoid hemorrhage

FOLLOW-UP
Patient Monitoring
- Clean intermittent catheterization
  - Frequent (at least 4 times daily)
- Regular bowel program
- Assess AD symptoms and BP at every appointment
- Teach SCI patients significance of AD
  - Symptoms should prompt patients to empty bladder and bowel

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Autonomic Dysreflexia Image 10
- Detrusor-Sphincter Dyssynergia
- Spinal Cord Injury

CODES
ICD9
- 337.3 Autonomic dysreflexia
- 596.89 Other specified disorders of bladder
- 599.0 Urinary tract infection, site not specified

ICD10
- G90.4 Autonomic dysreflexia
- N32.89 Other specified disorders of bladder
- N39.0 Urinary tract infection, site not specified

CLINICAL/SURGICAL PEARLS
- Most common triggers are from the genitourinary system such as bladder distention or instrumentation.
- AD occurs at and above level of T6.
- Chronic treatment with α-blockers may improve some symptoms of AD.
- Sphincterotomy or sphincter stent prosthesis allows reflex voiding with low-pressure bladder emptying into a condom catheter.
Epidemiology
Incidence (1)
- 0.3–0.5 episodes of bacteriuria per person per year among asymptomatic females aged 18–45
- Neonates: 1/105 (1–2 cases/100000 births)
- School age: Males: 0.04–0.2%; females: 0.7–2.7%
- Adult (involuted): Males <1%; females 4–6%
- Older adults: Males 11–13%; females 6–33%
- Almost 100% prevalence of bacteriuria in individuals with long-term, indwelling catheters

Prevalence
- Pregnancy: 2–7% of all pregnant females (2)
- Elderly: 20% of females, 10% of males (1)
- Pregnancy: 2–7% of all pregnant females (2)

Risk Factors
- Age, diabetes mellitus, sexual intercourse, use of diaphragm or spermaticide, delayed postpartum evacuation, history of recent infection, immunosuppression, long-term indwelling catheters, pregnancy, neurologic disorders, foreign bodies, stones, obstructive uropathy, telescopel reflux

Genetics
- Certain populations may be more susceptible to bacteriuria and recurrent UTI due to distinct molecular defects causing impaired host responses.
- Certain bacteria are more efficient at adhering to mucosal cells than others due to fimbria.
- Certain bacteria may be more efficient at adhering to mucosal cells than others due to fimbria.
- Cystitis prone: Certain patients are more prone to bacteriuria (transitional cell bacterial receptor sites).
- Cystitis: Clinical syndrome of dysuria, frequency, urgency occasionally with suprapubic pain.

Pathophysiology
- Urinary tract is normally sterile.
- Bacteriuria can also invade the urinary tract hematogenously or through direct transfer after instrumentation.
- Bacteriuria usually ascends up the urinary tract from the colonizing flora of the gut, vagina, or distal urethra.

Diagnosis
- History of childhood fevers: May imply UTIs and associated congenital abnormalities
- Problems with toilet training, urgency, incontinence
- U/S family history: Mothers, daughters, sisters
- History of a risk factor for bacteriuria

Physical Exam
- Suprapubic tenderness: Pyelonephritis
- Fever: Usually with upper tract infection
- Problems with toilet training, urgency, incontinence
- Children may have abdominal discomfort, tenderness, or distention

Diagnostic Tests & Interpretation
- Urine dipstick: Best for screening:
  - Leukocyte esterase test: 70–80% sensitivity for UTI
  - Pregnancy test: Can be used to differentiate infection from pregnancy

Microscopy:
- Rapid in-office test: 80% accurate, usually fresh sample
- Contains: Leukocytes, bacteria, erythrocytes,casts

Associated Conditions
- Diabetes mellitus, pregnancy, immunosuppression, structural urinary tract abnormalities, indwelling catheters

General Prevention
- Screening and treatment of asymptomatic bacteriuria in at-risk populations such as pregnant patients or prior to urologic intervention can prevent subsequent morbidity of 10%.
- Screening of asymptomatic spinal cord injury patients or those with indwelling Foley catheter is not recommended.

Bacteriuria and pyuria from an incompletely treated UTI may be avoided with the appropriate use of antibiotic class with sufficient duration; patient compliance should be encouraged.
DIFFERENTIAL DIAGNOSIS

- **Cystitis**: Pyuria, positive culture, abrupt onset
- **Unthritis**: Pyuria, negative urine culture, gradual onset
- **Vaginitis**: No pyuria, vaginal discharge, pruritus
- **Pyelonephritis**
- **Nephrolithiasis causes**: as in sterile pyuria
- **Contamination with vaginal/vulvar flora**

Diagnostic Procedures/Surgery

- **Localization of bacteria**: Segmented urine, ureteral catheterization
- **Immunologic antibody studies**

TREATMENT

**GENERAL MEASURES**

- **Obtain urine culture**: Indwelling catheters should be used as infrequently as possible
- **In patients with indwelling catheter**: urine specimen for culture should be obtained at the time catheter is changed under sterile conditions

**MEDICATION**

- **Asymptomatic bacteriuria is treated as a UTI in childhood, prior to urologic surgery, and in pregnancy**

**ADDITIONAL TREATMENT**

- **Radiation Therapy**

**ONGOING CARE**

- **Follow-up**: Repeat exam 2 wk posttreatment, not necessary in young women who are asymptomatic after therapy

**COMPLICATIONS**

- **Microscopic pyelitis and culture**
- **Periodic office visits to verify sterile urine**

**REFERENCE**


**ADDITIONAL READING**

BALANITIS AND BALANOPOSTHITIS
H. Henry Lai, MD, FACS
Gerald L. Andriole, MD, FACS

BASICS

DESCRIPTION
- Balanitis: Inflammation of the glans penis.
- Balanoposthitis: Inflammation of the foreskin and glans penis (affects uncircumcised men).

EPIDEMIOLOGY

Incidence
- Can occur at any age.
- No incidence studies of balanoposthitis have been reported in US.
- 1.5% of uncircumcised boys ages 0–15 were affected in a Japanese cohort.

Prevalence
- Common, the exact prevalence is unknown.
- Balanitis affects 11% of adult men and 3% of boys seen in urology clinics.

RISK FACTORS
- Presence of a foreskin (uncircumcised)
- Tight foreskin (phimosis)
- Poor genital hygiene
- Intertrigo (see below)
- Sexual contact (with or without infection)
- Poorly controlled diabetes mellitus
- Immunocompromised host
- Coexisting penile cancer

GENETICS
- N/A

PATHOPHYSIOLOGY

- The pathophysiology is usually different in young boys compared to adult men:
  - Boys: From bacterial invasion of tissue
  - Men: Combination of poor genital hygiene, intertrigo, irritant dermatitis, maceration injury, and bacterial, or candidal overgrowth
- Candida is the most common infectious cause
- Intertrigo refers to a condition in which damp, moist body areas are predisposed to inflammation:
  - Involves genitals, inner thighs, underbelly
  - Risk factors: Grossly overweight, diabetes, bed rest, diaper use, poor personal hygiene

ASSOCIATED CONDITIONS
- Diabetes mellitus

GENERAL PREVENTION
- Maintain good genital hygiene
- Retraction of foreskin to clean the glans
- Keep the glans and foreskin dry
- Circumcision
- Safe sexual contact
- Manage risk factors (eg, glycemic control)

DIAGNOSIS

HISTORY
- Symptoms may include: Pain, discharge, irritation, voiding symptom (dysuria, weak stream)
- Prior episodes and treatment
- Uncircumcised
- Foreskin retractability
- Genital hygiene habits
- Sexual contacts, sexually transmitted diseases
- Other genitourinary risk factors (eg, diabetes)

PHYSICAL EXAM
- Inspection (ulcers, mass, genital pus, edema)
- Palpation (tenderness, induration, mass)
- Inguinal lymph nodes should be nonpalpable

TREATMENT

GENERAL MEASURES
- Meticulous genital hygiene
- Keep the glans and foreskin clean and dry
- Expose the glans to air as often as possible
- Avoid excessive dampness in the genitals
- Avoid soaps while inflammation is present
- Cleaning with soap and water routinely
- Manage risk factors (eg, glycemic control)

MEDICATION
- Treatment depends on the underlying cause (infectious vs. inflammatory) and organisms

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis
- Serology for syphilis
- Venereal disease research laboratory (VDRL) or rapid plasma reagin (RPR)
- Herpes simplex virus (HSV)–1 and –2
- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Hepatitis A, B, and C
- Human immunodeficiency virus (HIV)
- Human T-lymphotropic virus type I (HTLV-I)
- Mycoplasma genitalium
- Ureaplasma urealyticum
- Trichomonas vaginalis
- Cytomegalovirus
- Enteroviruses
- Syphilis serology
- West Nile virus
- Human papillomavirus (HPV)

Imaging
- None

Diagnostic Procedures/Surgery
- Potassium hydroxide and Tzanck preparation for men
- Circumcision
- Potassium hydroxide smear evaluates for fungus
- Tzanck preparation for herpes virus

Pathologic Findings
- Biopsy is indicated for:
  - Balanitis that persists and in which the cause remains unclear warrants biopsy to rule out coexisting neoplasm or premalignant lesions
  - For definitive diagnosis of BXO

DIFFERENTIAL DIAGNOSIS
- Fixed drug eruption (allergic)
- Contact dermatitis
- Squamous cell carcinoma of the penis
- Carcinoma in situ of the penis
- Zoon (plasma cell) balanitis
- Psoriasis
- Reiter syndrome (Reactive arthritis/reactive arthritis triad) (with circinate balanitis)
- Human papilloma virus

42
**Balanitis and Balanoposthitis**

**First Line**
- **Candidal infection:** The most common cause of infectious balanitis.
  - Clotrimazole cream 1%
  - Miconazole cream 2%
  - Apply BID until symptoms resolve
  - Oral fluconazole if symptoms are severe
  - Nystatin cream if allergic to imidazole
  - Imidazole with hydrocortisone if inflammation

- **Anaerobic infection:**
  - Metronidazole 400 BID for 1 wk
  - Optimal dosage schedule is unknown
  - Alternatively, amoxicillin/clavulanic acid PO or clindamycin topically

- **Aerobic infection:**
  - Group A streptococci, Staphylococcus aureus, Gardnerella vaginalis are all reported cases of balanitis.
  - Treatment based on sensitivity of the culture (topical antibiotics, occasionally oral antibiotics)

- **BXO:**
  - Topical steroids (clobetasol propionate or betamethasone valerate) offers limited efficacy

- **Zoon (plasma cell) balanitis:**
  - Topical steroids with or without antibacterial cream

- **Circinate balanitis (Reiter syndrome):**
  - Hydrocortisone cream 1% apply BID
  - Treatment of associated infection

- **Irritant, allergic balanitis:**
  - Avoid exposure to irritants especially soaps
  - Emollients aqueous cream: Apply PRN and used as a soap substitute while inflammation is present
  - Hydrocortisone 1% apply QD or BID until symptoms resolve

**Second Line**
- **Radiation Therapy**
- **Additional Therapies**
- **Complementary & Alternative Therapies**

**Surgery/Other Procedures**
- Circumcision is reserved for recurrent balanitis, balanoposthitis, or phimosis that have failed conservative treatments.
- Occasionally dorsal slit may be performed.
- For BXO that does not respond to steroid.

**Surveillance**
- After acute episode and treatment is implemented, patients should be seen again to ensure resolution of symptoms and infection.
- Progression to cellulitis or gangrene may occur in diabetic patients with genital infection.
- Follow closely with genital dysplasia among those men with condyloma with a history of balanoposthitis than those with no such history.

**Patient Monitoring**
- Progression to cellulitis or gangrene may occur in diabetic patients with genital infection.
- Follow closely with genital dysplasia among those men with condyloma with a history of balanoposthitis than those with no such history.

**REFERENCES**

**ADDITIONAL READING**

**See Also**
- Balanitis and balanoposthitis image (p)
- Balanitis xerotica obliterans
- Balanitis, Zoon (Plasma Cell Balanitis)
- Lichen Sclerosis Et Atrophicus
- Penis, Lesion

**CODES**
- **ICD9**
  - 605 Redundant prepuce and phimosis
  - 607.1 Balanoposthitis
  - 607.81 Balanitis xerotica obliterans

- **ICD10**
  - N47.1 Phimosis
  - N47.6 Balanoposthitis
  - N48.1 Balanitis

**Clinical/Surgical Pearls**
- Maintaining good genital hygiene is a key preventive strategy (keep the foreskin and glans clean and dry).
- Underlying risk factors should also be managed (eg, glycemic control) in diabetes.
- Treatment depends on the underlying cause (infectious vs. inflammatory) and organisms.
- Circumcision is reserved for recurrent balanitis, balanoposthitis, or phimosis that have failed conservative treatments.
- Balanitis that persists and if the cause remains unclear warrants biopsy to rule out coexisting neoplasm or premalignant lesions.
BCG SEPSIS/BCG-OSIS

John B. Eifler, MD
Michael S. Cookson, MD

BASICS
DESCRIPTION
- BCG sepsis: Potentially life-threatening event secondary to intravasation of intravesical BCG resulting in cardiovascular collapse and acute respiratory distress
- Possible etiologies include hypersensitivity reaction and bacterial sepsis
- "BCG-osis" is a term used to refer to disseminated disease in patients treated with BCG
  - The lungs and liver are typically involved
  - Patients are usually hemodynamically stable

EPIDEMIOLOGY
Incidence
- >95% of patients treated with BCG have no significant morbidity (1)
- 1 in 15,000 patients treated with intravesical BCG will develop BCG sepsis (2)
- 10 reported deaths due to BCG sepsis (3)

Prevalence
N/A

RISK FACTORS
- Inadequate delay after transurethral instrumentation (TURBT or bladder biopsy)
- Traumatic catheterization or gross hematuria at time of intravesical instillation

GENETICS
N/A

PATHOPHYSIOLOGY
- BCG is live attenuated Mycobacterium bovis
- Intravasation of BCG through damaged urothelium with subsequent systemic response
- Symptoms may be related to mycobacterial infection and/or hypersensitivity reaction

ASSOCIATED CONDITIONS
- Recent transurethral instrumentation
- Traumatic catheterization
- Concomitant UTI
- Age >70

ASSOCIATED MEASURES
- Consultation with infectious disease specialist is recommended for septic patients (2)
- If antitubercular therapy required, intravesical BCG should be discontinued (2)

LAB DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Mild/moderate symptoms
  - Urine culture
  - Severe symptoms (Septic, severe cystitis symptoms >48 hr)
    - Urine, blood cultures
    - Liver function tests to assess for hepatitis
    - CXR to assess for pneumonitis
    - Acid-fast testing of urine
    - Consider PCR testing for mycobacterial DNA if disseminated BCG suspected
- Coagulation studies: PT/PTT/ fibrinogen if DIC suspected

Imaging
- See “Lab

Pathologic Findings
- Noncaseating granulomas
  - May be found in lung, liver, bone, prostate, kidney, epididymis

DIFFERENTIAL DIAGNOSIS
- Post-BCG bacterial cystitis
- BCG cystitis (cytokine release without intravasation of BCG)
- Gram-negative sepsis

TREATMENT
GENERAL MEASURES
- Consultation with infectious disease specialist is recommended for septic patients (2)
- If antitubercular therapy required, intravesical BCG should be discontinued (2)

MEDICATION
First Line
- Mild/moderate symptoms including low-grade fevers
  - Fluoroquinolone
    - Such as levofloxacin 500 mg
    - Helpful for bacterial cystitis and has mild antitubercular activity
- Neutropenic
  - SUCH AS Levofloxacin 500 mg
- Such as levofloxacin 500 mg
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSAIDs
  - All NSF
Antitubercular medications should be initiated for signs of sepsis or severe cystitis symptoms (>48 hr)

- Typically isoniazid 300 mg/d and rifampin 600 mg/d for 3–6 mo
- For solid organ involvement, ethambutol 15 mg/kg/d added
- BCG resistant to cycloserine and pyrazinamide
- Prednisone 40 mg/d recommended for septic shock or if hypersensitivity reaction suspected

**Second Line**

**SURGERY/OTHER PROCEDURES**

N/A

**ADDITIONAL TREATMENT**

**Radiation Therapy**

N/A

**Additional Therapies**

N/A

**Complementary & Alternative Therapies**

N/A

**ONGOING CARE**

**PROGNOSIS**

Good if treatment initiated in timely manner

**COMPLICATIONS**

Solid organ involvement

**FOLLOW-UP**

Patient Monitoring

IU admission with invasive monitoring for BCG sepsis

**Patient Resources**

N/A

**REFERENCES**


**ADDITIONAL READING**


**See Also (Topic, Algorithm, Media)**

- Bladder Cancer, General
- Bladder Cancer, Nonmuscle-Invasive Bladder Cancer (Ta, T1)
- Bladder Cancer, Urothelial, Superficial Carcinoma in Situ (CIS) (NMIBC)
- Urosepsis

**CODES**

**ICD9**

- 038.8 Other specified septicemias
- 995.91 Sepsis
- 995.39 Infection following other infusion, injection, transfusion, or vaccination

**ICD10**

- A41.89 Other specified sepsis
- T80.29KA Infct fol oth infusion, transfuse and therapeutic inject, iv

**CLINICAL/SURGICAL PEARLS**

- Patients undergoing intravesical BCG therapy who have traumatic catheterization or gross hematuria should delay therapy until symptoms resolve.
- Patients with high fever (>38.5°C/101.3°F) or severe cystitis symptoms lasting >48 hr should be hospitalized and undergo additional testing.
ASSOCIATED CONDITIONS
Pathophysiology
• May result from primary detrusor muscle failure (myogenic causes) and/or neurologic cause (eg, from lower motor neuron lesions, injury to spinal cord, multiple sclerosis).
• Patients often attempt to void by valsalva.
• Success of emptying depends on resistance of smooth and striated sphincter mechanisms.
• Continence depends on sphincter competence.

ASSOCIATED CONDITIONS
• Cause acute syndrome
• Diabetes mellitus
• Fowler syndrome (“nonneurogenic, neurogenic bladder”)
• Intervertebral disc diseases
• Longstanding bladder outlet obstruction with detrusor decompensation (myogenic failure)
• Lumbar sacral spinal surgery

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Blood: Creatinine to assess renal function.
• Urine: Urinalysis to assess renal infection.

Imaging
• Renal and bladder ultrasound (to assess renal stones, hydronephrosis).
BLADDER AREFLEXIA (DETROUSOR AREFLEXIA)

SURGERY/OTHER PROCEDURES
- Sacral neuromodulation (InterStim) in selected patients who do not have contraindications.
  - Effective in restoring voiding in patients with Fowler syndrome (1)
  - May be selectively considered in patients with nonobstructive urinary retention (2)
- Bladder augmentation may be considered in patients with poor detrusor compliance, and high detrusor leak point pressure and storage pressure.

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

ONGOING CARE
PROGNOSIS
- Most cases are irreversible, except the few circumstances described in “Differential Diagnosis”
- However, with proper urologic management, secondary complications may be minimized.

COMPICATIONS
- Bladder neoplasm from indwelling catheter
- Hydrophrosis and hydronephrosis
- Recurrent urinary tract infections
- Renal and bladder stones
- Renal insufficiency, failure, and dialysis
- Urethral erosion from chronic Foley catheter
- Urinary incontinence
- Urosepsis and death

FOLLOW-UP
Patient Monitoring
- Patients with poor detrusor compliance need periodic urodynamics studies, upper tract imaging, and urinary lab work to minimize complications.
- Patients who refuse to catheterize should be monitored closely.
- Patients with chronic indwelling catheter should undergo uroscopy periodically due to the increased risk of bladder neoplasm.

Patient Resources
- N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Bladder Areflexia (Detrusor Areflexia) Image
- Neurogenic Bladder, General Considerations
- Sacral Neuromodulation
- Spinal Cord Injury, Urologic Considerations
- Urodynamics, Indications, and Normal Values

CODES
ICD9
- 596.55 Detrusor sphincter dysynergia
- 788.39 Other specified retention of urine
- 798.38 Overflow incontinence

ICD10
- R33.8 Other retention of urine
- N36.44 Muscular disorders of urethra
- N39.490 Overflow incontinence

CLINICAL/SURGICAL PEARLS
- Detrusor areflexia requires urodynamics for diagnosis.
- Urodynamics can distinguish detrusor areflexia from bladder outlet obstruction.
- Intermittent catheterization is preferred over chronic indwelling catheters.
- Sacral neuromodulation (InterStim) may be selectively considered in patients with nonobstructive urinary retention or Fowler syndrome.
- Patients with chronic indwelling catheter should undergo uroscopy and urine cytology periodically due to the increased risk of bladder neoplasm.
BLADDER CALCULI (VESICAL CALCULI)

Mohamed S. Ismail, MBChB, MRCS, PhD
Francis Xavier Keeley, Jr., MD, FRCS

DESCRIPTION
Bladder calculi (also called bladder stones) are calcified material that are present in the bladder.
- It can originate primarily in the bladder.
- It can be a secondary renal stone that has formed in the kidney and passed into the bladder.
- Often associated with bladder outlet obstruction in the US.
- Historically the removal of bladder calculi was performed via an incision in the perineum with the patient in a supine position and the hips elevated (the origin of the term “lithotomy position”).

Epidemiology
Incidence
- The incidence of bladder calculus in the Western world has significantly dropped as a result of improved diet, nutrition, and infection control.
- Bladder calculi are endemic in Thailand, Burma, Indonesia, Middle East, and North Africa.
- Mostly in middle age men.
- In catheterized patients: The incidence of developing bladder calculus is 25% in 5 yr.
- The incidence in children has declined significantly in the developing countries; they are common in boys younger than 11 yr.
- Vaginal prolapse and urothelial surgery are common causes in women.

Prevalence
- Bladder calculus constitute 10–15% of the stone burden in adult and 15–30% in children.
- Data on the world-wide incidence are not available.

Risk Factors
- Urinary stasis
  - Bladder outlet obstruction
  - Benign prostatic hyperplasia
  - Urethral stricture
- Neurogenic bladder
- Foreign body such as urethral catheter and ureteric stent that act as nucleus for stone formation
- Urinary tract infection
- Urinary diversion and bladder substitution
  - Secondary to foreign body, infection, and systemic ailments
- Rarely patients may place foreign bodies in bladder that become calcified.

Genetics
N/A

PATHOPHYSIOLOGY
Bladder calculi are primarily formed in the bladder, rarely can be a secondary renal stone that has formed in the kidney and passed into the bladder.
- Foreign bodies, retained catheter bulbous fragments
- Patients with chronic intermittent catheterization may force pubic hair into the bladder that can become calcified over time.
- Stone analysis frequently reveals uric acid stone in 50% of the cases.
- Other constituents are ammonium urate, calcium oxalate, and calcium phosphate.
- In infected urine, struvite stones are the most common.
- In patients with spinal cord injury (SCI), bladder stones are often composed of struvite or calcium phosphate.
- In endemic areas, low phosphate diet results in increased ammonium excretion in the urine.
- Low intake of animal protein contributes to high urinary oxalate and low urinary citrate levels with increased risk of stone formation.
- Solitary stone are present in 75% of cases.

Associated Conditions
- Foreign bodies in the bladder
- Intermittent catheterization
- Low phosphate diet
- Urinary stasis (prostatic hyperplasia, stricture, congenital abnormalities [ureterocele], diverticulum, cystocele)
- Urinary tract infection

GENERAL PREVENTION
- Adequate hydration
- Treatment of bladder outlet obstruction
- Prevention of urinary tract infection
- Prevention of uricosuric as appropriate
  - Allopurinol for uric acid stones
- Reduce oxalate intake
- Increase urinary citrate
- Low sodium low protein diet

DIAGNOSIS

HISTORY
- Patients with SCI, neurogenic bladder may be at increased risk.
- Bladder calculi may be asymptomatic and may be incidental finding on imaging (plain x-ray, renal ultrasound, CT, or flexible cystoscopy).
- Patients commonly presents with:
  - Suprapubic or perineal pain
  - Irritative urinary symptoms
  - Intermittent urinary stream
  - Hematuria, gross, and microscopic
  - Resistant urinary tract infection

PHYSICAL EXAM
- Examine the abdomen for palpable bladder or kidney.
- Examine the external genitalia for any abnormalities (ureterocele) that may contribute to outlet obstruction.
- Digital rectal exam to assess for BPH and prostate cancer.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urine analysis: Hematuria, leukocytes, and crystalluria may be present
- Urine culture and sensitivity in case of suspected infection
- Urine cytology in the presence of calculi is nonspecific
- Serum creatinine
- Stone analysis should be considered when removed

Imaging
- Calculi stones can be visible on plain x-ray (KUB)
- Stones may be densely radiopaque
- Occasionally laminations may be visible on plain x-ray
- Uric acid and ammonium urate stones are radiolucent but will be seen on ultrasounds or CT scans.
- Bladder calculi may not be visible on MRI
- CT without contrast is highly sensitive and specific to detect calculi, however it is rarely used to diagnose bladder stones.
BLADDER CALCULI (VESICAL CALCULI)

Diagnostic Procedures/Surgery
- Cystoscopy to visualize the stone and guide subsequent removal of the stone.
- Allows evaluation of bladder outlet obstruction or other abnormality such as bladder diverticulum.

Pathologic Findings
- Acute and chronic inflammation.
- Squamous metaplasia and squamous cell carcinoma can result from chronic vesical calculus irritation.

Differential Diagnosis
- Bladder diverticulum.
- Bladder malignancy with or without calcification.
- Other bladder malignancies.
- Chronic pelvic pain syndrome.
- Fungal bezoar or blood clot.
- Intestinal cysts.
- Lower urinary tract symptoms due to bladder outlet obstruction.
- Oversecreting bladder.
- Urinary tract infection.
- Urinary unbladder.
- Vital unbladder stones can cause significant vesical irritation.

Treatment

General Measures
- Surgical removal is the mainstay treatment.
- Determining and correcting the cause (i.e., bladder outlet obstruction) should be a priority.

Medication
First Line
- Medical therapy is used to treat associated urinary tract infection.
- Cystoscopy/cystolitholapaxy using stone fragmenting forceps.
- Electrohydraulic, ultrasonic, laser, and pneumatic lithotrites are used for larger or harder stones.
- Large stones can be removed through small abdominal incision (open cystolitholapaxy).
- Cystolitholapaxy can be safely combined with procedures such as TURP or TUIP for bladder outlet obstruction.

Additional Treatment
- Radiation Therapy
- Additional Therapies
  - ESWL has a limited role in treating bladder calculi.
  - Bladder outlet procedure may be necessary if urinary stones are causing vesical calculi to improve bladder emptying.
  - Consideration to repair of bladder diverticulum or other anatomic abnormality if contributory.

Complementary & Alternative Therapies
- N/A

Ongoing Care

Prognosis
- Excellent with complete stone removal and associated bladder outlet obstruction are treated.
- Metabolic stone evaluation may be considered if appropriate (i.e., multiple upper tract calculi, recurrent bladder calculus, etc.).

Complications
- Recurrent urinary tract infection.
- Squamous metaplasia.
- Chronic irritation may result in secondary malignancy (i.e., squamous cell carcinoma).

Follow-Up
- Patient Monitoring
  - Urine analysis.
  - Flowmetry and postvoid residual.
  - Urinalysis for crystals.
- Renal ultrasonographic scan to screen for upper tract stone.

Patient Resources
- Published Health: Bladder Stones http://www.ncbi.nlm.nih.gov/pubmed/PMID002254

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Bladder Calculus (Vesical Calculus) Image 42
- Bladder Diverticulum
- Bladder Filling Defect
- Bladder Wall Calcification, Differential Diagnosis
- Fungal Infections, Genitourinary
- Unbladder, Adult, General Considerations

Codes
- ICD9
  - 594.0 Calculus in diverticulum of bladder
  - 594.1 Other calculus in bladder
- ICD10
  - N21.0 Calculus in bladder
  - N21.0 Bladder neck obstruction

Clinical/Surgical Pearls
- If an otherwise healthy person is found to have a bladder calculus, a complete evaluation is warranted to evaluate for causes such as urinary stones.
BLADDER CANCER, ADENOCARCINOMA

Matthew A. Young, MD
Sandip M. Prasad, MD, MPhil

BASICS

DESCRIPTION
- Adenocarcinoma of the bladder is an uncommon and frequently aggressive nonurothelial cancer.
- It is frequently muscle-invasive or metastatic at the time of diagnosis and therefore carries a poor prognosis.
- A common site is the urachus.

Epidemiology
- 0.3–0.5% of all primary bladder malignancies, making it the 3rd most common epithelial tumor of the bladder.
- Can arise from the urothelium or nonurothelial epithelium, or in association with ectopy of the bladder.
- Most common tumor arising in the bladder of ectopy patients, who have a 4% lifetime risk.
- A majority of nonurothelial, nonectopy-associated adenocarcinomas occur in men and are frequently associated with long-term inflammation or infection.
- Occurs more frequently in areas where Schistosoma is endemic.

Urachal cancer: <1% of primary bladder cancer; 1/10 of bladder adenocarcinomas

RISK FACTORS
In tissue-relevant studies, adenocarcinoma can be produced from bladder urothelium under the appropriate hormonal and neuroendocrine stimuli.

Genetics
- Associated with gain of function in regions 20q and 8p, or loss of function in regions 5q and 8p (1).

PATHOPHYSIOLOGY
Classification: 3 groups, related to site of tumor origin (2,3)
- Primary adenocarcinoma of bladder.
- Urethral adenocarcinoma.
- Extravesical adenocarcinoma (metastasis).
- Primary vesical adenocarcinoma: Can occur anywhere in the bladder, but the dome and the trigone of the bladder are common.
- Most common type of cancer in bladder exstrophy.
- All histologic variants of enteric carcinoma may occur in the bladder.
- Papillary or solid, most are mucin-producing.
- Most are poorly differentiated and invade at the time of diagnosis.

Urachal adenocarcinoma: For classification as a urachal carcinoma, there must be:
- Presence of a urachal remnant.
- Clear demarcation between the tumor and adjacent bladder mucosa.
- Predominant invasion of the muscularis propria or deeper structures of the bladder or extension to the space of Retzius, anterior abdominal wall, or umbilicus.
- Possible production of mucoid drainage from the umbilicus.

M.D. Anderson Cancer Center Diagnostic Criteria for Urachal Carcinoma:
- Location in bladder dome or elsewhere in the midline of the bladder.
- Sharp demarcation between tumor and normal surface epithelium.
- Supportive criteria:
  - Eutopic-type histology.
  - Absence of urothelial dysplasia.
  - Absence of cystitis cystica or cystitis glandularis transforming to the tumor.
  - Absence of primary adenocarcinoma of another organ.

- May produce stippled calcifications on plain films.
- Prognosis is worse for urachal carcinoma than for primary adenocarcinomas of the bladder.
- Urachal carcinoma demonstrates more extensive infiltration of the bladder wall, and for this reason, radical cystectomy is preferred over partial cystectomy, although the latter is still an option.
- Urachal carcinomas are not always adenocarcinomas: Most common type.
- Others include transitional cell carcinoma, squamous cell carcinoma, and rarely sarcoma.

Metastatic lesions are very rare:
- Adenocarcinomas from the colon, stomach, breast, ovary, endometrium, and prostate can metastasize to the bladder.
- Local invasion of a colonic primary tumor is more common than metastasis.
- Bladder adenocarcinoma is histologically indistinguishable from adenocarcinoma of the colon.

Sheldon Staging System for Urachal Carcinoma:
- Stage I: No invasion beyond the urachal mucosa.
- Stage II: Invasion confined to the urachus.
- Stage III: Local extension into the bladder (B3A).
- Stage IV: A - Abdominal wall (B3B).
- Stage IV: B - Peritoneum (B3C).
- Stage IV: C - Viscera other than bladder (B3D).
- Stage IV: D - Adenocarcinoma of the colon.

ASSOCIATED CONDITIONS
- Bladder exstrophy.
- Schistosomiasis.

GENERAL PREVENTION
Elimination of factors leading to chronic bladder inflammation.

DIAGNOSIS

HISTORY
- Hematuria, mucopurulent urethral discharge.
- Usually painless.
- Intermittent voiding symptoms (frequency, urgency, dysuria).
- Foreign body Schistosomiasis.
- Weight loss, flank pain, umbilical discharge (rare).
- Chronic infection.
- History of exstrophy or other bladder pathology.
- History of colon cancer or other malignancy, risk of metastatic lesion.

PHYSICAL EXAM
- Pelvic mass by bimanual rectal exam.
- Bloody or mucoid-umbilical discharge or umbilical mass.
- Digital rectal exam: Presence of blood in stool.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urine studies: Urinalysis, culture and sensitivity, urinocytology.
- Serum electrolytes: BUN/Creatinine, liver function tests.
- Carcinoembryonic antigen (CEA), CA125, and CA19-9 may be elevated in 40–60% of patients presenting with peritoneal carcinomatosis.

Imaging
- Urachal cancers may show stippled calcifications on plain x-ray films.
- 60% of bladder tumors are detected with IVU, which has been largely replaced with the CT scan.
- CT scan: Imaging method of choice for staging of bladder tumors; useful for detecting presence of pelvic lymphadenopathy and extravesical tumor extension.
- Sensitivity: 64–94%, specificity: 62–100%.
- Other investigations: CTA (staging), bone scan (imaging if bone pain is present), GI endoscopy, and breast exam (to exclude primary tumor) if clinically indicated.

Diagnositc Procedures/Surgery
- Diagnostic cystoscopy and biopsy:
  - Essential for definitive diagnosis.
  - Bloody efflux from ureteral orifices suspicious for upper tract pathology.

Pathologic Findings
- All histologic variants of enteric carcinoma may occur in the bladder.
- Adenocarcinomas can have glandular, mucinous, or signet ring patterns.
- Most produce mucin.
- Primary adenocarcinomas of the bladder are associated with cystitis glandularis and is thought to arise from glandular metaplasia of the urothelium.
- These tumors can be papillary or solid.
- Signet ring tumors produce limk plastic of the bladder.
- They are aggressive and radical surgical excision should be considered.
**Differential Diagnosis**
- Metastasis from ovary, prostate, or other adenocarcinoma
- Benign or malignant urothelial tumors

**Treatment**

**General Measures**
- Site of origin and tumor behavior are factors important in determining treatment
- Adenocarcinoma of the bladder is generally unresponsive to radiation and chemotherapy.
  - Radical cystectomy is treatment of choice.
  - Excision of the urachus and umbilicus is usually required if a urachal primary is suspected
- Adjunct chemotherapy or radiotherapy may be used, but surgery remains the most consistently effective treatment ([4,6])

**Medication**

**First Line**
- Generally unresponsive to radiation and cystotoxic chemotherapy ([7])
- Some response to standard regimens such as combination methotrexate, vinblastine, adriamycin, cisplatin (MVAC)
- Recently, 5-FU and cisplatin-based chemotherapy have demonstrated a modest response rate
- A clinical trial at M.D. Anderson using gemcitabine, 5-FU, leucovorin, and cisplatin (Gem-FLP) reported a clinical response rate in 30–40% of patients
- Currently there is no role for neoadjuvant chemotherapy for clinically node-negative resectable disease

**Second Line**
- 5-FU

**Surgery/Other Procedures**
- Radical cystectomy with pelvic lymph node dissection remains the gold standard
- Adjunct chemotherapy or radiotherapy has not improved survival significantly
- Partial cystectomy (with bladder mucosal sampling) with an en bloc removal of the urachus and umbilicus is an option for low-volume, low-stage urachal carcinoma

**Additional Treatment**

**Radiation Therapy**
- Urachal adenocarcinomas are radio resistant

**Additional Therapies**
- N/A
- Complementary & Alternative Therapies
- N/A

**Ongoing Care**

**Prognosis**
- Signet cell variant has a 50% mortality at 1 yr
- Urachal adenocarcinoma: Overall 11–15% 5-yr survival, but early-stage disease may have up to 90% 5-yr survival
- Nonurachal adenocarcinoma: 27–61% 5-yr survival
- Recurrence risk for urachal carcinoma
  - Positive margin
  - Urachal cysts or scarring are associated with a higher risk of relapse
  - Tumor involving the parietal surfaces or the abdominal wall
  - Occult length node metastases

**Complications**
- Urinary obstruction from local spread of tumor
- Metastasis to pelvic lymph nodes, liver, lung, mediastinum, and bone
- Surgical complications: Bleeding, infection, rectal injury

**Follow-Up**

**Patient Monitoring**
- Abdominal imaging (CT)
- Metastatic workup if suspected

**Patient Resources**
- American Cancer Society.
  - www.cancer.org
- National Cancer Institute
  - www.cancer.gov
- United Ostomy Association
  - www.uoa.org

**Ongoing Care**

**References**

**Additional Reading**

See Also (Topic, Algorithm, Media)
- Bladder Cancer, Adenocarcinoma Image
- Bladder Cancer, General
- Urachal Carcinoma

**Codes**

**ICD9**
- 188.1 Malignant neoplasm of dome of urinary bladder
- 188.7 Malignant neoplasm of urachus
- 188.9 Malignant neoplasm of bladder, part unspecified

**ICD10**
- C67.1 Malignant neoplasm of dome of urinary bladder
- C67.7 Malignant neoplasm of urachus
- C67.9 Malignant neoplasm of bladder, part unspecified

**Clinical/Surgical Pearls**
- Urachal adenocarcinoma may be involved in up to 7% of patients with adenocarcinoma of the bladder
- Most common tumor arising in the Bladder of exstrophy patients, who have a 4% lifetime risk
- Adenocarcinoma of the bladder is generally unresponsive to radiation and chemotherapy.
52

BLADDER CANCER, GENERAL
Matthew A. Young, MD
Sandip M. Prasad, MD, MPhil

PATHOPHYSIOLOGY

- 70% of tumors present as nonmuscle-invasive lesions
- 20% of these are Ta, 20% T1, 10% CIS
- Risk of recurrence
  - CIS: 50–90%
  - Ta low grade: 50–70%
  - Ta high grade: 60%
  - T1 high grade: 70–80%
  - Risk of recurrence in upper tracts 2–4%
- Risk of progression
  - CIS: >50%
  - Ta low grade: 5–10%
  - Ta high grade: 15–40%
  - T1 high grade: 30–50%
  - Most important prognostic factor is grade
  - Concurrent upper tract UCC in patients with bladder cancer is 2–4%

ASSOCIATED CONDITIONS

- Other smoking related illnesses (COPD)
- Adenocarcinoma, squamous cell
- Small-cell carcinoma
- Bone scan is recommended only in patients with bone pain, elevated calcium, or elevated alkaline phosphatase

DIAGNOSIS

HISTORY

- Gross painless hematuria is the most common presenting symptom
- Hematuria and flank tenderness (sensitivity 77%, specificity 98%)
- Urinalysis for hematuria screening
- High-fat diet has been associated with increased risk of bladder cancer

PHYSICAL EXAM

- Assess all urinary tract structures
- Painful, gross hematuria and may reveal palpable mass in bladder

DIAGNOSTIC TESTS & INTERPRETATION Lab

- Urinalysis with microscopy: RBCs
- Urine cytology
  - High specificity (96%), more sensitive for high-grade tumors (10%)
  - Other urinary markers
    - FISH (evaluate aneuploidy for chromosomes 3, 7, 17 and Bcl-2)
    - Sensitivity 77%, specificity 98%
    - MIB-1 (marker of aneuploid cells)
  - Sensitivity 56%, specificity 85%
- Renal function tests (BUN, Creatinine)
  - May indicate renal impairment secondary to ureteral obstruction
- Liver function tests
  - May be abnormal due to metastasis

Imaging

- CT abdomen/pelvis
  - Can detect lymphadenopathy and other intra-abdominal disease
  - Presence of hydronephrosis is suggestive of muscle invasive disease
- CT angiography has replaced IV as standard for evaluating upper tracts
- MRI may be useful for local staging
- Chest x-ray (CXR): Metastasis with muscle invasion
- Bone scan is recommended only in patients with bone pain, elevated calcium, or elevated alkaline phosphatase

Diagnostic Procedure/Surgery

- Cytoscopy is the most accurate initial diagnostic procedure
- Can be done in office with local anestheisia

Pathologic Findings

- Transitional cell carcinoma (urothelial carcinoma), 90%
- Squamous cell carcinoma, 3–7%
- Adenocarcinomas, <2%
- Small-cell carcinoma (lymphoma, carcinoma, lymphoblastoma, uncertain)
- Renal/gonadal and female reproductive system
- Bone pain, elevated calcium, or elevated alkaline phosphatase
- Blood in stool
- Urine in stool
- Hematuria: 85% have hematuria
- Congenital/familial causes: Cystinuria, hypercalciuria
- Renal/renal cell carcinoma
- Calcium stones (90% of adults with stones, gross hematuria and ~10% with painless microscopic hematuria have a malignancy), benign tumors, endometriosis
- Metabolic causes: (10% most common cause of hematuria in adults), other infections (diabetes mellitus, TB, syphilis, radiation cystitis)
- Rapidly progressive glomerulonephritis
- Schistosomiasis
- Urorheumatism
- Urothelial, 85% have hematuria
- Congenital/familial causes: Cystinuria, hypercalciuria
- Metabolic causes: (90% most common cause of hematuria in adults), other infections (diabetes mellitus, TB, syphilis, radiation cystitis)
- Renal/renal cell carcinoma
- Calcium stones (90% of adults with stones, gross hematuria and ~10% with painless microscopic hematuria have a malignancy), benign tumors, endometriosis
- Metabolic causes: (10% most common cause of hematuria in adults), other infections (diabetes mellitus, TB, syphilis, radiation cystitis)
- Renal/renal cell carcinoma
BLADDER CANCER, GENERAL

REFERENCES

ADDITIONAL READING
N/A

See Also (Topic, Algorithm, Media)
• Bladder Cancer, Adenocarcinoma
• Bladder Cancer, General Image D
• Bladder Cancer, Intravesical Agents (Table)
• Bladder Cancer, Nonmuscle-Invasive Bladder Cancer (Ta, T1)
• Bladder Cancer, Squamous Cell Carcinoma
• Bladder Cancer, Urthelial, Muscle Invasive (Clinical and Pathologic) T2/T3/T4 (MIBC) Neoadjuvant Therapy
• Bladder Cancer, Urthelial, Muscle Invasive (Clinical and Pathologic) T2/T3/T4 (MIBC)
• Bladder Cancer, Urthelial, Superficial Carcinoma In Situ (CIS) (NMIBC)
• Bladder Tumor Algorithm 2
• Hematuria, Gross and Microscopic, Adult
• Reference Tables: TNM Classification: Urinary Bladder Cancer

CODES

ICD 188.8 Malignant neoplasm of trigone of urinary bladder
188.8 Malignant neoplasm of other specified sites of bladder
186.9 Malignant neoplasm of bladder, part unspecified

ICD10
• C67.8 Malignant neoplasm of trigone of urinary bladder
• C67.8 Malignant neoplasm of other specified sites of bladder
• C67.8 Malignant neoplasm of bladder, part unspecified

CLINICAL/SURGICAL PEARLS
70% of bladder cancers present as nonmuscle-invasive lesions.
RISK FACTORS
- Tobacco smoking history (most common risk factor)
  - Overall 2.8x higher incidence in smokers
  - Risk increases with number of pack-years
  - 6x risk for 62 pack-year history
- Latency often >20 yr from time of exposure
- Quitting decreases risk
  - >15 yr after quitting, relative risk 1.1
- Occupational exposure
  - Organic chemicals, especially aromatic (Vin anilines)
  - Naphthoquinones, benzidine, aniline dyes, 4-aminoazobenzene
  - High-risk occupations: Petroleum/rubber/leather/paint/textile workers, hairdressers, truck drivers, aluminum electroplaters
- Asbestos contamination of drinking water
  - Latency may be 40 yr
- Chemoexposure with cyclophosphamide (Cytoxan)
- Helicobacter pylori
  - 4x increased risk after RT for cervical cancer
  - 1.5x risk after RT for prostate cancer
- Chronic hepatitis
  - SCC
- Indwelling catheters, chronic bladder catheter
- Cysts due to Schistosoma hematobium

PATHOPHYSIOLOGY
- Inciting genetic event
  - Low grade (LG). Deletion of part of chr 9 (RB gene) and/or mutation in FGFR-3
  - High grade (HG). Numerous mutations (particularly TP53), aneuploidy of chr 7, 9, 17
- NMIBC comprises ∼75% of bladder cancer
- Recurrence rate: ∼40% for LG, >80% for HG
- Most recurrences within 1st 6 mo after TURBT, but may occur after many years
- May also recur in upper tracts or prostate urethra
- Progression influenced by stage and grade
  - Stage Ta, LG: 5–10%; HG: 15–40% at 5 yr
  - Stage T1, HG 30–50% at 5 yr
- May also recur in upper tracts or prostate urethra
  - Stage T1, HG 30–50% at 5 yr
  - High-grade (HG) 10–25% for HG Ta, 33% for HG T1 (T1)
- Other risk factors for progression
  - Architecture: Non-papillary/broad based
  - Multifocality = >50%
  - Size >5 cm
  - Lymphovascular invasion
  - Focal lesions in FTA, RB, and PFEN predict poor prognosis

ASSOCIATED CONDITIONS
- See “Risk Factors”

GENERAL PREVENTION
- Smoking cessation
- Avoidance of occupational exposure
- Hydration long-term beneficial

DIAGNOSIS

HISTORY
- Most common in men >50; Males = females due to smoking prevalence
- 1st occurrence: 85% present with either gross or microscopic hematuria. Painless gross hematuria is hallmark of bladder CA
- Initial symptoms (eg, dysuria, urgency, frequency) occasionally due to bladder CA, especially CIS
- Microscopic hematuria typically present if due to cancer
- Smoking history:
  - Record total pack-years, current packs/day, and years since quitting if applicable
- Occupational risk factors

PHYSICAL EXAM
- Usually unrewarding for NMIBC

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - CBC including dipstick and micro evaluation for RBCs
  - Urine cytology: High specificity but low sensitivity.
  - Other urinary tests: urine cytology, BTA-Stat, NMP22, UrineVysion FISH: Low sensitivity and specificity for LG disease. Not generally recommended for routine workup of microscopic hematuria but may be considered for high-risk patients (see “Additional Reading”)
- Imaging:
  - CT urogram: Evaluate renal parenchyma, renal collecting system, and ureters
  - CT urogram (3-phase CT abdomen/pelvis with IV contrast): Study of choice for evaluation of gross/microscopic hematuria
  - If patient cannot receive IV contrast, consider MRI + RPR (intravenous pyelogram)

Diagnosing Procedure/Surgery
- Bladder CA typically detected on cystoscopy
- Cystoscopy indicated for gross hematuria and most cases of microscopic hematuria (see chapter “Hematuria, gross and microscopic, adult”)
- In-office, under local anesthesia, at time of initial presentation. It may be combined with biopsy
- TURBT under general or spinal anesthesia is definitive
- Retrograde pyelography may be used for equivocal CT urogram or when CT urogram/MRI contraindicated to exclude concomitant upper tract lesions in patients with hematuria or positive cystoscopy

Pathologic Findings
- Urine Cytology
  - Precursors to CIS/Unifocal cancer
- Papillosa
  - Papillary lesion with low recurrence risk (0–4%) or progression risk (1%)
- Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP)
  - Papillary growth, minimal cytologic atypia
  - Recurrence 35%, progression 4%
- CIS: See chapter “Bladder Cancer, urothelial, superficial, carcinoma in situ (CIS)”
- Bladder cancer: Confined to either urothelium (stage T1) or invasion of lamina propria (stage T1) and may be LG or HG

DIFFERENTIAL DIAGNOSIS
See Section 1 “Bladder cancer, general” for complete differential diagnosis of hematuria and bladder filling defects

Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- A papillary tumor confined to the mucousa is classified as stage Ta according to the Tumor, Node, Metastasis (TNM) classification system.
- Tumors that have invaded the lamina propria are classified as stage T1.
- Ta and T1 tumors can be removed by transurethral resection (TUR), and are called NMIBC (non-muscle-invasive bladder cancer).
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Challenging management: Due to recurrence and potential to progress to lethal disease
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenging management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
- Bladder cancer is a malignant neoplasm usually arising from the lining of the bladder (urothelium).
- Due to need for lifelong monitoring, highest cost per patient of any cancer
- Challenge management: Due to recurrence and potential to progress to lethal disease
- Most common histology: urothelial carcinoma (previously called transitional cell carcinoma/TCC)
- ∼75% of bladder cancers are non-muscle-invasive at presentation.
ADDITIONAL TREATMENT
Radiation Therapy
No role in superficial disease

Additional Therapies
Adjunct intravesical chemotherapy/immunotherapy (as above)

Compensatory & Alternative Therapies
Mediastinal seed (high intake of fruit, vegetables, legumes) thought to lower risk of urethral cancer (5)

ONGOING CARE

PROGNOSIS

CLINICAL/SURGICAL PEARLS

Greatest risk factor for progression to MIBC is high-grade disease.
Administration of mitomycin C at the time of TURBT for low-grade NMIBC decreases risk of recurrence but not progression.
Though the majority of men with high-grade NMIBC respond to BCG, most will ultimately recur.

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

ICD-10 C67.9 Malignant neoplasm of bladder, part unspecified

ICD-10 C67.9 Malignant neoplasm of bladder, unspecified

BLADDER CANCER, NON-MUSCLE-INVASIVE BLADDER CANCER (TA, T1) (NMIBC)

SURGERY/OTHER PROCEDURES

• Repeat TURBT indicated for T1 and HG. As many as 25–50% may harbor worse prognostic findings on 2nd TURBT.
• Bladder biopsies (random): Helpful if positive cytology with no obvious lesion.
• Laser electrofulguration useful for recurrent, small, LG, papillary tumors, may be performed under local anesthesia.
• Fluorescence “Blue Light” Cystoscopic. – Intravesical agents bind porphyrins in neoplastic tissue and fluoresces under Blue light.
• Improves detection of papillary tumors and CIS. – Decreases recurrence but not progression.
• Recommended by EAU guidelines.

Narrow band imaging (NBI) is an evolving endoscopic technology.

Radical cystectomy: Indicated in HG NMIBC. Narrow band imaging (NBI) is an evolving endoscopic technology.
BLADDER CANCER, SQUAMOUS CELL CARCINOMA

Daniel J. Canter, MD

PATHOPHYSIOLOGY (1)
- Schistosomiasis infection
- Transitional cell dedifferentiation
  - Transitional cells possess unique ability to
dedifferentiate into any cell type
- Chronic irritation of bladder mucosa due to a variety of
etiologies, especially SCCs
- Most common bladder sites are the lateral wall and
trigone

ASSOCIATED CONDITIONS
- Neurogenic bladder/SCIs
- Need for chronic indwelling Foley/CIC
- Smoking history
- Living and travel to areas endemic with
schistosomiasis

ASSOCIATED CONDITIONS
- Schistosomiasis infection
- Transitional cell carcinoma (TCC) can differentiate
into any histology
- Smoking
- Chronic bladder infection/irritation
  - Patients with SCIs
  - Chronic indwelling Foley catheter/CIC
  - Chronic infection
  - Bladder stones
  - Leukoplakia
  - Squamous metaplasia
- HPV infection
- Industrial exposures for workers involved in
the production of rubber, leather, textiles, and paint
(traditionally more associated with the development
of pure urothelial carcinoma)

Genetic
- Association with variations in inflammatory genes
- Epithelial growth factor receptor and p53
everexpression implicated as well as p16
abnormalities
- Keratin 10 and cavin-1 identified as potential
markers of differentiation from TCC to SCC

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis/culture
- Urinary cytology usually not reliable
- CBC
- Comprehensive metabolic panel, including (liver
function testing) LFTs, alkaline phosphatase, and
albumin

Imaging
- Cross-sectional imaging of the chest, abdomen, and
pelvis based on patient’s renal function (CT scan vs.
MRI)
- Bone scan if elevated calcium, alkaline phosphatase,
or unexplained pain

Diagnostic Procedures/Surgery
- Exam under anesthesia (USA) and transurethral
resection of bladder tumor (TURBT) of primary
tumor for histologic diagnosis and clinical staging
- Radical cystectomy with lymph node dissection and
primary diversion is considered for the treatment

Pathologic Findings
- Mixed urothelial and squamous carcinomas are
more common than pure SCCs
- The term SCC of the bladder is used only if tumor
is solely composed of squamous cell component,
with no urothelial carcinoma component
- Grading unreliable. Mostly considered a high-grade
neoplasm

Histologic findings
- Squamous metaplasia
- Keratinized islands
- Squamous pearls
- Interstitial bridges
- Histologic figures common

DIFFERENTIAL DIAGNOSIS
- Urothelial carcinoma of the bladder
- Squamous metaplasia
- Other histologic variant of bladder
(sarcomatoid, adenocarcinoma, etc.)
- Invasive cervical cancer: Often squamous cell

DIAGNOSIS
- History of living/travel to countries with endemic
schistosomiasis
- In general, in Western countries, patients who have
SCC of the bladder present in the same manner as
urothelial carcinoma of the bladder
- Hematuria
- Constitutional symptoms
- Flank/back pain due to ureteral obstruction
- History of chronic irritation to bladder mucosa

PHYSICAL EXAM
- Palpable mass on rectal/vaginal exam
- Gross hematuria

HISTORY
- History of living/travel to countries with endemic
schistosomiasis
- In general, in Western countries, patients who have
SCC of the bladder present in the same manner as
urothelial carcinoma of the bladder
- Hematuria
- Constitutional symptoms
- Flank/back pain due to ureteral obstruction
- History of chronic irritation to bladder mucosa

DESCRIPTION
- Squamous cell carcinoma (SCC) of the bladder is a
histologic variant of bladder cancer
- Most frequent histologic form of bladder cancer in
countries with endemic schistosomiasis
- SCC comprises 2–5% of all bladder
cancers—most common histologic variant in
Western countries

Epidemiology
Incidence
- 2–5% of bladder cancers in Western countries
- Originally reported that patients with spinal cord
injuries (SCIs) had an incidence of SCC of the
bladder of 2.3%—more recent data only suggests
0.39% incidence
- Approximately 75–80% of all bladder cancers are
SCCs in regions with endemic schistosomiasis

Prevalence
- Difficult to assess since so many of these patients will
ultimately die of bladder cancer

Risk Factors
- Schistosomiasis infection
- TransITIONAL cell carcinoma (TCC) can differentiate
into any histology
- Smoking
- Chronic bladder infection/irritation
  - Patients with SCIs
  - Chronic indwelling Foley catheter/CIC
  - Chronic infection
  - Bladder stones
  - Leukoplakia
  - Squamous metaplasia
- HPV infection
- Industrial exposures for workers involved in
the production of rubber, leather, textiles, and paint
(traditionally more associated with the development
of pure urothelial carcinoma)

Genetics
- Association with variations in inflammatory genes
- Epithelial growth factor receptor and p53
  neverexpression implicated as well as p16
  abnormalities
- Keratin 10 and cavin-1 identified as potential
  markers of differentiation from TCC to SCC
BLADDER CANCER, SQUAMOUS CELL CARCINOMA

TREATMENT

GENERAL MEASURES
• Treatment is related to stage
• In general, SCC of the bladder presents with locally advanced disease, and radical cystectomy with urinary diversion is an integral part of the treatment paradigm
• Although uncommon, noninvasive lesions can be treated with local resection and diligent surveillance

MEDICATION
First Line
• Systemic chemotherapies have been used with limited experience in treating SCC of the bladder
• Small series have reported positive responses to cisplatin-based therapies, similar to pure urothelial carcinoma
• At present, role for neoadjuvant/adjuvant chemotherapy is poorly defined

Second Line
N/A

SURGERY/OTHER PROCEDURES (2)
• After diagnosis is confirmed, radical cystectomy is 1st-line treatment
• Bladder-preserving therapies can be considered if tumor is nonmuscle invasive and completely resected, and patient is willing to commit to intensive surveillance protocol
• Limited experience with chemoradiotherapy as primary treatment modality

ADDITIONAL TREATMENT
Radiation Therapy
Can be used in adjunct setting for patients with positive surgical margins at time of surgery

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
• Related to pathologic stage (3)
• Evidence suggests that patients with SCC of the bladder tend to present with higher-stage (pT3/T4) disease at the time of radical cystectomy
• Overall survival has ranged from 4.8 to 50%
• 5-yr cancer-specific survival in contemporary series has ranged from 57 to 64%

COMPICATIONS
• Related to radical cystectomy and urinary diversion
  – Perioperative mortality approaches 2%
  – 40-50% of patients will experience a postoperative complication
  – Gastrointestinal complication is most common, e.g., ileus, small bowel obstruction

FOLLOW-UP
Patient Monitoring
• Related to tumor stage at the time of radical cystectomy
  – In general, patients are followed with history, physical exam, laboratory studies (CBC and comprehensive metabolic profile, including liver function tests) and cross-sectional imaging of chest, abdomen, and pelvis every 3–6 mo after surgery for the first 2 yr then semiannually for 2 yr then annually
  – Renal function needs to be followed annually as well

Patient Resources
Bladder Cancer Advocacy Network (www.bcan.org)

REFERENCES

ADDITIONAL READING
N/A

See Also (Topic, Algorithm, Media)
• Bladder Cancer, General
• Bladder Cancer, Squamous Cell Carcinoma Image
• Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (MIBC)

CODES

ICD9
188.9 Malignant neoplasm of bladder, part unspecified

ICD10
C67.9 Malignant neoplasm of bladder, unspecified

CLINICAL/SURGICAL PEARLS
• With the control of schistosomiasis in endemic regions, the rate of SCC is dropping relative to the diagnosis of urothelial carcinoma
• Radical cystectomy is the gold standard for muscle-invasive SCC of the bladder
BLADDER CANCER, UROTHELIAL, METASTATIC (CLINICAL AND PATHOLOGIC N+, M+)

Jean Hoffman-Censits, MD
Wm. Kevin Kelly, DO

GENERAL PREVENTION
• Smoking cessation
• Limit or modify chemical exposure
• Hydration may limit tumor exposure

DIAGNOSIS
• Many tumor recurrences are noted during routine radiographic surveillance, which is standard following radical cystectomy.
• Pain from bone metastasis, lymphatic progression in the retroperitoneum, bowel obstruction with carcinomatosis, and symptoms of visceral progression such as in the lungs and liver can be symptoms of metastatic bladder cancer.

PHYSICAL EXAM
• Most with early advanced or metastatic disease have no significant external exam findings.
• Palpable lymphadenopathy, hepatomegaly from liver involvement, as well as cachexia of malignancy can be noted.
• Low edema with venous thromboembolism is present (incidence 1-8%); higher incidence with platinum combination therapy.
• Poor nutrition and increased abdominal girth in setting of ascites and soft tissue intra-abdominal recurrence can contribute to edema.

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Lab abnormalities can include anemia of chronic disease, iron deficiency anemia in patients with longstanding hematuria, renal insufficiency in patients with ureteral obstruction, transaminitis (elevation of liver transaminases), and elevation in bilirubin in patients with liver involvement.
• Hypercalcemia is rare and associated with poor prognosis typically associated with squamous differentiation.
• No tumor marker for bladder cancer.

Imaging
• Staging guidelines recommend abdomen and pelvis imaging with CT or MRI.
• Imaging of the upper tract collecting system
• Chest imaging
• Bone scan if clinical suspicion of bone metastasis by pain or alkaline phosphate elevation
• PET may be useful but not standard of care
• Evaluation of normal cardiac ejection fraction required for Adriamycin

Pathologic Findings
• Urothelial (formerly transitional cell) carcinoma is the most common subtype, and for which the most data exists.
• Many sun-exposed patients may have urothelial cancer with squamous or other foci of differentiation.
• Less common histologic subtypes are squamous cell carcinoma, adenoscarcinoma, and small cell carcinoma.

DIFFERENTIAL DIAGNOSIS
• Pelvic and retroperitoneal adenopathy
• Metaplastic: lymphoma (non-Hodgkin, Hodgkin, others), metastatic (adrenal, renal, uterine, prostate, urethral, penile, germ cell, cerebral, ovarian, uterine), G3 carcinoma (lymphoma), colo-rectal, melanoma
• Infectious/inflammatory:
• Granulomatous: TB, sarcoidosis, histoplasmosis, lymphogranuloma venereum, Ca, tuberculosis, disease, etc.
• Nongranulomatus: Viral, bacterial (if abscess in local area), viral histiocytosis, retroperitoneal fibrosis
• Other: Crypt retnopatetal masses (lymphocele, urinoma, hemmorhage) aneurysms
• Bone lesions
• Congenital (bone islands, others)
• Endothrombotic (thrombophlebitis, Paget disease)
• Neoplasm primary (ovarian, melanoma) or secondary (prostate, breast, kidney, lung, thyroid)
• Trauma fracture (stress or healing)
• Others: Autoimmune diseases, drugs (Vitamin D, fluoroquinolones, infection (osteomyelitis), inflammatory/fibrosed tissue (hepatocele, others))
• Pulmonary nodules
• Infections: fungal, septic emboli, fungal (histoplasmosis, etc.), parasitic, mycobacterial, inflammatory conditions (Wegner granulomatosis), pulmonary APN, mycobacteriosis, silicosis
• Malignant: Primary lung cancer, bladder cancer, choroid carcinoma, renal and thyroid cancer, melanoma, Ewing’s sarcoma

TREATMENT
GENERAL MEASURES
• Treatment of urothelial (transitional cell) carcinoma with platinum-based chemotherpay has increased survival but curative rates are limited. With good performance status and renal function, platinum-based combination chemotherapy is the initial approach (Grade 1A/1)
• “Futility” for platinum-based therapy is not well defined. Generally assessment of renal function (daily; mgn, hearing >25 dB at 2 contiguous frequencies), performance status (WHO/ECOG, performance status 2 or less), baseline peripheral neuropathy and cardiac function (New York Heart Association [NYHA] Class I or better)
• In the setting of impaired renal function correct reversible causes (obstruction, etc.)
BLADDER CANCER, UROTHELIAL, METASTATIC (CLINICAL AND PATHOLOGIC N+, M+)

MEDICATION

First Line
• Cisplatin-based chemotherapy combinations are the most active and superior to carboplatin regimens. Survival outcome is similar in patients treated with standard multiagent MVAC (methotrexate, vinblastine, doxorubicin, cisplatin) compared to cisplatin with gemcitabine (GC), with less toxicity in the GC group (1,2).

• High-dose intensity chemotherapy with MVAC plus GEMC (2nd line-MVAC) compared to standard MVAC led to a better overall response rate (94% vs. 59%) and improved survival (21.8% in the MVAC-MVAC vs. 13.5%) at 7 y. The toxicity profile of MV-MVAC was superior with better dose intensity, and thus established MV-MVAC as an alternative to standard M-VAC (3).

• MC chemotherapy is usually given every 14 days with the AC given along each 28 days.

• MV-MVAC is also referred to as “dose dense” MVAC (DD-MVAC) regimen given the same drugs at the same doses clsoe together, all drugs every 14 days with hematopoietic growth factor support and is recommended by the NCCN guidelines.

• Adding paclitaxel to cisplatin and gemcitabine, compared to GC led to a modest but not significant improvement in survival and is not endorsed for most patients (4).

• Some typical regimens reported in the literature include:
  - MVAC: Methotrexate (30 mg/m² on days 1, 15,
  - vinblastine (3 mg/m² on days 2, 15, 22),
  - doxorubicin (30 mg/m² on day 2), and
  - cisplatin (70 mg/m²) repeated every 28 days for 6 cycles.
  - GC: Gemcitabine (1,000 mg/m² days 1, 8, 15) plus cisplatin (70 mg/m² day 2), repeated every 28 days for a maximum of 6 cycles.

Second Line
• There is no standard therapy for patients who have disease recurrence or progression following 1st line cisplatin/pemetrexed or MVAC chemotherapy, and clinical trial participation is encouraged.

• Small nonrandomized studies support the use of the following agents:
  - Gemcitabine, folic acid, and platinum combinations
  - Gemcitabine: Rash and cytopenias
  - Paclitaxel: Fluid retention, neuropathy, myelosuppression

• Ureteral obstruction (tumor or lymphadenopathy) is a common complication that requires stenting or percutaneous nephrostomy drainage.

SURGERY/OTHER PROCEDURES
• Retrospective series support consideration of salvage surgery for patients who initially present with uncontrollable or metastatic disease with robust chemotherapy responses (5). Survival rates were consistently better in those with pathologic complete response to induction chemotherapy and in those with node only metastasis. (See Section 1 “Bladder cancer, urothelial, muscle invasive (clinical and pathologic T2/T3/T4)”).

ADDITIONAL TREATMENT
• Radiation Therapy
  - Palliative radiation therapy is an option for patients with painful bony metastasis.

• Additional Therapies
  - Studies suggest benefit of zolendronic acid or denosumab in patients with metastatic bladder cancer to bone (6).
  - Granulocyte colony-stimulating factor can help limit myelosuppression with cisplatin and others.

Complementary & Alternative Therapies
• Supportive care includes adequate nutrition and hydration, particularly for patients undergoing multiresistance therapy.

ONGOING CARE

PROGNOSIS
• For patients with metastatic disease, ECOG status ≥1, hemoglobin ≤10, and visceral involvement are prognostic for overall survival (survival 14.2 mo for those with none of these features vs. 1.7 mo with all 3 features).

COMPILATIONS
• Cisplatin: Nephrotoxicity, ototoxicity, peripheral neuropathy, fatigue.
• Adriamycin (in MVAC regimen): Cardiac toxicity.

Myelosuppression, neutropenic fever, sepsis, mucositis, nausea, and vomiting are common (up to 56% may require readmission for toxicity).

• Neutropenia (including life-threatening febrile neutropenia) associated with multimodality chemotherapy for bladder cancer. Granulocyte growth factor is standard in the high-dose intensity MVAC regimen, and is used to support patients on gemcitabine and platinum combinations.

• Gemcitabine: Rash and cytopenias

• Taxanes (ie, paclitaxel): Fluid retention, neuropathy, myelosuppression

• Urinary obstruction (tumor or nephropathy) is common and can be alleviated with urinary stenting or percutaneous nephrostomy drainage.

FOLLOW-UP

Patient Monitoring
• In patients with metastatic disease on chemotherapy, imaging should be performed every 2–3 mo to assess response. In patients with durable responses of chemotherapy, imaging should be done every 3 mo for the 1st 2 yr of response.

Patient Resources
• Bladder Cancer Advocacy Network
  - http://www.bcan.org/

REFERENCES


ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Bladder Cancer, General
• Bladder Cancer, Nonurothelial
• Bladder Cancer, Squamous Cell Carcinoma

Codes
ICD-10
• C67.9 Secondary and unspecified malignant neoplasm of other specified sites.

ICD-9
• 188.9 Malignant neoplasm of bladder, part unspecified
• 196.9 Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified
• 198.89 Secondary malignant neoplasm of other specified sites.

CLINICAL/SURGICAL PEARLS
• Single-agent chemotherapy provides low response rates of usually short duration.
• For 1st line chemotherapy, performance status and the presence or absence of visceral metastases are independent prognostic factors for overall survival.
• Blisk drains help limit cisplatin renal toxicity.
BLADDER CANCER, UROTHELIAL, MUSCLE INVASIVE (CLINICAL AND PATHOLOGIC T2/T3/T4) (MIBC)

Zachary L. Smith, MD
S. Bruce Malkowicz, MD, FACS

ASSOCIATED CONDITIONS
Those secondary to smoking (lung disease, other malignancies)

GENERAL PREVENTION
- Avoidance of exposure to cigarette smoke and industrial risk factors
- Appropriate and timely workup of both microscopic and/or gross hematuria (early diagnosis, not prevention)

DIAGNOSIS

HISTORY
- History of smoking or other risk factors
- Prior bladder tumors in hematuria
- Family history of BCA
- Signs and symptoms:
  - Painless hematuria (80%)
  - Intermittent symptoms (frequency, urgency, dysuria) (35%)
  - Stigmata of locally invasive or metastatic disease (pelvic pain/fullness, palpable mass, incontinence, weight loss, bone pain)

PHYSICAL EXAM
- General: Nutritional status, abdominal/pelvic masses, lymphadenopathy
- Digital rectal exam (male), bimanual pelvic exam (female), which can be performed under anesthesia

DIAGNOSTIC TESTS & INTERPRETATION
- Blood: CBC, electrolytes, LFT (elevated alkaline phosphatase suggests liver or bone involvement)
- Urine:
  - Urinalysis with microscopy
  - Urine: Urinalysis with microscopy
- Imaging:
  - Abdominal imaging
  - CT urogram (triple phase: Noncontrast, nephrographic, excretory) is the current standard of care
  - MR urogram acceptable, where available
- Bone scan

Pathologic Findings
- BCA will be analyzed by pathologist for grade and depth of invasion
- Grading (WHO/ISUP, 2004):
  - High-grade urothelial neoplasm of low malignant potential (well-differentiated)
  - Low-grade (moderate differentiation)
  - High-grade (poorly differentiated)
- Depth of invasion:
  - Into detrusor muscle (T2)
  - Into perivesical fat (T3)
  - Into adjacent structures (prostate, uterus, vagina, pelvic/abdominal wall) (T4)

DIFFERENTIAL DIAGNOSIS
- Gynecologic and other pelvic tumors directly invading bladder
- Adenocarcinomas more likely to be metastatic in origin
- Mass seen at bladder base on imaging is sometimes actually prostate median lobe

TREATMENT

GENERAL MEASURES
- Preoperative evaluation, as most patients also have significant cardiorespiratory disease
- Discuss treatment options and urinary diversion options
- If ileal conduit, meet with stoma therapy nurse pre-op and preop for care/teaching
- For continent diversion, pre-op teaching imperative
- If bladder preservation chosen, coordinate with radiation oncology and medical oncology

MEDICATION
First Line
- Intravesical treatments not used for MIBC
- Neoadjuvant/adjuvant therapy with radical cystectomy (RC) urothelial carcinoma primarily

Second Line
- Carboplatin substituted for cisplatin in renal insufficiency
- Mitomycin-C-fluorouracil is a newer regimen which has emerging data to support its use
- Taxanes also promising as both single and combination agent
Surgery/Other Procedures

- RC with pelvic lymphadenectomy and urinary diversion considered gold standard therapy for MIBC (2).
  - Complete extirpation and pelvic lymphadenectomy provide best chances for control and cure
  - Unusual frozen sections to ensure negative margins before urinary tract reconstruction is standard practice
  - Patients with ≥T4 disease on clinical staging may be offered neoadjuvant chemotherapy
  - RC gives additional benefit in metastatic disease, but may be palliative in patients with intractable hematuria or pelvic pain
  - Lymphadenectomy may be prognostic and therapeutic
    - Positive nodes in ~25%
    - Patients with limited nodal burden have higher survival rates
    - Extended lymphadenectomy (to include paraaortic) and (paraavalvar nodules) may improve survival
    - May identify patients most suited for adjuvant therapeutics

- Urinary diversion (1):
  - Options include continent, catheterizable stoma, continent orthotopic neobladder, or ileal conduit
  - Each with advantages and disadvantages
  - Real conduit used most commonly, least complications
  - Neobladders typically reserved for younger, motivated patients who are able to perform self-catheterization if needed

- Partial cystectomy:
  - One patient selection criteria: Stage T2 only, solitary lesion allowing for 2 cm margins, lack of CIS, not involving trigone or seminal tracts
  - Recurrence common within 2 yr
  - Still allows for lymphadenectomy

- Radical TURBT:
  - As a sole therapy, outcomes poor for MIBC
  - Usually palliative in patients who will not tolerate RC or systemic therapy (such as elderly with significant comorbidities)

- Urethrectomy:
  - Simultaneous (during RC) or delayed urethrectomy if CIS or tumor involves prostatic urethra, ducts, or stroma
  - Orthotopic reconstruction should not be made until negative frozen section distal urethral margin is examined

Additional Treatment

Radiation Therapy

- RT as a monotherapy is considered inferior to RC
- RT in combination with chemotherapy has a role in selected patients undergoing organ preservation (see below)

Additional Therapies

- Combination RT and chemotherapy after TURBT is more efficacious bladder preservation technique
- Developed for patients who are either not candidates for or refuse RC
  - Ideal candidates for bladder preservation:
    - Complete visual resection on TURBT
    - Solitary tumor
    - No hydroaexitis
    - < 5-yr overall survival > 30–50%; better in T2 disease than T3-4

- Complementary & Alternative Therapies

Ongoing Care

- Prognostic factors:
  - Tumor cell type (SCC and adenocarcinoma less favorable)
  - Tumor grade and stage
  - Disease-free survival correlates with stage
  - Node burden (≥8 positive and node density （>20%)) has worse prognosis

- Survival rates after RC:
  - Disease-free survival (5 yr) without positive nodes: 72% (82–84%) for pT2; 45% (49–57%) for pT3; 24% (25–6%) for pT4
  - Disease-free survival with positive nodes: 30% (15–48%)

Complications

- General:
  - Common due to local invasion and advancement of disease
  - Urinary obstruction, hydronephrosis
  - Hematuria, clot retention
  - Malnutrition, infection, etc.

- Associated with RC:
  - 90-day hospital readmission: 32%
  - 90-day mortality: >4% (5–10%)
  - Bowel obstruction (4–10%), ureteral obstruction (0–36%)

Follow-Up

Patient Monitoring

- Follow-up remains controversial and dependent on disease severity
  - T1/T2 disease: Semiannual physical exam, serum chemistries, and CXR with CT scan every 2 yr (T1) or yearly (T2)
  - T3/T4 disease: Exam, labs, and CXR every 3 mo

- If disease free at 5 yr, surveillance can be lessened
  - T3/T4 disease: Exam, labs, and CXR every 3 mo
  - T1/T2 disease: Semiannual physical exam, serum chemistries, and CXR with CT scan every 2 yr (T1) or yearly (T2)

- Follow-up includes patients who will not tolerate RC or systemic therapy (such as elderly with significant comorbidities)

- Consider urethral washing or cystoscopy

Patient Resources

- Bladder Cancer Advocacy Network (BCAN): www.bcan.org

References


See Also (Topic, Algorithm, Media)

- General: Cancer, General
- Bladder Cancer, General
- Bladder Cancer, Nonmuscle-Invasive Bladder Cancer (Ta, T1)
- Bladder Cancer, Urinary, Metastatic (Clinical and Pathologic) N+ (M+)
- Bladder Cancer, Urinary, Muscle Invasive (Clinical and Pathologic) T2/T3/T4 (MIBC) Image
- Bladder Cancer, Urinary, Muscle Invasive (Clinical and Pathologic) T2/T3/T4 (MIBC) Neoadjuvant Therapy
- Bladder Mass
- Bladder Tumor Algorithm
- Bladder Tumors, Benign and Malignant, General Considerations
- Bladder Tumors, Benign and Malignant, General Considerations Algorithm
- Reference Tables: TNM Classification: Urinary Bladder Cancer

ICD10 188.9 Malignant neoplasm of bladder, part unspecified

ICD9 61 C67.9 Malignant neoplasm of bladder, unspecified


Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (MIBC)
BLADDER CANCER, UROTHELIAL, MUSCLE INVASIVE (CLINICAL AND PATHOLOGIC T2/T3/T4) (MIBC) NEOADJUVANT THERAPY

Jean Hoffman-Censits, MD
William Kevin Kelly, DO

ASSOCIATED CONDITIONS
- The majority of bladder cancer diagnosed in US has no other associations.
- In Egypt and regions in SE Asia, chronic bladder irritation from Schistosoma infection can lead to squamous cell carcinoma, as can chronic bladder irritation or inflammation, such as from chronic indwelling catheter use.

GENERAL PREVENTION
- Smoking cessation
- Limit or modify chemical exposure

RISK FACTORS
- Cigarette smoking
- Chemical and occupational exposure association
- Cigarette smoking
- Chemical and occupational exposure association
- Cytogenetic abnormalities:
  - Inactivating mutation in p53, p21, or Rb (MIBC)
  - Loss of chromosomes 17q, 5q, 3p (MIBC)
  - Multifactorial polygenic
  - Autosomal dominant
- Alterations in genes which contribute to toxin breakdown within the bladder (such as GST and AHR), may make some more likely to develop bladder cancer.
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.
- T2: Muscularis propria invasion
- T3: Perivesical tissue invasion
- T4: Invasion of pelvic structures (eg, prostate, small bowel, bladder, vagina, pelvic side wall, or abdominal wall)

EPIDEMIOLOGY
Incidence (1)
- 74,690 new cases of bladder cancer will be diagnosed in 2023.
- 500,000 in US (all stages)

Prevalence
- >50,000 in US (all stages)

DIAGNOSIS
- Gross or microscopic hematuria is the most common presenting sign.
- Dysuria, frequency, and urgency are common.
- Symptoms of locally advanced disease such as pelvic pain and constipation.
- Flank pain or renal insufficiency due to ureteral obstruction by tumor.

PATHOPHYSIOLOGY
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.

DIAGNOSTIC TESTS & INTERPRETATION
- Physical exam
- History
- General prevention
- Smoking cessation
- Limit or modify chemical exposure

BASICS

DESCRIPTION
- Bladder cancer is invasive, invasive bladder cancer (T2, T3, 4 MIBC) is much less common than noninvasive bladder cancer.
- May present with de novo invasive cancer, a minority progress from superficial bladder cancer.
- Radical cystectomy for muscle invasive bladder cancer is potentially curative, up to 50% of patients will develop recurrence within 1 yr.
- This high recurrence has led to the increasing use of neoadjuvant chem before cystectomy.
- Neoadjuvant cisplatin-based chemo has improved survival in radical cystectomy alone.

EPIDEMIOLOGY
Incidence (1)
- 74,690 new cases of bladder cancer will be diagnosed in 2023.
- 500,000 in US (all stages)

Prevalence
- >50,000 in US (all stages)

DIAGNOSIS
- Gross or microscopic hematuria is the most common presenting sign.
- Dysuria, frequency, and urgency are common.
- Symptoms of locally advanced disease such as pelvic pain and constipation.
- Flank pain or renal insufficiency due to ureteral obstruction by tumor.

PATHOPHYSIOLOGY
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.
- T2: Muscularis propria invasion
- T3: Perivesical tissue invasion
- T4: Invasion of pelvic structures (eg, prostate, small bowel, bladder, vagina, pelvic side wall, or abdominal wall)

ASSOCIATED CONDITIONS
- The majority of bladder cancer diagnosed in US has no other associations.
- In Egypt and regions in SE Asia, chronic bladder irritation from Schistosoma infection can lead to squamous cell carcinoma, as can chronic bladder irritation or inflammation, such as from chronic indwelling catheter use.

GENERAL PREVENTION
- Smoking cessation
- Limit or modify chemical exposure

RISK FACTORS
- Cigarette smoking
- Chemical and occupational exposure association
- Cigarette smoking
- Chemical and occupational exposure association
- Cytogenetic abnormalities:
  - Inactivating mutation in p53, p21, or Rb (MIBC)
  - Loss of chromosomes 17q, 5q, 3p (MIBC)
  - Multifactorial polygenic
  - Autosomal dominant
- Alterations in genes which contribute to toxin breakdown within the bladder (such as GST and AHR), may make some more likely to develop bladder cancer.
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.
- T2: Muscularis propria invasion
- T3: Perivesical tissue invasion
- T4: Invasion of pelvic structures (eg, prostate, small bowel, bladder, vagina, pelvic side wall, or abdominal wall)

EPIDEMIOLOGY
Incidence (1)
- 74,690 new cases of bladder cancer will be diagnosed in 2023.
- 500,000 in US (all stages)

Prevalence
- >50,000 in US (all stages)

DIAGNOSIS
- Gross or microscopic hematuria is the most common presenting sign.
- Dysuria, frequency, and urgency are common.
- Symptoms of locally advanced disease such as pelvic pain and constipation.
- Flank pain or renal insufficiency due to ureteral obstruction by tumor.

PATHOPHYSIOLOGY
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.
- T2: Muscularis propria invasion
- T3: Perivesical tissue invasion
- T4: Invasion of pelvic structures (eg, prostate, small bowel, bladder, vagina, pelvic side wall, or abdominal wall)

ASSOCIATED CONDITIONS
- The majority of bladder cancer diagnosed in US has no other associations.
- In Egypt and regions in SE Asia, chronic bladder irritation from Schistosoma infection can lead to squamous cell carcinoma, as can chronic bladder irritation or inflammation, such as from chronic indwelling catheter use.

GENERAL PREVENTION
- Smoking cessation
- Limit or modify chemical exposure

RISK FACTORS
- Cigarette smoking
- Chemical and occupational exposure association
- Cigarette smoking
- Chemical and occupational exposure association
- Cytogenetic abnormalities:
  - Inactivating mutation in p53, p21, or Rb (MIBC)
  - Loss of chromosomes 17q, 5q, 3p (MIBC)
  - Multifactorial polygenic
  - Autosomal dominant
- Alterations in genes which contribute to toxin breakdown within the bladder (such as GST and AHR), may make some more likely to develop bladder cancer.
- Tumor multifocality and the high rate of recurrence of urothelial cancer within the bladder, ureters, and renal pelvis in patients with a bladder cancer history can be due to the field effect in part from toxin exposure.
- T2: Muscularis propria invasion
- T3: Perivesical tissue invasion
- T4: Invasion of pelvic structures (eg, prostate, small bowel, bladder, vagina, pelvic side wall, or abdominal wall)
ADDITIONAL TREATMENT

**Radiation Therapy**
- Multimodality treatment with chemo-radiotherapy can be considered for patients who are medically inoperable or selected patients who wish for bladder preservation (8).
- If T2–T3, up to 5 cm, no carcinoma in situ, no hydroaestrosis, complete TURBT reaction, T3–T4, functional bladder at baseline.

**Neoadjuvant chemo** followed by cystectomy and chemo-radiotherapy have not been compared head to head in a prospective trial.

**Additional Therapies**
- Multidisciplinary evaluation should be considered to assess best plan of care
- For patients who have received standard cisplatin-based neoadjuvant chemo, there is currently no recommendation for adjuvant chemo following cystectomy
- For patients with invasive or node positive disease following cystectomy who did not receive neoadjuvant chemo, adjuvant platinum-based therapy should be considered
- Positive surgical margins can increase risk of local failure; consider adjuvant chemotherapy

**Complementary & Alternative Therapies**
- N/A

**ONGOING CARE**

**PROGNOSIS**
- Patients with pathologic complete response (pT0) at radical cystectomy have superior relapse free and overall survival outcomes compared to those with residual invasive disease
- 10.8% complete pathologic downstaging

**COMPLICATIONS**
- Cystitis, Nephrotoxicity, astrocitosis, peripheral neuropathy, and fatigue
- Adjuvant (in NAAC). Cardiac toxicity
- Neutropenia, including life threatening febrile neutropenia is associated with multimodality chemo for bladder cancer. Granulocyte growth factor is standard in the high-dose intensity HDM-EC regimen, and can be used to support patients on GC/platinum combinations
- GC: Rash and cystitis
- Ureteral obstruction (tumor or nodes): Alleviate with ureteral stenting or percutaneous nephrostomy to improve renal function
- 30-day perioperative mortality following cystectomy approximately 1%; average 30-day readmission rate 21–32%
- Perioperative morbidity following cystectomy: Infe, blood loss, infection, thromboembolism, wound complication, ostomy complications.

**FOLLOW-UP**

**Patient Monitoring**
- Following radical cystectomy, imaging of the chest, abdomen and pelvis including upper tract evaluation and CNE and electrolyte assessment should occur every 3–6 mo. Based on recurrence risk for the first 2 yr, then clinically indicated
- Urine cytology and electrolytes should be monitored every 3–6 mo. Based on recurrence risk for the first 2 yr, then as clinically indicated
- Continent diversion: Monitor 812 deficiency

**Patient Resources**
Bladder Cancer Advocacy Network
http://www.bcan.org

**REFERENCES**


**ADDITIONAL READING**


**See Also (Topic, Algorithm, Media)**
- Bladder Cancer, General
- Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (MIBC) Neoadjuvant Therapy
- Bladder Cancer, Urothelial, Metastatic (Clinical and Pathologic N+ or M+)
- Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (MIBC)
- Bladder Tumor Algorithm
- Reference Tables: TNM Classification: Urinary Bladder Cancer

**CODES**

ICD-O-MORPH
- 188.9 Malignant neoplasm of bladder, part unspecified

ICD-O-MORPH
- 188.9 Malignant neoplasm of bladder, unspecified

**CLINICAL/SURGICAL PEARLS**
- Outcomes after radical cystectomy indicate increased survival in patients who had more, rather than fewer, lymph nodes resected
- Patients with pathologic complete response following neoadjuvant chemotherapy appear to have the best long-term survival.
Carcinoma in situ (CIS) of the bladder is a flat, multifocal, “velvety” lesion of the urothelium. CIS is a flat, high-grade tumor that is confined to the mucosa. It can be occult and diagnosed by random biopsies of normal-appearing mucosa. Although it can occur alone, it most often seen with concurrent high-grade papillary lesions. CIS is considered high grade and aggressive with a propensity to invade the bladder wall and metastasize.

**EPIDEMIOLOGY**

**Incidence**

True incidence is not known given the flat superficial nature of this lesion, which can be destroyed by cautery effect during transurethral resection of bladder tumor (TURBT).

**Prevalence**

- Occurs as isolated CIS in 3–5% cases
- Estimated 5–10% of patients with noninvasive urothelial carcinoma have CIS
- 45–65% patients with invasive urothelial carcinoma have CIS

**RISK FACTORS**

- No risk factors specific for CIS beyond that of urothelial carcinoma
- Tobacco smoking
- Occupational exposure
- Medications
- Pelvic radiation
- Medications
- Occupational exposure
- Smoking history
- Family history of bladder cancer
- History of bladder cancer
- Irritative voiding symptoms—dysuria commonly
- Presence of gross hematuria
- Avoid occupational exposures
- Smoking cessation

**PATHOPHYSIOLOGY**

- CIS usually multifocal and can occur in the upper tracts, prostatic ducts, and urethra as well as the bladder
- Natural history—highly aggressive
- Progression to NMIBC in 54–83% of untreated cases
- Increase risk of recurrence if found with NMIBC papillary lesions.
- Bacillus Calmette-Guerin (BCG) reduces risk of progression by 35% compared with other intravesical therapies (1,3)
- BCG confers disease-free rate approximately 51% at 3–7 yr (1)
- If concurrent muscle-invasive lesion, prognosis and treatment depends on invasive lesion

**ASSOCIATED CONDITIONS**

- NMIBC (Ta,T1)
- Invasive bladder cancer (T2,T3,T4)

**GENERAL PREVENTION**

- Smoking cessation
- Avoid occupational exposures

**DIAGNOSIS**

**HISTORY**

- Age and sex
- Presence of gross hematuria
- Irritative voiding symptoms—dysuria commonly occurs with CIS
- History of bladder cancer
- Family history of bladder cancer
- Smoking history
- Occupational risk factors

**PHYSICAL EXAM**

- Usually unremarkable

- Biannual exam should be performed at time of cystoscopy/TURBT—if CIS is found in presence of advanced stage/invasive bladder cancer may appreciate palpable mass

**DIFFERENTIAL DIAGNOSIS**

- Noninvasive urothelial carcinoma
- Adenocarcinoma
- Metastatic disease

**DIAGNOSTIC TESTS & INTERPRETATION**

- Urinalysis, including microscopic evaluation
- Urethral cytology—highly specific and sensitive (>90%) for detecting CIS and high-grade urothelial carcinoma (5)
- Urilocystin, HA-HAase, and BLCA-4 have a high sensitivity to detect CIS however should not replace classic urine cytology (1, Grade B)

**IMAGING**

- No imaging specific for diagnosing CIS
- Renal/bladder ultrasound (US): Detects hydronephrosis that may be caused by ureteral obstruction from bladder tumor; bladder US can visualize larger bladder tumors
- Computed tomography (CT) urogram: Triple phase CT abdomen/pelvis is the gold standard for evaluation of pseudo-gross hematuria; can detect more advanced bladder tumors, hydronephrosis, and upper tract filling defects that may represent upper tract urothelial carcinoma.

**Diagnosis of Procedure/Surgery**

- Cystoscopy with bladder biopsy
  - Appearance can be flat, grossly erythematous, granular or cobblestone mucosa or visually normal
  - May be performed in office at initial visit
  - TURBT under general or spinal anesthesia may be required if papillary bladder tumor present
  - Retrograde urography also should be performed to assess the upper tracts if not already evaluated with a CT urogram.
  - Positive cytology with no visible tumor and negative random bladder biopsies suggests disease outside of bladder
  - Biopsy of prostatic urethra indicated
  - Selective cystoscopy from upper tracts; evaluate for urothelial carcinoma/CIS of renal pelvis or ureters. CIS of upper tracts suspected in absence of solid tumor and with positive cytology, rarely able to obtain adequate biopsy to confirm CIS histologically

- Fluorescent “Blue light” cystoscopy
  - More sensitive than conventional white light cystoscopy for detecting CIS
  - In a prospective study additional detection rate of 20% for all tumors and 23% for CIS
  - False positives can result in the presence of inflammation, recent TUR, or BCG instillation

**Pathologic Findings**

- Arias from surface uroepithelium
- Severe cystitis, atypia and mucosal aphasia (2)
- Large uniform hypochromatic nuclei
- Mitotic activity common
- Thought to be a precursor of invasive disease
- Some pathologists use the term “severe dysplasia” to describe CIS

**DIFFERENTIAL DIAGNOSIS**

- Nonurothelial cancers (squamous cell carcinoma, adenocarcinoma)
- Inflammatory lesion from prior radiation, intestinal cystitis, infection.
ADDITIONAL TREATMENTS

SURGERY/OTHER PROCEDURES

- **TURBT**—Resection of all visible papillary bladder tumors is essential prior to BCG therapy.
- For CIS refractory to intravesical therapy—radical cystectomy.
  - Disease-specific survival rates excellent if cystectomy performed early (instead of BCG instillation), however 40–50% could be overtreated.

MEDICATION

- **BCG**—live suspension of the attenuated Mycobacterium bovis vaccine strain
  - Standard of care for CIS
  - Therapy initiated no earlier than 2–4 wk after TURBT to give urothelium time to heal and prevent systemic complications of BCG
  - Administered as induction therapy—6 consecutive weekly bladder instillations; then maintenance treatment recommended for at least 1 yr (1) (Grade A)
  - BCG has the highest complete response rate and durable disease-free rates among all intravesical treatments (1) (Grade A)
  - Initial response rates approximately 70–90%; however up to 30% of patients will recur
  - Response to BCG instillation should be assessed at 3 mo
    - If no response can give another 6-wk course of BCG vs. proceed to radical cystectomy
    - Approximately 50% will respond to second course of BCG (1) (Grade B)

SECOND LINE

- **Intravesical chemotherapy**
  - Mitomycin C—an alternative for patients who cannot tolerate BCG.
  - Valrubicin—an option for poor surgical candidates with BCG-refractory disease—durable disease-free rates of all intravesical therapies.
  - Has side effect of dysuria and can be intolerable in some patients
  - Usually experienced within the first 6 mo of treatment.

FOLLOW-UP

- **Patient Monitoring**
  - At 3 mo patients should have urocytology and urine cytology. If negative, this should be repeated every 3 mo x 2 ye, every 6 mo thereafter until year 5 and then yearly (3)

PATIENT RESOURCES

American Cancer Society—Bladder Cancer
http://www.cancer.org/content/2003085.pdf

REFERENCES


ADDITIONAL READING


- See Also (Topic, Algorithm, Media)

  - **BCG Sepsis/BCGosis**
  - Bladder Cancer, General
  - Bladder Cancer, Intravesical Agents (table)
  - Bladder Cancer, Nonmuscle-Invasive Bladder Cancer (Ta, T1)
  - Bladder Cancer, Urthelial, Metastatic (Clinical and Pathologic T4a, M+)
  - Bladder Cancer, Urthelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (NMIBC)
  - Bladder Cancer, Urthelial, Superficial Carcinoma In Situ (CIS) (NMIBC) Image
  - Bladder Tumor Algorithm
  - Bladder Tumors, Bierie, and Multignant, General
  - Bladder Tumors, Bierie and Multignant, General Considerations
  - Reference Tables: TNM Classification: Urinary Bladder Cancer

ICD9

- 189.7 Carcinoma in situ of bladder

ICD10

- D09.0 Carcinoma in situ of bladder

CLINICAL/SURGICAL PEARLS

- Urine cytology is the best marker (>90% sensitivity/specificity) for diagnosis of CIS.

- Positive cytology in absence of visible bladder lesions—differential includes CIS bladder, prostatic urethra, or upper tract urothelial carcinoma.

- BCG is the treatment of choice for CIS of the bladder; highest response rate and most durable disease-free rates of all intravesical therapies.

- To prevent systemic complications of BCG do not administer after TURBT until urothelium healed (approximately 2 wk).

- For BCG refractory CIS: A second induction course can be administered vs. proceeding immediately to radical cystectomy.
BASICS

DESCRIPTION
- Bladder injury during surgery can be either intraperitoneal or extraperitoneal.
- The bladder is the urologic organ most subject to iatrogenic injury.
- Described during open, endoscopic, laparoscopic, or robotic procedures.
- May be blunt or sharp dissection, trosa, or electrocautery injury.
- Needle or trocar passage during transvaginal tape or dissection.
- Described during open, endoscopic, laparoscopic, or robotic procedures.
- Cystoscopy with overdistention and transurethral bladder tumor resections are also high risk for bladder perforation injury.

EPIDEMIOLOGY

Incidence (1,2)
- Intraoperative bladder injuries account for:
  - Laparoscopic injuries (0.2–8.3%)
  - Intraperitoneal (38–40%)
  - Extraperitoneal (53–56%) of injuries

Prevalence

Risk factors associated with specific conditions and procedures based on AUA review
- General factors
  - Previous caesarean delivery
  - Presence of labor
  - Presence of fetal part > +1
  - Fetal weight > 4 kg
  - Hysterectomy
  - Malignancy
  - Endometriosis
  - Prior pelvic surgery
  - Perforated anti-incontinence or pelvic organ prolapse surgery

- Risk factors associated with specific conditions and procedures based on AUA review

- Prior pelvic surgery
- Perforated anti-incontinence or pelvic organ prolapse surgery
- General surgery
- Malignancy
- Diverticulitis
- Inflammatory bowel disease

ASSOCIATED CONDITIONS
- Bladder cancer
- Prostate benign and malignant tumors
- Pelvic anatomic anomalies
- Prior pelvic surgery or radiation
- Pelvic trauma
- Tissue fibrosis or inflammation (eg, radiation, chronic catheter)

GENERAL PREVENTION
- Decompress bladder with a catheter placed before initial incision or trocar placement for laparoscopic cases
- Initial use of vesicure needle for insufflation
- Small bladder perforation not as significant as large perforation
- "Anatomic" trocar technique

Familiarity with bladder anatomy can minimize risk:
- Pediatric bladder is primarily intraperitoneal.
- Adult bladder is retroperitoneal and extraperitoneal.
- Peritoneum is clefted to bladder.
- Bladder is attached broadly and not as bladder neck.
- Bladder wall consists of 3 layers: mucosa, submucosa, muscularis.
- Ureters attached posteriorly in trigone
- Perforate bladder injury or TURBT with bladder at mid filling
- Avoid over or underdistention that can increase risk of perforation of bladder

DIAGNOSIS

HISTORY
- Determine any prior surgical or other interventions that can increase the risk of iatrogenic bladder injury
- Past surgical history such as bladder neck suspension, prostatectomy, partial cystectomy, urethral neobladder, any lower abdominal surgery that may result in the bladder adhering to the posterior fascia
- Prior pelvic radiation
- History of neurogenic bladder

PHYSICAL EXAM
- Intraperitoneal:
  - Findings may be subtle. Need high degree of suspicion
- Blood or gas in Foley, especially during transperitoneal laparoscopic procedure
  - Anesthesia may be first to recognize if monitoring catheter collection bag
- Urine in wound
- For transurethral surgery: Intraperitoneal abdominal distention/lifidity may be noted if hydrostatic irrigation is being used, patient may develop signs/symptoms of TUR syndrome
- Postoperative:
  - Distended abdomen
  - Peritonitis and abdominal rebound pain
  - Decreased urine production; oliguria or anuria
  - Abdominal/pelvic aches
  - Urine leakage from wound
  - Bloody urine
  - Fever

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- With urinary ascites elevation in serum BUN and creatinine as well as hyperkalemia and hypotension can be seen
- Elevated creatinine over serum level observed with urine leak due to systemic absorption
- Drain fluid sent for creatinine
- Urine vs. serum

Imaging
- Postoperative diagnosis (3):
  - Extraperitoneal Injury: Contrast contained in the extraperitoneal space
  - Intraperitoneal Injury: Contrast extravasates between loops of small bowel and the anterior paramesonephric fascia

CT cystogram can be done using standard technique or CT imaging with postcontrast evaluation (3):
- 300 cc gravity filling
- 3-view cystogram or CT cystogram
- All cystograms must include a postcontrast evacuation study to evaluate for residual contrast outside of the bladder
- SC can identify urinoma
- CT for pelvic ‘‘urinary’’ ascites or urinoma
- Intraperitoneal diagnosis during transurethral surgery. Intraperitoneal cystogram can be obtained
Diffuse detrusor usually causes urine leak
Rupture through mucosa, submucosa, and muscularis

**Diagnostic Procedures/Surgery (1,4)**

- Intraoperative extraperitoneal injury:
  - Initial catheter drainage with antibiotics
  - Exploratory laparotomy with repair
  - Foley or 2-layer repair
  - Open bladder/2-layer repair
  - 1-layer laparoscopic or robotic repair
- Intraperitoneal perforation
  - Usually managed with catheter drainage and close monitoring
  - Large perforations complicated by symptomatic collections require drainage, with or without formal closure of the perforation
- Bladder perforation during midurethral sling or transsacral mesh placement
  - Sling reinsertion and urethral catheterization
  - 11–12 days should be performed (4,8)

**ADEQUATE TREATMENT**

- For most bladder injuries Foley catheter for 24 hr
- Prompt recognition improves opportunity for formal closure of the perforation
- Prognosis worse if delayed diagnosis

**ADDITIONAL TREATMENT**

- In the setting of any bladder perforation during TURBT
- Intravesical postoperative chemotherapy should not be administered

**ONGOING CARE**

**PRONOSIS**

- Extraperitoneal: Usually heals with Foley catheter drainage and without further intervention
- Intraperitoneal: Good prognosis if identified intraperitoneally and repaired. Prognosis worse if delayed diagnosis

**COMPLICATIONS**

- Pericystitis or abscess
- Fever
- Hypotension

**FOLLOW-UP**

- Patient Monitoring
  - Foley catheter or suprapubic tube to monitor urine output
  - Usually no need for outpatient antibiotics

**REFERENCES**


**ADDITIONAL READING**

- See Also (Topic, Algorithm, Media)
  - Bladder Trauma
  - Trocar Syndrome
  - Ureter, Intraoperative Injury
  - Ureter, Trauma

**CODES**

- N99.72 Accidental puncture & laceration of a GU sys org during a GU sys procedure
- N99.71 Accidental puncture or laceration during a GU sys procedure
- 959.73 Accidental puncture & laceration of GU sys procedure during cath procedure
- 959.79 Accidental puncture & laceration of a GU sys procedure during other procedure
- 537.23–A Laceration of bladder, initial encounter

**PEARLS**

- Intraoperative visual inspection is a reliable method of assessing bladder injury
- Extraperitoneal: Usually heals with Foley catheter drainage and without further intervention
- Intraperitoneal: Good prognosis if identified intraperitoneally and repaired. Prognosis worse if delayed diagnosis
- All cystograms must include a postcontrast evacuation study to evaluate for residual contrast outside of the bladder.
BLADDER OUTLET OBSTRUCTION (BOO)

Michael J. Naslund, MD
Garjae D. Lavien, MD

DESCRIPTION

Bladder outlet obstruction (BOO) refers to a pathologic obstruction to urinary flow. Definitions include the following:

- A reduction in urinary flow to <12 cc/s during a sustained detrusor contraction of over 40–50 cm H₂O
- BOO index >40 on the International Continence Society nomogram based on urodynamic testing

EPIDEMIOLOGY

Incidence

2.2–6.8 events of acute urinary retention per 1,000 person years (1)

Prevalence
None

RISK FACTORS

- Increasing age
- Microscopic BPH starts as early as the 30s but clinical BPH usually presents after the age of 50
- Infection
- Urethral trauma
- Pelvic radiation
- Prior urologic procedures

GENETICS

None

PATHOPHYSIOLOGY

BOO can be due to both static and dynamic factors:

- Static factors:
  - Constricted outlet by enlarged prostatic tissue, bladder neck contracture, or urethral stricture
  - Outlet obstruction leads to detrusor hypertrophy and the symptoms of BOO

ASSOCIATED CONDITIONS

- BPH
- Urethral stricture disease
- Detrusor sphincter dyssynergia

GENERAL PREVENTION
None

DIAGNOSIS

HISTORY

- Detailed description of obstructive voiding symptoms consistent with BOO
- Slow urinary stream
- Urinary hesitancy
- Intermittent urinary stream
- Straining to void
- Sense of incomplete bladder emptying
- Urinary retention
- History of irritative symptoms
- Medical history of gynecologic, neurologic, and GI illness
- Past surgical history for pelvic and spinal procedures
- Medication review for anticholinergics, u-agonists, psychotropic agents
- Voiding diary
- International Prostate Symptom Score

PHYSICAL EXAM

- Abdominal palpation:
  - Palpate for bladder distention (>150 cc), needed to be palpable in an adult
- Rectal examination:
  - Note any findings suspicious for cancer: Nodules, firmness, and asymmetry
- Assess anal sphincter tone
- Pelvic exam (women) for pelvic organ prolapse and urethral diverticula
- Neurologic exam for gross defects

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PSA:
  - If elevated, consider prostate cancer, prostatic inflammation, benign prostatic hyperplasia
- Urinalysis:
  - If hematuria or urinary infection is present, further evaluation is necessary (see Chapter on “Hematuria, Gross and Microscopic, Adult”)
  - Renal and bladder US
- Urine culture
- Creatinine
- Test is necessary unless patient is in urinary retention

Imaging

- Radiographic and bladder US:
  - Evaluate for hydronephrosis if there is renal insufficiency
  - Allows noninvasive determination of PVR
- Upper tract imaging with CT urogram to evaluate causes of hematuria
  - Unilobar:
    - Measure peak flow, demonstrate voiding pattern, and voided volume
    - Peak flow <10–12 cc/s (for voided volume >150 cc) is suggestive of obstruction, although an uncorrectable bladder cannot be ruled out

- Cystoscopy: Endoscopic evaluation of urethra and bladder
- Videourodynamics: Fluoroscopy combined with urodynamics
- ICS nomogram is the most widely used
- Videourodynamics: Fluoroscopy combined with urodynamics

DIFFERENTIAL DIAGNOSIS

- Inflammatory bowel disease
- BOO after incontinence surgery
- Prostatic obstruction (BPH)
- Most common etiology of BOO in men
- Primary bladder neck obstruction
- Infection:
  - Prostatitis, intraurethral condyloma (men and women), periurethral abscess
- Neurogenic:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- Medications that affect bladder contractility:
  - Anticholinergics, antihypertensives, 
- Neuropathy:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- BOO after incontinence surgery
- Prostatic obstruction (BPH)
- Most common etiology of BOO in men
- Primary bladder neck obstruction
- Infection:
  - Prostatitis, intraurethral condyloma (men and women), periurethral abscess
- Neurogenic:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- Medications that affect bladder contractility:
  - Anticholinergics, antihypertensives, 
- Neuropathy:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- BOO after incontinence surgery
- Prostatic obstruction (BPH)
- Most common etiology of BOO in men
- Primary bladder neck obstruction
- Infection:
  - Prostatitis, intraurethral condyloma (men and women), periurethral abscess
- Neurogenic:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- Medications that affect bladder contractility:
  - Anticholinergics, antihypertensives, 
- Neuropathy:
  - Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- BOO after incontinence surgery
- Prostatic obstruction (BPH)
- Most common etiology of BOO in men
- Primary bladder neck obstruction
- A suprapubic tube is used if a urethral catheter cannot be placed (severe stricture or BPH) or urethral catheter is contraindicated (acute prostatitis).
- Long-term treatment of BOO is medical and surgical.
Therapies

N/A

Radiation Therapy

ADDITIONAL TREATMENT

Saw Palmetto (Serenoa Repens)

ADDITIONAL READING

If a male patient has lower urinary tract symptoms check to ensure a low post-void residual which generally confirms that treatment is not necessary.

Strong consideration should be given for evaluation for multiple sclerosis in young females with new onset urinary retention.

MEDICATION

First Line

- α-Blockers: Rapidly relax the smooth muscle of the bladder neck and prostate without impairing bladder contractility
  - Alfuzosin (10 mg/d)
  - Tamsulosin (0.4 mg to max 0.8 mg)
  - Silodosin (8 mg/d)
  - Terazosin (start 1 mg/d to max 20 mg)
  - Flutamide (5 mg/d)
  - Dutasteride (0.5 mg/d)

Second Line

- Phosphodiesterase-5 inhibitors (PDE5i) in males:
  - Sildenafil (50 mg to max 100 mg)
  - Tadalafil (20 mg)
  - Vardenafil (20 mg)
- α-Reductase inhibitors in males: Effective in larger glands (>40 cc) to reduce prostate size, improve symptoms, and reduce progression risk:
  - Finasteride (5 mg/d)
  - Dutasteride (0.5 mg/d)

SURGERY/OTHER PROCEDURES

- Urethral stents
- Clean intermittent catheterization
- Prostatic stents
- Bladder diverticula and fascial bladder
- Transabdominal prostatectomy
- Transperineal prostatectomy
- Transurethral prostatectomy
- Transurethral microwave therapy
- Transurethral needle ablation
- Open excision (with primary anastomosis, grafts, or flaps)
- Urethral dilation
- Urethral stents
- Transvaginal sphincterotomy
- Ureteral stents
- Urethral dilatation
- Urethral incision
- Urethral stents
- Urethral dilatation
- Urethral incision
- Urethral diverticulitis and fascial bladder
- Postobstructive diuresis:
  - Occurs with severe BOO and bilateral ureteral obstruction due to urinary retention
  - Severe hydronephrosis and renal failure
  - Serum electrolytes must be monitored closely

FOLLOW-UP

Patient Monitoring

- Periodic follow-up visits to assess symptom progression (PFS)
- Yearly urology and PSA measurement
- Serial measurement of uroflow and PVR urine
- Causal on the possibility of progression of symptoms and complications
- Management of BPH does not eliminate the risk of developing prostate cancer

Patient Resources

- Urology Care Foundation: www.urologyhealth.org

REFERENCES


ONGOING CARE

PROGNOSIS

Excellent with definitive management

COMPLICATIONS

- Urinary retention
- Bladder stones
- UTIs
- Sphincterotomy
- Dysuria
- No difference in reduction of lower urinary tract symptoms, and reduce progression risk:
- Finasteride (5 mg/d)
- Dutasteride (0.5 mg/d)

ADDITIONAL TREATMENT

Radiation Therapy

- Alpha-blockers: Rapidly relax the smooth muscle of the bladder neck and prostate without impairing bladder contractility
- Phosphodiesterase-5 inhibitors (PDE5i) in males:
  - Sildenafil (50 mg to max 100 mg)
  - Tadalafil (20 mg)
  - Vardenafil (20 mg)
- Alpha-reductase inhibitors in males: Effective in larger glands (>40 cc) to reduce prostate size, improve symptoms, and reduce progression risk:
  - Finasteride (5 mg/d)
  - Dutasteride (0.5 mg/d)
- Second Line
  - Phosphodiesterase-5 inhibitors (PDE5i) in males:
    - Tadalafil only FDA-approved by the FDA for treatment of LUTS in the setting of BPH with or without coexisting erectile dysfunction (ED)

SURGERY/OTHER PROCEDURES

- Urethral stents
- Clean intermittent catheterization
- Prostatic stents
- Bladder diverticula and fascial bladder
- Transabdominal prostatectomy
- Transperineal prostatectomy
- Transurethral prostatectomy
- Transurethral microwave therapy
- Transurethral needle ablation
- Open excision (with primary anastomosis, grafts, or flaps)
- Urethral dilatation
- Urethral incision
- Urethral diverticulitis and fascial bladder
- Postobstructive diuresis:
  - Occurs with severe BOO and bilateral ureteral obstruction due to urinary retention
  - Severe hydronephrosis and renal failure
  - Serum electrolytes must be monitored closely

FOLLOW-UP

Patient Monitoring

- Periodic follow-up visits to assess symptom progression (PFS)
- Yearly urology and PSA measurement
- Serial measurement of uroflow and PVR urine
- Causal on the possibility of progression of symptoms and complications
- Management of BPH does not eliminate the risk of developing prostate cancer

Patient Resources

- Urology Care Foundation: www.urologyhealth.org

REFERENCES


ONGOING CARE

PROGNOSIS

Excellent with definitive management

COMPLICATIONS

- Urinary retention
- Bladder stones
- UTIs
- Sphincterotomy
- Dysuria
- No difference in reduction of lower urinary tract symptoms, and reduce progression risk:
- Finasteride (5 mg/d)
- Dutasteride (0.5 mg/d)

ADDITIONAL TREATMENT

Radiation Therapy

- Alpha-blockers: Rapidly relax the smooth muscle of the bladder neck and prostate without impairing bladder contractility
- Phosphodiesterase-5 inhibitors (PDE5i) in males:
  - Sildenafil (50 mg to max 100 mg)
  - Tadalafil (20 mg)
  - Vardenafil (20 mg)
- Alpha-reductase inhibitors in males: Effective in larger glands (>40 cc) to reduce prostate size, improve symptoms, and reduce progression risk:
  - Finasteride (5 mg/d)
  - Dutasteride (0.5 mg/d)
- Second Line
  - Phosphodiesterase-5 inhibitors (PDE5i) in males:
    - Tadalafil only FDA-approved by the FDA for treatment of LUTS in the setting of BPH with or without coexisting erectile dysfunction (ED)

SURGERY/OTHER PROCEDURES

- Urethral stents
- Clean intermittent catheterization
- Prostatic stents
- Bladder diverticula and fascial bladder
- Transabdominal prostatectomy
- Transperineal prostatectomy
- Transurethral prostatectomy
- Transurethral microwave therapy
- Transurethral needle ablation
- Open excision (with primary anastomosis, grafts, or flaps)
- Urethral dilatation
- Urethral incision
- Urethral diverticulitis and fascial bladder
- Postobstructive diuresis:
  - Occurs with severe BOO and bilateral ureteral obstruction due to urinary retention
  - Severe hydronephrosis and renal failure
  - Serum electrolytes must be monitored closely

FOLLOW-UP

Patient Monitoring

- Periodic follow-up visits to assess symptom progression (PFS)
- Yearly urology and PSA measurement
- Serial measurement of uroflow and PVR urine
- Causal on the possibility of progression of symptoms and complications
- Management of BPH does not eliminate the risk of developing prostate cancer

Patient Resources

- Urology Care Foundation: www.urologyhealth.org

REFERENCES

BLADDER TRAUMA

Hunter Wessells, MD, FACS

DESCRIPTION
Bladder trauma generally comprises blunt and penetrating types of injury.
When not distended, bladder is protected from injury by bony pelvic
Pelvic fracture and bladder distention increase risk of traumatic injury.
Important to distinguish between extraperitoneal (EBR), intraperitoneal (IBR), and combined EBR/IBR.
Urogenic bladder injury is discussed in the section “Bladder Injury, Intraoperative.”

EPISTEMOLOGY
Incidence
1.6% of blunt abdominal trauma
Prevalence
Unknown

RISK FACTORS
Motor vehicle crashes (MVCs)
– Falls
– Industrial trauma (pelvic crush injury)
– Penetrating injuries to lower abdomen
– Bladder outlet obstruction
– Alcohol intoxication (bladder distention and decreased sensorium)
– Pelvic fracture
– 80% of bladder injuries associated with pelvic fracture
– 6% of patients with pelvic fracture sustain a bladder injury
– Urinalysis (UA) usually present

Genetics
N/A

PATHOPHYSIOLOGY
The bladder is generally well protected from blunt trauma unless significantly distended.
In an adult, the bladder lies in the true pelvis, but can rise to umbilicus when full.
In a child, bladder lies in abdomen and more prone to injury.
EBR or combined EBR/IBR
Pelvic fracture leads to shearing injury from bone fragment or compression with rupture
– Direct injury from penetrating trauma
– BFR
– How to lower abdomen in the presence of a full bladder

ASSOCIATED CONDITIONS
– Bladder neck injury
– Pelvic fracture
– Solid abdominal organ injury
– Urinary injury

GENERAL PREVENTION
– Avoid high risk activity
– Seatbelt proper positioning and use

DIAGNOSIS

HISTORY
– Type of blunt trauma to pelvis
– Associated injuries
– Penetrating injury, type of knife if known
– Gross hematuria
– Alcohol use
– Past urologic history
– Compliant:
– Location of lower abdominal pain
– Urinary retention
– Dysuria or voiding complaints

PHYSICAL EXAM
– Abdominal distention
– Lower abdominal/pelvic turgor
– Peristalsis
– Rectal and vaginal exam (assess integrity)
– Blood at meatus

– Site/extent/trajectory of penetrating objects
– Site/extent of abdominal/pelvic bruising
– Seatbelt sign
– Pelvic fracture and bladder distention increase risk of traumatic injury
– Bladder outlet obstruction
– Alcohol intoxication (bladder distention and decreased sensorium)
– Pelvic fracture
– 80% of bladder injuries associated with pelvic fracture
– 6% of patients with pelvic fracture sustain a bladder injury

ALERT
Gross hematuria is the hallmark sign of injury to the bladder.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
– Urinalysis (UA): Blood usually present
– Serum creatinine can be elevated with IBR due to intraperitoneal resorption of urine
– Hypertension, hypotension, uremia, azotemia can also be seen with urinary extravasation into the peritoneum
– CBC (look for leukocytosis and anemia)

Imaging
– Indications for performing cystography:
– Blunt trauma
– Pelvic ring fracture with gross or microscopic (≥3 or >10 RBC/HPF) hematuria
– Gross hematuria in presence of otherwise unexplained free intraperitoneal fluid
– High clinical suspicion (pelvic fluid collection, inability to void, elevated serum creatinine, abdominal distention, suprapubic tenderness, intesinocutaneous or unexplained, poorly functioning
– Foley catheter, displaced obturator ring fracture, or large public symphysis diastasis
– Perforating injury
– Trajectory suggests bladder injury
– Involvement of buttock, pelvic, or lower abdomen with any degree of hematuria
– High clinical suspicion

If urethral injury is suspected, this should be assessed preoperatively (CT with delayed images) or intraoperatively (retrograde pyelography/direct inspection)
When combined upper and lower tract urologic injuries are suspected, upper tract contrast study should be performed prior to cystogram (retained bladder contrast in abdomen or retroperitoneum can obscure upper tract pathology)

Diagnostic Procedures/Surgery
– Cystogram is easy to do and highly sensitive
– CT cystogram
– At least as sensitive as conventional cystography for diagnosing bladder rupture
– Dilute contrast to limit artifact (1:2)
– Postobstructive films not necessary
– Excellent visualization of bladder neck
– Readily identify foreign bodies
– Conventional cystoscopy
– Dilute contrast 1:2
– Scout, 40 oblique, and retrograde films
– For both CT and conventional cystography, fill bladder to capacity (at least 350 mL) in an adult, or determine by formula: (Age in years + 2) × 30.

ALERT
CT with delayed images is inadequate for the diagnosis of bladder injuries when bladder injury is suspected, a cystogram is mandatory.

Pathologic Findings
Injured tissue typically remains healthy, though there is potential for local ischemia (particularly if angio-embolization was performed for pelvic bleeding)

DIFFERENTIAL DIAGNOSIS
– Bladder contusion
– Urinalysis
– Renal or urethral injury

TREATMENT

GENERAL MEASURES
Stabilize patient if major trauma present

MEDICATION

First Line
For nonoperative management of EBR, antibiotics with gram-positive and gram-negative coverage are recommended while catheter is indwelling

Second Line
SPA
When associated with significant pelvic bleeding, open pelvic fractures, and abdominal solid organ injury, supportive care is indicated while more urgent injuries are temporized.

- **IBR**
  - Laceration is typically large (6–8 cm), at dome
  - Nonoperative management generally contraindicated secondary to size of defect and morbidity of chemical peritonitis
  - Should be closed in 2 layers with absorbable suture via midline incision
  - Laparoscopic repair has been reported in stable patients with no other injuries
  - Drain is not necessary
  - Foley catheter 7–10 days, with cystogram to confirm absence of extravasation

- **EBR**
  - Nonoperative management
  - Acceptable in the appropriate patient, but higher complication risk
  - 20-French or larger catheter
  - Cystogram after 10–14 days
  - Antibiotics with gram-positive and gram-negative coverage while catheter is indwelling
  - Contraindications to nonoperative management:
    - Inadequate catheter drainage
    - Vaginal or rectal injury
    - Bladder neck injury
    - Concomitant urethral injury
    - Internal fixation of pelvic fracture
    - Stable and undergoing laparotomy

**ADDITIONAL TREATMENT**

**Radiation Therapy**

**Additional Therapies**

**Complementary & Alternative Therapies**

**ONGOING CARE**

**PROGNOSIS**

- Prompt diagnosis and appropriate management allow excellent results and minimal morbidity.
- Complications usually are associated with delay in diagnosis and management.

**COMPLICATIONS**

- Unrecognized injury can result in fistula, sepsis, ileus, incontinence, and stricture.

**FOLLOW-UP**

- Monitor for signs/symptoms of:
  - Pelvic bleeding
  - Unrecognized abdominal injury
  - UTI
  - Urinary leak

**Patient Resources**

- www.urologyhealth.org/urology/index.cfm?article=99

**REFERENCES**


**ADDITIONAL READING**

**RISK FACTORS**

Estimated 437,180 male and 148,210 female bladder incidence

**DESCRIPTION**

**Gurdarshan S. Sandhu, MD**

**BLADDER TUMORS, BENIGN AND MALIGNANT, GENERAL**

**Epidemiology**

- **Incidence**
  - Bladder cancer: 9th most common cancer
  - Median age at diagnosis is 73
  - 3× more common in White than Black men
  - 1.5× more common in White than Black women
  - 14,880 total deaths in US in 2012 (10,510 males and 4,370 females)
  - Median age at diagnosis is 73
  - 14,880 total deaths in US in 2012 (10,510 males and 4,370 females)
  - 73,510 cases diagnosed in US in 2012 (55,600 males and 17,910 females)

**Prevalence**

- Estimated 437,180 male and 148,210 female bladder cancer cases in US as of 2012

**RISK FACTORS**

- Malignant bladder tumors
  - Smoking—main risk factor for bladder cancer
  - Risk is linearly dose and duration related, with 15–20 yr latency
  - 2nd hand smoke does not increase risk of bladder cancer formation

- Chemical exposure:
  - Especially aromatic dyes and amines
  - High-risk industries include textiles, aluminum, dye, leather, foundries, and rubber workers
  - Pelvic irradiation
  - Latency is 15–30 yr
  - Increased risk in prostate and cervical cancer treated with radiation

- **Chemotherapy**
  - Cyclophosphamide has a 4–9× increased risk for bladder cancer
  - Inflammation is a risk factor for squamous cell carcinoma (SCC)
  - Bladder cancer

- **Inflammation**
  - Chronic bladder stones
  - Schistosoma hematobium infection

- Genetics
  - Neoplastic cells carry a major role
  - History in a 1st-degree increases risk 2×
  - No clear inheritance patterns
  - p53 gene on chromosome 17
  - Overexpression leads to higher rates of progression and lower rates of response to chemotherapy
  - Loss of Retinoblastoma (RB) gene on chromosome 9
  - Development of superficial tumors
  - Slow metabolizers and slow acetylators more susceptible to environmental carcinogens

- **Pathophysiology**
  - **Patterns of spread of bladder cancer**
    - Symptomatic—hematuria
    - Hematogenous—lymph, lung, bone, etc.
    - Direct extension—prostate, urethra, uterus

- **ASSOCIATED CONDITIONS**
  - **None**

- **Diagnosis**
  - **General Prevention**
    - Smoking cessation
    - Antioxidants including vitamins A, C and E, and selenium
    - Mediterranean diet: Lowest bladder cancer risk
    - Avoid occupational exposures

- **DIAGNOSTIC TESTS & INTERPRETATION**
  - Urinalysis (for red blood cells and culture)
  - Urine cytology
  - More sensitive in high-grade disease and carcinoma in situ (90%)
  - Flow cytometry
  - Measures DNA content of cells to quantitate aneuploid cell populations
  - Other urine markers are commercially available (eg, BTA Stat, NMP 22, BladderChek), and have better sensitivities but worse specificities than cytology

- **Imaging**
  - Upper tract evaluation can be done with intravenous urography, retrograde urography, computerized tomography (CT), or magnetic resonance imaging
  - Metastatic evaluation includes chest imaging and bone scan

- **Diagnostic Procedures/Surgery**
  - Cystoscopy with bladder tumor resection or biopsy
  - Fluorescence cystoscopy may increase detection of carcinoma in situ or additional lesions

- **Pathologic Findings**
  - **Benign lesions**
    - Nonneoplastic adenoma: Metaplastic response to chronic inflammation
    - Von Brunn nests: Benign urothelial cells within the lamina propria
  - Squamous metaplasia: Common in women (40%)
  - Cystitis cystica: Central cystic degeneration of Von Brunn nests
  - Basaloid cysts
  - Malignant tumors
  - The primary tumor is urothelial—a single carcinoma

- **Associated Genes and Proteins**
  - Loss of Retinoblastoma (Rb) gene on chromosome 9
  - Inflammation is a risk factor for squamous cell carcinoma
  - Loss of Retinoblastoma (Rb) gene on chromosome 9
  - Inflammation is a risk factor for squamous cell carcinoma

- **Patterns of spread of bladder cancer**
  - Local extension—urothelial and smooth muscle
  - Lymphatic—lymph nodes, liver, bone, lung
  - Hematogenous—to liver, lung, bone, etc.

- **DIFFERENTIAL DIAGNOSIS**
  - Bladder wall mass: See “Pathologic findings”
  - Benign cystic lesions: Urinary calculi, interstitial cystitis, bladder cancer, chronic prostatitis

- **Diagnosis**
  - **Pathologic Findings**
    - **Benign lesions**
      - Nonneoplastic adenoma: Metaplastic response to chronic inflammation
      - Von Brunn nests: Benign urothelial cells within the lamina propria
    - Squamous metaplasia: Common in women (40%)
      - Cystitis cystica: Central cystic degeneration of Von Brunn nests
      - Basaloid cysts
      - Malignant tumors
      - The primary tumor is urothelial—a single carcinoma

- **Associated Genes and Proteins**
  - Loss of Retinoblastoma (Rb) gene on chromosome 9
  - Inflammation is a risk factor for squamous cell carcinoma
  - Loss of Retinoblastoma (Rb) gene on chromosome 9
  - Inflammation is a risk factor for squamous cell carcinoma

- **Patterns of spread of bladder cancer**
  - Local extension—urothelial and smooth muscle
  - Lymphatic—lymph nodes, liver, bone, lung
  - Hematogenous—to liver, lung, bone, etc.

- **DIFFERENTIAL DIAGNOSIS**
  - Bladder wall mass: See “Pathologic findings”
  - Benign cystic lesions: Urinary calculi, interstitial cystitis, bladder cancer, chronic prostatitis
SURGERY/OTHER PROCEDURES

TURBT
- Diagnostic: Consider repeat resection for T1 disease
- Therapeutic for non-muscle invasive disease
- Partial cystectomy
- For selected patients with unfavorable disease, unusual tumors, and tumors in diverticula
- Radical cystectomy
- For muscle invasive disease
- Consider for recurrent high-grade superficial disease

ADDITIONAL TREATMENT

Radiation Therapy
- Can be used in bladder sparing protocol
- Internal beam radiotherapy combined with chemotherapy to improve outcomes
- 5-y overall survival ~50%

Additional Therapies

- Cisplatin-based therapy is 1st line for small cell carcinoma
- Neoadjuvant chemotherapy for locally advanced disease prior to cystectomy
- Chemotherapy for metastatic disease with other gemcitabine, vinblastine, docetaxel and cisplatin, or gemcitabine and cisplatin

Complementary & Alternative Therapies

- Phototherapy: No long-term data
- Laser therapy
- Vitamins (6)

- Increased carotene intake, including beta-carotene, alpha-carotene and lycopene, is associated with decreased bladder cancer mortality associated with a decreased risk of bladder cancer
- Megadose multivitamins A, B6, C, and E plus zinc may decrease bladder tumor recurrence in patients receiving BCG immunotherapy
- Increased carotene intake, including beta-carotene, alpha carotene and lycopene, is associated with decreased bladder cancer risk

ONGOING CARE

PROGNOSIS

- Progression and recurrence depend upon grade, stage, size, the presence of CIS, multifocality, and frequency of prior recurrences.

COMPLICATIONS

- Bladder perforation from TURBT
- Disease progression and metastases
- Hematuria
- Urinary obstruction
- UTI or sepsis

FOLLOW-UP

Patient Monitoring
- History and physical, urinalysis, cystoscopy, and urine cytology every 3 mo for 2 yr, then every 6 mo to 2–3 yr, then once a year.
- Periodic upper tract imaging for high-risk patients

Patient Resources

- BCAN http://www.bcancer.org/bladder-cancer/support-group/

REFERENCES


ADDITIONAL READING

N/A

See Also (Topic, Algorithm, Media)

- Bladder Cancer, General Considerations
- Bladder Cancer, SCC
- Bladder Cancer, Urothelial, Superficial (Ta, T1) (NMIBC)
- Bladder Cancer, Urothelial, Metastatic (Clinical and Pathologic: N—, M—)
- Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic: T1/T2/T3/T4) (NMIBC)
- Bladder Cancer, Urothelial, Superficial Carcinoma In Situ (CIS) (NMIBC)
- Bladder Mass, Differenrtial Diagnosis
- Bladder Tumor Algorithm 1
- Bladder Tumors, Benign and Malignant, General Considerations Image 1
- Bladder Wall Calcification, Differential Diagnosis
- Bladder Wall Thickening, Differential Diagnosis
- Cystic Cystitis
- Cystitis Glandularis and Cystitis Glandularis of the Intestinal Type
- Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP)

CODES

ICD9
- 188.9 Malignant neoplasm of bladder, part unspecified
- 223.3 Benign neoplasm of bladder
- 295.7 Neoplasm of uncertain behavior of bladder

ICD10
- C99.9 Malignant neoplasm of bladder, unspecified
- D40.3 Benign neoplasm of bladder
- D41.4 Neoplasm of uncertain behavior of bladder

CLINICAL/SURGICAL PEARLS

- Painless gross hematuria must be investigated to rule out bladder cancer.
- Smoking is the most common risk factor for bladder cancer.
- TURBT with biopsy is mandatory for diagnosis and staging of all bladder tumors.
BOWEN DISEASE AND ERYTHROPLASIA OF QUEYRAT

Justin D. Ellett, MD, PhD
S. Walker Nickles, MD

DESCRIPTION
Bowen disease is squamous cell carcinoma in situ (CIS) of the foreskin-bearing epithelium of the shaft and scrotum.

Erythroplasia of Queyrat (EQ) is squamous cell carcinoma in situ (CIS) arising within the preputial mucocutaneous (mucosal) epithelium of the glans penis or inner side of the foreskin. 80–90% of cases are seen in uncircumcised men.

PREVALENCE
Most often occurs in Caucasian males
Mostly in uncircumcised men
Majority in men ages 50–70, but described in adult males of all ages

INCIDENCE
Coinfection of HPV type 8 and carcinogenic genital smegma though to be carcinogenic

EPIDEMIOLOGY
Incidence
Penile cancer occurs in 1% of all malignancies in men, and EQ and BE are a fraction of these

RISK FACTORS
Relative risk factors:
HPV types (16, 18, 39, 51) have been reported
Smegma thought to be carcinogenic
Phimosis present in 75% of cases
– Arsenic exposure from well-water and other sources
– Immunosuppression from HIV/AIDS
– Therapeutic immunosuppression for organ transplants
– Infections from HPV/AIDS
– Acetic exposure from well water and other sources
– Chronic injury and inflammation from poor hygiene, urine, smegma
– Radiation
– Chronic dermatoses
– Thermal injury
– Ionizing radiation
– Arsenic exposure
– Lichen sclerosis of the glans penis
– Relationship to other structures (submucosal, corpora spongiosa and/or cavernosa, urethra)

PATHOPHYSIOLOGY
Carcinogenesis results from:
– Chronic injury and inflammation from poor hygiene, urine, smegma
– Radiation
– Exposure to chemical carcinogens, such as arsenic or smoking
– HPV infection
– Decreased immune surveillance due to HIV/AIDS or medical immunosuppression

ASSOCIATED CONDITIONS
– Progression to invasive SCC in 5–30% of cases; more likely with EQ
– Lichen sclerosis, balanitis xerotica obliterans (BXO)

GENERAL PREVENTION
– Circumcision
– Daily genital hygiene by retraction of foreskin and cleansing
– Elimination of risk for HPV infection
– Early detection of lesions
– Treatment of phimosis

DIAGNOSIS

HISTORY
– Age: Median age 50
– Sexual promiscuity (increases risk for HPV infection)
– History of phimosis or difficulty retracting foreskin
– History of nonhealing wounds, pruritus, bleeding, discharge
– History of exposure to ionizing radiation or arsenic
– History of immunosuppression for organ transplants
– Sexual promiscuity
– Age: Median age 50
– Recent history of HPV infection
– Presence of ulceration increases likelihood of invasive SCC
– Presence of ulceration increases likelihood of invasive SCC
– Examination of inguinal nodes
– Important factors to assess:
– Diameter of lesion
– Location
– Number of lesions
– Histology (papillary, nodular, verrucous, or flat)
– Relationship to other structures (submucosal, corpora spongiosa and/or cavernosa, urethra)

PHYSICAL EXAM
– Solitary or multiple nontender erythematous plaques
– BD: Scaly, verrucoid plaque on shaft
– EQ: Velvety, smooth, shiny on glans
– BD: Usually at base of glans and penile shaft
– EQ: Usually on glans
– BD: Pearly, skin-toned papule or plaque, often with overlying telangiectasias
– EQ: Usually associated with lesions at other sites
– BD: Usually in uncircumcised men
– EQ: Majority in men ages 50–70
– BD: Scaly, verrucoid plaque on shaft

PATHOLOGY
Definitive diagnosis may only be made by biopsy

DIAGNOSTIC TESTS & INTERPRETATION
Lab
– Testing for carcinogenic HPV types

Imaging
– Imaging only indicated in instances of clinical suspicion of invasion, and would include MRI or ultrasound

DIFFERENTIAL DIAGNOSIS (1)
– Bowenoid papulosis
– Invasive SCC
– Benign course, but histologically similar except abnormal keratinocytes are spread discontinuously throughout epidermis
– Early invasion should be excluded via the use of multiple biopsies
– Usually spontaneously regresses

DIFFERENTIAL DIAGNOSIS (2)
– Squamous cell carcinoma
– Immunohistochemistry
– Ulceration
– Painful, coin-shaped plaques of small grouped papules on erythematous base
– Typical in younger patients (ages 25–30)
– Usually spontaneously regresses
– Usually at base of glans and penile shaft
– BD: Usually in uncircumcised men
– EQ: Majority in men ages 50–70
– BD: Scaly, verrucoid plaque on shaft
– EQ: Usually on glans
BOWEN DISEASE AND ERYTHROPLASIA OF QUEYRAT

- Balanitis circinata
  - Dry and scaling lesions of the glans in circumcised or uncircumcised males
  - Associated with Reiter’s syndrome
  - Can be moist and erythematous in uncircumcised males
- Candidal balanitis
  - Usually found in uncircumcised diabetics
  - Reddened and edematous lesions
  - Usually treated with antifungal therapy
  - In elderly, uncircumcised males
  - Usually distinguished from CIS on biopsy by band-like infiltrate of plasma cells

TREATMENT

GENERAL MEASURES (3)
Treatment based on multiple biopsy samples of adequate depth to rule out invasion

MEDICATION
First Line
- Topical therapy
  - 5-fluorouracil cream BID for 4–5 wk or
  - 5% imiquimod cream daily for 16 wk
  - Proven effective for large lesions not amenable to surgery or for recurrent lesions
  - Utilized with rubber condom to increase contact time

Second Line
N/A

SURGERY/OTHER PROCEDURES
- Circumcision can decrease likelihood of recurrence
- With lesions on the foreskin, circumcision, or excision with 5-mm margin is adequate for local control
- Lesions on the glans are difficult to excise with this strategy when trying to preserve penis anatomy
- Ensure adequate depth of resection to rule out invasion
- Mohs micrographic surgery has been utilized to accomplish adequate excision without disfigurement
- Nd:YAG, KTP, or carbon dioxide laser ablation has been shown to be effective
  - Nd:YAG preferred due to depth of penetration

ADDITIONAL TREATMENT
Radiation Therapy
Radiation therapy can be used for patients resistant to topical treatment or who are not surgical candidates

Additional Therapies
Additional therapies include cryotherapy, cautery, and photodynamic therapy, although their effectiveness is limited

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- 5–33% of cases have been reported to transform to SCC
  - 5–10% risk in BD, 10–33% in EQ
  - Carries significant risk of death
- All therapies have recurrence rates of 20–30%

COMPLICATIONS
Progression to invasive squamous cell carcinoma

FOLLOW-UP
Patient Monitoring
- BC and EQ surveillance parallels localized, invasive SCC of the penis with clinical exam:
  - Year 1–2, every 3 mo
  - Year 3–5, every 6 mo
  - Year 5–10, every 12 mo
  - Consider re-biopsy of recurrent lesions to rule out transformation to invasive SCC

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Bowen Disease and Erythroplasia of Queyrat Image
- Penis, Cutaneous Lesion
- Penis, Squamous Cell Carcinoma

CODES
ICD9
233.5 Carcinoma in situ of penis

ICD10
D07.4 Carcinoma in situ of penis

CLINICAL/SURGICAL PEARLS
- BC = SCC in situ arising on the glans or inner side of the foreskin.
- BD = SCC in situ of the penile shaft or corona.
- ED = 96% of cases seen in uncircumcised men.
- Progression to invasive SCC in 5–30%.
BURNS, EXTERNAL GENITALIA AND PERINEUM

Brad Figler, MD
Hunter Wessells, MD, FACS

BASICS

DESCRIPTION
Burns to the external genitalia and perineum can damage skin, subcutaneous tissue, and surrounding organs and can be due to thermal, electrical, or chemical contact.

Thermal (most common): Includes scalding and immersion injuries, direct contact with flames or hot objects.

Electrical: Passage of an electrical current from one point to another through the body.

Chemical: Corrosive and alkali substances found in household and industrial chemicals.

EPIDEMIOLOGY

Incidence
- Genital/perineal burns are rarely isolated.
- Genitals/perineum involved in 5–13% of burns treated at major burn centers.
- Abuse or neglect in 10–15% of childhood burn injuries (higher if <2 yr of age).

RISK FACTORS
- Age: Very young (scald burns common in abused children) and very old.
- Employment: Exposure to flames or caustic substances.
- Gender: Women are less likely to experience genital or perineal burns (less exposed).

PATHOPHYSIOLOGY

Classification (1)
- 1st-degree (superficial): Epidermis
  - Superficial (involving the superficial, papillary dermis)
  - Deep (involving reticular dermis)
- 2nd-degree (partial thickness): Dermis
  - Superficial (involving the superficial, papillary dermis)
  - Deep (involving reticular dermis)
- 3rd-degree: Unilateral subcutaneous tissue
  - Typically not painful due to nerve damage
- 4th-degree: Bone and muscle
  - Can lead to compartment syndrome
  - Often fatal

ASSOCIATED CONDITIONS
- Child sexual abuse
- Sexual abuse
- Myoglobinuria (electrical burns)

GENERAL PREVENTION
- Follow occupational-specific safety precautions.
- Handle caustic chemicals with care.

DIAGNOSIS

HISTORY
- Type of burn (thermal, chemical, or electrical)
- Causative agent or heat source (e.g., flame vs. water, nonionic substance)
- Location and area involved (Rule of Ns): External genitalia and perineum usually accounts for 1% of body surface area when using “Rule of Ns.”
- Possibility of other injuries (e.g., fractures from motor vehicle accidents, shrapnel).

PHYSICAL EXAM
- Complete assessment including ABCD’s of Advanced Trauma Life Support (ATLS). Often associated with concomitant injuries or further burns.
- With electrical burns determine any other entry/exit site of current.
- Rule of Ns: Based on total body surface involved. Genitalia/perineum accounts for 1% of body area.
- Vital signs (patients with electrical burns will require cardiac monitoring for at least 24 hr).
- Neurologic exam: Evaluate for compartment syndrome, peripheral pulses.
- GU: Examine for involvement of phallic, meatus, glans, and scrotum.
- Classification:
  - 1st-degree: Characterized by erythema, white plaques, and mild pain
  - 2nd-degree: Characterized by erythema, pain, superficial blisters
  - 3rd-degree: Characterized by eschar, blistering, and absence of pain due to loss of nerve fibers

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Electrolytes: Treatment of burns generally requires large amount of fluid resuscitation.
- With electrical burns, monitor creatine kinase and urine myoglobin.

Pathologic Findings
- Zone of coagulation: Occurs at point of maximum damage. In this zone, there is irreversible tissue loss due to coagulation of the constituent problem.
- Zone of stasis: Surrounding zone of stasis is characterized by decreased tissue perfusion. The tissue in this zone is potentially salvageable. The main aim of burn resuscitation is to increase tissue perfusion here and prevent any damage from becoming irreversible. Additional insults – such as prolonged hypotension, infection, or sepsis – can cause this zone into an area of complete tissue loss.
- Zone of hyperemia: In this outermost zone, tissue perfusion is increased. The tissue here will inevitably recover unless there is severe sepsis or prolonged hypoperfusion.

DIFFERENTIAL DIAGNOSIS

Diagnosis is usually apparent based on history and examination.

ALERT
- Treat any life-threatening conditions (ABCD’s).
- IVF: Resuscitation is critical if patient has severe burns.
**Burns, External Genitalia and Perineum**

**TREATMENT**

**GENERAL MEASURES**
- Treat any life-threatening conditions (ABCD)
  - Do not attempt to cool wound as this may cause more extensive injury
- Shock may occur; IVF critical
  - >20% total body surface area (TBSA), use modified Brooke formula:
    - 2 mL/kg/TBSA
- Most chemical burns should be copiously irrigated. If agent is known use guidelines:
  - Hydrofluoric acid: Irrigate with calcium gluconate
  - Hydrochloric acid or sulfuric acid: Use bicarbonate irrigation
  - Phenol: No irrigation

**MEDICATION**

**First Line**
- Silver sulfadiazine 1%: Apply to affected area
  - Does not penetrate eschar
- Mafenide acetate (Sulfamylon) 11.1%: Penetrates eschar
- Pain control
  - Narcotics
  - Anti-inflammatories
- Fluid resuscitation
- Electrolytes as needed
- Tetanus prophylaxis
- Antibiotic prophylaxis not necessary
  - Treat specific infections as they arise.

**SURGERY/OTHER PROCEDURES (2,3)**
- Most burns, particularly in children, should be managed with conservative treatment and require no surgical intervention.
- Foley catheter or suprapubic drainage may be used, but are often not necessary.
- Mainstay of surgical treatment, if needed, is careful debridement.
- Affected areas may require skin coverage:
  - Granulation indicates acceptable graft bed
  - Split-thickness skin grafts have reliable graft take and excellent cosmesis
  - Skin grafts can be meshed or unmeshed
  - If graft bed health is questionable, can use temporary xenograft
- Wound contractures are not uncommon; treat with z-plasty
- Urethral stricture may develop; should be treated in a delayed fashion (4)
  - Catheter drainage may be required in the interim

**ONGOING CARE**

**PROGNOSIS**
- Based on degree and extent of burn
- Most burns have matured by 6–12 mo; additional reconstruction may be required at that time

**COMPLICATIONS**
- Erectile dysfunction
- Scarring/disfigurement

**FOLLOW-UP**

**Patient Monitoring**
- Follow-up as indicated

**Patient Resources**
- American Burn Association
  - www.ameriburn.org
- Phoenix Society for Burn Survivors
  - www.phoenix-society.org

**REFERENCES**

**ADDITIONAL READING**

**SEe Also** (Topic, Algorithm, Media)
- Burns, External Genitalia and Perineum Image 6
- Penis, Trauma
- Scrotum and Testicle, Trauma

**CODES**

**ICD9**
- 942.05 Burn of unspecified degree of genitalia
- 942.15 Erythema (first degree) of genitalia
- 942.25 Blisters, epidermal loss (second degree) of genitalia

**ICD10**
- T21.06XA Burn of unsp degree of male genital region, init encntr
- T21.07XA Burn of unsp degree of female genital region, init encntr
- T21.16XA Burn of first degree of male genital region, init encntr
- T21.16XB Burn of first degree of female genital region, init encntr

**CLINICAL/SURGICAL PEARLS**
- Genital/perineal burns are rarely isolated.
- Favor conservative management initially.
- Excellent functional and cosmetic results are possible with split-thickness skin grafting.
CALYCEAL DIVERTICULA
Yaniv Shilo, MD
Timothy D. Averch, MD, FACS

## BASICS

### DESCRIPTION
- Calyceal diverticula are nonsecretory, transitional cell epithelium-lined cystic cavities within the renal parenchyma.
- The cavity is usually filled retrograde from urine in the collecting system.
- Mostly unilateral.
- Most prevalent in upper calyces (70%).
- No gender nor laterality predilection.
- Bilateral in 3%.
- Sometimes called pelvicaliceal diverticula.

### EPIDEMIOLOGY

#### Incidence
- Less than 1%.

#### Prevalence
- Found in up to 0.45% of routine intravenous pyelogram studies.

### RISK FACTORS

#### Genetics
- N/A.

### PATHOPHYSIOLOGY
- Congenital in origin due to failure of regression of ureteric bud.
- Urine enters diverticulum passively via narrow communication with collecting system.
- Urine trapped in diverticulum predisposes to infection and stone formation.

### ASSOCIATED CONDITIONS
- Flank pain.
- Calyceal calculi (9–50%).
- Recurrent urinary tract infection (UTI).
- Hematuria.

### GENERAL PREVENTION
- N/A.

## DIAGNOSIS

### HISTORY
- Mostly incidental finding on imaging.
- Flank pain.
- Microhematuria or macrohematuria.
- Recurrent UTI.

### PHYSICAL EXAM
- Usually not suggestive.

### DIAGNOSTIC TESTS & INTERPRETATION

#### Lab
- Urinalysis:
  - Microhematuria and pyuria.
- Urine culture:
  - Bacterial persistence.

#### Imaging
- Abdominal x-ray (KUB):
  - May demonstrate characteristic radiopaque "milk of calcium," which appears as a half moon or meniscus-shaped calcification.
  - Milk of calcium should change its location when changing positioning from erect to lateral decubitus.
- Case reports of confusion as being diagnosed as rib metastasis.
- Ultrasound (US):
  - Provide diagnosis in up to 90% of the cases.
- CT urography (CTU):
  - Delayed imaging is critical to demonstrate contrast medium within an apparent cystic mass.

### Diagnostic Procedures/Surgery

- Intravenous pyelography (IVP):
  - Detected imaging demonstrates the diverticulum, as it fills retrogradely from its connection to the renal pelvis or calyx.
- CT urography (CTU):
  - Delayed imaging is critical to demonstrate contrast medium within an apparent cystic mass.
- Retrograde pyelogram:
  - Allows greater distension of the collecting system than can be attained with IVP.
  - Delineating anatomy and assist in planning the appropriate treatment approach.

## Pathologic Findings
- Lined by nonsecretory transitional epithelium.
- Retrograde reflux of urine from the calyx via the diverticular neck can cause stasis with stones in calyceal diverticula in up to 50% of cases.

## DIFFERENTIAL DIAGNOSIS
- Calcified tumor.
- Complicated renal cyst.
- Kidney abscess.
- Nephrolithiasis.

## TREATMENT

### GENERAL MEASURES
- In case of uncomplicated, asymptomatic calyceal diverticulum treatment can be conservative with no further imaging follow-up.
- Indications for therapy include pain, recurrent infection, increased calculus growth, hematuria or large size that compresses or progressively damages contiguous renal parenchyma.

### MEDICATION

#### First Line
- Antibiotic treatment can be used for recurrent UTIs; otherwise no specific role.

#### Second Line
- N/A.

### SURGERY/OTHER PROCEDURES

- Shock wave lithotripsy (SWL):
  - May be suitable for calyceal diverticulum with small calculi and wide infundibulum (1).
  - Can resolve flank pain.
- Ureteroscopy (URS):
  - Most suitable as initial treatment for calculi <1.5 cm located in the middle or upper pole diverticulum and specifically in the anterior aspect.
  - Involves mechanical dilatation of the diverticular neck and removal of calculus if present.

- Abdomopacification of diverticular cavity is not a common practice.
CALYCEAL DIVERTICULA

**Percutaneous nephrolithotomy (PCNL):**
- Considered to be the definitive surgical treatment specifically for diverticula containing stone burden >1.5 cm in the posterior aspect.
- Challenging when only thin layer of parenchyma surrounding the diverticula or located anteriorly.
- Requires direct access to diverticulum and infundibulum widening.
- Ablation of the calyceal diverticulum cavity is recommended (2).

**Laparoscopic nephrolithotomy (LAP):**
- May be advantageous in cases of anterior diverticula, diverticula covered with thin layer, diverticula containing large calculi or large diverticula (3).
- Includes unroofing of the diverticulum and calculi removal if present.
- Ablation of the remaining cavity and neck.

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- N/A

**Complementary & Alternative Therapies**
- N/A

**ONGOING CARE**

**PROGNOSIS**
- Stone-free rate is relatively low (up to 60%).
- URS: Stone-free and symptom-free rates can be high when infundibulum is identified.
- PCNL: Excellent stone-free and symptom-free rates (over 80%).
- LAP: Initial results show high stone-free rate and diverticular ablation.

**COMPLICATIONS**
- Calyceal diverticula:
  - Secondary infection
  - Chronic pain with stones
  - Compression of surrounding tissue
  - Bleeding
  - Infection
  - Subcapsular or perinephric hematoma
- URS:
  - Bleeding
  - Thermal injury to ureteral wall or renal parenchyma
  - Urinary extravasation
  - Nephrothorax
  - Collecting system perforation

**FOLLOW-UP**

**Patient Monitoring**
- Radiographic imaging with either CTU, IVP, or kidney US should be done 6–8 wk postoperatively.
- Patients with calculi contained in diverticulum may need metabolic evaluation as these patients tend to have metabolic abnormalities similar to patients with nephrolithiasis (1).

**Patient Resources**
- N/A

**REFERENCES**

**ADDITIONAL READING**

**See Also** (Topic, Algorithm, Media)
- Calcifications, Renal
- Calyceal Diverticula Image
- Nephrocalcinosis
- Urolithiasis, Adult, General considerations
- Urolithiasis, Renal

**CODES**
- ICD9:
  - 592.0 Calculus of kidney
  - 593.89 Other specified disorders of kidney and ureter
  - 753.8 Other specified congenital malformations of kidney
- ICD10:
  - N20.0 Calculus of kidney
  - N28.89 Other specified disorders of kidney and ureter
  - Q63.8 Other specified congenital malformations of kidney

**CLINICAL/SURGICAL PEARLS**
- Usually located on upper calyces.
- Associate disorders include—calyceal calculus, recurrent UTI, and flank pain.
- URS is suitable for anterior midpole or upper diverticula with calculi <1.5 cm.
- PCNL is the treatment of choice in general for calyceal diverticula and specifically for posterior diverticula with thick layer of parenchyma surrounding with calculi >1.5 cm.
- Growing evidence for the effectiveness of LAP approach in cases of anterior diverticula, diverticula covered with thin layer, diverticulum containing large calculi or large diverticulum.
CATHETERIZABLE STOMA PROBLEMS
Zachary L. Smith, MD  S. Bruce Malkowicz, MD, FACS

PATHOPHYSIOLOGY
- Stomal stenosis can be attributed to infrequent catheterization, scar formation, ischemia secondary to compromised vascular supply to catheterizable channel, or a remnant-free mucocutaneous anastomosis.
- Difficulty catheterizing the CS channel can be attributed to angulation of a mobile and/or redundant channel.
- Significant weight loss or gain
- Improper creation of continence mechanism
- Incomplete detubularization or augmentation of the urinary reservoir can lead to incontinence secondary to low compliance and small reservoir capacity.
- Pouchitis (lower urinary tract infection) can cause temporary failure of the continence mechanism because of the hypercontractility of the bowel segment; can be caused by inflammation of the mucosa.

ASSOCIATED CONDITIONS
- Urologic, gynecologic, and colorectal malignancies
- Spinal dysraphisms
- Traumatic spinal cord injuries
- Incomplete detubularization or augmentation of the urinary reservoir can lead to incontinence secondary to low compliance and small reservoir capacity.
- Malignancy
- Incontinence (urinary vs. fecal)

DIAGNOSIS

HISTORY
- Date of surgery
- Indication for CS
- Incontinence (urinary vs. fecal)
- Malignancy
- Attempt to obtain operative reports
- Type of bowel utilized
- History of CS complications
- Catheterization details:
  - Typical catheterization regimen
  - Type and size of catheter used
  - Technique utilized (direction, amount of pressure, etc.)
- Normal catheterization volumes
- Time of last normal catheterization
- Character of urine at the time of last successful catheterization (color, odor, presence of debris, etc.)

PHYSICAL EXAM
- Vital signs may reveal tachycardia, hypotension, and fever in patients with peritonitis secondary to perforation of the catheterizable channel or urinary reservoir.
- Abdominal exam evaluating signs of peritonitis
- Inspection of the stoma, evaluating for:
  - Tenesmus
  - Mucosal ischemia
  - Abdominal wall deformity suggestive of parastomal hernia
  - Catheterization of CS to:
    - Evaluate patency of stoma
    - Determine capacity of urinary reservoir
    - Evaluate continence mechanism
    - Obtain urine sample
    - Inspect contrast for imaging.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Serum electrolytes:
  - Elevated serum creatinine may be noted in patients with urinary retention from the inability to catheterize.
  - Several metabolic abnormalities may be present in patients with urinary reservoirs, depending on bowel segment utilized.
    - Stomach: Hypochloremic, hypokalemic alkalosis
    - Jejunum: Hyponatremic, hypochloremic, hyperkalemic acidosis
    - Ileum: Hypochloremic, hyperkalemic acidosis
    - Colon: Hyperchloremic acidosis
  - CBC:
    - Leukocytosis suggestive of infection
    - Blood and urine cultures in patients presenting with abdominal pain and fever

Imaging
- Contrast study of catheterizable channel and urinary reservoir to evaluate for perforation
- Cross-sectional imaging of the kidneys assessing for the presence of hydronephrosis

ALERT
- Have a low threshold for obtaining a cross-sectional imaging study (CT/MRI) with contrast when a perforation of the CS or urinary reservoir is suspected, especially in patients with neurologic deficits.
DIFFERENTIAL DIAGNOSIS
- Parastomal hernia:
- Stomal stenosis:
- Fistula:
- Pouchitis:
- Perforation of CS conduit or urinary reservoir
- Inability to catheterize secondary to false passage or redundancy of CS channel:
- Fistula:
  - Electrolyte revision
  - Inability to catheterize secondary to false passage or redundancy of CS channel:
  - Electrolyte revision
  - Occasionally, minor false passages can be treated with an indwelling catheter for a short period to allow healing of channel.

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

- Stomal stenosis:
  - Routine catheterization schedule
  - Dilatation of stenosis
  - Local excision
  - Antibiotics
  - Catheterizable channels and the timing of their catheterization

Ongoing Care

Study following stoma revisions for stoma ranges from 80–95% (1). Complications

Follow-Up

Maintenance of routine catheterization schedule

Patient Monitoring

- Additional follow-up with enterostomal therapist

Patient Resources

- National Ostomy Association of America, Inc.
- Bladder Cancer Advocacy Network: www.bcan.org
- United Ostomy Associations of America, Inc.: www.ostomy.org

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Bladder Cancer, Urothelial, Muscle Invasive (Clinical and Pathologic T2/T3/T4) (NMSC)
- Bladder Cancer, Squamous Cell Carcinoma
- Catheterizable Stoma Problems Image
- Fistula
- Pouchitis
- Urinary Problems

CODES

ICD-9
- 598.82: Mechanical complication of cystostomy
- 598.83 Other complication of cystostomy
- V55.5: Attention to cystostomy

ICD-10
- N99.512: Cystostomy malfunction
- N99.518 Other cystostomy complication
- Z43.5: Encounter for attention to cystostomy

CLINICAL/SURGICAL PEARLS

- Catheterizable stoma are used for varying reasons throughout one’s life. Benign/neurogenic causes most common in children, malignant causes most common in adults.
- Stomal stenosis is by far the most common complication of catheterizable stomas.
- Surgical revision is often required for most catheterizable stoma complications.
- Good technique and catheterizable stoma maintenance with a routine catheterization schedule can prevent most complications.
CHordee
Jennifer A. Hagerty, DO

### BASICS

**DESCRIPTION**
- Chordee is ventral penile curvature that occurs with or without hypospadias.
  - Epispadias can occur with dorsal curvature.
  - Lateral curvature also can occur with or without hypospadias.

**EPIDEMIOLOGY**

**Incidence**
The incidence of chordee is unknown.

**Prevalence**
- 44% of fetuses through the 2nd trimester suggesting chordee is a normal part of development (1A).
- Hypospadias occurs in 1 of 250 live births (3A).
  - Chordee is identified in 1/3 of these patients (3A).

**RISK FACTORS**
- Congenital
- Prior penile surgery
- Trauma

**Genetics**
- Found in syndromes associated with hypospadias.
- Chromosomal abnormalities found in 22% of individuals with severe hypospadias associated with undescended testicles.
- 14% of hypospadias in siblings.
- 8% incidence in offspring.

**PATHOPHYSIOLOGY**
- Chordee could be considered an arrest of normal embryologic development.
- Different proposed etiologies for chordee without hypospadias (2,4):
  - Class I: Results when corpus spongiosum, dartos, and Buck fasciae are deficient over the involved portion of the urethra, urethra is just below the skin, and the dense fibrous tissue beneath the urethra is responsible for the chordee.
  - Class II: Spongiosum is normal while the dartos and Buck fasciae are dysgenetic.
  - Class III: Only the dartos fascia is deficient.
  - Class IV: Corporeal disproportion.

**ASSOCIATED CONDITIONS**
- Hypospadias
- Epispadias
- Penile torsion
- Cryptorchidism
- Disorders of sexual development

**GENERAL PREVENTION**
None known

### DIAGNOSIS

**HISTORY**
- Visualized curvature of the penis with an erection.
- Presence of hypospadias.

**PHYSICAL EXAM**
- Observe the individual's erection if possible.
  - Possible coexisting findings:
    - Hypospadias or epispadias
    - Incomplete foreskin ventrally
    - Penoscrotal webbing
    - Penile torsion
    - Hypoplasia of the ventral shaft skin
    - Cryptorchidism

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Routine lab testing not typically indicated.
- Chromosomal testing and/or biochemical testing in the individual with a suspected syndrome or disorder of sexual differentiation.

**Imaging**
- Renal and bladder ultrasound routinely recommended only in individuals with:
  - Severe hypospadias.
  - Hypospadias associated with other organ system anomalies.

**Diagnostic Procedures/Surgery**
- Intraoperative artificial erection test at the time of repair.
- Inflation of injectable saline into the corpora with a tourniquet at the base of the penis.

**Pathologic Findings**
N/A

### DIFFERENTIAL DIAGNOSIS
- Disorder of sex development
- Epispadias
- Hypospadias
- Normal penile variant
- Penile torsion

### TREATMENT

**GENERAL MEASURES**
- Chordee repair is the standard approach.

**MEDICATION**
- First Line: None usually indicated specifically for chordee.
- Second Line: N/A

**SURGERY/OTHER PROCEDURES**
- Specific surgery dependent on the associated conditions and the severity of the curvature.
- Performed typically after 6 mo of age.
  - General points:
    - Following penile skin release, induce artificial erection. This should be repeated to confirm correction.
    - Chordee without hypospadias often can be corrected by penile degloving with excision of the fibrous tissue superficial to Buck fascia.
    - More moderate chordee requires simple plication and/or excision of ellipses from the site of maximum curvature.
    - In the most severe cases, often associated with hypospadias, the urethra may be shortened and need to be transected.
Chordee secondary to corporeal disproportion involves incising the tunica albuginea on the ventral surface of the penis, transversely over the point of maximal curvature; then covering the defect with either a full-thickness, tunica vaginalis or single ply small intestinal submucosal (SIS) graft.

It is critical to identify and preserve the neurovascular bundles during dissection and plication.

Skin flaps may be required for penile skin coverage after correction of the chordee.

**ADDITIONAL TREATMENT**

**Radiation Therapy**

N/A

**Additional Therapies**

N/A

**Complementary & Alternative Therapies**

N/A

**ONGOING CARE**

**PROGNOSIS**

- Excellent prognosis postoperatively with a low complication rate
- There may be progression of chordee after puberty

**COMPLICATIONS**

Recurrence of chordee

**FOLLOW-UP**

**Patient Monitoring**

- Postoperative check-up within several weeks after surgery
- Consider follow-up after puberty

**PATIENT RESOURCES**


**REFERENCES**


**ADDITIONAL READING**


**CODES**

**ICD9**

- 607.89 Other specified disorders of penis
- 752.61 Hypospadias
- 752.63 Congenital chordee

**ICD10**

- N48.89 Other specified disorders of penis
- Q54.4 Congenital chordee
- Q54.9 Hypospadias, unspecified

**CLINICAL/SURGICAL PEARLS**

- Chordee most commonly occurs with hypospadias.
- Repair recommended after 6 mo of age.
- Consider ongoing monitoring after puberty.

**SEE ALSO (TOPIC, ALGORITHM, MEDIA)**

- Chordee Image
- Disorders of Sexual Development (DSD)
- Epispadias
- Hypospadias
CHRONIC KIDNEY DISEASE, ADULT (RENAL FAILURE, CHRONIC)
Shawn G.S. Grewal, MD
Gerald L. Andriole, MD, FACS

PATHOPHYSIOLOGY
Pathologic Findings
- Renal biopsy
- Nondiabetic kidney disease
- Nephrotic syndrome
- Acute/nephritic syndrome
- Acute/rapid progressive kidney disease
- Urologic evaluation if gross or microscopic hematuria
- Cytoscopy
- Upper tract imaging
- Angiography (CT or MR angiogram)

Differential Diagnosis
- Renal biopsy/kidney
- Nondiabetic kidney disease
- Nephrotic syndrome
- Acute/nephritic syndrome
- Acute/rapid progressive kidney disease
- May also be seen on nephrectomy/partial nephrectomy specimens

Diagnostic Procedures/Surgery
- Renal biopsy
- Nondiabetic kidney disease
- Nephrotic syndrome
- Acute/nephritic syndrome
- Acute/rapid progressive kidney disease
- Urologic evaluation if gross or microscopic hematuria
- Cytoscopy
- Upper tract imaging
- Angiography (CT or MR angiogram)

Diagnosis
- Silent, asymptomatic until late stages
- Evaluate for symptoms of associated conditions/risk factors
- May be seen on nephrectomy/partial nephrectomy specimens

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Chemistry
- Elevated creatinine
- Elevated blood urea nitrogen
- Hyperkalemia
- Acidosis
- Hyperphosphatemia
- Uremia with microcytosis
- Hemosiderin
- Casts: RBC (glomerulonephritis), WBC (interstitial nephritis)

Genetics
- Complex phenotype impacted by various genetic factors, with additional environmental factors
- CYP24A1 gene involved in renal bone reabsorption and is associated with increased risk in African Americans (6)
- APOL1 associated with focal segmental glomerulosclerosis and hypertension associated EDS (1)

Risk Factors
- Diabetes
- Hypertension
- Cardiovascular disease
- Family history
- Age >60
- Urinary tract obstruction
- Urinary calculi
- Nephrotic drugs
- Obesity
- Neplasia
- Loss of kidney mass
- Race
- African American, American Indian, Hispanic, Asian, or Pacific Islander

EPIDEMIOLOGY
Incidence
- 5% prevalence in noninstitutionalized adults
- Corresponds to 20 million people
- 398,000 treated by dialysis in 2000, expected to increase to 2 million people by 2030
- Prevalence in US population
- Stage 1: 1.1%
- Stage 2: 2.2%
- Stage 3: 7.7%
- Stage 4/5: 0.3% [1]

Associated Conditions
See risk factors

GFR (mL/min/1.73 m²) for:
- Stage 1: Kidney damage with normal renal function
- Stage 2: Mild renal dysfunction
- Stage 3: Moderate renal dysfunction
- Stage 4: Severe renal dysfunction
- Stage 5: Kidney failure (GFR < 15 or dialysis required)

Incidence
- Stage 1 or 2 CKD progress to more advanced stages at 0.5% per year
- Stage 1 or 2 CKD progress to end-stage renal disease at 1.5% per year

Hypertension
- African American, American Indian, Hispanic, Asian, or Pacific Islander

Description
- Complex phenotype impacted by various genetic factors, with additional environmental factors
- CYP24A1 gene involved in renal bone reabsorption and is associated with increased risk in African Americans
- APOL1 associated with focal segmental glomerulosclerosis and hypertension associated EDS

PHYSICAL EXAM
- Physical exam findings uncommon until late stages
- Differentiate from acute kidney disease based on duration and underlying etiology
- Acute kidney injury
- Acute nephritis
- Acute/nephritic syndrome
- Nondiabetic kidney disease
- Nephrotic syndrome
- Acute/rapid progressive kidney disease
- May also be seen on nephrectomy/partial nephrectomy specimens

PATHOBASIS
- Heterogenous condition with various causes
- Diabetic kidney disease
- Nephrotic kidney disease
- Glomerular disease
- Vascular disease
- Tubulointerstitial disease
- Cystic disease (polycystic kidney disease)
- Transplant nephropathy
- Acute rejection
- Chronic rejection
- Calcineurin toxicity
- Glomerulonephropathy

Associated Conditions
See risk factors

Screening and treatment of associated risk factors

Risk Factors
- Diabetes
- Hypertension
- Cardiovascular disease
- Family history
- Obesity
- Neplasia
- Loss of kidney mass
- Race
- African American, American Indian, Hispanic, Asian, or Pacific Islander

84
CHRONIC KIDNEY DISEASE, ADULT (RENAL FAILURE, CHRONIC)

TREATMENT
GENERAL MEASURES
- Use CKD staging to guide management (ie, risk for progression and complications of CKD). See Table II: “Chronic Kidney Disease (CKD).”
- Goal is reduction of morbidity and mortality from associated comorbidities.
- Patient more likely to die of cardiovascular disease than progress to dialysis (3).
- Blood glucose control (HbA1c <7).
- Treatment of proteinuria and hypertension.
- Treatment of dyslipidemia to prevent cardiovascular events.
- Addressing alterations in bone metabolism (hyperparathyroidism, Vitamin D deficiency).
- Prevention of contrast-induced nephropathy (patient at risk if GFR <60).
- Avoidance of herbal remedies which may have nephrotoxic effects.

ADDITIONAL TREATMENT
Surgery/Other Procedures
- Dialysis access as appropriate (vascular or peritoneal).
- Renal transplantation.

Procedures
- Skin biopsy (biopsy) if appropriate.
- Peritoneal dialysis.
- Arteriovenous fistula.
- Arteriovenous graft.

MEDICATION
First Line
- ACE inhibitors (ACE-I) (captopril, enalapril, ramipril, others).
- Angiotensin II receptor blockers (ARBs) (losartan, olmesartan, telmisartan others).
- Statin therapy.
- Statin therapy.
- Statin therapy.
- Statin therapy.

Second Line
- Thyroid hormone, erythropoietin, anabolic agents, or erythropoiesis-stimulating agents.
- Calcium and vitamin D supplements.
- Phosphorus binders.
- Paricalcitol.
- Denosumab.

Therapies
- Calcium and vitamin D supplements.
- Phosphorus binders.
- Paricalcitol.
- Denosumab.

Clotting
- Factor replacement therapy.
- Anticoagulants.

SURGERY/OTHER PROCEDURES
- Skin biopsy (biopsy) if appropriate.
- Peritoneal dialysis.
- Arteriovenous fistula.
- Arteriovenous graft.

PROGNOSIS
- Degree of proteinuria correlates with risk of progression.

FOLLOW-UP
Patient Monitoring
- Stage 1–2
  - Monitor GFR, proteinuria, and blood pressure.
  - Clinical abnormalities rare at this stage but patients must be monitored for progression.
  - Monitor heart rate and diastolic blood pressure in diabetics.
  - Renal function evaluation every 3 mo.
  - Serum electrolytes, and hemoglobin.

- Stage 3
  - MNT GFR, proteinuria, blood pressure, HbA1c, serum electrolytes, and hemoglobin.
  - Elevation of phosphorus, potassium, and anemia may be seen.

- Stage 4
  - Monitor GFR, proteinuria, blood pressure, HbA1c, serum electrolytes, and hemoglobin.
  - Significant electrolyte abnormalities common; monthly follow-up with nephrology.

- Stage 5
  - Severe electrolyte abnormalities and anemia present; ongoing follow-up with renal replacement therapy.

Patient Resources
- National Kidney Foundation.
- Kidney.org/patients.

ONGOING CARE
PROGNOSIS
- Variable depending on stage, patient risk factors, and management of comorbidities.
- 10–100× increased risk of cardiovascular complications in ESRD patients.
- 13–28% 1 yr mortality in patients initiating hemodialysis (5).

COMPLICATIONS
- CKD patients at increased risk of progression.
- Cardiovascular disease, hypertension, anemia, disorders of mineral metabolism, and death.

PEARLS
- Degree of proteinuria correlates with risk of progression.

CLINICAL/SURGICAL PERILS
- Degree of proteinuria predicts progression.

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media).
- See Table in Section II “Chronic Kidney Disease (CKD).”
**CHRONIC KIDNEY DISEASE, PEDIATRIC (RENAL FAILURE, CHRONIC)**

**Timothy E. Bunchman, MD**

**Megan M. Lo, MD**

**PATHOPHYSIOLOGY**

- In interstitial renal diseases, the degree of CKD is related to the amount of renal mass. In those patients who were born with small kidneys or have associated obstructive uropathy (POCUS, UPJ, megaloureteric syndrome) often will have early progressive loss of renal function.
- Glomerular-based renal disease is more common in the school-age and greater population.
- The clinical presentation of glomerulonephritis is associated with edema, hypertension, as well as blood and protein in the urine, most need a renal biopsy.

**ASSOCIATED CONDITIONS**

- Hypertension
- Short stature

**GENERAL PREVENTION**

- In CKD associated with congenital renal disease there is no true prevention.
- In TID, the presence of polyuria, polydipsia, and congenital diseases and/or syndromes.
- Prevention from a glomerular-based renal disease is limited as these are usually related to autoimmune diseases. Therefore, the general prevention in all areas of CKD is prevention of complications of CKD.

**DIAGNOSIS**

- In glomerular-based renal disease the history is associated with grossly bloody urine, hematuria, proteinuria, hypertension, and edema. Tissue pathology is generally needed for diagnosis.
- In the review of systems, the findings of polyuria, polydipsia, and exclusion of diabetes is important.
- Family history is important in certain renal disease, specifically in the area of the familial renal disease such as IgA nephropathy, Alport, polycystic kidney disease, and rarely benign familial hematuria.
- In addition, eliciting a history of reflux and congenital renal abnormalities within the family is important.
- Further, a family history of dialysis or transplantation or unexplained hypertension earlier in life may be important.
- In the classic Alport syndrome (a male predominant disease) there is an association with high-frequency hearing loss, often in the 2nd or 3rd decade of life.

**PHYSICAL EXAM**

- Often these children have a bivirg exam

- In TID, the blood pressure and poor growth are important.
- In CGD, kids often have hypertension.
- Can have associated edema, anorexia, and cardiovascular abnormalities.

**DIAGNOSTIC TESTS & INTERPRETATION**

- **Lab**
  - Basic metabolic panel, renal function testing
  - Regardless of the etiology of CKD, at levels of CKD 3 or greater (roughly 50% kidney function), one can have:
    - Metabolic acidosis (low CO2)
    - Abnormal parathyroid activity
    - Low calcium, elevated phosphorus, and elevated PTH
    - Anemia that is usually related to a combination of iron deficiency, as well as the lack of natural erythropoiesis.
  - C3-C4 complement
  - Decreased in some glomerulonephritis and lupus nephritis.
  - Urinalysis:
    - In TID, the urine is usually benign with inability to concentrate the urine regardless of the time of day.
    - In CGD, often these patients can have blood and protein and red cell casts.
    - Urine protein: Creatinine ratio, usually 24 hr urine for protein.

- **Imaging**
  - In TID if the renal imaging is important.
    - Often these patients can have normal to small looking kidneys seen on ultrasound. The echogenic texture will be important. Further, some degree of obstructive uropathy may be seen.
    - Voiding cystourethrogram may be indicated
    - In those patients who have obstructive uropathy, either a UBT or IVU, a diuretic renal scan or MAG3 scan may be important.
  
  - In CGD, renal imaging may show nephromegaly. Otherwise, ultrasound will be non-specific.

**Diagnosis Procedure/Surgery**

- In glomerular-based renal diseases renal biopsy is often required.
- Indication for biopsy in patients with CGD is a non-complementable glomerulonephritis or a persistant low C3, and a low C4.
- Other indications: Glomerulonephritis associated with an elevated anti-dsDNA (lupus), hemoptysis with associated renal glomerulonephritis (pulmonary, renal disease), and in patients with persistent low C3 without normalization after 12 wk, which would be postinfectious glomerulonephritis. (Historically poststreptococcal glomerulonephritis).

**Pathologic Findings**

- Histologic analysis in interstitial renal disease is not essential.
- In glomerular-based renal diseases, renal biopsy is often required.
- Depending on underlying cause, the pathologic findings are vastly different on H&E, immunofluorescence, and electron microscopy.
DIFFERENTIAL DIAGNOSIS
• As mentioned for TID, polycystic kidney disease can also be associated with diabetes, which is an easy diagnosis to exclude based on urinalysis and blood work.
• Differential diagnosis of CKD is limited to underlying disease—Congenital renal anomalies: Obstructive uropathy, renal hypoplasia or dysplasia, reflux nephropathy, polycystic kidney disease—Glomerular disease: Focal segmental glomerulosclerosis (FSGS).—Others: Hemolytic uremic syndrome, genetic diseases (tyrosinosis, oculocutaneous Alport syndrome), interstitial nephritis—Rare in childhood: Diabetic nephropathy and hypertension

TREATMENT
GENERAL MEASURES
• In chronic interstitial renal disease with polyuria/polydipsia, more fluid and sodium are needed to maintain euvolemia.
• In both groups, attention to potassium and phosphorus load is important.
• ACE inhibitors and angiotensin receptor blockers (ARB) are used for glomerular-based renal disease because of proteinuria but are contraindicated in possible pregnancy (birth defects) and low GFR (renal failure, hyperkalemia).
• All NSAIDS should be avoided. Levels of potential hypertensive agents (epoetin, darbepoetin) are used for anemia.
• Protein restriction, used in adult CKD to slow disease progression, cannot be used with kids as this would further hinder their growth and development.
• Nutrition is important: At least 2 g/kg/d protein stores and growth.
• Other renal diseases such as focal sclerosis maybe less amenable to therapy.

TREATMENT
First Line
• Treatment of metabolic acids with either liquid form of Bicara or the pill form of bicarbonate to normalize the CO₂. This will preserve growth as well as bone integrity.
• Treatment of phosphorus restriction, phosphorus binders such as calcium acetate or sevelamer products, and institution of vitamin D to preserve and prevent secondary hyperparathyroidism and prevent bone disease.

Second Line
• Those that were mentioned above including antihypertensive agents if indicated.
• Often ACE inhibitors and angiotensin receptor blockers (ARB) are used for glomerular-based renal disease because of proteinuria but are contraindicated in possible pregnancy (birth defects) and low GFR (renal failure, hyperkalemia).

SURGERY/OTHER PROCEDURES
In TID, patients may require cystoscopy with ablation of PUV. UPJ or UVJ obstructions may need to be corrected. Reflux may need to be corrected, if high grade and not resolving spontaneously.

ADDITIONAL TREATMENT
Radiation Therapy
• NJA.

Additional Therapies
• Diagnosis is oral or intravenous pyelogram to identify dilated renal calyces.
• Ability to retain contrast during the radiologic procedures.

Complementary & Alternative Therapies
• Nutrition: It is important to provide adequate intake of calories and protein to ensure growth.

ONGOING CARE
PROGNOSIS
• Difficult to predict early in life.
• Lack of renal growth with a creatinine greater than 1 at a year of age, associated hematuria, proteinuria, and hypertension in patients with TID portends the need for future dialysis and transplantation.

COMPLICATIONS
• Growth impairment in children is a known complication, independent of the etiology of CKD (2).
• Hypertension is also a risk factor.
• Protein restriction, used in adult CKD to slow disease progression, cannot be used with kids as this would further hinder their growth and development.

FOLLOW-UP
• Neonates and infants should be seen as frequently as they develop, in order to ensure maintenance of euvelema.
• Primary care physicians need to be instructed that patients with interstitial disease will get dehydrated more quickly than the average patient; therefore, attention to their care at the time of vomiting and diarrhea is important for these patients will become volume depleted in a hurry.

Patient Monitoring
• Glomerular based renal diseases are associated with salt and water restriction as well as blood pressure control.

Patient Resources
• American Society of Pediatric Nephrology. www.aspneph.com/patient/patient.asp
• National Kidney Disease Educational Program. www.kidney.org/patients
• NKF Care, Patient Information Center. www.kidney.org/patients

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Acute Kidney Injury, Pediatric (Renal Failure, Acute)
• Megacyst, Congenital
• Pediatric Urethral Valves
• Prune Belly (Eagle-Barrett or Triad) Syndrome

CODES
ICD9
• 586.39 Other congenital malformations of bladder and urethra

ICD10
• N03.9 Chronic kidney disease, unspecified
• N05.8 Other specified anomalies of bladder and urethra

CLINICAL/SURGICAL PEARLS
• Patients with interstitial disease or obstructive uropathy require IU hydration while APD prior to procedures.
• In contrast to adults, diabetes nephropathy and hypertension are rare causes of CKD in children.
• Small changes in creatinine reflect large changes in GFR for children with CKD.
• Baseline creatinine with attention to any changes after potential renal insult (CT contrast, hypervolemia/hypertension, medications, etc.) is an important measure for monitoring and prevention of progression of CKD.
CHYLOUS ASCITES
Brett S. Carver, MD

BASICS
DESCRIPTION
Chylous ascites is characterized by the accumulation of chyle in the peritoneal cavity. Results from the obstruction or injury of the thoracic duct or cisterna chyli of the lymphatic system. Lymphatic leakage from the lymph vessels draining the intestines. Characterized as a milky fluid due to the high triglyceride component. This section focuses primarily on chylous ascites associated with retroperitoneal lymph node dissection (RPLND) for testicular cancer.

EPIDEMIOLOGY
Incidence
Chylous ascites is reported to occur in ~1% of patients undergoing a primary RPLND for testicular cancer and 3% of postchemotherapy RPLNDs.

PREVALENCE
N/A

RISK FACTORS
Predisposing factors for chylous ascites associated with RPLND:
– Surgical resection of the vena cava.
– Suprahilar dissection.
– Simultaneous hepatic resection.
– In addition, patients undergoing reoperative RPLND are at an increased risk.

Genetics
N/A

PATHOPHYSIOLOGY (1)
Chylous ascites is caused by injury or obstruction of the thoracic duct or cisterna chyli. Surgical injury, ligation of the thoracic duct. Retroperitoneal tumor associated with obstruction of the thoracic duct. Leakage of fat containing lymphatic fluid into the peritoneum.

ASSOCIATED CONDITIONS
– Testicular cancer
– Peritonitis
– Fist or small-bowel obstruction
– Failure to thrive

DIAGNOSIS
HISTORY
Patients often present following RPLND with symptoms of abdominal distention and pain, decreased appetite, nausea, and vomiting. Shortness of breath may also be present associated with increased abdominal pressures. Secondary infection associated with peritonitis with symptoms of fever, chills, abdominal pain, and lethargy.

PHYSICAL EXAM
The most common finding on physical exam is distension of the abdomen with flank bulging. The abdomen is dull to percussion and may demonstrate a fluid wave upon palpation.

DIAGNOSTIC TESTS & INTERPRETATION
Lab
Serum tumor markers (AFP, HCG, LDH) should be obtained to rule out recurrence.
– Aspiration of the abdominal fluid reveals a milky white fluid, which should be sent for triglyceride testing and culture to rule out a secondary infection.
– A fluid triglyceride level >110 mg/dL is diagnostic.

Imaging
– CT scan of the abdomen and pelvis is the imaging modality of choice to evaluate for the presence of ascites and rule out retroperitoneal recurrent disease.
– Abdominal ultrasonography may be used to document ascites and guide aspiration.

Diagnostic Procedures/Surgery
Abdominal paracentesis is performed to aspirate the ascites for diagnostic testing.

Pathologic Findings
Chylous ascites is grossly defined as a milky white fluid. Lab testing will reveal elevated triglyceride content.

DIFFERENTIAL DIAGNOSIS
Chylous ascites can be caused by other conditions beyond RPLND for testicular cancer:
– Postoperative
– Abdominal aneurysm repair
– Peritoneal dialysis catheter placement
– Infectious/inflammatory
– Pancreatitis
– Retroperitoneal irradiation
– Renal disease
– Geriatric disease
– Retroperitoneal fibrosis
– Sarcoid
– TB
– Filariasis
– Mycobacterium avium-intracellulare (AIDS related)
– Neoplasm
– Lymphoma
– Kaposi sarcoma
– Other solid tumors
– Other causes
– Cirrhosis
– Carcinoid
– Nephrotic syndrome
– Trauma
– Right-sided heart failure
– Dilated cardiomyopathy
– Idiopathic
– Congenital causes (defects of lacteal formation)
CHYLOUS ASCITES

TREATMENT

GENERAL MEASURES
- All patients with abdominal distention following an RPLND should be evaluated for:
  - Ascites (nonchylous)
  - Ileus
  - Small-bowel obstruction
  - Recurrent disease in the abdomen or retroperitoneum.
- The majority of chylous effusions will heal spontaneously. Abdominal paracentesis is diagnostic and often therapeutic in relieving symptoms associated with increased abdominal pressures.

MEDICATION
First Line
- Low lipid, high medium chain triglyceride oral diet.
  - MCT oil supplement
    - 1 tablespoon (15 mL) 3–4 times/d
    - Mix with juices or otherwise incorporated into low-fat diet
  - Do not use in patients with advanced cirrhosis: Risk of narcosis and coma
- Somatostatin analogs have been demonstrated to be effective in reducing lymphorrhagia.
  - Octreotide 100 mcg administered subcutaneously 3 times per day

Second Line
- Total parental nutrition is to be utilized in patients who fail oral diet modifications.
  - Bowel rest may enhance recovery if conservative approaches are not successful

SURGERY/OTHER PROCEDURES
- Abdominal paracentesis, repeated as necessary.
- Surgical exploration with direct ligation of lymphatic vessels for persistent chylous ascites.
- Peritoneal venous shunts for refractory chylous ascites.
- Direct lymphatic vessel ligation or embolization of large leaking vessels using interventional radiologic techniques.

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
Orlistat (Xenical) has been used successfully in a nontesticular cancer case of chylous ascites (3).

ONGOING CARE

PROGNOSIS
The prognosis is excellent for the vast majority of cases as most will respond to conservative management.

COMPLICATIONS
- The complications of chylous ascites related to increased abdominal pressure:
  - Renal failure
  - Venous thrombosis
  - Pulmonary embolism
  - Atelectasis
  - Pneumonia
- The gastrointestinal complications of chylous ascites include ileus and small-bowel obstruction.
  - Malnutrition and failure to thrive may also occur due to protein-losing enteropathy with chylous diarrhea (steatorrhea), malabsorption, and malnutrition

FOLLOW-UP
Patient Monitoring
- Follow-up protocols should be followed according to guidelines established by the National Comprehensive Cancer Network for testicular cancer patients.
- After initial treatment of chylous ascites, patients should be seen in follow-up to monitor for recurrent ascites.

Patient Resources
N/A

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
  - Chylous Ascites Image ID
  - Lymphatic Ascites
  - Testis Cancer, Adult General Considerations

CODES

ICD9
- 225.9 Unspecified filariasis
- 407.8 Other noninfectious disorders of lymphatic vessels

ICD10
- B74.9 Filariasis, unspecified
- I89.8 Other noninfective disorders of lymphatic vessels and nodes

CLINICAL/SURGICAL
- Chylous ascites occurs in ~1–3% of patients undergoing a RPLND.
- Risk factors include vena cava resection, suprahilar dissections, and concomitant hepatic surgery.
- Initial management includes pancrtoscopy for symptom of pain or pulmonary compromise and low lipid, high medium-chain triglyceride oral diet.

REFERENCES
CHYLURIA
Matthew A. Uhlman, MD, MBA

BASICS

DESCRIPTION
- Chyluria is the presence of chyle (a combination of lymphatic fluid and triglycerides) in urine
- Presents as milky white urine that can be constant or present primarily after meals
- Often self-limited or resolves with conservative treatment including dietary changes
- Extended chyluria can lead to malabsorption, vitamin deficiencies, and immunosuppression (due to depletion of fat soluble vitamins)[1][C]

EPIDEMIOLOGY

Incidence
- 2–10% of patients infected with filariasis can develop chyluria [2][C]
- Extremely low rates of clinically significant chyluria [1][C]
- Clinically significant in <1% of postoperative patients

Prevalence
- 120 million people suffer from filariasis worldwide, primarily in Asia, Africa, Pacific Islands, and South America [2][C]
- Chyluria is a manifestation of chronic infection, most often by Wuchereria bancrofti, Brugia malayi, or Brugia timori [2][C]
- Rare in developed countries

Nontropical chyluria
- Most often caused by trauma, renal surgery, infection, mass effect (AAA, tumor, abscess), pregnancy, or congenital abnormality [1][C]

RISK FACTORS

Parasitic chyluria
- In B. bancrofti, B. malayi, and B. timori are primary causes of filariasis. All are transmitted by mosquitoes. Less common parasitic infections have been reported to cause chyluria (Leishmania, Behcets, diphtheria, ascariasis) [1,2][C]

Nontropical chyluria
- Renal parenchymal surgery (most often radical or partial nephrectomy, RFA, or renal tumors) [1,3][C]
- Trauma
- Mass effect: Renal tumors (primary or metastatic) or lymphangiography
- Infection: TB, abscess
- Acute aneurysm
- Pregnancy
- Congenital fistula or lymphangioma

PATHOPHYSIOLOGY

Parasitic
- Adult filariae cause lymphangiitis
- Obstruction of suprarenal lymphatics (thoracic duct or upper retroperitoneal lymph drainage)
- Results in rupture of lymphatic vesicles in the thoracic duct, forming intestinal lymphatic urinary fistula
- Lymphatic HTN, with vascular incompetence:
- With obstruction between intestinal vessels and thoracic duct, the resulting cavernoous malformation opens into the urinary system, creating a fistula
- Common fistula sites are renal venous, pelvicalyceal system, urethra, and ureter
- Less commonly caused by external compression or trauma

Nontropical
- Disruption of peripelvic lymphatics during surgery allows backflow into pelvicalyceal system [1][C]
- Congenital fistulous connections between urinary tract and lymphatic system have been described, primarily in children

ASSOCIATED CONDITIONS

W. bancrofti, B. malayi, and B. timori are considered the three causative agents of lymphatic filariasis. Mosquitoes serve as vectors for all 3 nematodes [2][C]

GENERAL PREVENTION

Control of mosquito vector that transmits W. bancrofti, B. malayi, and B. timori [2][C]
- Insect repellent and mosquito nets in endemic areas
- Diethylcarbamazine (DEC) fortified salt
- Annual DEC + albendazole are used to treat asymptomatic filariasis via action on microfilariae

DIAGNOSIS

HISTORY
- Patient complaints of intermittent or continuous milky or cloudy urine
- If intermittent, most often occurs following meals
- Country of origin of patient:
- Asia, Africa, Pacific Islands, South America
- Travel to tropical regions
- History of trauma
- History of renal surgery within prior 2 yr
- History of TB exposure/infection
- Significant weight loss, anemia, lower urinary tract symptoms (frequency, urgency, dysuria), hematuria, nutritional deficiency, proteinuria, or signs of immunosuppression
- Heavy chyluria can cause distal colic or rarely, urinary retention

PHYSICAL EXAM
- Evaluation of lower limbs and genitals
- Lymphadenopathy/lymphangitis
- Male groin exam may reveal hydrocele or epididymitis
- Palpable abdominal or flank mass
- Chylous output from surgical wound or surgical drain

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis typically positive for albuminuria
- Roserandurinary triglycerides
- Fat globules in urine identified by Sudan III stain
- Peripheral blood eosinophilia, may indicate parasitic infection
- Evaluate for TB (if clinically indicated) (tuberculin test, urine stain, and culture for acid fast bacillus)
- ICT antigen card test (immunochromatographic card test, a commercial assay) is widely used in the diagnosis of W. bancrofti
- WBR rapid and panel rapid (2 commercially available assays) tests detect W. bancrofti, B. malayi, and B. timori

Imaging
- Abdominal/pelvic CT (3,4)[B]
- Include retroperitoneal mass
- Fat fluid level seen in the urinary tract
- Can demonstrate contrast communication between collecting system and perinephric collection but does not show communications between perirenal collection and lymphatics
- Lymphangiography (traditional or magnetic resonance) demonstrates abnormal lymphatics and entrance of contrast material into renal collecting system
- Angiography: Can be useful in delineating site of fistula, though not as precise as lymphangiography

Retrograde pyelography
- Rarely warranted, but may show effuse pyelographic backflow

Diagnostic Procedures/Surgery
- Blood smear: Examine for microfilaria (early stage in life cycle of nematodes) using Giemsa stain
- Cystourethroscopy: Can help localize site of milky effusion of urine. Rarely, effuse seen from bladder or posterior urethra
- Retrograde pyelography: Rarely warranted, but may show effuse pyelographic backflow
**Parasitic Chyluria**

Some fats—recommendations are often for fat-free or very low-fat diet, though this should not be observed for 90% of which are in the form of triglycerides.

**TREATMENT**

**GENERAL MEASURES**

- **Nontropical**
  - Up to 50% of cases resolve spontaneously under dietary restriction (10).  
  - Bed rest and/or use of abdominal binder to increase abdominal pressure may allow spontaneous closure.
  - Medium-chain triglyceride (MCT) diet (avoids chylomicrons through lymphatics)
  - Ureteral stent placement to reduce renal pelvis pressure

**MEDICATION**

Dietary modifications to reduce chylomicrons in diet—recommendations are often for fat-free or very low-fat diet, though this should not be observed for more than several weeks given the body’s need for some fats.

**Parasitic Chyluria**

- **DEC and albendazole, or levamisole and albendazole**
- **DEC fortified salt** can be used to treat and prevent lymphatic filariasis.

**SURGERY/OTHER PROCEDURES**

- Procedures of choice involve disconnection of renal plexus lymphatics (5,13,6)[C]
  - **Nephrolysis**: Stripping and ligation of all lymphatic vessels to the kidney and upper ureter; open and laparoscopic techniques described
  - Laparoscopic transabdominal and retroperitoneoscopic approaches described
  - Success rates 80–98%; recurrence rates 3–25%
  - Endoscopic coagulation of fistula
  - Lymphangiovenous anastomosis with ligation of renal lymphatics
  - Renal autotransplantation
  - Nephrectomy was described prior to minimally invasive techniques

**FOLLOW-UP**

**Patient Monitoring**

- Treatment failures are readily apparent as urine returns to milky color (1,13)[CA]
- Re-evaluate if chyluria recurs following treatment; consider the contralateral kidney as the source

**Patient Resources**

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- **Chyluria Image**
- **Filariasis, Urologic Considerations**
- **Urine, Abnormal Colored**
CIRCUMCISION, ADULT CONSIDERATIONS
Irvin H. Hirsch, MD

BASICS

DESCRIPTION
Circumcision involves the removal of the prepuce. This section addresses adult circumcision issues.

Adult circumcision is indicated for elective treatment of balanitis (glans inflammation), posthitis (prepuce inflammation), removal of preputial lesions, and at patient request for cultural and religious preference.

Emergent circumcision may be necessary for treatment of paraphimosis after failed attempt at manual reduction.

Circumcision may be necessary as part of surgical procedures requiring degloving exposure of the penis (penile fracture repair or Peyronie disease).

Circumcision is the most common operation performed worldwide.

There is some controversy concerning the need for circumcision and potential effects on sexual satisfaction. This is weighed against the potential health benefits.

EPIDEMIOLOGY
Incidence
N/A

Prevalence
Male circumcision, largely in newborns, is performed in 77% of US males and in 30% of males worldwide.

Circumcision rate in newborns has declined from 83% in the 1960s to 77% in 2010.

These incidence rates do not include out-of-hospital circumcisions.

Increasingly adult circumcision has been advocated as an important adjunct to STD and HIV prevention in developing countries (1).

RISK FACTORS
Diabetes mellitus
Genital lesions

PATHOPHYSIOLOGY

The prepuce serves as a specialized, junctional mucocutaneous tissue marking the boundary between mucosa and skin; it is similar to the eyelids, anus, and lips.

Conditions that can cause problems:
- Lack of genital hygiene
- Chronic balanoposthitis may lead to phimosis

ASSOCIATED CONDITIONS
- Diabetes mellitus
- Balanitis
- Lichen sclerosus/enthesial stricture
- Penile condylomata
- Squamous cell carcinoma
- Erectile dysfunction
- Peyronie disease

ALERT
The American Urologic Association (AUA) policy statement now considers circumcision to be of a health benefit, citing a 50-60% risk reduction in HIV transmission in some African nations.

GENERAL PREVENTION
Local hygiene measures may prevent balanitis and its sequelae.

Although male circumcision should not be substituted for other HIV risk-reduction strategies, it has been shown to reduce the risk for HIV and some STIs in heterosexual men.

Despite these data, male circumcision has not been demonstrated to reduce the risk for HIV or other STIs among men who have sex with men (MSM).

Good visualization of the glans penis is crucial in all cases of circumcision to limit complications.

DIAGNOSIS

HISTORY
- Penile pain with or without erection
- Dyspareunia
- Postcoital pain

PHYSICAL EXAM
- Inability to retract prepuce (phimosis)
- Inability to reduce prepuce (paraphimosis)
- Penile erythema or exocytosis
- Glans erythema
- Malodorous secretion (smegma)
- Associated penile lesion

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- UA
- Urine culture if indicated
- STD testing if indicated

Imaging
N/A

Diagnostic Procedures/Surgery
N/A

Pathologic Findings
- Acute and chronic inflammation
- Plasma cell infiltrate (Zoon balanitis)
- Lichen sclerosus (BMD balanitis xerotica obliterans)

DIFFERENTIAL DIAGNOSIS
N/A

TREATMENT

GENERAL MEASURES
Circumcision for balanitis in adults should be performed after exhausting nonsurgical medical approaches.

MEDICATION
First Line
- Topical antibiotics
- Topical steroids
- Topical antifungals

Second Line
N/A

SURGERY/OTHER PROCEDURES

General anesthesia may be utilized.

Local anesthesia is recommended when tolerated.

Ultrasonic/bipolar cautery is injected at the level of the infrapubic bone and around the base of the penis. Avoid epinephrine.

Technique is selected based on surgeon’s preference: Sleeve technique or dorsal slit circumcision.
CIRCUMCISION, ADULT CONSIDERATIONS

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
For high risk or anticoagulated patients an isolated dorsal slit may be oversewn without circumcision.
Nonsurgical preputial compression devices are currently under investigation for HPV, HSV, and HIV risk reduction programs in developing countries (Prepex or Shang Ring). The prepuce sloughs after 7 days.

ONGOING CARE

PROGNOSIS
Patient satisfaction is high

COMPICATIONS (2)
- The majority of complications relating to circumcision are minor and should be easily treated
- While very infrequent, challenging complications requiring complex reconstructive surgery and should be referred to a center specializing in these reconstructions.
  - Early
    - Hematoma and bleeding
    - Infection
    - Urethral stricture due to tight bandaging
    - Glans necrosis
    - Removal of inadequate or excessive skin
    - Partial penile amputation
  - Late
    - Urethral injury/urethrocutaneous fistula
    - Neural stress
    - Hyperesthesia or hypoesthesia of penis
    - Penile scarring and deformity
    - Skin bridges between the glans and penile shaft
    - Concealed/buried penis
    - Inclusion cysts
    - Erectile dysfunction

FOLLOW-UP

Patient Monitoring
- Routine postoperative care.
- Follow for alterations in penile sensation and erectile function.

Patient Resources
www.aafp.org/afp/1999/0315/p1514.html

REFERENCES

ADDITIONAL READING
- Cold CJ, Taylor JR. The prepuce. BJU Int. 1999;83(suppl 1):4–44.

See Also (Topic, Algorithm, Media)
- Circumcision, Pediatric Considerations
- Penis, Cysts
- Phimosis and Paraphimosis

CODES
- IC90
  - 605 Redundant prepuce and phimosis
  - 607.1 Balanoposthitis
- ICD-10
  - N47.2 Paraphimosis
  - N48.1 Balanitis
  - Z41.2 Encounter for routine and ritual male circumcision

CLINICAL/SURGICAL PEARLS
- These measures reduce risk of neural injury: minimize use of electrocautery and limit excision superficial to Buck fascia
- Ablate hemostasis of tunica albuginea
CIRCUMCISION, PEDIATRIC CONSIDERATIONS

Mary Ellen T. Dolat, MD
Harry P. Koo, MD, FAAP, FACS

DESCRIPTION

Circumcision: are the surgical removal of the foreskin (prepuce) from the penis.

- One of the oldest surgical procedures
- One of the most commonly performed surgical procedures in practice today.
- There is some controversy concerning the need for circumcision and potential effects on sexual dissatisfaction in adulthood. This is weighed against the potential health benefits.

EPIDEMIOLOGY

- Few data are available to help estimate accurately the number of newborns circumcised worldwide.
- Countries of origin, ethnicity, religious affiliation, and birth in a rural vs. an urban hospital clearly influence a child’s likelihood of being circumcised.
- In addition, lack of (or the type of) health insurance may influence a child’s likelihood of being circumcised.
- Most common reasons reported by US parents for choosing circumcision:
  - Health/medical benefits including hygiene (40–60%),
  - Social concerns (23–37%),
  - Religious requirements (11–19%)

Incidence

- Circumcision rate in newborns has declined from 83% in the 1960s to 77% in 2010.
- These incidence rates do not include out-of-hospital circumcisions.
- 79% of men surveyed reported being circumcised prior to sexual activity.

Prevalence

- Most neonates have a physiologic phimosis or balanitis.
- A small percentage (5–10%) of newborns are at risk for infection.
- The penis should be carefully examined before the infant is circumcised.

Risk Factors

- Urinary tract infection
  - An increased risk for UTI in uncircumcised males younger than 1 yr: risk being greatest toward the 1st 6 mo.
  - Given that the risk of UTI in infant males is ~1%, the number needed to circumcise to prevent UTI is ~100.
  - The benefits of male circumcision are, therefore, likely to be greater in boys at higher risk for UTI, such as infants with underlying anatomical defects:
    - Need for future circumcision
    - Future medical complications for boys (and men) who are uncircumcised as newborns: balanitis, severe phimosis, and paraphimosis.
    - For parents, there exists a ~2–5% risk that their sons will need a circumcision for a medical indication if they choose not to circumcise their sons as newborns (2)

PATHOPHYSIOLOGY

- The foreskin serves as a specialized, junctional mucocutaneous tissue marking the boundary between mucosa and skin. It is similar to the eyelids, anus, and lips.
- Most neonates have a physiologic phimosis, affecting most newborns until about 1 month of age.
- During childhood, the growth of the prepuce body, accumulation of epithelial cells, and intermittent penile erections eventually separate the prepuce from the glans, permitting retraction.
- During the first 6 mo of life, there are more uropathogenic organisms around the urethral meatus of an uncircumcised male infant than around those of circumcised male infants; this colonization decreases in both groups after the first 6 mo (3).
- Boys with vesicoureteral reflux who are uncircumcised have a higher risk of UTI.

ASSOCIATED CONDITIONS

- Phimosis
- Paraphimosis

GENERAL PREVENTION

- Gentle periodic retraction during the newborn period will help prevent phimosis for the inability to retract foreskin later in life.

DIAGNOSIS

- History
  - Prior history of phimosis or balanitis
  - Prior history of meatalitis
  - Report of “ballooning” of the distal foreskin during voiding
  - Prior history of circumcision
    - Incomplete removal of foreskin
    - Congenital phimosis
  - Some parents report “infected whitish pus,” which in most instances is due to normal secretion of smegma

PHYSICAL EXAM

- In newborns, perform a complete male genital exam in a baby with nonpalpable testes may be due to congenital adrenal hyperplasia
- Look for penile developmental variations that may be a contraindication of a newborn circumcision (see “Diagnosis”)
- Same instance with newborns with incomplete foreskin development (ie, does not have natural phimosis), may still be amenable to a newborn clamp circumcision

DIAGNOSTIC TESTS & INTERPRETATION

- Lab: Not necessary unless there is suspicion for intersex anomaly
- Imaging: Not necessary unless there is suspicion for intersex anomaly
- Diagnostic Procedures/Surgery: Not necessary unless there is suspicion for intersex anomaly

PATHOLOGIC FINDINGS

- Risk

DIFFERENTIAL DIAGNOSIS

- The foreskin should be carefully examined before the procedure to identify the following conditions that may preclude a circumcision:
  - HYPOSPADIA
  - EPISPADIAS
  - HYPOSPADIAS
  - CHordee
  - Microphallus
  - Foreskin that obstructs voiding

- Recommend obtaining a pediatric urology consultation to determine whether the baby would be a candidate for newborn circumcision

TREATMENT

- Remove the foreskin
- Circumcision: 2 ways of preventing penile cancer:
  - Western nations: “Routine” newborn circumcision (not recommended)
  - Scandinavian countries (low prevalence of circumcision) and in Israel (high prevalence of circumcision) and in Scandinavian countries (low prevalence of circumcision).
  - Recommend obtaining a pediatric urology consultation to determine whether the baby would be a candidate for newborn circumcision

ALERT

- In cases of Disorders of Sexual Development (DSD) with sex assignment concerns or significant anomaly such as hypospadias the infant should not undergo newborn circumcision.

GENERAL MEASURES

- The AAP states that the health benefits of newborn male circumcision outweigh the risks but the scientific evidence is not strong enough for the AAP to recommend routine circumcision of all newborns. The AAP advises parents to learn the facts about circumcision and weigh the risks and benefits.

- Most routine circumcision is performed between 2 and 10 days of life.
### Ongoing Care

**Prognosis**

Some groups believe that circumcision may reduce or increase the possibility of the risk of the penis, potentially impacting sexual pleasure later in life. The data are conflicting and mostly these subjective findings are not conclusive.

**Complications**

- **Large US hospital-based studies estimate the risk of a significant acute circumcision complication to be between 0.19–0.22%**.
- **From newborn circumcisions using clamp techniques**:
  - **Gomo clamp**: Mainly related to technical factors
  - **Insufficient or inadequate skin removal requiring additional revision procedure**: Since the metal bell completely covers the glans, glans injury is extremely rare
  - **Plastibell**: Insufficient or inadequate skin removal requiring additional revision procedure
  - **Incomplete circumcision**: Retained Plastibell ring
  - **Mogen clamp**: Potential for injury to glans, including partial amputation
  - **Immediate complications**: Significant bleeding (0.08–0.18%)
  - **Postcircumcision bleeding may be the 1st manifestation on an underlying bleeding disorder**
  - **Significant infection (0.36%)**: Significant penile injury (0.04%)
  - **Late complications**: Phimosis (acquired)
  - **Adhesions**: Skin bridges
  - **Excess skin**: Insufficient penile skin
  - **Peri-urethral infection**: Peri-urethral infection
  - **Peri-urethral inflammation**: Peri-urethral inflammation
  - **Hymenostomy fistula**: Peri-urethral fistula

**Follow-up**

- **Patient Monitoring**: A small amount of petroleum jelly may help with discomfort due to diaper friction the 1st few days postop.
- **Bandaging** is optional after the 1st 1–2 days.
- **Diapering** usually takes place within 10 days.
- **Clean site with warm water and avoid baby diaper wipes**.

**Patient Resources**

American Academy of Pediatrics, Patient Education ONLINE. www.patiented.aap.org

### Codes

- **ICD9**: Z41.2 Encounter for routine and ritual male circumcision
- **ICD10**: Z90.872 Male genital surgical procedures; not elsewhere classified

### Additional Reading


### Additional Pearls

- Make sure to carefully inspect the penis for any congenital defects such as hypospadias or chordee before proceeding with neonatal circumcision. It is best to delay circumcision until the primary defect can be repaired as the foreskin may be used in reconstructive procedures.
- The choice of neonatal circumcision is a matter of the physician’s personal preference. For circumcisions using a Gomo clamp, or Plastibell, select the correct size of the bell; this would ensure adequate foreskin removal.
- Always consider the cultural and religious beliefs of the family when counseling about newborn circumcision.

### Additional Treatment

- **Radiation Therapy**: Not recommended
- **Additional Therapies**: Not recommended
- **Complementary & Alternative Therapies**: Traditional religious providers perform the procedures in community settings.
CONDYLOMA ACUMINATA (VENERAL WARTS)
Neal Patel, MD
Allen D. Seftel, MD

**DESCRIPTION**
- Anogenital epidermal lesions caused by the transmission of human papilloma virus (HPV).
- The most common viral sexually transmitted infection in the US, they are also called genital warts, or venereal warts.
- Most common sites: Penis, vulva, vagina, cervix, perineum, and perianal area.
- Less commonly, urethra, bladder, oropharynx, larynx, and trachea.

**Epidemiology**
- **Incidence:**
  - Most common STD
  - ~ 1% of sexually active adults in the US
- **Prevalence:**
  - Highest prevalence: 18–28 yr olds and exceeds 50% of the US population
  - HPV 6 and 11 account >90% of visible genital warts.

**Risk Factors**
- Increased risk with number of sex partners, frequency of sexual activity, early coitus, and presence of condylomata on partners.
- Age <25
- Immunocompromised status
- Cigarette smoking and oral contraceptives may be associated with an increased risk.
- Onset of sexual activity at an early age

**Pathophysiology**
- HPV is a double-stranded, circular DNA genome consisting of ~8,000 base pairs. Subtypes 6 and 11 are associated with the majority of genital warts.
- Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 80 different subtypes can potentially associate with condylomata.
- Basal layer of epidermis is invaded by the virus.
- Transmission is by direct sexual contact.
- Less common route is autoinoculation from nongenital lesions.
- Vascular layer of epithelium is invaded by the virus.

**Associated Conditions**
- Perineal cancer
- Anogenital lesions
- Buschke-Löwenstein tumor
- Male: Examine penis, meatus, scrotum, perineum, and suprapubic, and perianal region.

**Diagnosis**
- **History:**
  - Age and sex of patient
  - History of recent sexual exposure
  - Number of partners and frequency of sexual intercourse
  - Visible warts usually seen within 2–3 mo after exposure
  - Practice of anal intercourse
  - Immunocompromised state

**Physical Exam**
- Lesions are pinkish to red-grayish white, papillary lesions found on moist surfaces, often coalescing.
- Lesions appear pearly-white and granular.
- Larger lesions may be verrucous or flat in configuration.
- With magnification, a central vascular can be seen within each projection.
- Male: Examine penis, meatus, scrotum, perineum, suprapubic, and perianal region.
- Female: Labia, introitus, perineum, cervix, and perianal region.
- Examine for evidence of coexisting STD (ulcers, discharge, adenopathy).

**Diagnostic Tests & Interpretation**
- The most common viral sexually transmitted disease in the US, they are also called genital warts.
- **Onset of sexual activity at an early age**

**Pathologic Findings**
- Branching, villous, papillary connective tissue stroma covered by epithelium.
- Superficial hyperkeratosis and thickening of the epidermis (acanthosis).
- Clear vacuolization of the prickle cells (koilocytosis), characteristic of HPV infection, is seen.
- There is no evidence of invasion of the underlying stroma.

**Differential Diagnosis**
- Bowen disease and erythroplasia of Queyrat
- Bowenoid papulosis
- Basal cell carcinoma
- Condyloma latum (syphilis)
- Extramammary Paget disease
- Fibroepitheliomas
- Herpes simplex virus
- Malignant melanoma
- Mild mucocutaneous candidiasis
- Nevi
- Pearly penile papules
- Seborrheic keratosis
- Squamous cell carcinomabasaloid cell carcinoma

**Treatment**
- **First Line**
  - Podophyll (Podophyllin 25%, Podcon, Podofilin): Applied to lesion (concentration 10–25%) by hand physician
  - Podophyll (Cordyline): Self-application of 0.5% solution to warts twice daily for 3 days, followed by 4 days without treatment; can be repeated 4–6 times.
- **Second Line**
  - 5-FU (Efudex, Fluoroplex): Topical therapy may take up to 3 mo to observe a response.
  - 5-FU (Cordyline): Self-application of 0.5% cream 1–3 times per day for several weeks, as needed. Maybe also used as an intralesional instillation but not without intensive complications.
CONDYLOMA ACUMINATA (VENERAL WARTS)

- **Therapeutic agents (Immunotherapy):**
  - An 80–90% virological cure of therapeutic agents; apply directly to lesions; repeat weekly
  - Ipratrophine (4mg)
    - Agents of interferon-α, which enhances cell-mediated cytolytic activity. Available as a 5% cream applied to external lesions 3 times per week up to a maximum of 16 wk

**Second Line Procedures**

- **Electrocoagulation/Laser: Application of liquid nitrogen on skin lesions**; local anesthesia is usually sufficient
- **Holmium laser can be used to remove intraurethral warts**; magnification necessary to maximize efficacy; may produce less scarring
- **Cryotherapy: Application of liquid nitrogen on patients without extensive disease**; this procedure can be repeated at 1- or 2-wk intervals.
- **Interferon-α– Potent inducer of interferon cell-mediated cytolytic activity. Available as a 5% cream applied to external lesions 3 times per week up to a maximum of 16 wk**

**ONGOING CARE**

**PROGNOSIS**

- Subclinical infections are probably not curative.
- Women should still undergo routine Pap smears.
- Malignant transformation of genital cells, but it may be a cofactor in development of malignancy. HPV 6 and 11 are considered low-risk subtypes, and are seldom associated with malignancy.
- Nonsmokers are at 25–50 times greater risk for malignancy

**COMPLICATIONS**

- Malignant transformation: Perineal carcinoma, cervical carcinoma, anal carcinoma, and Buschke-Löwenstein tumor

**FOLLOW-UP**

**Patient Monitoring**

- Educate the patient about self-exam.
- Patients should be examined shortly after therapy, to evaluate initial response rates.
- Encourage use of condoms if sexually active.
- Surveillance urothroscopy is recommended 3–6 mo after treatment of intrarectal lesions.

**Patient Resources**

- Centers for Disease Control and Prevention – http://www.cdc.gov/std/default.htm

**REFERENCES**


**ADDITIONAL READING**


**See Also (Topic, Algorithm, Media)**

- Bowenoid Papulosis
- Buschke-Lowenstein Tumor
- Condylomata Latum (Syphilis)
- Fibroepitheliomas
- Herpes Simplex Virus
- Malignant Melanoma
- Multilokum Condylomata
- Pearly Penile Papules
- Penis, Cancer General
- Penis, Sexion
- Seborrhic Keratosis
- Urethra, Condyloma (Warts)

**ICD9**

- 079.31 Condylooma acuminatum
- 079.4 Human papillomavirus in conditions classified elsewhere and of unspecified site

**ICD10**

- A63.0 Anogenital (veneral) warts
- B97.7 Papillomaviruses as the cause of diseases classified elsewhere
CONTRAST ALLERGY AND REACTIONS

Edouard J. Trabulsi, MD, FACS
Leonard G. Gomella, MD, FACS

DESCRIPTION

Allergy reactions to IV contrast used for radiologic imaging are common, can range from mild to moderate, and occasionally life threatening.

Often an immune system-based response to IV administration of contrast used for common urologic studies such as excretory urography and CT.

Contrast allergy and reactions can be divided into 3 groups:

- Idiosyncratic anaphylactoid reactions
- Nonidiosyncratic reactions
- Delayed reactions

Reactions to MRI contrast media are discussed in Section II "Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy (NSF/NFD)."

"Contrast Induced Nephropathy" is discussed in Section II.

RISK FACTORS

History of allergy or atopy

Previous ADR

Dehydration

Cardiac disease

Asthma

Renal disease

Sickle cell disease

Renal insufficiency

Previous reaction (5 times), allergy or atopy

Dehydration

Cardiac disease

Asthma

Renal disease

Sickle cell disease

Renal insufficiency

GENERAL PREVENTION

Use of alternative imaging in patients with history of previous ADR

Preprocedure hydration

Patients with normal renal function on dialysis

Patients with pre-existing renal impairment should stop metformin before the procedure and be well hydrated to avoid RCM-related biguanide lactic acidosis and contrast-induced nephropathy.

In patients with normal renal function on metformin the following comorbidities should prompt discontinuation of metformin before the contrast:

- Liver dysfunction, alcohol abuse, cardiac failure, myoccardial or peripheral muscle ischemia, orpsis

- Limit risk for contrast-induced nephropathy, special arrangements should be made with the radiology department for any patient with a GFR <60 mL/min/1.73 m².

- Prevention in patient with known allergy:
  - Review radiology department procedures at site where testing scheduled.
  - Give methylprednisolone (Medrol) 32 mg PO 12 and 2 hr prior to scheduled test and 50 mg diphenhydramine

- Patients with allergies to other substances (food, medicines), with history of asthma, who are allergic to iodinated contrast, who are undergoing guthabism (or those with allergy to guthabism who we to receive IV contrast) DO NOT need steroid preop.

DIAGNOSIS

HISTORY (4)

- Previous ADR
- Cardiac or renal disease
- Metformin with chronic renal disease
- Allergies

PHYSICAL EXAM

- Monitor vital signs (BP, heart rate, respiratory)

- Hypotension and rare shock

- Observe for:
  - Urticaria, bronchospasm, wheezing, stridor
  - Shorness of breath, flushing, pruritus, angioedema

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- In acute setting, no labs are usually needed

- Blood gas may be useful

- Blood gas may be useful

- In patients with normal renal function on metformin the following comorbidities should prompt discontinuation of metformin before the contrast:

- Liver dysfunction, alcohol abuse, cardiac failure, myoccardial or peripheral muscle ischemia, orpsis

- Limit risk for contrast-induced nephropathy, special arrangements should be made with the radiology department for any patient with a GFR <60 mL/min/1.73 m².

- Prevention in patient with known allergy:
  - Review radiology department procedures at site where testing scheduled.
  - Give methylprednisolone (Medrol) 32 mg PO 12 and 2 hr prior to scheduled test and 50 mg diphenhydramine

- Patients with allergies to other substances (food, medicines), with history of asthma, who are allergic to iodinated contrast, who are undergoing guthabism (or those with allergy to guthabism who we to receive IV contrast) DO NOT need steroid preop.

- Review radiology department procedures at site where testing scheduled.

- Give methylprednisolone (Medrol) 32 mg PO 12 and 2 hr prior to scheduled test and 50 mg diphenhydramine

- Patients with allergies to other substances (food, medicines), with history of asthma, who are allergic to iodinated contrast, who are undergoing guthabism (or those with allergy to guthabism who we to receive IV contrast) DO NOT need steroid preop.

- Review radiology department procedures at site where testing scheduled.

- Give methylprednisolone (Medrol) 32 mg PO 12 and 2 hr prior to scheduled test and 50 mg diphenhydramine

- Patients with allergies to other substances (food, medicines), with history of asthma, who are allergic to iodinated contrast, who are undergoing guthabism (or those with allergy to guthabism who we to receive IV contrast) DO NOT need steroid preop.
First Line

Based on guidelines noted above (5):

- If hypotension MS or LR IV bolus 1 L
  with fluid response considered manifest by HR improvements
  with volume administration.
  - Hypertensive crisis (DBP > 90 mm Hg)
  - Benadryl
  - Albuterol: 2 puffs (90 mcg/puff)
  - Diffuse erythema: IV access, monitor vitals, pulse oximeter
  - Reaction rebound prevention: IV steroids help
  - Anxiety/panic attack: Diagnosis of exclusion; lorazepam 2–4 mg PO slow push; 4 mg max
  - Hypoglycemia: IV access, O2 mask; oral 2 sugar tablets
  - Pulmonary edema: IV access, monitor vitals, pulse oximeter
  - Bronchospasm: IV access, monitor vitals, pulse oximeter
  - Seizures: Protect patient; turn on side to avoid aspiration
  - With tachycardia (pulse > 100 BPM)
  - With bradycardia (pulse < 60 BPM [vasovagal])
  - Furosemide 20–40 mg PO
  - Neofundic: 180 mg PO
  - Glucagon: 1 mg IM
  - Hydrocortisone 200 mg IV over 2 min
  - Labetalol: 20 mg IV over 2 min; double dose every 10 min PRN
  - Epinephrine: 0.4 mg IV or SQ push every 5–10 min PRN
  - Nitroglycerin: 0.4 mg tablet SQ repeat every
  - Oximeter, O2 mask; consider rapid response team/911

Second Line

N/A

SURGERY/OTHER PROCEDURES

N/A

ADDITIONAL TREATMENT

Radiation Therapy

N/A

ADDITIONAL THERAPIES

For life-threatening reactions: ABCs of resuscitation, IV fluids, vasopressors for BP support if IV fluids not effective

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

- Depends on severity of the anaphylactic reaction and the severity of the underlying condition
- Mortality risk in severe cases: 1 in 170,000

COMPLICATIONS

- Risk of death of 1 in 170,000 for both ionic HOCM and nonionic LOCM

FOLLOW-UP

- Appropriate supportive measures until recovery
- Appropriate follow-up recommendations

PATIENT MONITORING

- Appropriate supportive measures until recovery

PATIENT RESOURCES

N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Contrast-Induced Nephropathy (CIN)
- Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy (NSF/ND)
- Reference Tables: Contrast Agents, Genitourinary Contrast Agents

ICD9

- 708.0 Allergic urticaria
- 995.0 Other anaphylactic reaction
- 995.37 Other drug allergy

ICD10

- L50.0 Allergic urticaria
- T88.6XXA Anaphylactic reaction due to adverse drug reaction
- L50.0 Allergic urticaria
- 970.808A Adverse effect of diagnostic agents, initial encounter

CLINICAL/SURGICAL PEARLS

A shellfish or iodine allergy does not correlate with contrast media allergy.
CUSHING DISEASE AND SYNDROME

John B. Eifler, MD
Michael S. Cookson, MD

BASICS

DESCRIPTION
Cushing disease is hypercortisolism due to an ACTH-secreting pituitary adenoma.
Cushing syndrome is the cluster of symptoms attributable to hypercortisolism.

GENERAL PREVENTION
Diligent management of glucocorticoid administration.

EPIDEMIOLOGY
Incidence
N/A

RISK FACTORS
Intragastric exposure to glucocorticoids
− Includes steroid creams or nasal sprays.

GENETICS
− Associated with MEN-1, Carney complex.
− GNAS1 gene mutation (McCune-Albright syndrome).

PATHOPHYSIOLOGY
− Elevated serum levels of cortisol, either from endogenous or exogenous sources.
− Hypothalamus-pituitary-adrenal (HPA) axis dysregulation.

HISTORY
− Progressive weight gain
− Fatigue
− Proximal myopathy
− Skin abnormalities: Easy bruisability, striae, and thinning of skin.

LAB
− CBC, serum electrolytes, glucose, lipids
− Elevated late-night salivary cortisol: In Cushing hypercortisolemia, not etiology
− Hyperglycemia, hypokalemia, neutrophilia, lymphopenia, hyperlipidemia consistent with Cushing syndrome.

DIAGNOSTIC TESTS & INTERPRETATION
− Plasma ACTH concentration
− Elevated late-night salivary cortisol: In Cushing syndrome, diurnal variation of cortisol levels is lost.
− ACTH-secreting tumor (failure to suppress cortisol by DST)
− ACTH-independent hypercortisolism to evaluate for adrenal adenoma/carcinoma.

IMAGING
− Brain MRI if pituitary lesion suspected.
− CT abdomen/pelvis adrenal protocol for ACTH-independent hypercortisolism to evaluate for adrenal adenoma/carcinoma.

DIFFERENTIAL DIAGNOSIS
− Alcoholism (pseudo-Cushing).
− Adrenal adenoma.
− Adrenal adenocarcinoma.
− Micronodular/macro-nodular adrenal hyperplasia.

TREATMENT
GENERIC MEASURES
− Multidisciplinary approach: Endocrinologist, neurosurgeon, adrenal surgeon.
− Surgical therapy is the mainstay of treatment.

MEDICATION
− Ketoconazole: Considered medical treatment of choice; not FDA approved for this indication.
− Mitotane: 500–750 mg 3 or 4 times a day.
− Primarily used for adrenocortical carcinoma.
− Inhibits 11β-hydroxylase.
− Side effects: Reversible hepatotoxicity, headaches, sedation, nausea, and vomiting.

REFERENCES
− Ectopic ACTH production may lead to metastases.
− Rimostil: Suppresses cortisol production by inhibiting 11β-hydroxylase.
− Primarily used for adenocortical carcinoma.

SIDE EFFECTS
− Mitotane: Supresses cortisol production by inhibiting 11β-hydroxylase.
− Metopirone: Inhibit 11β-hydroxylase.
− Gynecomastia, decreased libido, and impotence in males.
− Reduced androgen production may lead to decreased libido, decreased muscle mass.
CUSHING DISEASE AND SYNDROME

Second Line

SURGERY/OTHER PROCEDURES

- Cushing disease:
  - Trans-sphenoidal resection of pituitary adenoma: Gold standard
    - Cure in 60–80% of patients
  - Bilateral adrenalectomy if disease refractory to pituitary surgery or if life-threatening hypercortisolism
  - Ectopic ACTH-secreting tumor: Surgical resection

- Ectopic ACTH-secreting tumor: Surgical resection

- Bilateral adrenalectomy reserved for unresectable disease

- Ipsilateral adrenalectomy for primary cortisol-secreting adrenal masses

ADDITIONAL TREATMENT

Radiation Therapy

Pituitary irradiation effective in 15% of refractory cases—not considered primary therapy

ADDITIONAL THERAPIES

N/A

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

- Prognosis good for adrenal adenoma or Cushing disease, worse for adrenocortical carcinoma

- Prognosis for ectopic ACTH-producing tumors typically poor

COMPLICATIONS

- Bilateral adrenalectomy
  - Adrenal insufficiency
  - Osteoporosis
  - Increased infection risk
  - Nelson syndrome (pituitary adenoma)

FOLLOW-UP

- Patient Monitoring
  - Postoperative monitoring for adrenal insufficiency
  - Pre- and postoperative management is complex and should be coordinated by endocrinologists
  - Post operative hydrocortisone replacement with prolonged wean to allow pituitary adrenal axis to recalibrate
  - After primary treatment (pituitary surgery), any new-onset symptoms → reevaluation

Patient Resources


REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Adrenal Adenoma
- Adrenal Cortical carcinoma
- Adrenal Mass
- Cushing Syndrome Algorithm
- Nelson Syndrome

CODES

ICD9

255.0 Cushing’s syndrome

ICD10

- E24.0 Pituitary-dependent Cushing’s disease
- E24.8 Other Cushing’s syndrome
- E24.9 Cushing’s syndrome, unspecified

CLINICAL/SURGICAL PEARLS

- Initial diagnostic studies for suspected Cushing syndrome include late-night salivary cortisol and 24-h urinary free cortisol.
- Most common cause of endogenous Cushing syndrome is a pituitary adenoma.
- Muscle weakness +/− skin hyperpigmentation after bilateral adrenalectomy may be due to pituitary adenoma (Nelson syndrome).

101
CYSTITIS, GENERAL CONSIDERATIONS
Kelly A. Healy, MD
Demetrios H. Bagley, MD, FACS

DESCRIPTION

Bacterial cystitis:
- Occurs more frequently in women.
- In men, isolated cystitis is rare and often associated with prostatitis that results in secondary bacterial infection of the bladder.
- Clinical syndrome of dysuria, frequency, urgency, and suprapubic pain.
- Can be caused by infection (bacterial, viral, fungal), less commonly parasitic, radiation, interstitial cystitis (IC) or due to other irritants (drugs), or a complication of another illness.

Incidence
- Young women: Sexual activity, use of spermicidal agents.
- Adenovirus in the urine preceding transplantation.
- Postmenopausal alterations in the perineal skin and mucosa as blood type or maternal history of recurrent cystitis.
- Postmenopausal changes in the perineal skin and mucosa.
- Bacterial cystitis in females is usually an ascending infection.
- Obstetric endarteritis causing ischemia.
- Common cause of hemorrhagic cystitis thought to be due to acrolein metabolite dwelling in bladder.

Risk Factors
- Bacterial cystitis:
  - Young women: Sexual activity, use of spermicidal condoms or diaphragm, and genetic factors such as blood type or maternal history of recurrent cystitis.
  - Healthy, noninstitutionalized older women: Postmenopausal changes in the perineal epithelium and vaginal microflora, incontinence, diabetes, and history of cystitis.

Genetics
- N/A

PATHOPHYSIOLOGY

Bacterial cystitis in females is usually an ascending infection.
- In males, it occurs in association with urethral or prostatic obstruction, prostatitis, foreign bodies, or tumors.
- Increased in tumor necrosis factor in bladder mucosa.
- Increased mast cell degranulation and histamine release.
- Changes in purinergic signaling

ASSOCIATED CONDITIONS

See “Differential Diagnosis.”

GENERAL PREVENTION

- Infectious: Minimize bacterial exposure, avoid indwelling Foley catheter if possible, intermittent catheterization if prolonged catheter needed.
- Hemorrhagic: Avoid radiation or cyclophosphamide/iphosphamide exposure.

PHYSICAL EXAM

- Characterization of symptoms: Frequency, urgency, dysuria, suprapubic pain, perineal or scrotal pain, dyspareunia.
- Exposure to radiation:
  - Obliterative endarteritis causing ischemia.
  - Common cause of hemorrhagic cystitis thought to be due to acrolein metabolite dwelling in bladder.
- History of UTI; previous treatments.
- Exposure to radiation:
  - Suspect viral or fungal infection.
  - Use of personal hygiene products that can cause local irritation (douches, vaginal preparations).
- Mucosal damage:
  - Escherichia coli
  - Cystitis cystica, cystitis glandularis
  - Chronic pelvic pain syndromes
  - Interstitial cystitis
  - Dyspareunia
  - Bacterial vaginosis, lichen sclerosus
  - Gynecologic pain
  - Urethritis
  - Urethral syndrome

DIAGNOSIS

- Characterization of symptoms: Frequency, urgency, dysuria, suprapubic pain, perineal or scrotal pain, dyspareunia.
- Exposure to radiation:
  - Obliterative endarteritis causing ischemia.
  - Common cause of hemorrhagic cystitis thought to be due to acrolein metabolite dwelling in bladder.
- History of UTI; previous treatments.
- Exposure to radiation:
  - Suspect viral or fungal infection.
  - Use of personal hygiene products that can cause local irritation (douches, vaginal preparations).
- Mucosal damage:
  - Escherichia coli
  - Cystitis cystica, cystitis glandularis
  - Chronic pelvic pain syndromes
  - Interstitial cystitis
  - Dyspareunia
  - Bacterial vaginosis, lichen sclerosus
  - Gynecologic pain
  - Urethritis
  - Urethral syndrome

DIAGNOSTIC TESTS & INTERPRETATION

- Urine culture:
  - Ananemic, sterile
  - Midstream standard
  - Catheter sample if concerns about contamination.
- Fungal and viral cultures only if high suspicion.
- CT urogram or US:
  - To rule out vesicoureteral reflux if considering intravesical formalin treatment for hemorrhagic cystitis.

DIAGNOSTIC PROCEDURES/SURGERY

- Cystoscopy for hematuria workup or if the diagnosis is not apparent.
- Cystoscopy with hydrodistention for the diagnosis of IC.
- Cystoscopy for hemorrhagic cystitis due to acrolein metabolite dwelling in bladder.
- Cystoscopy for urothelial carcinoma in situ for tissue culture.

Pathologic Findings

- Evidence of acute or chronic inflammation.
- Michaelis-Gutierrez bodies in necrotic epidermis.

DIFFERENTIAL DIAGNOSIS

- Anxiety
- Diabetes mellitus
- Bladder cancer or other malignancy
- Chronic pelvic pain syndromes
- Interstitial cystitis
- Diabetes insipidus
- Excess fluid intake
- Bladder biopsy
- Yeasts
- Candidiasis
- Eosinophilic cystitis
- Bacterial cystitis
- Yeasts
- Endometriosis
- Urethral syndrome
Based on culture if initial antibiotic not successful in Second Line

**TREATMENT**

**GENERAL MEASURES**
- Encourage adequate hydration.
- Cystoscopy with clot evacuation and electro or laser fulguration.
- Cystoscopy with hydrodistention to diagnose IC; look for characteristic glomerulations.
- Encourage voiding immediately before and after exposure to pathogens
- Encourage adequate hydration.

**COMPlications**
- Hemorrhagic cystitis may recur and/or be refractory requiring cystoscopy and fulguration.
- Simple bacterial cystitis prognosis is excellent.

**PROGNOSIS**
- Depends on etiology of cystitis
- Prostatitis
- Neurogenic bladder, chronic urinary retention
- IC (painful bladder syndrome)
- Infectious cystitis: Bacterial, viral, parasitic, fungal
- Hemorrhagic cystitis
- Extrinsic bladder compression (eg, pelvic tumor, radiation-induced fibrosis)
- EPIdymitis
- Cystitis, Radiation
- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Cystitis, Radiation
- Acute cystitis in females is most commonly bacterial and typically responds to a short course of antibiotic.

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- May induce radiation cystitis

**Additional Therapies**
- Hyperbaric oxygen for hemorrhagic cystitis.
- Complementary & Alternative Therapies
- Cranberry tablets for prevention of recurrent bacterial cystitis; evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs.

**ONGOING CARE**

**PROGNOSIS**
- Simple bacterial cystitis prognosis is excellent.
- Depends on etiology of cystitis
- Prostatitis
- Neurogenic bladder, chronic urinary retention
- IC (painful bladder syndrome)
- Infectious cystitis: Bacterial, viral, parasitic, fungal
- Hemorrhagic cystitis
- Extrinsic bladder compression (eg, pelvic tumor, radiation-induced fibrosis)
- EPIdymitis
- Cystitis, Radiation
- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Cystitis, Radiation
- Acute cystitis in females is most commonly bacterial and typically responds to a short course of antibiotic.

**ADDITIONAL READING**

See Also (Topic, Algorithm, Media)
- Bacterias and Pyuria
- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Cystitis, Radiation
- Intraocular Cystitis
- Prostatitis, General
- Pyuria Algorithm
- Urinary tract infection (UTI), Adult Female
- Urinary tract infection (UTI), Adult Male
- Urinary tract infection (UTI), Pediatric

**Ongoing Care**
- History and physical exam
- Patients with > 3 episodes of cystitis per year should be considered candidates for prophylaxis.
- Single dose at bedtime or at time of intercourse is recommended.

**FOLLOW-UP**

**Patient Monitoring**
- Symptomatic
- History and physical exam
- Patients with > 3 episodes of cystitis per year should be considered candidates for prophylaxis.
- Single dose at bedtime or at time of intercourse is recommended.

**Additional Therapies**
- Cranberry tablets for prevention of recurrent bacterial cystitis; evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs.

**Additional Treatment**

**Radiation Therapy**
- May induce radiation cystitis

**Additional Therapies**
- Hyperbaric oxygen for hemorrhagic cystitis.
- Complementary & Alternative Therapies
- Cranberry tablets for prevention of recurrent bacterial cystitis; evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs.

**Ongoing Care**
- History and physical exam
- Patients with > 3 episodes of cystitis per year should be considered candidates for prophylaxis.
- Single dose at bedtime or at time of intercourse is recommended.

**Follow-Up**
- Symptomatic
- History and physical exam
- Patients with > 3 episodes of cystitis per year should be considered candidates for prophylaxis.
- Single dose at bedtime or at time of intercourse is recommended.
CYSTITIS, HEMORRHAGIC (INFECTIOUS, NONINFECTIOUS, RADIATION)
Ahmad Shabsigh, MD, FACS

BASICS
DESCRIPTION
- Inflammation leading to damage of the bladder’s urothelium and blood vessels, causing hematuria and irritative voiding symptoms.
- Hemorrhagic cystitis (HC) is commonly caused by severe infection, cyclophosphamide, and radiation therapy induced.

EPIDEMIOLOGY
Incidence
- Cyclophosphamide-induced HC: 5–7%
- 7–70% of hematopoietic stem cell transplants.

ASSOCIATED CONDITIONS
RISK FACTORS
- No. epip, iv, or oral premedication.
- Infections.
- Exposure to certain industrial chemicals, such as aniline or toluidine derivatives.
- Previous treatment with oxazaphosphorine agents (e.g., cyclophosphamide, isophosphamide).
- History of prior pelvic radiation (prostate and cervical cancers).
- Resection of BK virus (BKV) infection in bone marrow transplant patients.

GENETICS
N/A

PATHOPHYSIOLOGY
- Cyclophosphamide: Acrolein enters the urethelium. Activates platelet-activating factor, nitric oxide, tumor necrosis factor-α, and IL-1, eventually forming peroxynitrite that causes damage.
- Radiation-induced cystitis results from a progressive osmotic abnormality leading to mucosal ischemia, ulceration, and necrosis.
- Peroxynitrite toxicity is immune-mediated, whereas danazol toxicity is likely from damaging vascular changes.

ASSOCIATED CONDITIONS
See “Differential Diagnosis.”

GENERAL PREVENTION
- Patients treated with cyclophosphamide once had a high incidence of HC (~70%), with high mortality rates (as high as 75%) if became severe.
- IV hydration, frequent bladder emptying, and sometimes indwelling catheters with bladder irrigations are used to reduce the time toxins are in contact with the bladder wall.
- Mepacrine phosphate (nocarboxylic) binds to acrolein, creating nontoxic compounds.
- WF-10 (2-A), sodium pentosan polysulfate (Epilone), and amifostine (Ethyol) have been creating nontoxic compounds.
- N-acetylcysteine (Mucomyst) binds to acrolein, forming peroxynitrite that causes damage.

TREATMENT
GENERAL MEASURES
- Catheterization/bladder irrigation with normal saline to clear bleeding and evacuate clots.
- Remove the offending train.
- Treat the infectious agent.
- Hydration and diuresis.
- Blood products transfusion, when necessary.

DIAGNOSIS

HISTORY
- Gross hematuria (with or without pain).
- Frequency, urgency, dysuria.
- Urinary retention from clots.
- Oliguria/microscopical hematuria.
- Suprapubic pain.
- Revers with drills.
- Occasional mucosal sloughing.
- Large hypertrophied tongue: Amyloidosis.

DIAGNOSTIC TESTS & INTERPRETATION
- Urine for analysis, cytology, and cultures (including fungal and viral cultures, if indicated).
- Coagulation factors (especially platelets), which can be depleted.
- Serial hematocrits.
- Blood tests for collagen disease markers, if indicated.

IMAGING
- CT-urogram: – Often done as part of hematuria workup. – Rules out other urologic abnormalities. – Usually not able to diagnose HC, but may show clots in the lumen, a widened irregular bladder wall, and/or small capacity.
- Radiopaque studies: – Penicillin, piperacillin, methicillin, carbenicillin, nonoxynol-9 contraceptive.
- Catheterization/bladder irrigation with normal saline to clear bleeding and evacuate clots.

DIFFERENTIAL DIAGNOSIS
- Acute UTIs.
- Carcinomas of the urinary tract.
- Other infections rarely cause severe HC.

Pathologic Findings
- Usually initiated by bladder distension, minor trauma, infection, instrumentation.
- Acute episodes wane within 12–18 mo.
- Can recur as late as 15–20 yr after exposure.

Acute episodes wane within 12–18 mo.
- Can recur as late as 15–20 yr after exposure.

Relief: – Usually induced by bladder distension, minor trauma, infection, instrumentation.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.
- – Usually initiated by bladder distension, minor trauma, infection, instrumentation.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.

Viral infection:
- Typically seen in immunocompromised patients after BMT.
- May present dramatically, but usually resolves spontaneously in ~2 wk.
- Other infections rarely cause severe HC.
- – Bacterial: E. coli, Enterococcus.
- – Prophylaxis: – Acute infections.
- – Can occur as late as 15–20 yr after exposure.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.

Medications:
- Typically seen in immunocompromised patients after BMT.
- May present dramatically, but usually resolves spontaneously in ~2 wk.
- Other infections rarely cause severe HC.
- – Bacterial: E. coli, Enterococcus.
- Systemic hematologic disease: Rare; often refractory to fulguration and irrigation.
- Systemic amyloidosis associated with rheumatoid arthritis or CREST disease.
- – Chemical toxic: – Acute, subacute, and chronic hematuria.
- – Systemic hematologic disease: Rare; often refractory to fulguration and irrigation.
- – Systemic amyloidosis associated with rheumatoid arthritis or CREST disease.
- Chemical toxic: – Acute, subacute, and chronic hematuria.

- Penicillin, piperacillin, methicillin, carbenicillin, nonoxynol-9 contraceptive.
- – Prophylaxis: – Acute infections.
- – Can occur as late as 15–20 yr after exposure.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.

- Penicillin, piperacillin, methicillin, carbenicillin, nonoxynol-9 contraceptive.
- – Prophylaxis: – Acute infections.
- – Can occur as late as 15–20 yr after exposure.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.

- Penicillin, piperacillin, methicillin, carbenicillin, nonoxynol-9 contraceptive.
- – Prophylaxis: – Acute infections.
- – Can occur as late as 15–20 yr after exposure.
- – Acute episodes wane within 12–18 mo.
- – Can recur as late as 15–20 yr after exposure.
Consider the following after all conservative modalities have failed, and patient is unstable.

- Adverse effects: Reflux could cause ureteral fibrosis and obstruction or papillary necrosis; vasoconstriction and platelet aggregation always be readily available.
- High rate of recurrence.
- Selective hypogastric artery embolization:
  - Stabilizes membranes, decreasing edema; causes vasoconstriction and platelet aggregation.
  - Adverse effect: Build-up can clog catheters.
  - Duration of response is often short.
- Hyaluronic acid:
  -  30 mL 100% phenol in 30 mL of glycine for 1 min, followed by saline flush.
  - May need repeat cystoscopy for hemorrhagic radiation cystitis.
  - May need surgical reconstruction.
- Phenol instillation:
  - 0.5–1% solution in bladder for 10–20 min, followed by saline flush.
  - Very painful, requires anesthesia.
  - Duration of response is often short.
- Prostaglandin instillation:
  - 5 mg/kg in 60 mL of 0.9% NaCl intravesical over 15 min.
  - Duration of response is often short.
- Aminocaproic acid (Amicar):
  - 0.25–0.5 g/kg per day for 5–7 days.
  - Low morbidity: No anesthesia required, no renal absorption.
  - Low success, as most bleeding is venous.

**COMPLICATIONS**

- Vesicoureteral reflux resulting from bladder fibrosis.
- Secondary UTIs from prolonged catheterization.
- Anemia, renal failure.
- Long term increases risk of secondary urothelial malignancy.
- Hyperbaric oxygen (4): Promotes granulation tissue and neovascularization, causes vasoconstriction.
- Higher rate of recurrence.
- Better for radiation-induced cystitis.
- Ureteral obstruction.
- Complications: Global classification, bladder necrosis, lower limb paralysis, anticoagulation.
- Low-lying branches of hypogastric artery.
- Low-dose cidofovir (3):
  - Low-dose cidofovir (3): 5 mg/kg in 60 mL of 0.9% NaCl intravesical over 15 min.
  - Duration of response is often short.
- Prostaglandin instillation:
  - 5 mg/kg in 60 mL of 0.9% NaCl intravesical over 15 min.
  - Duration of response is often short.
- Hyaluronic acid:
  -  30 mL 100% phenol in 30 mL of glycine for 1 min, followed by saline flush.
  - May need repeat cystoscopy for hemorrhagic radiation cystitis.
  - May need surgical reconstruction.
- Phenol instillation:
  - 0.5–1% solution in bladder for 10–20 min, followed by saline flush.
  - Very painful, requires anesthesia.
  - Duration of response is often short.
- Prostaglandin instillation:
  - 5 mg/kg in 60 mL of 0.9% NaCl intravesical over 15 min.
  - Duration of response is often short.
- Aminocaproic acid (Amicar):
  - 0.25–0.5 g/kg per day for 5–7 days.
  - Low morbidity: No anesthesia required, no renal absorption.
  - Low success, as most bleeding is venous.

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- Contralateral, a recognized cause of HC.

**Additional Therapies**

- Hypertonic saline.
  - Promotes granulation tissue and neovascularization, causes vasoconstriction.
  - Better for radiation-induced cystitis.
  - Requires a hypertonic chamber, which may not always be readily available.
  - May require 30–40 daily treatments.
- Polyoma Virus (BK, JC), Urologic Consideration
- Cytoxan (Cyclophosphamide) Toxicity
- Radiation Therapy
- Radiation) Image
- Polyoma Virus (BK, JC), Urologic Consideration
- CYSTITIS, HEMORRHAGIC (INFECTIOUS, NONINFECTIOUS, RADIATION)

**ADDITIONAL READING**

- See Also (Topic, Algorithm, Media)
  - Chemotherapy Toxicity, Urologic Consideration
  - Cystitis, General Considerations
  - Cystitis, Hemorrhagic (Infectious, Non-Infectious, Radiation) Image
  - Cystitis, Radiation
  - Cystitis, Vidal
  - Cystitis, Vidal
  - Polyoma Virus (BK, JC), Urologic Consideration

**CODES**

- ICD9: 595.89 Other specified types of cystitis
- ICD10: N30.91 Cystitis, unspecified with hematuria
- N30.90 Cystitis, unspecified without hematuria
- N30.89 Other specified types of cystitis

**CLINICAL/SURGICAL PEARLS**

Optimum treatment for chemotherapy-induced HC is prevention (aggressive hydration and/or prophylactic mesna therapy).
CYSOTOCELE
Alana M. Murphy, MD

ASSOCIATED CONDITIONS
- Multicompartment POP
  - Always suspect concurrent apical prolapse in the setting of stage ≥3 cystocele
- Storage symptoms/signs: Stress UI, urinary urgency, urgency urinary incontinence (UI)
- Voiding symptoms/signs: Weak urinary stream, urinary hesitancy, elevated postvoid residual (PVR)
- Related to bladder outlet obstruction, urinary retention

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- No lab testing is required for the diagnosis of a cystocele
  - Urinalysis and urine culture as indicated
Imaging
- No imaging is required for the diagnosis or management of a cystocele
  - A cystocele may inadvertently be detected on imaging studies, such as a cystogram
  - Dynamic magnetic resonance imaging (MRI) with contrast
    - Evaluates pelvic structures in relation to one another during a Valsalva maneuver
    - Aids in differentiation between a cystocele and an enterocele
    - Aids in assessment of multicompartment POP

Diagnostic Procedures/Surgery
- Pelvic exam
  - Employ standardized staging system (POP-Q or Baden-Walker)
  - PVR assessment
  - Urinalysis
  - Only indicated to characterize associated storage and voiding symptoms/signs

Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS
- Cystocele
- Enterocele
- Anterior vaginal wall masses: Urethral diverticulum, Skene gland cyst, epidermal inclusion cyst, cesophageal, Bartholin duct cyst, Gartner duct cyst

TREATMENT
GENERAL MEASURES
- Observation
- Pelvic floor exercises (Kegel exercises) (E/R)
- Vaginal pessary
- Surgical repair

MEDICATION
First Line
- There are no data to support systemic or topical estrogen or other medications as a therapy for the treatment of cystoceles

Second Line
N/A

BASICS
DESCRIPTION
- Cystocele is prolapse of the bladder into the vagina
- Also referred to as anterior compartment prolapse

EPIDEMIOLOGY
Prevalence
- Difficult to determine due to several factors:
  - Data mostly reported in the context of surgical treatment
  - Cystocele may be asymptomatic
- Diagnosis requires a vaginal exam
- POP quantification (POP-Q) distribution in an observational study of women 18–82 yr old seeking routine gynecologic care (2):
  - POP-Q stage 0: 6.4%
  - POP-Q stage 1: 43.9%
  - POP-Q stage 2: 47.7%
  - POP-Q stage 3: 2.6%

RISK FACTORS
- Increasing age
- Family
- Vaginal delivery (nerve, muscle, and connective tissue damage)
  - Instrumented vaginal delivery may be associated with a higher risk of POP compared to spontaneous vaginal delivery
- Race (3):
  - Hispanic women have highest prevalence of POP
  - Increased intra-abdominal pressure (obesity, chronic cough, constipation)
- Pelvic surgery (hysterectomy, radical cystectomy)
- Congenital connective tissue disorders (Ehlers–Danlos syndrome)

Genetics
- Connective tissue disorders, bladder exstrophy
- POP prevalence rates differ according to race suggesting a genetic component (3)

PATHOPHYSIOLOGY
- Weakness of supporting and suspending structures:
  - Cardinal ligaments, uterosacral ligaments, endopelvic fascia, pubocervical fascia, levator ani muscles
- Defect locations:
  - Central: Attenuation of the pubocervical fascia in the midline
  - Lateral: Disruption of lateral attachments of the endopelvic fascia to the arcus tendineus fascia pelvis (ATFP)
- Combined defects

ASSOCIATED CONDITIONS
- Multicompartment POP
  - Always suspect concurrent apical prolapse in the setting of stage ≥3 cystocele
- Storage symptoms/signs: Stress UI, urinary urgency, urgency urinary incontinence (UI)
- Voiding symptoms/signs: Weak urinary stream, urinary hesitancy, elevated postvoid residual (PVR)
- Related to bladder outlet obstruction, urinary retention

DIAGNOSIS
HISTORY
- Symptoms/signs: Pelvic pressure, vaginal pressure, sensation of a vaginal bulge, stress/urgency/overflow UI, obstructive voiding symptoms, recurrent urinary tract infections (UTIs)
- Previous pelvic/vaginal surgical procedures
- Hormonal status
- Obstetric history
- Comorbidities

PHYSICAL EXAM
- Assessment of POP should be performed during a Valsalva maneuver
- Leading edge of POP should be used for staging purposes
- Examining a patient in a standing position may help determine the maximum extent of POP
- Assessment of the anterior compartment should be performed with support of the apical and posterior compartment to ensure the elimination of potentially distracting apical and posterior POP

BADEN–WALKER GRADING SCALE
- Grade 0: No POP
- Grade 1: Leading edge descends halfway to the hymen
- Grade 2: Leading edge descends to the hymen
- Grade 3: Leading edge descends halfway past the hymen
- Grade 4: Procidentia or vault eversion

POP-Q STAGING SYSTEM
- Stage 0: No POP
- Stage 1: Leading edge is between 1 cm above and 1 cm below the hymen
- Stage 2: Leading edge is <1 cm below the hymen but not less than total vaginal length – 2 cm (TVL – 2 cm)
- Stage 3: Leading edge is below hymen by more than TVL – 2 cm
**ADDITIONAL TREATMENT**

**Radiation Therapy**

N/A

Additional Therapies

- Observation
  - Appropriate if a patient is not symptomatic
  - Close to 30% of women will require reoperation for symptomatic POP (1)

- Pelvic floor exercises (Kegel exercises) (4)[B]
  - Good option for poor surgical candidates
  - May be used as a temporary solution
  - Risk of vaginal discharge, vaginal ulceration, vestibulovaginal fissure formation

**Complementary & Alternative Therapies**

N/A

**ONGOING CARE**

**PROGNOSIS**

- Recurrence rates as high as 30–70%
- Close to 35% of women will require reoperation for symptomatic POP (1)

**COMPLICATIONS**

- Blood loss
- Urinary injury/obstruction
- Bladder
- Dysesthesia
- de novo stress UI
- Recurrent cystocele

**FOLLOW-UP**

**Patient Monitoring**

Evaluation for recurrent POP should largely be based on symptoms or clinical signs (elevated PVR, urinary retention, recurrent UTIs)

**Patient Resources**

- American Urogynecologic Society.

**REFERENCES**


**ADDITIONAL READING**


**See Also** (Topic, Algorithm, Media)

- Baden-Walker Staging
- Cystocele, Grading
- Cystocele Enterocele Algorithm
- Cystocele Image ID
- Pelvic Organ Prolapse (Cystocele and Enterocele)
- Pelvic Organ Prolapse Quantification System (POP-Q)
- Recurrence, Urologic Considerations
- Vaginal Mesh Eversion
- Vaginal Pessaries, Urologic Considerations
- Vaginal Prolapse

**CODIES**

- ICD9
  - 618.01 Cystocele, midline
  - 618.02 Cystocele, lateral

- ICD10
  - N81.10 Cystocele, unspecified
  - N81.11 Cystocele, midline
  - N81.12 Cystocele, lateral

**CLINICAL/SURGICAL**

- Management of a cystocele should largely be based on patient preference and symptoms.
- Always suspect concomitant apical prolapse in the setting of stage ≥3 cystocele or a recurrent cystocele.
- Mesh grafts for cystocele repair provide a superior anatomic outcome but they are associated with higher complication rates.
DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLUS, UROLOGIC CONSIDERATIONS

Joshua D. Roth, MD
Michael O. Koch, MD, FACS

BASICS

DESCRIPTION

Deep vein thrombosis (DVT): Aggregation of platelets and fibrin within a deep vein of the leg or pelvic that may lead to venous obstruction.

Pulmonary embolism (PE): Blockage of the pulmonary artery or one of its branches by a thrombus that has traveled from elsewhere in the body through the bloodstream. Can be an acute life-threatening illness.

Genetics

- Inherited risk factors for DVT/PE (3):
  - Family history
  - Factor V Leiden mutation
  - Protein C deficiency
  - Protein S deficiency
  - Antithrombin deficiency
  - Sickle cell trait

PHYSIOLOGY

- Most PEs arise from DVTs:
  - Hypercoagulability: Regional activation of coagulation cascade leading to obstruction, edema, pain
  - Static: Stagnant hypoxemia causes endothelial injury
  - Injury: Platelet accumulation and fibrin deposition
  - Need to differentiate from superficial thrombophlebitis/thrombosis that does not usually lead to DVT

ASSOCIATED CONDITIONS

- Paradoxical embolism: Systemic embolisms of venous origin that occur in patients with atrial or ventricular septal defects, which allow the embolus to pass into the arterial circulation

GENERAL PREVENTION

- DVT prophylaxis (pPx):
  - Mechanical (nonpharmacologic) therapies
    - Early postoperative ambulation
    - Graduated compression stockings (GCSs)
    - Intermittent pneumatic compression (IPC)
  - Pharmacologic therapies
    - Subcutaneous low-molecular-weight heparin (LMWH)
    - Subcutaneous low-dose unfractionated heparin (LDUH)

- Recommendations (4):
  - High-risk patients who are at high risk for bleeding complications:
    - LMWH/LDUH (B), or mechanical pPx, preferably with IPC (C)
  - Moderate-risk surgery (VTE risk 0.5–3.0%):
    - LMWH/LDUH (B) or mechanical pPx, preferably with IPC (C)
  - Low-risk surgery (VTE risk <0.5%):
    - No specific pharmacologic (B) or mechanical (C) pPx

IMAGING

- Recent high-risk surgery, or other risk factors for VTE:
  - History of prolonged immobilization, postoperative status, especially in patient with risk factors
  - Complaint of calf pain, swelling, or discoloration
  - High clinical suspicion with above history
  - Acute onset of dyspnea, tachycardia, arrhythmia, hypotension

LAB

- D-dimers: Sensitivity approaches 95% for ELISA method
  - PE: ~80 mm Hg
  - ALB: Increased PA–aO2 gradient
  - D–dimer: >80 mg/dL

DIAGNOSTIC TESTS & INTERPRETATION

- Grayscale US to visualize the structure of the veins and color Doppler US to visualize the flow of blood through the vein; more accurate than Doppler and phlebography

108
DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLUS, UROLOGIC CONSIDERATIONS

**MEDICATION**

**GENERAL MEASURES**
- Thrombi are a woven congealed mass of fibrin and platelets.
- Overall management of anticoagulation and antiplatelet therapy can be found in Section VII: Reference Tables: Anticoagulation and Antiplatelet Therapy in Urologic Practice

**DVT**
- Extremity elevation, early ambulation, pain relief
- If necessary LMWH therapy can be followed by unfractionated heparin

**PE**
- Pneumonitis/pneumonia, pneumothorax, CHF, DVT: Cellulitis, thrombophlebitis, muscle destruction of valves leads to chronic pain, swelling, skin necrosis, ulceration

**TREATMENT**

**ALERT**
- DVT and PE are potentially life-threatening and acute decline in status can occur. This condition must be treated/diagnosed quickly and level of suspicion must always be high in postoperative patients.

**GENERAL MEASURES**
- DVT: Extremity elevation, early ambulation, pain relief
- PE: Oxygen therapy, fluid resuscitation, maintain cardiac output with pressures if needed
- Overall management of anticoagulation and antiplatelet therapy can be found in Section VII: Reference Tables: Anticoagulation and Antiplatelet Therapy in Urologic Practice

**MEDICATION**

**First Line**
- DVT proximal to knee anticoagulation with (4):
  - Unfractionated heparin (UFH)
  - Fondaparinux
- Early mobilization of oral warfarin, with continued parenteral anticoagulation until INR is reached for >24 hr.
- DVT Distal to knee
  - Without severe symptoms/factors: Serial noninvasive imaging for 2 wk or anticoagulation (C). If thrombus extends, recommend therapeutic anticoagulation (B/C).
  - With severe symptoms/factors: Anticoagulation (as above) over imaging (C).
- PE
  - Systemic anticoagulation as for DVT (B/C)
  - PE with hypoxemia: Systemic thrombolysis with streptokinase is recommended (C).

**Second Line**
- DVT/PE
  - In patients with hepatic insufficiency thromboprophylaxis (HVT), UAW (argatroban, lepirudin, and danaparoid) can be used

**SURGERY/OTHER PROCEDURES**
- DVT
  - Venous thromboembolism: Rarely needed
  - SVC filter
    - Used as prophylaxis in high-risk or multitrauma patients
    - Recommended for acute DVT with contradi-
      ction to anticoagulation (4/B)
  - PE
    - Pulmonary emboloscopy: Considered rarely for patient who remains in shock despite medical therapy

**ADDITIONAL TREATMENT**

**Therapy**
- N/A

**Additional Therapies**
- Will need 3 mo of anticoagulation therapy for postsurgical DVT/PE
  - Prostakon can reverse unfractionated heparin if needed. Protamine is not as effective with LMWH but should be used if excessive bleeding is encountered

**Complementary & Alternative Therapies**
- N/A

**ONGOING CARE**

**PROGNOSIS**
- 10–30% of all patients with VTE suffer mortality within 30 days (3)
- Following anticoagulation therapy, 1/3 of all VTE patients will experience a recurrence within 10 yr (3)
- Highest risk of recurrence is in the 1st year (3)
- 1/3–1/2 of those with LE DVTs develop postthrombotic syndrome (3)

**COMPLICATIONS**
- DVT: Pulmonary embolism and postthrombotic syndrome: Destruction of valves leads to chronic pain, swelling, skin necrosis, ulceration
- PE: Death, pulmonary infarction, pain, atrhythmia, shortness of breath
- VTE: Requires anticoagulation with its associated risk factors (increased bleeding risk), increased healthcare costs, prolonged hospitalization, rehospitalizations
- Heparin-induced thrombocytopenia with unfractionated heparin

**FOLLOW-UP**

**Patient Monitoring**
- Patients on heparin: Follow aPTT
- If necessary LMWH therapy can be followed by antifactor Xa assays
- Patients on warfarin need close monitoring of their INR for a goal between 2.0 and 3.0 (3/B)

**Patient Resources**
- The Coalition to Prevent Deep-Vein Thrombosis
  - http://www.preventdvt.org
- The National Blood Clot Alliance

**REFERENCES**


**ADDITIONAL READING**


See also (Topic, Algorithm, Media)
- Reference Tables: Anticoagulation and Antiplatelet Therapy in Urologic Practice
- Deep Venous Thrombosis and Pulmonary Embolism, Urologic Considerations Image
- Deep Venous Thrombosis, Prophylaxis, AUA Guidelines

**ICD9**
- 415.10 Acute venous embolism and thrombosis of unspecified deep vessels of lower extremity
- 415.11 Iatrogenic pulmonary embolism and deep venous thrombosis, not elsewhere classified
- 453.40 Acute venous embolism and thrombosis of unspecified deep veins of lower extremity
- 997.2 Peripheral vascular complications, not elsewhere classified

**ICD10**
- I26.99 Other pulmonary embolism without acute cor pulmonale
- T81.72XA Complication of vein following a surgical procedure, NEC, init

**CLINICAL/SURGICAL PEARLS**
- Prophylaxis can help prevent DVT/PE
- PE usually develops from a venous thrombus involving the proximal lower extremity
- Early diagnosis and treatment are key.
DETRUSOR OVERACTIVITY
Lysanne Campeau, MD, CM, PhD, FRCSC
Victor W. Nitti, MD, FACS

PATHOPHYSIOLOGY
- Increased connectivity and excitability between detrusor muscle and nerves
- Inflammation
- Increasedafferent activity
- Neurologic lesions of the CNS above the sacral micturition center

ASSOCIATED CONDITIONS
- DO, pelvic floor disorders, urinary incontinence, bladder outlet obstruction, neurologic lesions above the sacral micturition center, detrusor external sphincter dyssynergia

GENERAL PREVENTION
- Avoiding large fluid intake or the consumption of “bladder irritants” such as caffeine.
- Timed voiding and avoiding bladder overdistension

DIAGNOSIS

ALERT
DO, by definition can only be diagnosed by urodynamic testing. Therefore it is not practical to talk in terms of diagnosing DO.

HISTORY (3)
- Past medical and surgical history
- Medications (diuretics, psychoactive drugs)
- Lower urinary tract symptoms survey
- Women with DO and OAB:
  - Are twice as likely to have urge urinary incontinence.
  - Have a higher symptom score on questionnaires
  - Higher episodes of daytime voiding and nocturia
  - Have lower functional bladder capacities
- Higher episodes of daytime voiding and nocturia
- Higher symptom scores on questionnaires
- Women with OAB:
  - Have lower functional bladder capacities

PHYSICAL EXAM
- Rule out the presence of exacerbating conditions
- Pelvic and vaginal exam
- Neurologic exam: Peripheral sensation and motor assessment
- Postvoid residual

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis: Determine presence of infection, hematuria, glycosuria
- Urine culture: Rule out infection
- Urine cytology: Rule out malignancy

Surgical
- Diagnostic Procedures/Surgery
  - Urodynamic testing
  - Filling cystometry: Measurement of the pressure/volume relationship of the bladder during filling

Imaging
- Can involve urodynamic testing with cystogram and voiding cystourethrogram
- Renal ultrasound can also rule out the presence of hydronephrosis caused by high bladder pressures

Pathologic Findings
DO is characterized by the presence of contractions that produce a wave form on urodynamic testing of variable duration and amplitude

DIFFERENTIAL DIAGNOSIS
- Bladder calculus
- Bladder cancer/tumor in situ
- Bladder outlet obstruction/Prostatic hypertrophy
- Congestive heart failure
- Detrusor external sphincter dyssynergia
- Diabetic neuropathy
- Interstitial cystitis/Painful bladder syndrome
- Medications
- Neurogenic bladder
- Pelvic organ prolapse
- Polyuria/polydipsia
- Sexually transmitted infection
- Stress incontinence
- Testing artifacts during UDS evaluation (false positive)
- Urinal tract infection
- UTI

GENERAL MEASURES
- Treatment aimed at inhibiting involuntary detrusor contractions and decreasing vesical pressures
- There are a number of options used to treat symptoms associated with DO. Only antimuscarinics, biofeedback, and augmentation cystoplasty have been proven to actually reduce or eliminate DO
- Behavioral modifications: Timed voiding, decrease fluid intake, avoid caffeine
- Pelvic floor exercises (Kegels): With or without biofeedback
DETRUSOR OVERACTIVITY

MEDICATION
- Antimuscarinics: Inhibit the effect of acetylcholine at postjunctional muscarinic receptors on detrusor muscle cells
  - Tolterodine (2–4 mg/d)
  - Trospium XR (60 mg/d)
  - Solifenacin (5–10 mg/d)
  - Oxybutynin (IR 7.5–20 mg/d, XL 5–30 mg/d, patch twice weekly)
  - Fesoterodine (4–8 mg/d)
- β3-adrenergic receptor agonist: Promotes detrusor muscle relaxation
  - Intravesical botulinum toxin (OnabotulinumtoxinA) injection
  - Sacral neuromodulation: Stimulation of S3 nerve root (InterStim)
  - Posterior tibial nerve stimulation (PTNS): Urgent PCTM
- Augmentation cystoplasty/Urinary diversion: Increase functional bladder capacity and reduce intravesical pressure
- Pelvic floor reconstruction: If concomitant pelvic floor disorder

FOLLOW-UP
- Patient Monitoring
  - Periodic patient follow-up
  - Symptom assessment
  - Treatment compliance
  - Minimize medication side effects

Patient Resources
- National Association for Continence: www.nafc.org/bladder-health

REFERENCES

ADDITIONAL READING

ONCOLOGIC/SURGICAL PEARLS
- OAB is not synonymous with detrusor overactivity, the key symptom of OAB is urinary urgency.
- DO demonstrated on cystometry needs to be correlated with patient’s symptoms.
- Treatment indicated if potential complications or patient driven.
- Only antimuscarinics, botulinum toxin, and augmentation cystoplasty have been proven to actually reduce or eliminate DO.

ADDITIONAL THERAPIES
- Infection prophylaxis
- Clean intermittent catheterization
- Decrease bladder pressure if urinary retention present

Ongoing Care
- Stepwise approach to treatment with least invasive pharmacologic options as first line
- May develop refractory OAB that may require second- or third-line treatment

FOLLOW-UP
- Periodic patient follow-up
- Symptom assessment
- Treatment compliance
- Minimize medication side effects

Patient Resources
- National Association for Continence: www.nafc.org/bladder-health

REFERENCES

ADDITIONAL READING

CODES
ICD9
- 596.51 Hypertonicity of bladder
- 718.41 Urinary frequency
- 718.63 Urgency of urination

ICD10
- N32.81 Overactive bladder
- R35.0 Frequency of micturition
- R39.15 Urgency of urination

CLINICAL/SURGICAL PEARLS
- OAB is not synonymous with detrusor overactivity, the key symptom of OAB is urinary urgency.
- DO demonstrated on cystometry needs to be correlated with patient’s symptoms.
- Treatment indicated if potential complications or patient driven.
- Only antimuscarinics, botulinum toxin, and augmentation cystoplasty have been proven to actually reduce or eliminate DO.

Ongoing Care
- Stepwise approach to treatment with least invasive pharmacologic options as first line
- May develop refractory OAB that may require second- or third-line treatment

FOLLOW-UP
- Periodic patient follow-up
- Symptom assessment
- Treatment compliance
- Minimize medication side effects

Patient Resources
- National Association for Continence: www.nafc.org/bladder-health

REFERENCES

ADDITIONAL READING

CODES
ICD9
- 596.51 Hypertonicity of bladder
- 718.41 Urinary frequency
- 718.63 Urgency of urination

ICD10
- N32.81 Overactive bladder
- R35.0 Frequency of micturition
- R39.15 Urgency of urination

CLINICAL/SURGICAL PEARLS
- OAB is not synonymous with detrusor overactivity, the key symptom of OAB is urinary urgency.
- DO demonstrated on cystometry needs to be correlated with patient’s symptoms.
- Treatment indicated if potential complications or patient driven.
- Only antimuscarinics, botulinum toxin, and augmentation cystoplasty have been proven to actually reduce or eliminate DO.
DETRUSOR SPHINCTER DYSSYNERGIA (DSD)
Michael J. Amirian, MD
Patrick J. Shenot, MD, FACS

BASICS
DESCRIPTION
- Detrusor sphincter dyssynergia (DSD) is found in cases of neurogenic lower urinary tract dysfunction
- DSD is contraction of the sphincter mechanism occurring simultaneously with uninhibited involuntary contraction of the bladder detrusor muscle (neurogenic detrusor overactivity [NDO])

EPIDEMIOLOGY
Incidence
- Unknown
  - Depends on incidence of underlying neurologic condition
Prevalence
- Prevalent in those with spinal cord lesions
  - More prevalent at higher levels (cervical) than lower (sacral) injury or disease
- May affect those with multiple sclerosis (MS), spinal cord tumor, traumatic spinal cord injury (SCI), arteriovenous malformation
- Unilateral involuntary detrusor contraction (ie, NDO) must be present for DSD to occur

RISK FACTORS
- Neurologic processes affecting central nervous system (CNS)
  - Below level of the pons
- Associated with autonomic hyperreflexia

GENETICS
None

PATHOPHYSIOLOGY
- DSD causes functional outflow obstruction
- DSD causes chronic detrusor overactivity
  - Damaged elevation of intravesical pressure
  - Damaged urethral sphincter tone
  - Damaged urethral sphincter function
  - Nonrelaxing stenotic urothelial obstruction
  - Impaired transmission of coordinating influences from the pons during reflex detrusor contraction
- Uninhibited detrusor contraction stimulates a reflex sphincter contraction, resulting in bladder outflow obstruction
- 10–20% patients have internal (bladder neck) sphincter dyssynergia coexistent with external sphincter dyssynergia

ASSOCIATED CONDITIONS
- SCI
- MS
- Transverse myelitis

GENERAL PREVENTION
N/A

DIAGNOSIS
HISTORY
- Neurologic disease
  - Date of onset, duration of process
- Urinary voiding symptoms
  - Frequency, urgency, urge incontinence
- Method of urinary management
  - Condom catheter urinary collection
  - Intermittent self-catheterization
- Indwelling urethral suprapubic catheter
- Urinary tract infection (UTI)
  - Severity of infection
  - Response to antibiotics
  - Need for parenteral antibiotics
  - Frequency of occurrence of infection
  - Urinalysis
  - Episodes of UTI
- Surgical intervention

PHYSICAL EXAM
- Fever
- Parenteral UTI
  - Men
  - Prostate, testes/epididymis, renal
  - Female
  - Pelvic
  - Hypertension
- Hypertension
  - During manipulation of GU/GI systems, autonomic hyperreflexia may result
  - Generalized edema
  - Sexual renal insufficiency
  - Filial rectal mass
  - Secondary hydrominosis
  - Flank tenderness
  - Ureteral obstruction
  - Pelvitis
  - Abdominal mass
  - Distended bladder, urinary retention
  - Incontinence of urine
  - Spontaneously
  - With stress maneuvers
  - During abdominal/pelvic palpation
  - With stress maneuvers
  - During abnormally high palpation
  - Testicular mass
  - Epidydymitis-orchitis/epididymitis
  - Secondary abscess formation
  - Hydrocele from recurrent infection
  - Prostate mass/Node
  - Prostatic prostatitis
  - Prostate abscess

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Blood studies
  - Serum chemistry
  - Renal function, electrolyte levels
  - Complete blood count
  - Secondary anemia due to decreased renal function or chronic infection
- Urine studies
  - Urinalysis
  - Proteinuria: Renal dysfunction
  - Pyuria, nitrite, leukocyte esterase: Acute or chronic infection
  - Hematuria: Infection or lithiasis

Imaging
- Renal ultrasound (US)
  - Effective in screening for upper urinary tracts
  - Calculi
  - Hydroureteronephrosis
  - Masses
  - Sonography (USG)
  - Contraindicated in those with decreased renal function (serum creatinine > 2.0)
- Delayed secretion of contrast with high urinary storage pressures
  - Hydroureteronephrosis
  - Marked elevation of intravesical pressure
  - May be due to urinary calculi
  - Voiding cystourethrogram
  - Bladder
    - Wall thickening
    - Trabeculation
    - Shuntreflux
    - Incomplete emptying
    - Ultrasound
      - Vesicoureteral reflux
      - Hydrocele
      - Hydroureteronephrosis
      - Ureteral
        - Prostatic urethral dilatation
        - Membranous urethra persistently narrow, stenotic, constricting
        - Distal urethra normal
        - Rule out stricture
        - Nuclear medicine renal scan
          - Objective quantification of GFR
          - Sequential studies can detect deterioration of renal function prior to elevation of serum creatinine
  - Diagnostic Procedures/Surgery
  - Ultrasound evaluation
    - Essential to diagnose detrusor overactivity with detrusor sphincter dyssynergia
  - Cystoscopy
    - Normal galea urethral
    - Spanning, nonrelaxing, stenotic membranous urethral
    - Dilated prostatic urethra
    - Bladder trabeculation/external trabeculation
    - Rule out calculus or bladder tumor

Pathologic Findings
None
DIFFERENTIAL DIAGNOSIS
- Detrusor instability and bladder outflow obstruction
- Bony prostatic hypertrophy
- Adenocarcinoma of the prostate
- Urethral stricture disease
- Urinary retention
- Impaired detrusor contractility
- Detrusor areflexia
- Urinary retention/incomplete emptying and neurogenic disease
- Decrease intravesical pressure
- Decrease bladder contractility
- Detrusor areflexia
- Urethral tumor
- Adenocarcinoma of the prostate
- Urethral stricture disease
- Neurogenic bladder
- Kyphoscoliosis

TREATMENT
GENERAL MEASURES
- Intermitent catheterization
- Decrease intravesical pressure
- Decrease bladder contractility
- Detrusor areflexia
- Decrease urinary storage

MEDICATION
First Line
- Anticholinergic therapy
  - Effective in improving urinary storage under low pressure
  - Phosphodiesterase 5 inhibitors
  - β-Adrenergic blockade
  - α-Adrenergic blockade
- Endoscopic sphincter ablation
- Botulinum toxin injection into the external sphincter

Second Line
- Botulinum toxin injection into the external sphincter for DSD
- Adrenergic blockade
- Anticholinergic therapy
- Endoscopic sphincter ablation
- Botulinum toxin injection into the external sphincter

SPECIAL CONSIDERATIONS
- Urinary retention
- Detrusor areflexia
- Urethral stricture disease
- Neurogenic bladder
- Kyphoscoliosis

OTHER PROCEDURES
- Endoscopic sphincterotomy
- Electrosurgical or laser sphincterotomy
- Nerve root stimulation allows control over detrusor contraction
- Conduit of ileum connecting dome of bladder to anterior abdominal wall

Ongoing Care
- Excellent prognosis if effectively treated
- Uninked, ~50% of men will develop significant complication

COMPLICATIONS
- Detrusor instability
- Neurogenic bladder
- Urethral stricture disease
- Neurogenic bladder

ADDITIONAL READING

REFERENCES
1.14

DIABETES MELLITUS, UROLOGIC CONSIDERATIONS

Thomas M. Facelle, MD
Mark L. Jordan, MD, FACS

BASICS

DESCRIPTION
- Hyperglycemia with secondary metabolic abnormalities
- Two subtypes including insulin deficiency (DM1) and insulin resistance (DM2)

EPIDEMIOLOGY

Risk factors
- Genetic predisposition
- Environmental factors

Prevalence
- 8.3% of US population in 2010 was diabetic (1)

Incidence
- 30% with DM1 and 10–40% with DM2 will develop kidney failure
- 59% with DM will have urologic complications

Risk factors
- Genetics
  - Strong hereditary component for DM2
  - DM1: Approx one-third genetic contribution
- Environmental
  - Visceral obesity for DM2

DIAGNOSIS

History
- General
  - Polyuria, polydipsia
  - Weight loss, malaise
- Family history
- Previous DM
- Weight loss, malaise
- Polyuria, polydipsia

Physical Exam
- General
  - Symmetry, nodules, tenderness
  - Abdomen
  - Flank
  - External genitalia
  - Prostate
  - Rectal
- History
  - Infertility
  - Voiding dysfunction
  - UTI

Assessments
- Laboratory
  - Fasting glucose
  - Oral GTT, 2-hr value
  - Microalbuminuria
  - Uric acid
  - Erythrocyte sedimentation rate

DIFFERENTIAL DIAGNOSIS

- Bladder cancer
- Increased incidence and mortality seen in men and women with DM

ASSOCIATED CONDITIONS
- Obesity
- Metabolic syndrome
- Neuropathy
- Renal failure

GENERAL PREVENTION
- Glycemic control
- Weight reduction

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Urinalysis
- Urine culture, and sensitivities
- Microalbuminuria

DIFFERENTIAL DIAGNOSIS

- UTI
- Pyelonephritis
- Urinary tract infection
- Urinary tract obstruction
- Urinary tract infection
- Urethral stricture
- Neurogenic bladder
- Urethral stricture
- Neurogenic bladder
- Urethral stricture
- Neurogenic bladder
DIABETES MELLITUS, UROLOGIC CONSIDERATIONS

TREATMENT

GENERAL MEASURES
- Educate patients regarding urologic manifestations of diabetes
- Glycemic control
  - Dietary improvement, weight loss, exercise

MEDICATION

First Line
- UTI
  - DM is an underlying condition that makes any UTI a complicated UTI
  - Antibiotics (oral vs. intravenous)
  - Fluid resuscitation
- ED
  - Oral phosphodiesterase inhibitors (sildenafil, vardenafil, vardenafl, avanafil)
- Voiding dysfunction
  - α-blockers if outlet obstruction (benign)
  - Bladder stimulation (anticholinergic, cholinergic)
- Voiding dysfunction
  - α-blockers if bladder outlet obstruction (benign)
- UTI
  - Voiding dysfunction
  - α-blockers if bladder outlet obstruction
- Voiding dysfunction
  - α-blockers if bladder outlet obstruction
- ED
  - α-blockers if bladder outlet obstruction

Second Line
- ED
  - Intravesical suppository (MUSE)
- Voiding dysfunction
  - α-blockers if bladder outlet obstruction
- UTI
  - Voiding dysfunction
  - α-blockers if bladder outlet obstruction

SURGERY/OTHER PROCEDURES
- UTI
  - Retention: Catheter placement, suprapubic tube
  - Urolithiasis: Urine electrolytes, nephrostomy tube, ureteroscopy, extracorporeal shock wave lithotripsy
- ED
  - Penile prosthesis
- Voiding dysfunction
  - Cystoscopic resection (transurethral)- efficacy for overactivity and retention
- Bladder outlet obstruction: Trans urethral resection of prostate, photoselective vaporization of prostate, etc.
- Lower urinary diversion (urostomy, ileal conduit)
- Incontinence
  - Artificial urinary sphincter
- Bladder cancer
  - Transurethral resection, cystectomy

ADDITIONAL TREATMENT

Radiation Therapy
- ED
  - Radiation therapy
- Voiding dysfunction
  - Radiation therapy
- Erectile dysfunction
  - Vascular dysfunction

Complementary & Alternative Therapies

- UTI
  - Cranberry extract
- Voiding dysfunction
  - Acupuncture to sacral dermatome

ONGOING CARE

PROGNOSIS
- Good with tight glycemic control
- Late presentation and progression of symptoms

COMPLICATIONS
- UTI
  - Upper tract infection
  - Staphylococcus, KPC
- Renal failure
- Voiding dysfunction
  - UTI
- Upper tract damage/renal failure
- Incontinence
- Bladder stones
- Atonic bladder
- Diabetic nephropathy
  - ESRD
- Dialysis dependence

FOLLOW-UP

Patient Monitoring
- General
  - Periodic serum glucose
  - HbA1c
- Glycemic control
  - Urine protein and microalbuminuria
- ED
  - Testosterone replacement: Check serum testosterone, prostate specific antigen (PSA), renal function for eligibility
- Voiding dysfunction
  - Symptomatology
  - RU/PH/CT
- Incontinence
  - Repeat urodynamics as needed

Patient Resources
- Centers for Disease Control and Prevention, Diabetes Public Health Resource: http://www.cdc.gov/diabetes
- American Diabetes Association: http://www.diabetes.org
- National Diabetes Education Foundation: http://neph.org

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Diabetes Mellitus, Urologic Considerations Image A
- Erectile Dysfunction (ED)/Impotence
- Hyperglycemia, Urologic Considerations
- Neurourology
- Prostate, Benign: BPH
- Prostate, Benign: HYPP
- Urology, General
- urology/surgical

CODES

ICD9
- 250.40 Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled
- 250.41 Diabetes with renal manifestations, type I (juvenile type), not stated as uncontrolled
- 585.6 E10.29 Type 1 diabetes mellitus w/oth diabetic kidney complication
- 585.7 Type 2 diabetes mellitus w/oth diabetic kidney complication
- N04.6.1 E10.29 Type 1 diabetes mellitus w/oth diabetic kidney complication
- N17.8 E10.29 Type 2 diabetes mellitus w/oth diabetic kidney complication
- 585.6.1 E10.29 Type 1 diabetes mellitus w/oth diabetic kidney complication
- 585.7.1 E10.29 Type 2 diabetes mellitus w/oth diabetic kidney complication

ICD10
- E10.29 Type 1 diabetes mellitus woth diabetic kidney complication
- E11.29 Type 2 diabetes mellitus woth diabetic kidney complication
- N05.6 E10.29 Type 1 diabetes mellitus woth diabetic kidney complication
- N17.8 E10.29 Type 2 diabetes mellitus woth diabetic kidney complication
- N17.8.1 E10.29 Type 1 diabetes mellitus woth diabetic kidney complication

CLINICAL/SURGICAL PEARLS
- DM predisposes to urinary infections of greater severity with likely upper tract involvement.
- Most common voiding symptom is overactivity.
- ED may be the presenting sign of DM.
- Tight glycemic control is necessary to reduce progression of symptoms.
DISORDERS OF SEXUAL DEVELOPMENT (DSD)

Luigi Avolio, MD

BASICS

DESCRIPTION
- Congenital condition in which development of chromosomal, gonadal, or anatomic sex is atypical (1)
- Chromosomal sex is inconsistent with phenotypical sex
- DSD is the result of a discordance among the 3 sex determination processes (chromosomal, gonadal, and phenotypical)
- Ambiguous genitalia and intersex disorders are no longer considered correct terms
  - Classification
    - See chromosome DSD
    - XX DSD
    - XY DSD

EPIEDELOLOGY

Incidence
- 1 in 5,000 live births
  - Congenital adrenal hyperplasia (CAH) represents 60–70% of neonatal DSD (1 case per 15,000 live births)

Prevalence
- N/A

RISK FACTORS
- Family history of DSD
- In utero exposure to androgens
  - Dietary teratogens
  - Maternal injection

Genetics
- XX DSD
  - CF21-gene-ch1q13.13. Autosomal recessive
  - 3β-hydroxysteroid dehydrogenase deficiency, MIM#201910, 150822 genes-ch1.p2.1. Autosomal recessive
- XX DSD
  - P450 oxidoreductase deficiency, MIM#201910, 150822 genes-ch1.p2.1. Autosomal recessive
  - Persistence of mullerian duct syndrome (PMDS)

ASSOCIATED CONDITIONS
- Turner syndrome
- Klinefelter syndrome
- Rettinsen syndrome
- Inguinal hernia
- Congenital adrenal hyperplasia
- Amenorrhea
- Infertility

GENERAL PREVENTION
- Prenatal treatment of tissues at risk for CAH with dexamethasone
- Chorionic villus sample
- Amniocentesis

DIAGNOSIS

HISTORY
- Family anamnesis
  - DSDs, genital abnormalities, amenorrhea, sterility, hirsutism
  - Early infant deaths (missed adrenocortical syndrome)
- Maternal exposure to androgens
- History of maternal virilization (androgen-producing tumor)

PHYSICAL EXAM
- External genitalia
  - Phalic structure (length, breadth, and amount of erectile tissue)
- Abdomen
  - Mass referable to enlarged uterus

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Karyotype
- Serum levels of sodium, potassium, and 17hydroxyprogesterone
- Androgens (testosterone, dehydroepiandrosterone, androstenedione)
- Cortisol, gonadotrophins, and AMH levels
- Stimulation test with human chorionic gonadotropin (suspected defect of androgen production)
DISORDERS OF SEXUAL DEVELOPMENT (DSD)

Imaging
- Abdominal pelvic ultrasonography (renal presence)
- Cystogram/urogram (visualisation of vagina, lithotripsy)
- MRI

Diagnostic Procedures/Surgery
- Laparoscopy to define internal anatomy
- Cystoscopy to confirm anatomy and level of confluence of urogenital sinus
- Gonadal biopsy to analyse presence of ovarian and/or testicular tissue
- Skin biopsy to obtain cellular lines

Pathologic Findings
Identification of ovarian tissue, testicular tissue, ovotestes, or streak gonads according to related specific disorders

DIFFERENTIAL DIAGNOSIS
- Hypothyroidism
- Hypospadias
- Hydrocele and hernia
- Menstruation disorders
- Microphallus
- Gonadal dysgenesis

TREATMENT
GENERAL MEASURES
- Gender assignment avoiding hasty decision
- Expert evaluation by an experienced multidisciplinary team

MEDICATION
First Line
- Nifedipine with self-washing CAH
- Fluid and electrolyte replacement
- Glucocorticoid and mineralocorticoid replacement
- Hydrocortisone 10 mg/m2/d
- Fludrocortisone 0.1–0.2 mg/d
- Oral sodium chloride, 1–2 g/d added to formula or breast milk

Second Line
- Pseudoephedrine

SURGERY/OTHER PROCEDURES
- Masculinizing genitoplasty (between the ages of 6 and 18 mos)
  - Hormonal treatment with testosterone preparation to stimulate phallic development
  - Surgical excision of Müllerian structures
  - Phaloplasty (hypospadias repair, chordee correction, corporal transposition)
  - Orchidopexy
  - Rectal injury (urogenital sinus mobilization)
- Feminizing genitoplasty (during the 1st 6 mo of life)
- Clitoroplasty preserving innervation to reduce the size of the gland and shaft
- Vaginoplasty and labioplasty to separate vagina and urethra from the common urogenital sinus
- Gonads
  - 46XX DSD: Normal ovaries, no treatment necessary
  - 46XY DSD: Gonadal biopsy
  - Female gender assigned: Orchiectomy (timing is subject of debate)
  - Male gender assigned: Orchidopexy
  - Gonadal dysgenesis
- Exclusion of dysgenetic gonads (steak)

- Müllerian remnants
  - Small asymmetries are managed conservatively
  - Symptomatic remnants are treated surgically (endoscopic excision or unfolding, laparoscopic robotic excision)

ADDITIONAL TREATMENT
Radiation Therapy
No

Additional Therapies
No

Complementary & Alternative Therapies
No

ONGOING CARE
PROGNOSIS
Many patients can remain fertile (CAH, some ovotesticular DSD, XY DSD with X0)

COMPLICATIONS
- Acute adrenal insufficiency in CAH not adequately treated
- Damage to clitoral innervation (clitoroplasty)
- Steroid of the vaginal introitus (laparoplasty)
- Urinary obstruction (urogenital sinus mobilization)

FOLLOW-UP
Patient Monitoring
- Sexual function (adequate vaginal introitus, adequate penile reconstruction)
- Risk of gonadoblastoma in gonadal dysgenesis is 12% (occurrence of neoplasia is primarily associated with the Y chromosome containing karyotype)
- Lifetime psychosocial support mandatory for all patients with DSD

Patient Resources
- http://www.toukipschilddis.org (all DSDs)
- http://www.accordancealliance.org (all DSDs)
- http://www.kidn.org (all DSDs)
- http://www.carebundation.org (CAH)
- http://www.nhm.org.uk (CAH)
- http://healthtalk.org (hypospadias and epispadias)
- http://www.isdod.org (Androgen Insensitivity Syndrome)

REFERENCES

ADDITIONAL READING
- http://www.mendelian.inheritanceinman.org/mim/ (Online Mendelian Inheritance in Man™)
- See Also (Topic, Algorithm, Media)
  - Androgen Insensitivity Syndrome (46,XY, Androgen Resistance Syndrome), Complete (CAIS) and Partial (PAIS)
  - Müllerian Duct Remnants and Persistent Müllerian Duct Syndrome (PMDS)
  - Pseudohermaphroditism, Male and Female

CODES

- ICD9
  - 259.80 Congenital adrenogenital disorders
  - 293.90 Androgen insensitivity, unspecified
  - 752.7 Intersex and reproductive defects
  - 756.4 Intersex and reproductive defects

- ICD10
  - E25.0 Congenital adrenogenital disorders associw engine deficiency
  - E34.50 Androgen insensitivity syndrome, unspecified
  - Q56.4 Intersex and reproductive defects

CLINICAL/SURGICAL PEARLS
- DSD should be managed by a specialized multidisciplinary team
- Gender assignment should be made after thorough investigation by the team
- DSD is a heterogeneous group of conditions with different underlying molecular causes. Many disease genes remain to be identified
- Infants with a DSD and who present with truly ambiguous genitalia are a rare occurrence.
DYSFUNCTIONAL ELIMINATION SYNDROME
Jennifer A. Hagerty, DO

BASICS
DESCRIPTION
- Dysfunctional voiding; various symptoms from mild daytime frequency and postvoid dribbling to daytime and nighttime wetting, urgency, urge incontinence, pelvic holding maneuvers, and urinary tract infections (UTIs)
- Sometimes referred to as bowel bladder dysfunction (BBD)
- Dysfunctional voiding often associated with bowel dysfunction; constipation, encopresis, or fecal impaction
- Constipation and rectal dilation interfere with normal bladder function
- No identifiable neurologic cause

EPIDEMIOLOGY
Incidence
- Constipation is present in up to 50% of children with dysfunctional voiding

Prevalence
- 20–30% school-aged children have dysfunctional voiding

RISK FACTORS
- UTIs
- Sexual abuse
- Attention deficit/hyperactivity disorder
- Stressors during or after toilet training

Genetics
- Ochoa syndrome, a genetic disorder with an autosomal recessive inheritance pattern
  - Associated with dysfunctional voiding

PATHOPHYSIOLOGY
- Voiding dysfunction (variable etiologies):
  - Small bladder capacity
  - Large bladder capacity secondary to urine holding
  - Disordinated voiding with difficulty relaxing the sphincter during voiding
  - Often associated with constipation
  - Rectum close to posterior wall of bladder
  - Large amount stool
  - Obstruction by compression of the bladder and bladder neck
  - Obstruction by compression of the bladder and bladder neck

ASSOCIATED CONDITIONS
- Vesicoureteral reflux (VUR)
- UTIs
- Encopresis
- Incontinence
- VUR
- Urge syndrome

GENERAL PREVENTION
- None have been identified

DIAGNOSIS
HISTORY
- Present typically after toilet training
- Diurnal and/or nocturnal enuresis
- Frequency and urgency
- Hegidity
- UTIs
- Difficulty stooling, hard or infrequent stools
- Encopresis

PHYSICAL EXAM
- Typically normal physical exam
  - Evaluate for neurologic dysfunction
  - Examine the external genitalia for anatomic causes of symptoms
  - Evaluate for a distended bladder and palpable stool
  - Consider rectal exam for fecal retention

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis and urine culture; rule out bacteriuria and glucosuria

Imaging
- Renal/bladder ultrasound; evaluate for hydronephrosis, thickened and/or distended bladder, post-void residual, stool in the rectum
- MRI lumbar spine if concern for a neurogenic cause to evaluate for a tethered cord
- Voiding cystourethrogram to evaluate for VUR in patients with febrile UTIs.
  - Also information on bladder capacity and emptying, and appearance of the bladder and urethra
  - Spinning top urethra; widening of the urethra in females during voiding

Diagnostic Procedures/Surgery
- Voiding and stooling diary to assess frequency and volume of voids and stooling frequency and consistency
- Uroflowmetry evaluate pattern
  - Flow rates different than adults and less reliable; curve more diagnostic
  - Bell shaped—normal
  - Tower shaped—overactive bladder
  - Low flat curve—obturator obstruction
  - Staccato pattern—sphincter overactivity
  - Interrupted flow—underactive bladder
- Urodynamic; patients refractory to conventional therapy
  - Evaluate the filling and emptying phases of the bladder
  - Can be done in conjunction with fluoroscopy

DIFFERENTIAL DIAGNOSIS
- Nonneurogenic neurogenic bladder
- Neurogenic bladder
- Ochoa syndrome
- Overactive bladder
- Giggle Incontinence

TREATMENT
GENERAL MEASURES
- Behavioral modification: Education on voiding patterns
  - Timed voiding
  - Correct positions to void
  - Relaxation techniques
  - Proper hydration
  - Bowel management
  - Education on correlation between the bladder and bowel activity
  - Daily toilet time
  - Dietary modifications; high fiber

MEDICATION
First Line
- Treatment of constipation prior to medications for bladder symptoms; disimpaction followed by maintenance therapy
  - Initial treatment with laxatives and enemas
  - Maintain soft daily stools with a combination of fiber, fluids, laxatives, and softeners
DYSFUNCTIONAL ELIMINATION SYNDROME

- Antimuscarinics; overactive bladders
  - Reduce the intensity and frequency of bladder contractions
- α-Adrenergic blockers; bladder neck obstruction
  - Relaxation of the bladder neck to improve bladder emptying
- Prophylactic antibiotics; prevention of recurrent UTIs until dysfunctional elimination improved

Second Line
- Tricyclic antidepressants for urge incontinence
  - Mechanism not known; not FDA approved in children

SURGERY/OTHER PROCEDURES
- Biofeedback
- Transcutaneous electrical nerve stimulation

ADDITIONAL TREATMENT
Radiation Therapy
N/A

ADDITIONAL THERAPIES
Clean intermittent catheterization with impaired bladder contractility
Complementary & Alternative Therapies
- Acupuncture
  - Low utility in children given use of needles
- Probiotics, prevention of UTIs and treatment of constipation
- Cranberry supplements; potential for UTI prevention

ONGOING CARE
PROGNOSIS
Most children have resolution of symptoms in a short period of time with behavioral modifications; however, some children may have persistence requiring more intensive management.

COMPILATIONS
- UTIs
- Urinary incontinence
- Urinary retention
- Hydronephrosis

FOLLOW-UP
Patient Monitoring
- Voiding/stooling diary
- Uroflowmetry
- Post-void residual monitoring

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Enuresis, Pediatric
- Incontinence, Urinary, Pediatric
- Urinary Retention, Pediatric
- Urinary Tract Infection, Pediatric
- Vesicoureteral Reflux, Pediatric
- Dysfunctional Elimination Syndrome Image

CODES
ICD9
- 599.0 Urinary tract infection, site not specified
- 788.3 Urinary incontinence
- 788.41 Urinary frequency

ICD10
- N39.0 Urinary tract infection, site not specified
- R32 Unspecified urinary incontinence
- R35.0 Frequency of micturition

CLINICAL/SURGICAL PEARS
- Constipation is often associated with bladder dysfunction in children.
- Treatment of constipation alone may lead to complete resolution of urinary complaints.
- Vesicoureteral reflux may resolve after treatment of voiding dysfunction.
- Education of the correlation between stooling patterns and voiding complaints is a very important part of treatment; if understanding is poor there is often low compliance.

119
DYSORGASMIA (PAINFUL ORGASM), MALE
John Patrick Mulhall, MBCh, FACS, FECSM

BASICS

DESCRIPTION

• Dysorgasmia specifically refers to pain that occurs immediately preceding, at or immediately following orgasm.
• The pain is usually located in the penis or testicles but may be present in the lower abdomen, groin, perineum, or elsewhere.
• The severity of pain ranges from mild and of nuisance value to crippling and may last seconds to hours after orgasm.
• The condition is best identified and studied in the postradical prostatectomy setting.
• Ejaculatory pain may be seen in other conditions such as chronic prostatitis/chronic pelvic pain syndrome (CPPS), or NIH category III prostatitis, and is discussed in Section II (“Ejaculation, painful”).

EPIDEMIOLOGY

Incidence

• The most frequent correlate of dysorgasmia is radical prostatectomy and this condition occurs in about 10–15% of patients.
• In this population, the pain is usually self-limiting with most sufferers experiencing complete resolution by 2 yr postoperatively.

Prevalence

N/A

RISK FACTORS

• Radical prostatectomy
• Prostate radiation
• Chronic pelvic pain syndrome (CPPS)

Genetics

None known

PATHOPHYSIOLOGY

• While unproven one of the postulated mechanisms is that the pain is related to pelvic floor or bladder neck spasm.
• This is the rationale for the use of α-blockers.
• Dysorgasmia decreases in frequency and degree over time after RP.

ASSOCIATED CONDITIONS

• Chronic pelvic pain syndrome (NIH category III prostatitis)
• Erectile dysfunction (1)
• Prostate cancer

GENERAL PREVENTION

None known

DIAGNOSIS

HISTORY

• Medical history
• Focusing on assessment of orgasmic pain location, severity and duration.
• Prior history of radical prostatectomy, radiation therapy, or CPPS.

PHYSICAL EXAM

• General physical exam
• Genital exam (although often there are no specific findings)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

None are useful

Imaging

None are useful

Diagnostic Procedures/Surgery

None

Pathologic findings

None

DIFFERENTIAL DIAGNOSIS

• Pelvic pain:
  – Perineal compressive neuropathy
  – Perineal trauma
  – Perineal disease
  – Sexually transmitted infection (STI)
  – Urinary stone
• Testicular pain:
  – Epididymitis
  – Orchitis
  – Testicular tumor
  – Trauma

TREATMENT

GENERAL MEASURES

Reassurance that the condition is most often self-limiting

MEDICATION

First Line

• α-Blockers (daily initially; if successful attempt on-demand) (2)
• Up to 70% of men using α-blockers will have significant improvement in pain.
• Side effects include syncope, orthostasis, retrograde ejaculation, asthenia, and nasal congestion
  – Alfuzosin 10 mg/d
  – Doxazosin start 1 mg/d to max 8 mg
  – Silodosin 8 mg/d
  – Tamsulosin start 0.4 mg to max 0.8 mg
  – Terazosin start 1 mg/d to max 20 mg

Second Line

• Centrally acting pain relievers
• Optimum dose and duration not established
  – Gabapentin
  – 900 to 1,800 mg/d and given in divided doses (3 times a day) using 300 or 400 mg capsules
  – Pregabalin
  – Begin dosing at 150 mg/d, increase to 300 mg/d within 1 wk. Maximum dose of 600 mg/d

SURGERY/OTHER PROCEDURES

Cases reports exist of excision of retained seminal vesicle following radical prostatectomy with relief of symptoms (3)

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

N/A

Complementary & Alternative Therapies

N/A
DYSORGASMIA (PAINFUL ORGASM), MALE

ongoing care

PROGNOSIS
• Recovery is expected following radical prostatectomy.
• At 24 mo, a statistically significant decrease in symptoms was seen in one study (4).
  – 72%, 26%, and 7% of patients still complained of pain at 1, 18, and 24 mo, respectively.

COMPlications

FollOW-UP

Patient Monitoring
Routine radical prostatectomy follow-up appears most appropriate.

Patient Resources

RefErEnces


additional ReadiIng

• See also (Topic, Algorithm, Media)
  • Ejaculatory Disorders (Delayed, Decreased, or Absent)
  • Ejaculation, Painful
  • Post-organ Fibrosis Syndrome (POS)
  • Prostatitis, Chronic Nonbacterial, Inflammatory and Noninflammatory (NIH CP/CPPS III A and B)

cliniCal/Surgical pearlS

• Dysorgasmia is common after radical prostatectomy.
• It is usually self-limiting.
• It is often responsive to α-blocker therapy.

codes

ICD-9
• 607.89 Other specified disorders of penis
• 608.89 Other specified disorders of male genital organs
• 789.09 Abdominal pain, other specified site

ICD-10
• N48.89 Other specified disorders of penis
• N50.8 Other specified disorders of male genital organs
• N53.12 Painful ejaculation

clinical/surgical pearlS

• Dysorgasmia is common after radical prostatectomy.
• It is usually self-limiting.
• It is often responsive to α-blocker therapy.
DYSPAREUNIA, FEMALE
Bradley C. Gill, MD, MS
Sandip P. Vasavada, MD, FACS

BASICS

DESCRIPTION
Dyspareunia is defined as pain associated with sexual intercourse. Most often used in association with female sexual dysfunction and is the focus of this section.

- Present since 1st (primary) intercourse or acquired (secondary) thereafter.
- Etiologies can be physiologic and/or psychological.

Epidemiology
Incidence
Lack of disclosure to clinicians and treatment pursuit suggests underestimation

Prevalence
Up to 60% prevalence in women, but varies widely by sample and definition.

RISK FACTORS
- Menopause (physiologic or iatrogenic)
- Physical trauma (physiologic or iatrogenic)
- Psychological trauma (supporting evidence is mixed)
- Tissue irritation (infection, inflammation, malignancy, etc.)
- Urinary tract infection

Genetics
Early menopause should be considered

PATHOPHYSIOLOGY
- Pain results from irritation or trauma to the female urogenital anatomy (congenital)
- Etiologies can be physiologic and/or psychological.
- Present since 1st (primary) intercourse or acquired (secondary) thereafter.

ASSOCIATED CONDITIONS
- Vaginal atrophy
- Urinary conditions
- Pelvic inflammatory disease
- Systemic conditions
- Menopause (physiologic or iatrogenic)
- Other chronic diseases

GENERAL PREVENTION
- Maintenance of vaginal mucosal integrity
- Good hygiene and health maintenance

DIAGNOSIS

DESCRIPTION
Dyspareunia is defined as pain associated with sexual intercourse.

- Most often used in association with female sexual dysfunction and is the focus of this section.
- Present since 1st (primary) intercourse or acquired (secondary) thereafter.
- Etiologies can be physiologic and/or psychological.

HISTORY
- Description of pain
  - Positioning, specific maneuvers, location
  - Use of lubricants, condoms, sex toys, hygiene products
  - Specific partners or partner-related factors
  - Timing of menstrual cycle
  - Bowel or bladder habits
  - Urinogenital conditions
  - Sexually transmitted or urinary tract infections
  - Complicated pregnancies
  - Endometriosis
  - Uterine fibroids
  - Inflammatory bowel disease
  - Urinogenital trauma
  - Vaginal childbirth injuries
  - Difficult or forced intercourse
  - Systemic conditions
  - Menopause (physiologic or iatrogenic)
  - Pain disorders or fibromyalgia
  - Cancer
  - Other chronic diseases
  - Vaginal trauma
- Current or prior abuse
  - Sexual abuse
  - Verbal or physical abuse

PHYSICAL EXAM
- Visual inspection of external genitalia
  - Distribution of pubic hair
  - Diffuse vulvo-vestibular
  - Lacerations, puncture, discharge, bleeding
  - Inflamed Bartholin or Skene glands
  - Prolapsed urethra, vagina, or cervix
  - Skin or mucosal lesions suspicious for cancer
  - Speculum exam
    - Diffuse vaginitis or cervicitis
    - Mucosal rugae, moisture, thinning, or excoriation
  - Vaginal wall masses
  - Ulcerations, pustules, discharge, or bleeding
    - Diffuse vaginitis or cervicitis
    - Vaginal wall masses
    - Lacerations suspicious for cancer

Diagnostic sampling with cervical surface scrapings, brushings, and culture swabs
- Lacerations, punctures, or discharge
- Masses, skin changes, mucosal changes, bleeding
- Palpation of external genitalia, vaginal sidewalls, pelvic floor muscles, cervix, and ovaries
  - Bartholins or Skene gland tenderness
  - Urethral or vaginal sidewall mass
  - Surgically placed foreign bodies
  - Pelvic floor muscle tension, spasm, or tenderness
  - Cervical motion, ovulatory, or adrenal tenderness
  - Vaginal cul-de-sac mass or tenderness

FACTORS ALTERING THE PAIN
- Positioning, specific maneuvers, location
- Use of lubricants, condoms, sex toys, hygiene products
- Specific partners or partner-related factors
- Timing of menstrual cycle
- Bowel or bladder habits
- Urinogenital conditions
- Sexually transmitted or urinary tract infections
- Complicated pregnancies
- Endometriosis
- Uterine fibroids
- Inflammatory bowel disease
- Urinogenital trauma
- Vaginal childbirth injuries
- Difficult or forced intercourse
- Systemic conditions
- Menopause (physiologic or iatrogenic)
- Pain disorders or fibromyalgia
- Cancer
- Other chronic diseases
- Vaginal trauma
- Current or prior abuse
- Sexual abuse
- Verbal or physical abuse

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Urinalysis and urine culture to screen for infection or cystitis
  - Endometrial swabs for gonorrhea, chlamydia, or bacterial vaginosis
  - Cervical scrapings or brushings for malignancy and human papilloma virus
  - Vaginal pH, wet mount, or whiff test for bacterial or fungal infection

Imaging
- Transvaginal ultrasound for reproductive organ or pelvic masses
- Transabdominal ultrasound for abdominal masses
- Pelvic magnetic resonance imaging for uterine diverticula or pelvic masses

Diagnostic Procedures/Surgery
- Cystourethroscopy for cystitis, urethritis, urethral diverticula
- Double-balloon urethrography for urethral diverticula
- Colposcopy for human papilloma virus or uterocervical malignancies
- Colonoscopy for inflammatory bowel disease or colo-rectal malignancy
- Diagnostic laparoscopy for endometriosis or pelvic masses

DIFFERENTIAL DIAGNOSIS
- Congenital
  - Vaginal agenesis, vaginal malformation, imperforate hymen, sigil hymen, retroverted uterus
- Gynecologic
  - Structural: Hymenal remnant, introital or vaginal stenosis, polyps, childbirth, adhesions
  - Inflammatory: Vaginal atrophy, lichen sclerosus, vulvar lichen planus
  - Infectious: Sexually transmitted, viral, bacterial vaginosis, fungal, pelvic inflammatory disease
  - Allergic: Contact dermatitis, vulvar lichen planus, latex, semen, vaccine product, etc.
  - Reproductive: Endometriosis, fibroids, ectopic pregnancy, adenomatous cysts, ovarian cyst
  - Iatrogenic: Implant erosion, exposed sutures, postoperative fistula

Urologic
- Urinary prolapse, urethral carcinoma, urethral diverticulum, urethral cancer, urethritis, cystitis
- Colorectal
  - Inflammatory bowel disease, abscess, hemorrhoids, constipation, rectal cancer
- Musculoskeletal
  - Vaginismus, pelvic floor muscle spasm, trauma, chronic pain disorder, fibromyalgia

Psychological
- Posttraumatic stress disorder, sexual aversion disorders, genital sexual arousal disorder
TREATMENT

GENERAL MEASURES
- Behavioral (1,2)
  - Identify and eliminate any allergy-related hygienic or sexual practices
  - Encourage using water-based lubrication or hypoallergenic products
- Use infection prophylaxis like postcoital voiding when appropriate for UTI issues
- Psychological counseling, couples therapy, or relaxation exercises as indicated
- Careful consideration of replacing condoms or other barrier devices with another contraceptive

MEDICATION

First Line
- Trigger point injections for muscle spasm
- Excision of implanted mesh, eroded sutures, or other foreign body
- Urethral diverticulectomy if indicated
- Laparoscopic sacral colpopexy for problematic retroverted uterus
- Laparoscopic lysis of adhesions if indicated
- Laparoscopic endometriosis excision or ablation
- Topical corticosteroids for vulvar hyperplasia or testicle for lichen sclerosis
- Topical estrogen for atrophy considering benefits and risks

Second Line
- Appropriate dose and duration of antibiotics or antifungals for infection
- Use of antibiotics or estrogen agonist/antagonist or fluconazole concomitantly
- Careful consideration of replacing condoms or other barrier devices with another contraceptive

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
- Daily passive dilatation with progressive vaginal dilators for stenosis
- Use of pressure for problematic retroverted uterus
- Pain/flat physiotherapy or biofeedback for muscle spasms
- Ultrasound or electrical stimulation for persistent muscle spasm
- Tibolone (synthetic, steroid) is commonly used in Europe in postmenopausal women with desire and arousal disorders

Complementary & Alternative Therapies
- Education, sex therapy, psychotherapy, and cognitive behavioral therapy are also important in the multidisciplinary management of sexual dysfunction including those with a history of sexual abuse.
- Currently there are limited studies on the effectiveness of herbal remedies to aid female sexual dysfunction in general.

ONGOING CARE

PROGNOSIS
- Results vary with etiology and treatment of many is long term
- Minimal risk to approach any etiology should be most beneficial

FOLLOW-UP

Patient Monitoring
- Frequent follow-up with initiation of new behavioral or medical therapies is best
- Upon resolution and improved patient satisfaction follow-up may be spaced out

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Dyspareunia
  - Dyspareunia Algorithm
  - Dyspareunia, Female Sexual Dysfunction
  - Urinary Tract Infections
  - Urogenital Prolapse
  - Urethra, Diverticulum, Female (Urethral Diverticulum)
  - Vaginal Atrophy, Urologic Considerations

CODES

ICD9
- 627.3 Postmenopausal atrophic vaginitis
- 627.9 Other atrophic vaginitis

ICD10
- F52.6 Dyspareunia not due to a substance or known physical condition
- N94.1 Dyspareunia
- N95.2 Postmenopausal atrophic vaginitis

CLINICAL/SURGICAL PEARLS
- Do not discount behavioral interventions.
- Topical estrogen can work wonders.
- Changing the hygienic routine can help.
DYSURIA
Mohamed S. Ismail, MBChB, MRCS, PhD
Francis Xavier Keeley, Jr., MD, FRCS

DESCRIPTION
Dysuria is the symptom of discomfort, burning, or pain during urination.
It is often associated with other lower urinary tract symptoms.

EPIDEMIOLOGY
Incidence
Dysuria accounts for up to 15% of visits to family doctors.
In men the incidence increases with age and 5% of men seek medical help for dysuria.

Prevalence
In the United States the reported prevalence of dysuria is 25%.

RISK FACTORS
See associated conditions.

GENETICS
N/A

PATHOPHYSIOLOGY
• Dysuria results from the irritation of the urethra or bladder by inflammation or irritants.
• The transient receptor potential subfamily vanilloid type 1 receptor (TRPV1) exists in the urethra.
• Inflammatory mediators such as leukotrienes activate TRPV1 and result in pain and burning during voiding.

ASSOCIATED CONDITIONS
• Bladder or urethral cancer
• BPH
• Connective tissue diseases
• Behcet (reactive arthritis) syndrome
• STD
• Urethral stricture disease
• Urinary tract infection
• Urolithiasis

GENERAL PREVENTION
• Hydration to flush out the urinary tract
• Women should wipe from front to back after bowel movements.
• Women should empty the bladder immediately after intercourse.
• Keep the genital area clean and dry.
• Avoid irritating soap and vaginal products.
• Treat infection with antibiotics.

DIAGNOSIS

UNEXPLAINED DYSURIA MAY INDICATE CANCER IN SITU OF THE BLADDER.

HISTORY
• The cause of dysuria can be challenging to diagnose.
• Dysuria is frequently associated with other lower urinary tract symptoms such as urinary frequency, hesitancy, urgency, and nocturia (1).
• Age and sex (2):
  • Dysuria is more common in women.
  • The most common cause in young women is urethritis, in middle age women genitourinary causes, and in elderly women urinary tract infection.
• The most common cause in young men is urolithiasis and in elderly men benign prostatic hyperplasia (BPH) and urinary tract infection.
• Dysuria in children may suggest sexually transmitted diseases (STD).
• Onset:
  • Sudden onset symptoms suggest acute bacterial infection.
  • Gradual onset symptoms may suggest Chlamydia trachomatis infection.
• Timing of pain:
  • At the onset of voiding indicates inflammation such as urethritis.
  • At the middle of voiding indicates obstruction such as urethral stenosis or BPH.
  • At the end of voiding usually indicates bladder pathology such as cystitis.
• Location of pain:
  • External discomfort associated with vaginal infection or inflammation.
  • Internal discomfort indicates bladder or urethral origin.
• Associated symptoms:
  • Frequency, urgency, and suprapubic pain suggest diagnosis of interstitial cystitis.
  • Frequency, nocturia, and reduced flow suggest bladder outlet obstruction or urethral stricture.
  • Fever, rigor, and flank pain suggest pyelonephritis or urethritis.
• Urethral discharge in young age indicates sexually transmitted diseases.
• Vaginal irritation, discharge, and dyspareunia indicate genital tract infection such as:
  • Virovaginitis, atrophic vaginitis, or sexually transmitted diseases.
• Urethral discharge in young age indicates sexually transmitted diseases.
• Vaginal irritation, discharge, and dyspareunia indicate genital tract infection such as:
  • Virovaginitis, atrophic vaginitis, or sexually transmitted diseases.
• Dyspareunia + dribbling + dysuria (“3 Ds”) suggests a urethral diverticulum in females.
• The presence of joint or back pain may indicate connective tissue diseases.
• Significant urgency occurs as a result of irritation of the bladder trigone and posterior urethra due to inflammation, bladder stone, or tumor.
• Oral and genital ulcers, vesicles, ulcers with dysuria suggest Behcet disease.
• History of recent surgery such as urethral instrumentation or continent surgery and history of recent catheterization should be obtained to rule out infection, inflammation, and urethral erosion.
• Sexual history:
  • Sexual behavior
  • The use of contraceptives, diaphragms, condoms, etc.
• Previous history of sexually transmitted diseases and history of urethral straining.
• Drug history: Drugs associated with dysuria are morphine, perindopril, ciprofloxacin, saw palmetto, dopamine.

PHYSICAL EXAM
• General exam and observation should be recorded.
• Abdominal exam:
  • Inspection: Look for skin rash and abdominal distension which indicate full bladder.
  • Palpation: Feel for loin tenderness, palpable bladder, suprapubic tenderness, abdominal masses, and midline pulsation.
  • Percussion: To detect full bladder or any other abdominal masses.
• Association: To rule out other causes of abdominal distension.
• Male genital exam:
  • Look for any penile lesions, urethral discharge, muscular tendons, balanitis, perineal bruising, and abnormalities in the foreskin.
  • Examine the scrotum for swelling, tenderness, and testicular masses.
• Digital rectal exam to rule out prostatitis, benign prostatic enlargement, and prostate cancer.
• Female genital exam (3):
  • Look for vaginal and urethral discharge.
  • Vulval lesions such as ulcers, vesicles, and rash.
  • Identify urethral lumps that indicate urethral fenestration, diverticulum, or stones. Look for signs of atrophic vaginitis.
  • Pelvic exam: Adnexal and cervical tenderness which indicates pelvic inflammatory disease, uterine tenderness, and uterine masses.
  • Bimanual exam to look for pelvic masses.

DIAGNOSTIC TESTS & INTERPRETATION LAB
• Urine dipstick is a useful and easy test to screen for urinary tract infection.
• A positive test for nitrites is suggestive of urinary tract infection. A negative test does not rule out infection.
• A positive leukocyte esterase suggests the presence of white blood cells in the urine which is associated with inflammation. It has 75% sensitivity to detect infection.
• Urine microscopy:
  • Pyuria is defined by the presence of 3–5 white blood cells per high power field.
  • Hematuria is defined by the presence of 3–5 red blood cells per high power field.
• Sterile pyuria is present in urinalysis, transitional cell carcinoma, and atypical microorganisms such as tubercle.
DIFFERENTIAL DIAGNOSIS

Based on specific diagnosis

Pathologic Findings

DIFFERENTIAL DIAGNOSIS

- Disease of the urinary tract
  - Urinary tract infection
  - Urolithiasis, bladder calculus, crystalluria
  - Intestinal cystitis
  - Prostatitis (acute, chronic bacterial and chronic pelvic pain syndrome)
  - Gynecologic (cervical in situ, prostate cancer, urethral cancer)
- Disease of the genital tract
  - Sexually transmitted disease
  - Gonorrhea, Chlamydia, and herpes simplex infection
  - Vulvo-vaginitis, orchitis, pelvic inflammatory disease
- Epidermitis
- Urethral diverticulum
- Systems diseases
  - Connective tissue diseases: Reiter reactive arthritis syndrome and Behcet disease
  - Local irritants
    - Chemical irritants: Cystophosphamide, laundry detergents, bubble baths, intraurethral lubricants
    - Mechanical irritation: Radiation cystitis
  - Infections and adolescents
  - Laceration
  - Exploratory sexual activity, masturbation

Diagnosis

- Gram staining demonstrate the urinary pathogens
- Urine culture and sensitivity identify the causative microorganism of urinary tract infection and its antimicrobial susceptibilities
- Bacterial count of more than 1,000 colony forming units is diagnostic
- Vaginal and uterine smears: Important for the diagnosis of sexually transmitted diseases
- Vaginal pH measurement, potassium hydroxide

Diagnostic Procedures/Surgery

- Visual vaistoscopy: Allows careful assessment of the urethra
- Imaging
  - Renal ultrasound scan in suspected cases of upper tract pathology, urethral, and bladder abnormalities
  - Plain abdominal x-ray in suspected cases of urethralis and ephymematous peritonitis and pyoneum
- Other imaging modalities can be arranged according to the suspected diagnosis such as voiding cystourethrogram, retrograde urethrogram, computed tomogram with intravenous contrast, magnetic resonance imaging

Medication

- Erythromycin: Used as a primary treatment for gonorrhea
- Antibiotics according to the causative organism

Surgical management is reserved for specific causes

ADDITIONAL TREATMENT

Dysuria

- Treat the primary cause
- Personal hygiene
- Protection measures against STD
- Treat the primary cause

PROGNOSIS

- Unexplained persistent dysuria should NEVER be ignored; must rule out occult malignancy, such as carcinoma in situ of the bladder
- Persistent hematuria after adequate treatment of dysuria related to UTI must have formal hematuria workup.
EDEMA, EXTERNAL GENITALIA (LYMPHADEMA, PENO-SCROTAL EDEMA)
Megan M. Merrill, DO

ASSOCIATED CONDITIONS
- Advanced prostate cancer
- Anemia
- Acute/chronic failure
- Congestive heart failure
- Renal failure
- Symmetrical lymphedema (lymphangitis filariasis)
- Paraphimosis
- Renal insufficiency/renal failure
- Retroperitoneal lymphadenopathy
- Testicular torsion

DIAGNOSIS
- EDEMA: The penis and scrotum in an uncircumcised male may indicate paraphimosis, which requires immediate foreskin reduction to avoid glans penis vascular compromise (1).
- EDEMA of the scrotum with areas of necrosis or devitalized skin may indicate Fournier gangrene and requires emergent urologic consultation and surgical debridement.

PHYSICAL EXAM
- Palpate for an increase in subcutaneous tissue and may suggest etiology.
- Foul odor associated with Fournier gangrene
- Bruising or induration with crepitance seen in Fournier gangrene

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- No specific lab tests
- Elevated brain natriuretic peptide (BNP) associated with hypervolemia
- Fractional sodium excretion may suggest fluid overload

Imaging
- Scrotal ultrasound (US) confirms thickened subcutaneous tissue and may suggest etiology.
- CT may suggest retroperitoneal etiology.

Diagnostic Procedures/Surgery
- Physical exam significant for indicating edema of the genital skin
- Pathologic Findings
- Edematous subcutaneous tissue of the scrotum and perineal skin with possible areas of devitalized skin or necrosis

DESCRIPTION
- Pitting or nonpitting edema of the penis shaft and scrotal skin due to the accumulation of transudative fluid in the dartos (scrotal) or subcutaneous layer of the penis

EPIDEMIOLOGY
- Incidence
- Prevalence
- Risk Factors
- Genetic
- Prevalent condition in nursing home and hospitalized patients
- Incidence is not well documented

PATHOPHYSIOLOGY
- Accumulation of transudate within the subcutaneous tissue of the penis and scrotum
- May be localized to the genital region or part of generalized lower extremity edema or massive body edema (anasarca).
- In generalized edema capillary hemodynamics are altered and fluid moves from vascular space to interstitium according to Starling’s law (2).

BASICS
- Physical manifestation of macro-orchidism/scrotal edema that becomes more apparent in puberty (1).

ASSOCIATED CONDITIONS
- Advanced prostate cancer
- Anemia
- Acute/chronic failure
- Congestive heart failure
- Renal failure
- Symmetrical lymphedema (lymphangitis filariasis)
- Paraphimosis
- Renal insufficiency/renal failure
- Retroperitoneal lymphadenopathy
- Testicular torsion

DIAGNOSIS
- EDEMA: The penis and scrotum in an uncircumcised male may indicate paraphimosis, which requires immediate foreskin reduction to avoid glans penis vascular compromise (1).
- EDEMA of the scrotum with areas of necrosis or devitalized skin may indicate Fournier gangrene and requires emergent urologic consultation and surgical debridement.

PHYSICAL EXAM
- Palpate for an increase in subcutaneous tissue and may suggest etiology.
- Foul odor associated with Fournier gangrene
- Bruising or induration with crepitance seen in Fournier gangrene

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- No specific lab tests
- Elevated brain natriuretic peptide (BNP) associated with hypervolemia
- Fractional sodium excretion may suggest fluid overload

Imaging
- Scrotal ultrasound (US) confirms thickened subcutaneous tissue and may suggest etiology.
- CT may suggest retroperitoneal etiology.

Diagnostic Procedures/Surgery
- Physical exam significant for indicating edema of the genital skin
- Pathologic Findings
- Edematous subcutaneous tissue of the scrotum and perineal skin with possible areas of devitalized skin or necrosis
DIFFERENTIAL DIAGNOSIS
- Acute idiopathic scrotal edema
- Angiokeratoma of the genital skin
- Cellulitis
- Chemical or allergic dermatitis
- Elephantiasis
- Epidermolysis-architects
- Fourier gangrene
- Hydrocele
- Lymphoedema of scrotal edema (usually children)
- Inguinal hernia
- Paraphimosis
- Retropertioneal mass
- Squamous carcinoma of penis
- Testicular torsion
- Varicocele

ADDITIONAL TREATMENT
Radiation Therapy
While this can be a cause of genital lymphedema, it may have a role in primary palliative treatment of prostate, penis, and retroperitoneal malignancies causing scrotal edema.

Additional Therapies
Supportive undergarments/briefs for patient comfort

Complementary & Alternative Therapies
N/A

ONGOING CARE
PROGNOSIS
Depends on etiology

COMPLICATIONS
- Skin breakdown/ulceration
- Urinary retention/obstructive voiding
- Genital and scrotal compression is NOT recommended

FOLLOW-UP
Patient Monitoring
- Physical exam for resolution
- Monitor underlying condition, appropriate labs, nutritional status

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Edema, Lower Extremity, Urologic Considerations
- Fourier Gangrene
- Testicular Torsion
- Paraphimosis
- Edema, External Genitalia (Lymphedema, Peno-Scrotal Edema) Image

CODES
ICD9
- 605 Redundant prepuce and phimosis
- 607.83 Edema of penis
- 608.86 Edema of male genital organs

ICD10
- N47.1 Phimosis
- N48.89 Other specified disorders of penis
- N50.8 Other specified disorders of male genital organs

CLINICAL/SURGICAL PEARLS
- Determine the patient’s fluid status to rule out hypervolemia as the cause of genital edema.
- Acute scrotal pain, swelling, lack of cremasteric reflex, and a high-riding ipsilateral testis could indicate testicular torsion.
- Evaluate for paraphimosis in uncircumcised males.
- Crepitance, induration, necrosis, and foul odor suggest Fournier gangrene and require emergent surgical debridement.
- Complications of edema may include urinary retention and skin breakdown—these should be evaluated for and treated accordingly.
EJACULATION, PREMATURE (PREMATURE EJACULATION)

Elizabeth K. Peacock, MD
James S. Rosoff, MD

**BASICS**

**DESCRIPTION**

- Definition of premature ejaculation (PE) remains controversial:
  - ISSM (2008): Ejaculation within about a minute and inability to delay ejaculation with all or nearly all vaginal penetrations causing negative personal consequences (1)
  - WHO (2004): Inability to delay ejaculation with intercourse before/soon after starting intercourse (15 s)
  - AUA (2004): Ejaculation sooner than desired, before or shortly after penetration that causes distress to 1/both partners
  - EAU (2001): Inability to control ejaculation for sufficient time before vaginal penetration
  - APA (2001): Persistent or recurrent ejaculation with minimal sexual stimulation

- May also be classified as primary (lifelong PE) or secondary (acquired PE)

- ICD-10 uses 15 s of intravaginal ejaculatory latency time (IELT) as a cutoff

**EPIDEMIOLOGY**

- Incidence: Unknown
- Prevalence: PE is the most common sexual dysfunction in men <40
  - Approximately 20–30% in this group

**RISK FACTORS**

- Increased levels of arousal due to new partner or situation
- Low frequency of sexual activity
- Genetics
  - Polymorphism in the serotonin transporter promoter region (5-HTTLPR) may play a genetic role in the etiology and/or treatment of PE, though this is controversial.

**PATHOPHYSIOLOGY**

- Serotonin receptor stimulation (5-hydroxytryptamine):
  - Serotonin 5-HT 2c receptors inhibit ejaculation, 5-HT 1a receptors facilitate ejaculation
  - Hyposensitivity of 5-HT 2c or hypersensitivity of 5-HT 1a may cause PE
  - Increase in serotonin transporter (5-HTT) may play a genetic role in PE
- Consider psychological factors, hormone alterations, penile sensitivity, circumcision status, chronic prostatitis as potential causes though with limited evidence supporting these

**ASSOCIATED CONDITIONS**

- Erectile dysfunction
- General anxiety
- Situational anxiety
- Depression
- Substance abuse
- Relationship distress
- Prostatitis

**GENERAL PREVENTION**

**DIAGNOSIS**

**HISTORY**

- Time to ejaculation is essential
- Duration/frequency of PE
- Rate of occurrence of PE
- Degree of sexual stimulation causing PE
- Nature/frequency of sexual activity including foreplay, masturbation, and intercourse
- Discuss length of time experiencing PE, perceived lack of control, and resultant sexual dissatisfaction
- Any indication of ED
- Issues with the partner, such as dyspareunia or other medical problems
- Rule out symptoms consistent with cystitis or prostatitis
- Medication history: Consider PE due to withdrawal from narcotics or trifluoperazine (Stelazine)
- Sexual History
  - Global to all sexual encounters, or with specific situations and/or partners
  - Religious upbringing
  - Early sexual experiences
  - Sexual relationships, past and present
  - Religious upbringing
  - Early sexual experiences
  - Sexual relationships, past and present
  - Conflicts or concerns within current relationship
  - Traumatic sexual experiences

**PHYSICAL EXAM**

- Complete physical exam with focus to rule out biologic causes including recent pelvic surgery or infectious source
- Recall exam to assess for prostatitis
- Rare to have findings on exam that would define etiology or change management

**TREATMENT**

**GENERAL MEASURES**

- Behavioral treatment:
  - Stop–squeeze method (Masters and Johnson) involves removal of penis at point of ejaculation with squeezing of glans or frenulum
  - Start–stop method (Seman) involves a pause in intercourse at point of ejaculation
  - High initial success rates are reported, but poor long-term rates are present due to the time-consuming nature of treatment
- Psychotherapy may be beneficial
- Combination of pharmacotherapy and psychotherapy is suggested as current model for treatment

**DIAGNOSTIC TESTS & INTERPRETATION**

- Lab: Usually unnecessary
- Imaging: N/A
- Pathologic Findings: N/A
- Diagnostic Procedures/Surgery: N/A
- Pathologic Findings: N/A
EJACULATION, PREMATURE (PREMATURE EJACULATION)

MEDICATION

First Line

- No medications are approved for treatment of PE in the United States
  - SSRIs:
    - Elevates level of serotonin in synapse that results in prolongation of ejaculatory latency time
    - 1st-line pharmacotherapeutic approach (off-label)
    - Daily treatment with PO paroxetine 20–40 mg (greatest evidence), sertraline 25–200 mg, fluoxetine 5–20 mg
    - Newer agents have not been effective (fluvoxamine/venlafaxine)
    - Dapoxetine approved in Europe only for on-demand dosing for PE

- Topical agents:
  - EMLA: Lidocaine–prilocaine 2.5% cream
  - TEMPE: Metered-dose aerosol spray with lidocaine 7.5 mg and prilocaine 2.5 mg per spray

Second Line

- Clomipramine:
  - Tricyclic antidepressant
  - Daily treatment with 25–50 mg or on-demand treatment with 50 mg 5 hrs prior to intercourse

- Tramadol (synthetic opioid analgesic) with potential treatment role in PE (little evidence) (2)

SURGERY/OTHER PROCEDURES

CT-guided cryoablation of unilateral dorsal penile nerve (single study, 24 patients) (3)

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) has recommended authorization of a cutaneous spray containing a mixture of 150 mg lidocaine and 50 mg prilocaine per milliliter applied to the glans

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

Varies by treatment modality. May have up to 80% success rate with medication and/or behavioral modification

COMPLICATIONS

- Medications carry side effects, but complications of PE are limited
- Rarely, a problem with fertility may exist due to inability to complete intercourse
- May provoke anxiety or depression if PE is severe
- May interfere with development of sexual relationship

FOLLOW-UP

Patient Monitoring

N/A

Patient Resources

Urology Care Foundation. http://www.urologyhealth.org/urologyindex.cfm?article=122

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Dysorgasmia (Painful Orgasm), Male
- Ejaculatory Disturbances (Delayed, Decreased, or Absent)
- Ejaculation Premature Algorithm

CODES

ICD9

302.75 Premature ejaculation

ICD10

P52.4 Premature ejaculation

CLINICAL/SURGICAL PEARLS

- Exact definition of PE remains controversial.
- Combination of pharmacotherapy (off-label use) and psychotherapy is likely the most beneficial treatment.
EJACULATORY DISTURBANCES (DELAYED, DECREASED, ABSENT)

Pravin K. Rao, MD

BASICS

DESCRIPTION
- Anorgasmia or delayed orgasm/ejaculation
- Difficulty/habitual to reach orgasm
- Low-volume ejaculates
- Testosterone analysis
- Aspermia
- Orgasm with zero ejaculate volume
- Retrograde ejaculation
- Sperm seen in post-ejaculatory urine
- Ejaculatory duct obstruction (EDO)
- Congenital, acquired, iatrogenic
- Failure of emissions
- Can also cause low/zero volume

EPIDEMIOLOGY

Incidence
- Increased in aging (age 50–80 yr) men with
  BPH/LUTS (11B)
  ~46% decreased ejaculation
- ~15–30% anejaculation
  ~90% report decreased ejaculatory volume
- Selective serotonin reuptake inhibitors (SSRIs)
  ~16–37% delayed or difficult orgasm
- Anorgasmia is rare:
  ~0.14–0.4% in general population
- Prevalence

RISK FACTORS

- Age
- Benign prostatic hyperplasia
- Lower urinary tract symptoms
- Prostatitis/Ejaculatory duct stones
- Depression and related medications
- Hypogonadism
- Hypertension medications
- Prostate/retroperitoneal/Bladder neck surgery
- Retropertoneal lymph node dissection (RPLND)
- Cystic fibrosis
- Neurologic conditions/Diabetes
  - Multiple sclerosis, spinal cord injury (SCI), spina bifida, diabetes
- Rectal surgery
- Radiation therapy

Genetics
- N/A

PATHOPHYSIOLOGY

- Normal ejaculation:
  - Central control in multiple brain regions
  - Can promote or inhibit ejaculation
  - Sympathetic (T12-L3):
    - Sympathetic (T12–L3):
      - Hypogastric nerve (thoracolumbar)
      - Seminal emission by contraction of epididymis, vas deferens/ampulla, seminal vesicle (SV), and prostate smooth muscle
  - Bladder neck closure preventing retrograde ejaculation
  - Parasympathetic (S2–S4):
    - Pelvic nerve
    - Gland secretions of prostate SV
      - Prostatectomy or removal of prostate bump
      - Sensory
    - Prostatic nerve
    - Efferents from sacral cord
      - Relaxation of external urethral sphincter
      - Pelvic nerve
      - Prostate smooth muscle
      - Ejaculation requiring intact, properly developed, and coordinated accessory sex organs
      - Ejaculation requires intact, properly developed, and coordinated accessory sex organs, nerves, and muscles
      - Congenital, acquired, iatrogenic, infectious, inflammatory causes can all prevent normal ejaculation
      - Functional causes may lead to the complaint of decreased force of ejaculation
      - Ejaculate volume commonly decreases by ~0.03 mL each year with advanced age

ASSOCIATED CONDITIONS

- Psychological/Psychiatric conditions
  - See Risk Factors

GENERAL PREVENTION

- Avoidance of bladder neck procedures
  - Transurethral prostate, bladder neck surgery
- Avoidance/reduced use of medications
  - SSRI, v-blockers, 5a-reductase inhibitors
- Nerve sparing at time of RPLND
- Strict diabetic control

DIAGNOSIS

HISTORY

- Duration of symptoms
  - No defined criteria for diagnosis of delayed ejaculation
  - Mostly normal men ejaculate after 4–10 min of penetration
  - Presence of significant distress to patient or partner important to diagnosis
  - Presence or absence of orgasm
  - Perceived ejaculate volume
  - Sources of stress/psychological disturbance
  - Past medical history
  - Retroperitoneal and genitourinary operations
  - Family history of erectile dysfunction
  - See vas deferens, congenital absence
  - Medications:
    - Antidepressants/antipsychotics
    - Bladder outlet medications
  - Anorgasmia/Delayed orgasm

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Semen analysis
  - Volume: Suspect if ejaculate volume <1.5 cc
  - Concentration: Low volume azoospermia suspicious for EDO
  - Absence of seminal fructose suggests EDO
  - Post-ejaculatory urine analysis (PEU): >10–15 sperm/HPF demonstrates retrograde ejaculation

Imaging

- Transrectal ultrasound (TRUS)
  - Visualization for low volume azoospermia
  - For patients with negative PEU
  - Normal SV A-P diameter <1.5 cm
  - MRI
  - Can help identify structural abnormalities

PHYSICAL EXAM

- Absence or diminished development of epididymides and vas deferens
  - Congenital bilateral or unilateral absence of the vas deferens (CBVD/CUAVD)
  - Enlarged SV
  - EDO
  - Hypospadias or epispadias
  - Hypogonadism

DIAGNOSTIC TESTS & INTERPRETATION
EJACULATORY DISTURBANCES (DELAYED, DECREASED, ABSENT)

Diagnostic Procedures/Surgery
- TRUS with TV aspiration: Presence of numerous sperm suggests obstruction
- Cystoscopy
- Retrograde ejaculation
- Vas Deferens, Congenital Absence
- Retrograde Ejaculation
- Varicoceles

Pathologic Findings
Scar tissue at ejaculatory duct

DIFFERENTIAL DIAGNOSIS
- Anorgasmia
- Retarded/Delayed orgasm
- Erectile dysfunction
- Pathologic Findings
  - May present as inability to reach orgasm, or with weak force of ejaculation
  - Retrograde ejaculation
  - Aspermia

MEDICATION
- EDO (ejaculatory duct obstruction)

GENERAL MEASURES
- Remove/modify correctible causes
  - Psychological/Stress factors
  - See images of PVS devices:
    - Procedure: Apply to ventral/frenular region for 1–3 min at a time, with 1 min rest periods, for up to 15–20 min
    - See images of PVS devices:
      - Fentices
      - Vibrates (dorsal and ventral stimulation)
      - Electroejaculation (EEJ) via rectal probe

- Autonomic dysreflexia
- Risk for SCI lesions above T6
  - Can occur with PVS or EEJ
- Consider nifedipine 10–20 mg PO 10–15 min before treatment initiated
  - Monitor at risk patients for hypertension, tachycardia, sweats
  - Retrieval of sperm from bladder
    - See “Retrograde Ejaculation”
  - Testicular or epididymal sperm retrieval
    - Requires IVF/ICSI
  - Donor sperm or adoption may circumvent the need to (IVF/ICSI)

TREATMENT

GENERAL MEASURES
- Treat erectile dysfunction
  - Psychological assessment/counseling
  - Treat erectile dysfunction
  - Sexual counseling on techniques for optimal arousal

MEDICATION

First Line
- Alphaline 21% vs. tamsulosin 90% of patients
- Psychological/Stress factors
- Psychological assessment/counseling
- Treat erectile dysfunction
- Sexual counseling on techniques for optimal arousal

SECOND LINE

RADIOGRAPHIC THERAPY
- Radiation Therapy

ADDITIONAL TREATMENT

RADIOGRAPHIC THERAPY
- Radiation Therapy

Additional Therapies
- Penile/flex physical therapy for associated symptoms of pain or voiding symptoms
- Cognitive-behavioral sex therapy
- Changing idiosyncratic masturbation style if present

COMPLEMENTARY & ALTERNATIVE THERAPIES

ONGOING CARE

PROGNOSIS
- Depends on the etiology, duration, and severity
- >40% SCI men doing PVS with home insemination of their partners can achieve pregnancy (33B)

COMPLICATIONS
- Infertility implications
- Relationship stress and difficulty

FOLLOW-UP

Patient Monitoring
Based on response to therapy and needs of specific patient

Patient Resources
N/A

REFERENCES

ADDITIONAL READING
2. Nelson CI, Mulhall JP. Male organic disorders: What do we know? Contemp Urol. 2007;February

See Also (Topic, Algorithm, Media)
- Anorgasmia/Dysorgasmia
- Ejaculation, Painful
- Ejaculation, Premature
- Ejaculatory Disturbances (Delayed, Decreased, or Absent) Images &
- Ejaculatory Duct Obstruction
- Vas Defects, Congenital Absence

CODES

ICD9
- 302.79 Psychosocial dysfunction with other specified psychosexual dysfunctions
- 608.87 Retrograde ejaculation
- 608.89 Other specified disorders of male genital organs

ICD10
- F52.3 Male organic disorder
- N53.14 Retrograde ejaculation
- N53.19 Other ejaculatory dysfunction

Inclusion of partner in treatment important if recommending change in sexual practice.
ENURESIS, ADULT
Katie S. Murray, DO
Tomas L. Griebling, MD, MPH, FACS

BASICS

DESCRIPTION
- Enuresis is repeated inability to control urine
  - Primary: Starts in childhood and never resolves and continues into adulthood
  - Secondary: New onset in adulthood
- Nocturnal enuresis (NE) is involuntary urination while asleep after the age at which bladder control usually occurs

ASSOCIATED CONDITIONS
- Pathophysiology
  - Genetics
    - 2.3% of adult population affected
  - Risk Factors
    - Family history of NE
    - If both parents have NE, children have 80% chance
  - Epidemiology
    - Enuresis is repeated inability to control urine
    - Nocturnal enuresis (NE) is involuntary urination while asleep after the age at which bladder control usually occurs

RISK FACTORS
- 35% of a 24-hr urine volume
- Urine production increased in recumbent position
- Disturbance in sensation, cortical arousal, or urinary sphincter function
- Decreased bladder capacity initiating involuntary voiding reflex
- Nocturnal polyuria because vasopressin secretion or reduction in renal sensitivity to the antidiuretic hormone (ADH)
- Detrusor instability during filling phase
- Bladder diaries/frequency-volume charts

PATHOPHYSIOLOGY
- Unknown in most situations
- Recognized hypotheses
  - Obstructive sleep apnea causing diminished vasopressin secretion
  - Decreased bladder capacity initiating involuntary voiding reflex
- Nocturnal polyuria
  - Due to decreased nocturnal excretion of urine
  - Caused by conditions affecting the kidneys
  - Associated with conditions affecting the heart
- Normal physiology decreases nighttime, relative to daytime, urinary output. Excess production of urine at night, in the setting of a normal 24-hr urine output, is termed nocturnal polyuria
- Nocturnal polyuria is the baseline of 24-hr urine volume

ASSOCIATED CONDITIONS
- Benign prostatic hypertrophy
- Daytime urinary incontinence
- Psychopathological disorders including depression
- Sleep apnea

GENERAL PREVENTION
- Timed voiding
- Complete bladder emptying
- Avoidance of caffeine and alcohol
- Adjust timing of fluid intake

DIAGNOSIS

HISTORY
- Have never achieved nocturnal continence of urine
- Non-specific urinary symptoms
- Ask about known or potential medical history
- Complete surgical and trauma incident history
- Obtain record of fluid intake habits
- Review medications and times of administration
- Voiding diaries to evaluate frequency, volume, and patterns
- International prostate symptom score (IPSS) in men

PHYSICAL EXAM
- Full urologic exam (pelvic exam in women and DRE in men)
- Full neurologic exam

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Urinalysis and urine culture: Rule out urinary tract infection, hematuria, proteinuria, glycosuria
  - Creatinine: Rule out renal insufficiency
- Urine cytology (if other symptoms such as irritative voiding symptoms make carcinoma a concern)
- Imaging
  - Post void residual bladder scan
  - Imaging: Imaging for possible abnormalities such as ectopic ureters
- CT urography
- Renal ultrasound

Diagnostic Procedures/Surgery
- Bladder diaries/frequency-volume charts
- Cystoscopy with retrograde pyelograms to evaluate bladder and ureters
- Urine cytology
- Vescouretal testing (VET)
- Bladder diaries/frequency-volume charts
- Cystoscopy with retrograde pyelograms to evaluate bladder and ureters
- Urodynamic testing (VET)
- Urodynamic testing: Test for abnormalities such as ectopic ureters
- CT urography
- Renal ultrasound
- Urodynamic testing: Test for abnormalities such as ectopic ureters
- CT urography

Pathologic Findings
- N/A

DIFFERENTIAL DIAGNOSIS
- Prostatic hypertrophy
- Neurogenic bladder
- Idiopathic detrusor instability
- Neurologic disorders

TREATMENT

GENERAL MEASURES
- Conservative measures have varying success rates
- Education is key when attempting to improve enuresis without medical therapy
- Timed voiding
  - Complete bladder emptying
  - If associated with BPH in men management with α-blockers for 5α-reductase inhibitors
- Avoidance of caffeine and alcohol
- Adjust timing of fluid intake
- Restrict fluid intake in evening to reduce urine output at night
- Take diuretics medications early in a day

MEDICATION

First Line
- If due to prostatic hypertrophy: See Section I
- "Bladder Outlet Obstruction (BOO)."
- Antimuscarinics or α3-agonists (α3)
  - Inhibit the effect of acetylcholine at postsynaptic muscarinic receptors on detrusor muscle cells
  - α3-Adrenergic agonist promotes detrusor muscle relaxation
  - Varying results (5–40%), depends on whether detrusor instability is not cause of enuresis
  - Side effects: Dry mouth, constipation, blurred vision, confusion

Antimuscarinics
- Ttolterodine (2–4 mg)
- Trospium XR (60 mg)
- Oxybutynin (5–15 mg)
- Solifenacin (5–10 mg)
- Oxybutynin ER (7.5–20 mg), XL 5–30 mg; patch twice-weekly
- Tolterodine (4–8 mg)
- α3-adrenergic agonist
  - Mirabegron (25–50 mg)

3-Adrenergic agonist

Mirabegron (25–50 mg)

Trospium XR (60 mg)

Oxybutynin (5–15 mg)

Solifenacin (5–10 mg)

Oxybutynin ER (7.5–20 mg), XL 5–30 mg; patch twice-weekly

Tolterodine (4–8 mg)

α3-adrenergic agonist

Mirabegron (25–50 mg)
Second Line

- **DDAVP (Desmopressin)** (5)
  - Not currently FDA approved for this clinical indication (has European regulatory approval)
  - Analog of vasopressin
  - Decreases urine production for about 5 hr
  - Decreases number of enuresis events but may not eliminate it completely
    - Oral 0.2 mg at bedtime, increase to 0.6 mg to response
    - Intranasal formulations are no longer indicated for the treatment of primary NE due to risk for severe hyponatremia with seizures and death
  - Side effects: Nasal irritation, dry mouth, sleep disruption, water intoxication, seizures, heart failure, electrolyte disturbances, hyponatremic coma
  - Use with extreme caution if at all in geriatric patients (>65 yr) due to risk of severe hyponatremia and other adverse events

- **Imipramine** (5)
  - Tricyclic antidepressant
  - Mild anticholinergic effect and α-action to increase internal sphincter tone
  - Side effects: Sleep abnormalities, decrease appetite, personality disturbances

SURGERY/OTHER PROCEDURES

- Consideration after all conservative and pharmacologic measures have failed
- If urodynamic testing shows detrusor overactivity, may consider additional interventions
  - Botulinum toxin injections
  - Sacral neuromodulation
  - Posterior tibial neuromodulation
  - Augmentation cystoplasty
  - Urinary diversion

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies

- Psychological counseling
- Assist with coping mechanisms and finding any potential underlying issues

Complementary & Alternative Therapies

- Enuresis (bedwetting) alarms
- Timed voiding through the day and night
- Decrease fluid hydration prior to bed
- Empty bladder to completion prior to bed

ONGOING CARE

PROGNOSIS

- Many patients may eventually become dry
  - This is more likely in children

COMPPLICATIONS

- Urea dermatitis
- Skin breakdown and superficial ulcers from direct contact of urine on skin
- Psychological effects
  - Job changes/decreased work performance
  - Depression
  - Low self-esteem
  - Decreased social activities

FOLLOW-UP

Patient Monitoring

- Long-term follow-up until resolution or satisfaction by the patient
- Psychological counseling and follow-up if necessary

Patient Resources

- The Simon Foundation for Continence (simonfoundation.org)
- National Association for Continence (www.nafc.org)

REFERENCES


ADDITIONAL READING

- http://www.nafc.org/Bladder-Bowel/Bedwetting/Adult-Bedwetting/

See Also (Topic, Algorithm, Media)

- Bladder Outlet Obstruction (BOO)
- Enuresis Algorithm
- Enuresis, Pediatrics
- Incontinence, Adult Male
- Nocturia
- Urge Incontinence
- Urgency, Urinary (Frequency and Urgency)

CODES

**ICD9**

- 307.6 Enuresis
- 788.30 Urinary incontinence, unspecified
- 788.36 Nocturnal enuresis

**ICD10**

- F98.0 Enuresis not due to a substance or known physiol condition
- N39.44 Nocturnal enuresis
- R32 Unspecified urinary incontinence

CLINICAL/SURGICAL PEARLS

- Evaluating for underlying conditions is important in new onset enuresis.
- Social implications are common.
- Enuresis raised the risk for nighttime falls in elderly.
BASICS
DESCRIPTION
• Primary (idiopathic) or secondary (neurogenic) – Incontinence due to pooling of urine in the vagina
• Nocturnal polyuria

ASSOCIATED CONDITIONS
• Neuropsychiatric disorders (children with attention deficit hyperactivity disorder 2.7 x more likely to have NE)
• Upper urinary obstruction and nocturnal sleep apnea. Apnea episodes result in increased secretion of atrial natriuretic factor
• Constipation
• Urinary tract infection

GENERAL PREVENTION
MNE may not be preventable but parents should maintain regular voiding and bowel patterns—may help reduce risk of developing MNE with UTIs.

DIAGNOSIC TESTS & INTERPRETATION
Diagnostic Procedures/Surgery
- Cystoscopy: Routine use should be avoided
- Urodynamics: Helpful in evaluating bladder or posterior urethral dysfunctions
- Uroflowmetry: Assesses bladder outlet obstruction
- VCUG when diagnosis suggests posterior urethral valves or in older males; also used to evaluate for bladder structure (unusual)
- Abdominal u-vue to evaluate for vesical abnormalities
- Abdominal ultrasound may be helpful in the assessment of select patients with potential anatomic causes

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Macroscopic urinalysis (dipstick) to determine glucosuria, proteinuria, UT. If glucosuria present, serum glucose at that time
- Urine文化学：May be considered in male patients, especially those who have failed initial therapy to ensure no anatomic problem
- SMH of the spine for children suspected of having a neurogenic bladder as etiology, for those patients who are compliant and fail all therapeutic alternatives for NMNE, or who have a neurocutaneous signature or other physical findings on the lower spine or physical exam

PATHOPHYSIOLOGY
• Complex, involving central nervous system, circadian rhythm (sleep and diuresis), and bladder function abnormalities

PHYSICAL EXAM
- Abdominal exam for distended bowel/bladder
- Lower limb inspection for stigmata of occult spinal dysraphism/behelvel cord (sacral dimple, hair tuft, hemangioma, lipoma or other neurocutaneous signatures, absence of a palpable sacrum, or excess fat overlying the sacral region suggestive of a lumbosacral abnormality)
- Genital exam for congenital anomalies such as ectopic ureter or a urogenital sinus (with or without a palpable sacral dimple or excess fat overlying the sacral region)
- Labial adhesions in girls
- Urethral abnormalities or phimosis in boys
- Gait abnormalities, high arched foot

DIFFERENTIAL DIAGNOSIS
• Ectopic ureter
• Posterior urethral valves
• Urinary structure

PATHOLOGIC FINDINGS
• Neurogenic bladder
• Ectopic ureter
• Posterior urethral valves
• Urinary structure

DIAGNOSTIC PROCEDURES/SURGERY
- Ultrasound: Aids in evaluating bladder compliance and function in children with known dysfunctional voiding or enuresis due to neurogenic bladder or posterior urethral valves
- Cystoscopy: Routine use should be avoided
- May be helpful in the assessment of select patients with potential anatomic causes

ASSOCIATED CONDITIONS
• Neuropsychiatric disorders (children with attention deficit hyperactivity disorder 2.7 x more likely to have NE)
• Upper urinary obstruction and nocturnal sleep apnea. Apnea episodes result in increased secretion of atrial natriuretic factor
• Constipation
• Urinary tract infection

GENERAL PREVENTION
MNE may not be preventable but parents should maintain regular voiding and bowel patterns—may help reduce risk of developing MNE with UTIs.

DIAGNOSTIC TESTS & INTERPRETATION
Diagnostic Procedures/Surgery
- Cystoscopy: Routine use should be avoided
- Urodynamics: Helpful in evaluating bladder or posterior urethral dysfunctions
- Uroflowmetry: Assesses bladder outlet obstruction
- VCUG when diagnosis suggests posterior urethral valves or in older males; also used to evaluate for bladder structure (unusual)
- Abdominal u-vue to evaluate for vesical abnormalities
- Abdominal ultrasound may be helpful in the assessment of select patients with potential anatomic causes

PATHOPHYSIOLOGY
• Complex, involving central nervous system, circadian rhythm (sleep and diuresis), and bladder function abnormalities

PHYSICAL EXAM
- Abdominal exam for distended bowel/bladder
- Lower limb inspection for stigmata of occult spinal dysraphism/behelvel cord (sacral dimple, hair tuft, hemangioma, lipoma or other neurocutaneous signatures, absence of a palpable sacrum, or excess fat overlying the sacral region suggestive of a lumbosacral abnormality)
- Genital exam for congenital anomalies such as ectopic ureter or a urogenital sinus (with or without a palpable sacral dimple or excess fat overlying the sacral region)
- Labial adhesions in girls
- Urethral abnormalities or phimosis in boys
- Gait abnormalities, high arched foot

DIFFERENTIAL DIAGNOSIS
• Ectopic ureter
• Posterior urethral valves
• Urinary structure

PATHOLOGIC FINDINGS
• Neurogenic bladder
• Ectopic ureter
• Posterior urethral valves
• Urinary structure

DIAGNOSTIC PROCEDURES/SURGERY
- Ultrasound: Aids in evaluating bladder compliance and function in children with known dysfunctional voiding or enuresis due to neurogenic bladder or posterior urethral valves
- Cystoscopy: Routine use should be avoided
- May be helpful in the assessment of select patients with potential anatomic causes
TREATMENT

GENERAL MEASURES (2–4)
- Before embarking on any therapy, the interest and ability of the child and family to comply should be determined.
- Patience and compliance should be emphasized, because many months may be required to achieve improvement or resolution.
- Motivational therapy should be encouraged in almost every case; it is useful in conjunction with other treatments.
- Behavioral therapy is prerequisite to medications in most patients with nonspontaneous NE.
- Enuresis alarm for MNE works with well motivated families and children.
  - Treatment may take 2–3 mo.
  - Mechanism of action for behavioral therapy unclear.
  - Initial cure rate as high as 75%, suggest 4 mo of conservative dryness.
  - Relapse can be high, but 50% achieve long-term care.

MEDICATION

First Line
- DDAVP (desmopressin) for NE:
  - 0.2–0.6 mg PO 1 hr before bed. No fluid intake 2 hr before and 8 hr after bedtime.
  - Success rate 70–80%.
- Caution in patients with cystic fibrosis (hyponatremic dehydration)
- Tapering schedule imperative.
- Give parents copy of FDA warning (Dec 2007).
- Tapering schedule imperative.
- Caution in patients with cystic fibrosis.
- ∼2 hr before and 8 hr after bedtime.
- Give parents copy of FDA warning (Dec 2007).
- Tapering schedule imperative.
- Caution in patients with cystic fibrosis.
- ∼2 hr before and 8 hr after bedtime.
- Give parents copy of FDA warning (Dec 2007).
- Tapering schedule imperative.
- Caution in patients with cystic fibrosis.

Second Line
- Imipramine for NE:
  - Tricyclic antidepressant with prolonged QT interval.
  - Imipramine overdose can result in seizure.
  - Tapering dose 25–50 mg.
  - Success rates of 25–40%, but relapse rates can be high.
  - ∼2 hr before and 8 hr after bedtime.
  - Give parents copy of FDA warning (Dec 2007).
  - Tapering schedule imperative.
  - Caution in patients with cystic fibrosis.

THERAPIES

- Behavioral therapy is effective in cases of dysfunctional voiding. Most helpful in addition to improved voiding and bowel habits.
- Child must have sufficient cognitive ability to understand teaching.

ONGOING CARE

PROGNOSIS
- After age 6: spontaneous resolution rate of 15%/yr for bedwetters.
- After age 15, <1% have NE.
- Over 6.5 yr of follow-up:
  - 84% no longer wet at night.
  - 20–50% dry during the day.
  - Persistence of enuresis into adulthood (2–3%)
- After age 5, spontaneous resolution rate of 15%/yr.
- After age 15, spontaneous resolution rate of 15%/yr.
- After age 5, spontaneous resolution rate of 15%/yr.

FOLLOW-UP

Patient Monitoring
- Children with history of UTI or organic causes of enuresis should be followed for the specific condition.
- Monitor closely while on medication to treat the primary condition.

Patient Resources
- International Children’s Continence Society.
  - http://iccs.org/pamphlets/

SURGERY/OTHER PROCEDURES
- Only in cases of congenital anomalies (ectopic ureter, posterior urethral valves, etc.)
- Neurosurgical intervention for spinal anomalies, tethered cord.

ADDITIONAL TREATMENT

Radiation Therapy

- Additional Therapies
  - Children with dysfunctional voiding/elimination syndromes may benefit from elimination training program and selective use of anticholinergic medications.
  - Bacteriuria with LUTS and voiding dysfunction.

REFERENCES


ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Dysfunctional elimination syndrome
- Enuresis, Adult
- Enuresis, Pediatric Algorithm
- Urinary Tract Infection, Pediatric
- Vesicourethral Reflex, Pediatric

CODES

ICD9
- 596.6 Enuresis
  - 788.30 Urinary incontinence, unspecified
  - 788.36 Nocturnal enuresis

ICD10
- N38.4 Nocturnal enuresis
- R32 Unspecified urinary incontinence

CLINICAL/SURGICAL PEARLS

The primary therapy for all children with NE should be initial behavioral management before relying on medications.
EPIDIDYMIS, MASS (EPIDIDYMAL TUMORS AND CYSTS)
Ramiro J. Madden-Fuentes, MD
Judd W. Moul, MD, FACS

PHYSICAL EXAM
• Sandal exam—Identify location of mass—single or multiple
  • Compare with contralateral scrotal contents
  • Evaluate if fluid, mobile, indurated, or encroaching on other structures
  • Identify spermatic cord defects
  • Scars from vasectomy—sperm granuloma, epididymal inclusion cyst
  • Bowel mass for associated masses
• Intrapelvic exam—Evaluate for lymphadenopathy
• Hema

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Urinalysis: To evaluate for UTI. Include urine culture if suspicious for infection
  • Tumor markers if any concern for testicular mass
• Serum α-fetoprotein (AFP), β-human chorionic gonadotropin (β-hCG), lactate dehydrogenase (LDH)
• Purified protein derivative (PPD) if TB suspected

Imaging
• Sonar ultrasound—Solid vs. cystic
  • Location—testicular or paratesticular
  • Vascular or avascular
  • Cannot reliably differentiate between malignant or benign
  • Chest x-ray if TB suspected
• If mbenign tumor and >10 yr old—CT scan of the abdomen and pelvis with contrast to evaluate for retroperitoneal nodes (23A)

Diagnostic Procedures/Surgery
• Raney needle for epididymal lesions
• Painful approach
• Frozen section for pathology, proceed to orchiectomy with high cord ligation if malignant

Pathologic Findings
• Benign
  • Adenomatoid—Epididymal cystadenoma/papillary cystadenoma
  • Spermatocele
• Malignant
  • Rhabdomyosarcoma
  • Leiomyosarcoma
  • Fibrosarcoma
  • Metastatic carcinoma

DIFFERENTIAL DIAGNOSIS
• Adenomatous tumor of the epididymis:
  • Most common solid tumor of the epididymis
• Ectopic tissue:
  • Adrenal cortical rests
  • Sphenogonadal fusion
• Epididymal cyst

• Epididymal cystadenoma/papillary cystadenoma:
  • 2/3 associated with von Hippel–Lindau syndrome
  • 1/3 of all epididymal tumors
• Testicular tumors:
  • Acute, very tender on exam
  • Chronic; may have secondary calcification
  • Common cause of epididymal pain
• Renal cysts
• Fibrous pseudotumor
• Reticulosis
• Granulomas: Sarcoidosis, TB, histoplasmosis
• Varicocele
• Hydrocele of the cord
• Leiomysarcoma
• Malignant epididymal tumor:
  • Primary (very rare): Liposarcoma, rhabdomyosarcoma (high on differential in children), leiomyosarcoma, adenocarcinoma, lymphoma
  • Metastatic: Prostate, kidney, stomach most common
• Repillary cystadenoma
• Polyorchidism
• Sperm granuloma:
  • Sarcoid
  • Spem granuloma:
  • Seen in 40% postvasectomy or 2.5% idiopathic in general population
  • Granulomatous lesion with few giant cells
  • Consequence of extravasation of spermatozoa generally postvasectomy (al vascocenized men and general population)
• Testicular tumors:
  • TB of the epididymis
• Vasitis
• Vasa and vasiis nodosa (usually associated with epididymitis)
• Young syndrome (obstructive azoospermia, sinusitis, bronchiectasis)
Therapies
Complementary & Alternative

Use of radiation for local control of
Radiation Therapy
ADDITIONAL TREATMENT

SURGERY/OTHER PROCEDURES
- Excision of suspicious lesion via inguinal approach
- Frozen section
- If positive for malignancy, radical orchiectomy
- Doxycycline 100 mg PO BID
- Levofoxacin 500 mg PO daily x 10 days

EPIDIDYMIS, MASS (EPIDIDYMAL TUMORS AND CYSTS)

Ongoing care
Prognosis
- Adenomatoid tumors
- Benign, excellent prognosis
- Rhabdomyosarcoma
- In children with low stage disease survival may be as high as 90%; Worst stage (IV), survival is ~5.2% (4A)

Complications
- Uninfected epididymitis can cause severe systemic illness
- More advanced infections can present with testicular swelling and pain (epididymo-orchitis)
- If radiation or chemotherapy needed:
- Vincristine, cyclophosphamide, dactinomycin

Ongoing care
Prognosis
- Adenomatoid tumors
- Benign, excellent prognosis
- Rhabdomyosarcoma
- In children with low stage disease survival may be as high as 90%; Worst stage (IV), survival is ~5.2% (4A)

Complications
- Uninfected epididymitis can cause severe systemic illness
- More advanced infections can present with testicular swelling and pain (epididymo-orchitis)
- If radiation or chemotherapy needed:
- Vincristine, cyclophosphamide, dactinomycin

Follow-up
Patient Monitoring
- Oncologic follow-up if malignant disease
- Teach patient testicular self-exam

Patient Resources
Patient

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Adenomatous Tumors, Testicular and Paratesticular
- Epithelial cystadenoma/Papillary Cystadenoma
- Epithelium, Mass (Epithelial Tumor and Cyst)
- Images 4D
- Epidemiology, Metastasis to
- Epididymitis
- Hydrocele
- Paratesticular tumors
- Sarcoma and Other Masses
- Sexually Transmitted Infections (STIs) (Sexually Transmitted Diseases, STDS), General
- Sperm Granuloma
- Spermatocele
- Von Hippel-Lindau Disease

Additional treatments
Radiation Therapy
Use of radiation for local control of rhabdomyosarcoma in young patient is controversial

Additional Therapies
- Chemotherapy
- Vincristine, cyclophosphamide, dactinomycin may have a role in rhabdomyosarcoma depending on extent of disease and oncologist recommendations (4A)

Complementary & Alternative Therapies

Other
- Epididymitis (3[A]
- TB: Treat according to current CDC guidelines
- In young men and treat accordingly (See “Sexually Transmitted Diseases Treatment Guidelines”, General)
- Older men more likely to be infected by enteric organisms (Escherichia coli)
- As most epididymal lesions are benign, observation may be as high as 90%; Worst stage (IV), survival is ~5.2% (4A)
- If positive for malignancy, radical orchiectomy
- Frozen section
- Excision of suspicious lesion via inguinal approach
- Doxycycline 100 mg PO BID x 10 days
- Levofoxacin 500 mg PO daily x 10 days
- - Vincristine, cyclophosphamide, dactinomycin
- - If radiation or chemotherapy needed:
- - Vincristine, cyclophosphamide, dactinomycin

Diagnosis
- Ultrasonography
- Testicular self-exam
- Physical exam

Follow-up
Patient Monitoring
- Oncologic follow-up if malignant disease
- Teach patient testicular self-exam

Patient Resources
- Patient

References

Diagnosis
- Ultrasonography
- Testicular self-exam
- Physical exam

Follow-up
Patient Monitoring
- Oncologic follow-up if malignant disease
- Teach patient testicular self-exam

Patient Resources
- Patient

References

Epididymitis
- Most epididymal lesions are benign and should be followed serially.
- Treatment for epididymitis is guided by risk of STIs as a source.
- Ultrasonography is important to delineate a testicular vs paratesticular origin of the mass.
- Ultrasonography can reliably differentiate malignant solid tumors from benign tumors.
- Rhabdomyosarcoma predominantly occurs in children.
EPIDIDYMITIS
Jonathan H. Huang, MD
Wayland Hsiao, MD

BASICS
DESCRIPTION
• Epididymitis is an inflammatory condition of the epididymis
  • Acute epididymitis is a clinical syndrome consisting of pain, swelling, and inflammation of the epididymis that lasts <6 wk
  • Usually infectious but occasionally inflammatory due to trauma or other cause
  • Chronic epididymitis is characterized by a >6-wk history of symptoms of discomfort and/or pain in the scrotum, testicle, or epididymis
  • Infectious epididymitis is often associated with orchitis
  • Left untreated, localized infectious epididymitis can lead to more extensive infection to include the testicle
  • Thought to be the most common cause of scrotal pain in men

EPIDEMIOLOGY (1)
Incidence
• Estimated at 1 in 100 males in the United States

Prevalence
• 42% of cases are in males 20–39 yr old
• Reported from infancy to the elderly population

RISK FACTORS
• High-risk sexual behavior (multiple sexual partners, sex without condoms)
• Poor hygiene
• Being uncircumcised
• Poor hygiene
• High-risk sexual behavior (multiple sexual partners, sex without condoms)
• Instrumentation of the genitourinary tract
• Catheterization, transurethral surgery
• Urinary tract obstruction (benign prostate hypertrophy, urethral strictures, bladder cancer, prostatic cancer)
• Amiodarone usage
• Testicular pain
• Gradually worsens in epididymitis

ASSOCIATED CONDITIONS
• Orchitis
• Hydrocele
• Immunosuppression

GENERAL PREVENTION
• Condom usage
• Proper hygiene
• Avoiding unnecessary instrumentation of the genitourinary tract

ALERT
Emergency evaluation for testicular torsion is indicated when the onset of pain is sudden, pain is severe, or the test results available during the initial examination do not support a diagnosis of infection.

DIAGNOSIS
HISTORY
• Testicular pain
• Gradually worsens in epididymitis
• Rapid onset and intense in testicular torsion
• Sexual intercourse without condom including anal receptive unprotected sex
• Instrumentation of the genitourinary tract
• Review of systems may help elucidate other causes (ie, amiodarone usage, TB, Behçet disease, sarcoidosis)
• Chronic Epididymitis Symptom Index (CESI) has been described for cases that last >3 mo

Other infectious causes:
• Bacterial
 ◦ Escherichia coli, Salmonella enterica
 ◦ Chlamydia pneumoniae
 ◦ Mycoplasma genitalium, Ureaplasma urealyticum
 ◦ Brucella abortus, Brucella canis, Brucella canis, Brucella melitensis, Brucella gormanii
 ◦ Fungal (more common with HIV)
 ◦ Cryptococcus neoformans
 ◦ Mucormycosis
 ◦ Nocardiosis
 ◦ Actinomycosis
 ◦ Tuberculosis
 ◦ Tuberculosis
 ◦ Sarcoidosis
 ◦ Trauma
 ◦ Amiodarone usage
 ◦ Antiretroviral antibodies interact with the elevated concentration of amiodarone in the epididymis, leading to inflammation
 ◦ Behçet disease
 ◦ Etiology of epididymitis is unclear
 ◦ Sarcoidosis
 ◦ Noncaseating granulomas in the epididymis lead to inflammation
 ◦ Chronic epididymitis (>6-wk duration)
 ◦ Inadequately treated acute epididymitis
 ◦ Postprostatectomy syndrome
 ◦ Reported in 1 in 100 males
 ◦ TB
 ◦ Suspected to be due to hematogenous spread; usually a chronic granulomatous reaction
 ◦ BCG treatment for superficial bladder cancer can lead to epididymitis

PHYSICAL EXAM
• Epidermal tenderness
• Positive in 90–97% of patients
• Epidemidal and constrictional testicle may be involved
• Erythema
• Spermatic cord may be involved
• Enlargement of the scrotum
• Fever
• Genital exam
• UI symptoms related to STDs
• Urinalysis
• Ulcerations from Behçet disease
• Hydrocele
• A reactive process sometimes related to the epididymal inflammation
• Prostate exam
• Rule out prostatitis, especially in males with chronic epididymitis
• Pain sign
• Used to rule out testicular torsion
• Allallowment of pain, with elevation of the testicle, is more consistent with epididymitis (negative Pain sign)
• Only positive in 8% of children with epididymitis

DIAGNOSTIC TESTS & INTERPRETATION
Lab (3)
• Used to rule in a source of infection
• Urinalysis
• Gram stain with at least 5 white blood cells (WBCs) per high power field
• Gram-negative bacilli is suggestive of E. coli infection and underlying cystitis
• Intracellular gram-negative diplococci suggests a diagnosis of N. gonorrhoeae infection
• Findings of only WBCs are suggestive of E. chaffeensis in 2/3 of cases
• Send for culture and sensitivity
• Urosepsis
• Assess for leukocyturia or at least 10 WBCs per high power field
• Urine culture (midstream clean catch)
• Send for culture and sensitivity
• C-reactive protein
• Acute phase protein that is elevated in epididymitis
• Sensitivity of 96.2%, specificity of 94.2%
• When an STD is suspected, the patient should be screened for other STDs, including human immunodeficiency virus (HIV)

Imaging (4.5)
• Color Doppler scrotal ultrasound (US)
• Hypoechoic and swelling in epididymitis
• Sensitivity of 70%, specificity of 88%
• Negative US, when positive clinical findings, should not necessarily alter management
• Decreased blood flow in testicular torsion
• Sensitivity of 100%
• Rule out testicular torsion
• Ultrasound imaging with Testicular perfusion
• High sensitivity and specificity in differentiating testicular torsion from epididymitis
• Rarely used in the United States

PHYSICAL EXAM
• Epidermal tenderness
• Positive in 90–97% of patients
• Epidemidal and constrictional testicle may be involved
• Erythema
• Spermatic cord may be involved
• Enlargement of the scrotum
• Fever
• Genital exam
• UI symptoms related to STDs
• Urinalysis
• Ulcerations from Behçet disease
• Hydrocele
• A reactive process sometimes related to the epididymal inflammation
• Prostate exam
• Rule out prostatitis, especially in males with chronic epididymitis
• Pain sign
• Used to rule out testicular torsion
• Allallowment of pain, with elevation of the testicle, is more consistent with epididymitis (negative Pain sign)
• Only positive in 8% of children with epididymitis

DIAGNOSTIC TESTS & INTERPRETATION
Lab (3)
• Used to rule in a source of infection
• Urinalysis
• Gram stain with at least 5 white blood cells (WBCs) per high power field
• Gram-negative bacilli is suggestive of E. coli infection and underlying cystitis
• Intracellular gram-negative diplococci suggests a diagnosis of N. gonorrhoeae infection
• Findings of only WBCs are suggestive of E. chaffeensis in 2/3 of cases
• Send for culture and sensitivity
• Urosepsis
• Assess for leukocyturia or at least 10 WBCs per high power field
• Urine culture (midstream clean catch)
• Send for culture and sensitivity
• C-reactive protein
• Acute phase protein that is elevated in epididymitis
• Sensitivity of 96.2%, specificity of 94.2%
• When an STD is suspected, the patient should be screened for other STDs, including human immunodeficiency virus (HIV)

Imaging (4.5)
• Color Doppler scrotal ultrasound (US)
• Hypoechoic and swelling in epididymitis
• Sensitivity of 70%, specificity of 88%
• Negative US, when positive clinical findings, should not necessarily alter management
• Decreased blood flow in testicular torsion
• Sensitivity of 100%
• Rule out testicular torsion
• Ultrasound imaging with Testicular perfusion
• High sensitivity and specificity in differentiating testicular torsion from epididymitis
• Rarely used in the United States
MEDICATION (1)

GENERAL MEASURES

Empiric therapy to treat infections tailoring therapy to age and history

For infections tailor therapy to age and history

Chronic epididymitis

Acute epididymitis

Varicocele

Testicular torsion

Testicular cancer

Spermatocele

Referred pain (inguinal hernia renal colic, aneurysm, hip pain, lower back pain)

Spermatic cord torsion

Interstitial cystitis

Chronic pelvic pain syndrome

Abscess

Possible fibrosis

Infection

Inflammation

In infants and children with epididymitis, up to 75%

Ciprofloxacin and other quinolones are no longer recommended when there are clinical signs of epididymitis and a positive urine culture.

– Levofloxacin 500 mg orally once daily for 10 days

– Ciprofloxacin and other quinolones are no longer recommended when there are clinical signs of epididymitis and a positive urine culture.

– Local heat therapy/Sitz baths

– Scrotal support

– Course of antibiotics is appropriate initially; if no improvement in symptoms, consider:

Avoid sexual activity for at least 1 wk following the initiation of treatment, especially if symptoms have not improved

Infections due to resistance

Fertility issues need to be addressed

Outcomes appear improved in the setting of posthysterectomy chronic epididymitis

– Patient needs to understand that there is only at a 10% chance of pain relief

– Outcomes appear improved in the setting of posthysterectomy chronic epididymitis

– Festivity issues need to be addressed

– Testicular denervation

– Not widely used

– Reserved for patients who failed conservative management

– Pain relief noted in 71% of cases

SECOND LINE

SURGERY/OTHER PROCEDURES

– Drainage if abscess present

– Epididymectomy

– Reserved for patients who failed conservative management

– Pain relief noted in 71% of cases

ADDITIONAL TREATMENT

Radiation Therapy

Epididymitis Image

Complementary & Alternative Therapies

FOLLOW-UP

Patient Monitoring

In men < 35 yr old STI/STD with C. trachomatis and N. gonorrhoeae are the most common organisms responsible for bacterial epididymitis.

In older men suspect coliform bacteria.

Testicular torsion needs to be ruled out in cases of acute scrotal pain (clinical exam and Doppler US as appropriate).

REFERENCES


ADDITIONAL READING

N/A

See Also (Topic, Algorithm, Media)

Acute Scrotum

Acute Scrotum Algorithm

Epididymitis Image

Bacterial Prostatitis

Orchitis, General Considerations

Scrotum and Testicle, Mass

Scrotum and Testicle, Mass Algorithm

ICD9

016.40 Tuberculosis of epididymis, unspecified

098.0 Gonococcal infection (acute) of lower genitourinary tract

604.90 Orchitis and epididymitis, unspecified

ICD10

A13.13 Tuberculosis of other male genital organs

A54.23 Gonococcal infection of other male genital organs

N45.1 Epididymitis

CLINICAL/SURGICAL PEARLS

Clinical Pearls

In men < 35 yr old STI/STD with C. trachomatis and N. gonorrhoeae are the most common organisms responsible for bacterial epididymitis.

In older men suspect coliform bacteria.

Testicular torsion needs to be ruled out in cases of acute scrotal pain (clinical exam and Doppler US as appropriate).

EPISPADIAS

Sarah M. Lambert, MD
Pasquale Casale, MD, FACS
Paul H. Noh, MD, FACS, FAAP

DIAGNOSIS

HISTORY
- Usually recognized at birth
- Less severe forms, especially in females, may go unrecognized until the child experiences persistent urinary incontinence after toilet training or UTIs
- Urinary incontinence due to open bladder outlet and absence of urinary sphincter. The more proximal the urethral meatus, the greater the degree of incontinence
- There may be a family history of exstrophy–epispadias, although rare

PHYSICAL EXAM
- Males:
  - Displaced urogenital sinus, ranging from plans to perineal to peno-pubic region to subpubic location
  - Open urethral plate visible on dorsum of phallus
  - Divergent peno-pubic attachments due to public diastasis, resulting in splaying of corporal cavernosa and a short, pendular penis with dorsal chordee
  - 3 degrees of female epispadias, according to Davis (1)
  - Assess position of testes
  - Ventral hood of foreskin
  - Divergent peno-pubic attachments due to public diastasis
  - Open urethral plate visible on dorsum of phallus
- Females:
  - 3 degrees of female epispadias, according to Davis (1)
  - Urethral orifice appears patulous
  - Labia minora poorly developed and terminated anteriorly at clitoris
  - Vagina and internal genitalia usually normal
  - Assess position of clitoris

LABORATORY
- CBC, renal profile

Diagnostic Procedures/Surgery
- Voiding cystourethrogram to assess bladder capacity, bladder outlet, presence/absence of VUR
- Renal/bladder US to assess presence/absence of 2 kidneys and presence/absence of hydronephrosis, due to increased risk of renal agenesis, ectopic renal location, and VUR
- Urodynamic program to assess bladder capacity, bladder outlet, presence/absence of VUR

Pathologic Findings
- N/A

DIFFERENTIAL DIAGNOSIS
- Varying degrees of epispadias
- Classic bladder exstrophy

TREATMENT

First Line
- Anticholinergic therapy may help with bladder overactivity and modeling to promote increased capacity with good compliance once surgery has increased outlet resistance

Second Line
- N/A

SURGERY/OTHER PROCEDURES

Goals:
- Protection of upper tracts, including correction of VUR and maintenance of a low-pressure system
- Achieve urinary continence
- Reconstruction of external genitalia for optimal functional and cosmetic results

Type of Surgery
- Bladder closure between 3 to 6 m of age. Patient is left with an epispadias
- Can also be done as a single stage with bladder closure and urethral reconstruction known as the “Complete Primary Repair of Exstrophy.” Higher incidence of glanular loss than staged repair
- Ureterectomies are needed if the public diastasis is 4 cm or greater on plain x-ray. It was once thought that if the surgery was done in the 1st 48 hr of life that ureterectomies are not needed. Current management favors ureterectomies to maximize continence
- Patients need to be immobilized after surgery to allow pelvic bone healing if osteotomies are needed

Imaging
- Plain x-ray to assess orientation of pelvic bones; osteotomies should be done if public diastasis is > 4 cm
- Renal/bladder US to assess presence/absence of 2 kidneys and presence/absence of hydronephrosis, due to increased risk of renal agenesis, ectopic renal location, and VUR

BASICS

DESCRIPTION
- Congenital anomaly characterized by a dorsal opening of the urethra, resulting in dorsal chordee and widely displaced corporeal bodies
- Often associated with the so-called “exstrophy–epispadias complex” – a wide spectrum of abnormalities that can include classic bladder exstrophy, epispadias, and cloacal exstrophy
- Each of these anomalies is considered to arise from the same basic embryologic defect

EPIDEMIOLOGY

Incidence
- 1 in 117,000 newborn males (1)[A]
- 1 in 484,000 newborn females (1)[A]
- Males: 1 in 117,000 newborn males (1)[A]
- Females: 1 in 484,000 newborn females (1)[A]

Prevalence
- N/A

RISK FACTORS
- N/A

PATHOPHYSIOLOGY
- On the same spectrum of exstrophy
- Failure of medial migration of mesenchyme between the ectodermal and endodermal layers of the cloacal membrane due to premature rupture of the cloacal membrane
- The mesenchyme that forms the genital tubercles at the 5th wk of gestation fails to migrate completely toward the midline, resulting in a defect in the dorsal urethral wall

ASSOCIATED CONDITIONS
- Exstrophy
- Urinary incontinence
- VUR: Incidence of 30–75% (1)
- Inguinal hernias: Incidence of 33% (1)
- Failure of medial migration of mesenchyme between the ectodermal and endodermal layers of the cloacal membrane
- On the same spectrum of exstrophy–epispadias, imperforate anus most common
- Concomitant colorectal anomalies with 1.8%–2.8% concomitant renal anomalies, duplicated collecting system most common
- Congenital anomaly characterized by a dorsal opening of the urethra, resulting in dorsal chordee and widely displaced corporeal bodies

GENETIC
- None identified

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Males:
  - Displaced urogenital sinus, ranging from plans to perineal to peno-pubic region to subpubic location
  - Divergent peno-pubic attachments due to public diastasis, resulting in splaying of corporal cavernosa and a short, pendular penis with dorsal chordee
- Females:
  - 3 degrees of female epispadias, according to Davis (1)
  - Urethral orifice appears patulous
  - Place is left with an epispadias

LABORATORY
- CBC, renal profile

SURGERY/OTHER PROCEDURES

Goals:
- Protection of upper tracts, including correction of VUR and maintenance of a low-pressure system
- Achieve urinary continence
- Reconstruction of external genitalia for optimal functional and cosmetic results
- First stage:
  - Bladder closure between 3 to 6 m of age. Patient is left with an epispadias
  - Can also be done as a single stage with bladder closure and urethral reconstruction known as the “Complete Primary Repair of Exstrophy.” Higher incidence of glanular loss than staged repair
  - Ureterectomies are needed if the public diastasis is 4 cm or greater on plain x-ray. It was once thought that if the surgery was done in the 1st 48 hr of life that ureterectomies are not needed. Current management favors ureterectomies to maximize continence
- Patients need to be immobilized after surgery to allow pelvic bone healing if osteotomies are needed
**PROGNOSIS**

- Continence rates after bladder neck reconstruction range from 70% to 87% [2,5].
- Satisfactory condoms after penile reconstruction range from 50% to 85% (8,17).
- Erectile function is almost universally preserved.
- The ability to participate in satisfactory intercourse and to have children is difficult to assess, as this requires long-term follow-up. Most reports aim to indicate the majority of patients can have intercourse and many males have even fathered children.

**COMPLICATIONS**

- The most common is fistula formation, with an incidence of 4–40% after urethropasty in males, although many of these will close spontaneously (2,4,7).
- Other less common complications are stricture, meatal stenosis, wound infection, diverticulum, and urothelial obstruction.
- If there is tension on the closure, dehiscence is a major complication that might result.

**FOLLOW-UP**

**Patient Monitoring**

- **After epispadias repair:**
  - Remove urethral catheter 1–2 wk after surgery
  - Regular urology to assess urethra and bladder capacity
  - Regular upper tract monitoring with urodynamics US in cases of persistent incontinence or infection

  **After bladder neck repair:**
  - Urodynamics may be necessary with cystometrogram and urethral pressure profilometry
  - Continuation of prophylactic antibiotics until PVRS are minimal
  - Can remove SP tube once PVRS are minimal
  - Can remove urethral catheter 1–2 wk after surgery
  - Urodynamics may be necessary with cystometrogram and urethral pressure profilometry
  - Can remove SP tube once PVRS are minimal

**Patient Resources**


**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- Epispadias in HPG
- Exstrophy, Bladder (Classic Exstrophy)
- Exstrophy, Clival
- Exstrophy-Epispadias Complex

**ICD9**

- 752.62 Epispadias
- 752.5 Exstrophy of urinary bladder
- 752.8 Other specified anomalies of bladder and urethra

**ICD10**

- Q64.0 Exstrophy
- O64.0 Epispadias
- O64.10 Exstrophy of urinary bladder, unspecified

**CLINICAL/SURGICAL PEARLS**

- Female epispadias is not well recognized. It often presents after birth because of complaints of incontinence.
- Antenatal ultrasound may be suggestive of exstrophy-epispadias complex. Findings of abnormal genitalia, low set umbilical cord, inability to identify bladder on ultrasound.
ASSOCIATED CONDITIONS

Treatment effects are generally dependent upon the modality used and are discussed elsewhere.

GENERAL PREVENTION

• Pelvic surgery/RP:
  – Cavernous nerve sparing surgery
  – Sparing of accessory pudendal arteries intraperitoneally
  – RT:
  – Reducing volume of tissue irradiated is postulated to reduce likelihood of ED
  – No definitive evidence supporting use of intensity-modulated radiation therapy (IMRT), RT, or proton beam RT to reduce ED
  – Treatment plans limiting RT to the corpora cavernosa may have a beneficial effect
  – Penile rehabilitation:
    – Signals from studies suggesting early rehabilitation (phosphodiesterase type 5 inhibitors (PDE5i), intracavernosal injections) can impact postoperative erectile status after RP and RT
    – Goals: Cavernosal oxygenation, preservation of endothelial function, prevention of corporal smooth muscle fibrosis.
    – Optimal regimen for rehabilitation is not understood

DIAGNOSIS

HISTORY

• Medical history:
  – Risk factors for general ED
  – Cardiovascular disease
  – Diabetes mellitus
  – Smoking
  – Hypertension
  – Depression
  – Alcoholism
  – Surgical history
  – Type and date of surgery
  – Nerve sparing status (if RP or radical cystectomy)
  – Type and date of surgery
  – Radiation history
  – Dose, template, radiation modality, and date
  – Use of ADT
  – Radiation history
  – Dose, template, radiation modality, and date
  – Use of ADT
  – Radiation history
  – Dose, template, radiation modality, and date
  – Use of ADT

PHYSICAL EXAM

• General physical exam
  – Medical history
  – Presence of nocturnal erections
  – Consistency of erectile quality
  – Onset and severity of ED
  – Validated questionnaires, ie, International Index of Erectile Function (IIEF)
  – Peak systolic velocity < 30 cm/s indicative of CVOD
  – Peak systolic velocity > 30 cm/s indicative of arterial insufficiency
  – Testicular volume and consistency as screening for hypogonadism

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• Generally noncontributory.
  – If evidence of hypogonadism, check early morning serum testosterone.
  – Testosterone levels < 300 ng/dL

Imaging

• Duplex Doppler ultrasound of the penis
  – Can be used to evaluate for presence of vasculogenic ED
  – Peak systolic velocity < 30 cm/s indicative of arterial insufficiency
  – Testicular volume < 5 cm³ indicative of CVOD

Diagnostic Procedures/Surgery

• Pathologic findings

DIFFERENTIAL DIAGNOSIS

• Hypoactive sexual desire disorder
  – Medication induced: Antihypertensives, psychotropics, antidepressants
  – Neurogenic ED
  – Psychogenic ED
  – Vascular ED

TREATMENT

GENERAL MEASURES

• Perform cardiovascular risk assessment to evaluate fitness for sexual activity prior to treatment.
  – Patient and partner should be informed of relevant treatment options, risks, and benefits.

MEDICATION

First Line

• PDE5i (USA)
  – Likely to be ineffective immediately after surgery given cavernosal nerve injury
  – Daily dosing frequently used in rehabilitation regimens
  – When used on-demand only, decreased response noted 2–3 yr after RT

• Medications:
  – Sildenafil 50–100 mg: Onset 15–60 min, duration of action 4 hr
  – Vardenafil 10–20 mg: Onset 15–60 min, duration of action 4–8 hr
  – Tadalafil 10–20 mg: Onset 15–120 min, duration of action 24–36 hr
  – Avanafil 100–200 mg

• Combinations to PDE5i use:
  – Absolute contraindications: Use of nitrites
  – Sildenafil, Tadalafil, Vardenafil: Should be postponed for 4 hr after taking the nitric oxide antagonists
  – Vardenafil: Should not be taken with type 1A or type 3 sodium channel blockers

• Side effects: All associated with headache, dyspepsia, facial flushing

• Sildenafil, Tadalafil: Blurred vision—reacts with PDE6 in retina
Erectile Dysfunction, Following Pelvic Surgery or Radiation

Second Line
- Intracavernosal Injection therapy
  - Highly effective with up to an 85% response rate post-RT (SEC)
  - Risks include priapism, penile pain, ecchymosis
  - Used in a variety of formulations
  - Single agent: Prostaglandin E1
  - Bimix: Papaverine and phentolamine
  - Trimix: Papaverine, phentolamine, and prostaglandin E1
- Intravesical prostaglandin E1 suppository (MUSE)
  - Variable efficacy
  - Penile pain frequently reported, especially in the immediate postoperative period

Surgery/Other Procedures
- Vacuum constriction devices
  - Low patient satisfaction given cumbersome application
- Penile prosthesis implantation
  - Definitive therapy for patients failing or refusing 1st- and 2nd-line treatments
  - Generally, postponed until 2 yr post-RT as regeneration of cavernous nerves during this time may preclude need for surgical therapy
  - High patient satisfaction in appropriately selected population
- Implant infection and malfunction risk must be discussed with patient preoperatively

Additional Treatment
Radiation Therapy
- 1st- and 2nd-line treatments
  - Limited data on combining modalities has been reported
- Level 3 evidence: PDE5i ± either transurethral or intracavernosal injection therapy generates better efficacy than either monotherapy alone
- Level 4 evidence: Enhanced efficacy with the combination of vacuum-erection therapy ± either PDE5i or transurethral PGE1 or intracavernosal injection therapy

Complementary & Alternative Therapies
- Data does not support use of trazodone, yohimbine, and herbal therapies. These medications are not recommended for use in ED by the American Urological Association
- Testosterone therapy
  - Noted to be strongest predictor of patient satisfaction after prostate cancer therapy, particularly in patients with a history of prostate cancer

Prognosis
- Improvement in erectile function can be noted after pelvic surgery, with maximal improvement noted between 18 and 24 mo postoperatively.
- Low likelihood of improvement in erectile quality after 2 yr postoperatively.
- Nadir of erectile function 3 to 5 yr after RT.
- Penile rehabilitation likely improves the prognosis of postsurgical/post-RT ED. Definitive data are pending.

Complications
- Significant effects on patient quality of life
- Noted to be strongest predictor of patient satisfaction after prostate cancer therapy
- Depression

Follow-Up
- Variable dependent upon patient response to treatment.
- Close follow-up is recommended in patients on rehabilitation protocols to evaluate for erectile recovery.

Patient Resources

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Erectile Dysfunction/Impotence, General Considerations
- Penile Doppler Ultrasound, Indications and Parameters
- Penile Rehabilitation

Codes
ICD9
- 527.84 Impotence of organic origin
- N52.31 Erectile dysfunction following radical prostatectomy
- N52.32 Erectile dysfunction following radical cytoreduction
- N52.39 Other post-surgical erectile dysfunction

Clinical/Surgical Pearls
- ED after pelvic surgery and RT is highly prevalent and frequently underdiagnosed in physicians, marketing materials.
- ED after pelvic surgery is immediate in onset with 18–24 mo time to maximal recovery. 
- ED after RT has a minimal onset, with nadir of erectile function at 9–12 mo post-RT.
- Data on penile rehabilitation is conflicting but increasingly shows an improvement in posttreatment erectile recovery.
- The majority of postpelvic surgery/RT ED patients are effectively treated with PDE5i in intracavernosal injection therapy.
Erectile Dysfunction/Impotence, General Considerations

Trinity J. Bivalacqua, MD, PhD

RISK FACTORS

Prevalence

EPIDEMIOLOGY

Incidence

• Crude incidence: 26 cases/1,000 man years
  – Incidence increases with each decade above 40
  ◦ 12 cases/1,000 man years: 40–49 yr
  ◦ 30 cases/1,000 man years: 50–59 yr
  ◦ 46 cases/1,000 man years: 60–69 yr

Prevalence

• Increases universally with age and medical comorbidities (cardiovascular disease, hypertension, smoking, inactivity, obesity)
  – Prevalence by age
    ◦ Below age 40: 1–9%
    ◦ 40–49 yr: 10–20%
    ◦ 50–69 yr: 20–40%
    ◦ >70 yr: 50–75%

PATHOPHYSIOLOGY

Mechanism of erection

– Relaxation of cavernosal smooth muscle (contracted in flaccid state inhibiting inflow of blood)
  ◦ Mediated by NO release from pelvic nerves and endothelial cells
  ◦ Increased cyclic GMP (cGMP) and cyclic AMP (cAMP) trigger signaling pathways leading to decreased intracellular calcium causing smooth muscle relaxation, increased penile blood flow, and tumescence
  ◦ Smooth muscle relaxation further promoted due to inhibition of rho-kinase
  ◦ Veno-occlusive mechanism prevents outflow of blood from penis and maintains erection

CASES

– Associated with 14 times increased risk of cardiovascular morbidity and mortality
  – Cardiovascular disease (hypertension, hyperlipidemia, peripheral vascular disease)
  – Lower urinary tract symptoms/Benign prostatic hyperplasia (BPH)

ASSOCIATED CONDITIONS

– Chronic renal failure, chronic liver disease
– Endocrine disorders (hypogonadism, Cushing disease)

– Prior abdominal/pelvic surgery, radiation, trauma
  – Plasmod, Peyronie disease
  – Neurologic disease (Parkinson disease, dementia, stroke)
  – Depression/psychological disorders

– Long distance cycling
– Smoking

– Medications
  ◦ Antihypertensives (thiazide diuretics, β-blockers, α2 agonists)
  ◦ ACE inhibitors, angiotensin receptor blockers, and calcium channel blockers cause less ED by improving erectile function
  ◦ Psychotropics (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, lithium)

– Antidepressants
  – Antidepresants (clomipramine, sertraline, paroxetine, marijuana)
  – Tobacco smoking

DIAGNOSIS

HISTORY

– Medical history—comorbid conditions, medications, alcohol, tobacco, recreational drug use, history of cycling
– Surgical history
– Psychosocial history
  – Status of current relationship
  – Level of libido/interest in sex
  – Quality of erection
  – Duration of ED
  – Onset of ED (sudden vs. gradual)
– Presence of nocturnal or morning erections
– Presence of penile curvature, plaque, pain
– International Index of Erectile Function

PHYSICAL EXAM

– Neurologic: Stroke, TIA, CNS disease; visual field defects, neuropsych, perimodal vision
– Endocrinologic: Atrophic testes, gynecomastia, loss of secondary sexual characteristics
– Cardiovascular: Blood pressure, femoral/pedal pulses, lower extremity ischemia
– Penile: Curvature, Peyronie disease plaques
– Rectal exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

– Complete blood count
– Serum chemistries
– Fasting glucose level, hemoglobin A1C
– Lipid profile
– Serum total testosterone
– Thyroid function tests (optional)
– PSA (suspect prostate pathology)
– Urinalysis (glucose as indicator of diabetes)

Imaging

– Duplex penile ultrasound—most reliable and least invasive modality for assessing ED
– Provides imaging evaluation and quantification of penile blood flow

ASSOCIATED CONDITIONS

– Atherosclerosis
  – Diabetic mellitus
  – Hypertension, stroke
  – Depression
  – Parkinson disease, multiple sclerosis
  – Psoriasis
  – Peyronie disease
  – Prostate cancer

GENERAL PREVENTION

– Avoidance of tobacco use
– Optimal medical management of common associated conditions
  – Increase exercise/weight loss
  – Split bicycle seat for long-distance cycling

Genetics

– Several gene polymorphisms linked with ED
  – Angiotensin-converting enzyme (ACE) polymorphisms may be risk factors for vasculogenic ED and endothelial nitric oxide synthase (eNOS) polymorphisms alone or in combination with other genetic polymorphisms implicated in ED

BASICS

DESCRIPTION

Consistent or recurrent inability to attain and/or maintain an erection sufficient for satisfactory sexual activity

ASSOCIATED CONDITIONS

– Medications
  – Smoking
  – Long-distance cycling
  – Depression/Psychological disorders
  – Neurologic disease (Parkinson disease, dementia, prior stroke)
  – Priapism, Peyronie disease
  – Prior abdominal/pelvic surgery, radiation or trauma
  – Endocrinopathies (hypogonadism, Cushing disease)
  – Lower urinary tract symptoms/Benign prostatic hyperplasia (BPH)

RISK FACTORS

Probability of ED increases with presence of each risk factor

– Diabetes mellitus
  – Presence of ED 3 times higher in diabetic men

– ED occurs at earlier age and increases with disease duration

– Associated with 14 times increased risk of cardiovascular morbidity and mortality

– Cardiovascular disease (hypertension, hyperlipidemia, peripheral vascular disease)

– Lower urinary tract symptoms/Benign prostatic hyperplasia (BPH)

– Chronic renal failure, chronic liver disease

– Endocrine disorders (hypogonadism, Cushing disease)

– Prior abdominal/pelvic surgery, radiation, trauma

– Plasmod, Peyronie disease

– Neurologic disease (Parkinson disease, dementia, stroke)

– Depression/psychological disorders

– Long distance cycling

– Smoking

– Medications

– Antihypertensives (thiazide diuretics, β-blockers, α2 agonists)

– ACE inhibitors, angiotensin receptor blockers, and calcium channel blockers cause less ED by improving erectile function

– Psychotropics (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, lithium)

– Antidepressants

– Antidepresants (clomipramine, sertraline, paroxetine, marijuana)

– Tobacco smoking
Erectile Dysfunction/Impotence, General Considerations

**Differential Diagnosis**

Psychogenic erectile dysfunction, depression, possible early sign of cardiovascular disease

**Treatment**

**General Measures**

- Treatment choice should be made among physician, patient, and partner after evaluation of risk/benefit of all treatment choices
- Cardiovascular risk assessment should be performed before initiating therapy
  - Low risk: Asymptomatic, <3 risk factors—may proceed with medical therapy
  - Intermediate risk: Asymptomatic, 3-5 risk factors, stable angina, or mild heart failure—requires full cardiovascular assessment to reclassify as high vs. low risk
  - High risk: Unstable angina, recent myocardial infarction, advanced heart failure or valvular disease—defer until cardiac condition stabilized

**Medication**

- **First Line**
  - PDE5 inhibitors (PDE5i): Inhibit breakdown of cGMP promoting smooth muscle relaxation
    - Sildenafil 50–100 mg: Onset 15–60 min, duration of action 4 hr
    - Vardenafil 10–20 mg: Onset 15–60 min, duration of action 2–8 hr
    - Tadalafil 10–20 mg: Onset 15–120 min, duration of action 24–36 hr
    - Avanafil 100–200 mg
  - Combinations to PDE5i use:
    - Absolute contraindications: Use of nitrates
    - Should be postponed for 4 hr after taking inhibitors or α-adrenergic antagonists

  - **Second Line**
    - Intracavernous injection therapy
    - Mechanism: Self-injection of vasoactive agent into corpora cavernosa producing rapid erection
    - Drugs:
      - Alprostadil (PGE1)
      - Bimane: Papaverine and phentolamine
      - Trimix: Papaverine, phentolamine, and prostaglandin E1
    - Side effects: Fibrosis, priapism, painful erection, hematoma
    - Complications: Monoxide oxide medication usage, decreased manual dexterity
    - Efficacy: 80–90% effective in wide range of patients
      - Intracutaneous therapy
      - MUSE (Medicated urethral system for erection)
    - Mechanism: Insertion of abbot containing pellet into distal urethral, absorbed into corpora cavernosa production erection within 30 min
    - Side effects: Penile ischemia, pain, abnormal color of penis

**Surgery/Other Procedures**

- **IP**
  - Indications: Failed 1st- and 2nd-line pharmacotherapy or vacuum device treatment
  - Mechanism: Definitive ED treatment with placement of inflatable cylinders into corpora cavernosa
  - Complications: Infection (<1%), erosion (<5%), mechanical malfunction (5–10%)
  - Penile neurovascularization
    - Reserved for select young patients with clearly documented arterial occlusion

**Additional Treatment**

**Radiation Therapy**

**Additional Therapies**

- Psychosocial therapy: Referral for sex therapy in patients with psychogenic ED
- Cognitive behavioral intervention identifies sexual stressors and refines maladaptive thought processes

**Complementary & Alternative Therapies**

- No FDA-approved dietary supplements or herbal medications for ED but ginseng, ginko biloba, red ginseng, yohimbine reportedly improve ED

**Ongoing Care**

- Excellent if reduction of cardiovascular risk factors, weight loss, exercise, smoking cessation

**Complications**

- N/A

**Follow-Up**

**Patient Monitoring**

- Patients to be reviewed periodically with follow-up considerations:
  - Progress to initial therapy
  - Need for dose titration
  - Patient education on proper medication use (specific PDE5i on empty stomach, use of local injection therapy)
  - Need for progression to 2nd-line therapy/surgery based on therapeutic effectiveness and patient satisfaction

**Patient Resources**


**References**


**Additional Reading**


See Also (Topic, Algorithm, Media)

- Erectile Dysfunction Algorithm

- Erectile Dysfunction, Following Pelvic Surgery or Radiation

- Erectile Dysfunction/Impotence, General Considerations

- Penile Rehabilitation

**Additional Pearls**

- ED is a symptom of multiple underlying diseases that affect the following: penis nerve, artery, endothelial or smooth muscle function
- Cardiac risk assessment should occur prior to initiation of therapy
- Surgical therapy (penile prosthesis) is an essential therapy when medical treatment has failed or is contraindicated.
EXSTROPHY, BLADDER (CLASSIC EXSTROPHY)
Grahame H.H. Smith, MBBS

DIAGNOSIS

HISTORY

- Any family history of exstrophy

PHYSICAL EXAM

- Bladder exposed on abdominal wall
- Bladder plate size
- Lateral ureteric orifices
- Males have an open bladder neck and prostate, the short and broad phallus is open dorsally with dorsal chordee
- Females have an open bladder neck and urethra, bifid clitoris lateral to urethra and anteriorly situated vagina
- Rectus diastasis with external rotation of pelvis
- Low-set umbilicus with foreshortened distance to pubis
- Public dialogue with external rotation of pelvis

DIAGNOSTIC TESTS & INTERPRETATION

- Antenatal ultrasound
- Renal ultrasound
- Blood type and cross-match in preparation for surgery

PHYSICAL EXAM

- Any family history of exstrophy

TREATMENT

GENERAL MEASURES

- Anterograde
  - Consider MRI assessment and karyotyping
- Options for termination may be discussed
- Immediate postnatal care
- 2-0 silk suture on abdominal cord as close to abdominal wall as possible
- Cover bladder with a nonadherent dressing
- Irrigate with normal saline and apply a new dressing with each diaper change

SURGERY/OTHER PROCEDURES

- Ideally the exstrophy is closed on next elective list with two senior staff in attendance
- Requires an adequate bladder plate but the minimum size is not defined
- If unable to easily approximate pubis, then may need pelvic osteotomy
- Pelvic osteotomy may reduce the incidence of delirium and subsequent prolapse in females
- Avoid latex exposure to prevent latex allergy

DIFFERENTIAL DIAGNOSIS

- Bladder exstrophy
- Omphalocele
- Gastrochisis
- Epispadias

BASICS

DESCRIPTION

- Classic bladder exstrophy is a major genitourinary anomaly characterized by the bladder lying open on the abdominal wall with an associated lower midline abdominal wall hernia. The defect extends from the umbilicus to the distal end of the phallus, resulting in concurrent epispadias in males and a bifid clitoris in females.
- Classic exstrophy is considered midway in severity between cloacal exstrophy and epispadias, as part of exstrophy–epispadias complex.

Epidemiology

- Incidence
  - 1 in 10,000–50,000
  - Male > Female (2:1)

- Prevalence
  - N/A

RISK FACTORS

- Genetics
  - Multifactorial etiology without definite genetic link
  - 1st theory postulates that an incomplete ingrowth of mesoderm is unable to reinforce cloacal membrane, which results in premature rupture and subsequent failure to develop ectoderm and mesoderm. The timing of the rupture determines cloacal (earlier) vs. classic exstrophy (later)
  - 2nd theory describes an overgrowth of cloacal mesenchymal tissue. Bladder smooth muscle cells in exstrophy patients show lower intracellular calcium concentrations and enhanced migration

ASSOCIATED CONDITIONS

- Usually healthy without any other major organ system defects
- Subsequent inguinal hernia common
- Rarely may be associated with duplication of bladder or urethra, colorectal abnormalities (2%), duodenal and palate, subsequent testis tumors
- In contrast, classic exstrophy has much more extensive anomalies

GENERAL PREVENTION

N/A

DIFFERENTIAL DIAGNOSIS

- Bladder exstrophy
- Omphalocele
- Gastrochisis
- Epispadias

DISCUSSION

PATHOPHYSIOLOGY

- Risk in sibling is 1 in 100; risk in offspring is 1 in 70

- Male
  - 1 in 10,000–50,000

- Female
  - 19q13.31–41, and 22q11.21 may harbor genes associated with exstrophy

- Cloacal exstrophy
  - Associated with p63 gene dysregulation

- Classic bladder exstrophy
  - Considered midway in severity between cloacal exstrophy and epispadias (later)

- Risk in sibling is 1 in 100; risk in offspring is 1 in 70

- Male
  - 1 in 10,000–50,000

- Female
  - 2:1

- 1st theory postulates that an incomplete ingrowth of mesoderm is unable to reinforce cloacal membrane, which results in premature rupture and subsequent failure to develop ectoderm and mesoderm. The timing of the rupture determines cloacal (earlier) vs. classic exstrophy (later)

- 2nd theory describes an overgrowth of cloacal mesenchymal tissue. Bladder smooth muscle cells in exstrophy patients show lower intracellular calcium concentrations and enhanced migration
ADDITIONAL TREATMENT

ADDITIONAL THERAPIES

Radiation Therapy
N/A

Additional Therapies
- Delayed closure in the case of a late presentation
- All need osteotomy with option of external fixation
- Inadequate bladder plate
  - Delay closure with osteotomies, once adequate
  - If remains inadequate consider augmentation at time of closure
- Postoperative
  - Ensure maximal urinary drainage with ureteric stents, suprapubic tube, and urethral catheter
  - With or without pelvic immobilization (traction, Buck, Bryant, Mermaid dressing, spica cast)
  - Optimal duration of immobilization not established
  - Remove stents one at a time; suprapubic only removed after ensuring appropriate bladder emptying

Complementary & Alternative Therapies
N/A

ONGOING CARE
- Subsequent operative treatment options:
  - Bladder neck plasty (failure rate 50%)
  - Bladder neck closure (failure rate 2%) with augmentation and Mitrofanoff conduit
  - Ureterosigmoidostomy (plus or minus Mainz II pouch)
  - Umbilicoplasty
  - Radial forearm flap phalloplasty (males)
  - Vaginoplasty, clitoroplasty (females)

PROGNOSIS
- Life expectancy normal
- Urinary continence in 50–90%; definition of continence disputed; most common definition of continence is dry with voiding or catheterization every 3 hr
- May require multiple surgeries
- Quality of life scores are less than the normal.
- Functional results seem to be the most likely predictive factor of health-related QOL score

COMPLICATIONS
- Failure of primary closure: 10%
- Failure to store (urinary incontinence secondary to incompetent outlet plus or minus poor bladder compliance)
- Failure to empty (after closure or after bladder neck procedure)
- Upper tract damage and renal failure due to high bladder pressures and/or high outlet resistance
- Developmental psychopathology

- Male: Infertility, retrograde ejaculation, urethrocystourethrectomy fistula, loss of phallus (complete penis disassembly, Kelly repair), incontinence, testis tumors
- Female:
  - Vaginal genitus, requiring vaginoplasty
  - Degree of bladerness association with risk of uterine prolapse
  - Enterocystoplasty may lead to false-positive pregnancy test
  - Normal fertility possible, Cesarean delivery suggested
  - Increased risk of adenocarcinoma of bladder
  - Increased risk of cutaneous adenocarcinoma after urotoagmosidotony

FOLLOW-UP
- After discharge:
  - Antibiotic prophylaxis to prevent urinary tract infections
  - Regular ultrasound to assess for hydronephrosis, residual volume, and bladder volume
  - Vaginoplasty, clitoroplasty (females)

Patient Monitoring
- Yearly colonoscopy starting 10 yr after ureterosigmoidostomy

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Epispadias
- Exstrophy, Cloacal
- Exstrophy–Epispadias Complex
- Exstrophy, Bladder (Classic Exstrophy) Images

CODES
- ICD9
  - 753.5 Exstrophy of urinary bladder
  - Q64.11 Supravesical fissure of urinary bladder
  - Q64.19 Other exstrophy of urinary bladder

- ICD10
  - Q64.11 Supravesical fissure of urinary bladder
  - Q64.19 Other exstrophy of urinary bladder

CLINICAL/SURGICAL PEARLS
- Achieving normal urinary continence with normal voiding after repair is uncommon. It is almost always possible to achieve continence if the patient is willing to undertake clean intermittent catheterization.
- Males will tend to be unhappy about the length of their penis. However, what they lack in length they gain in width.
- For the inexperienced clinician it is sometimes difficult to identify the gender of a newborn baby with bladder exstrophy. Boys almost always have bilateral palpable gonads.

147
EXSTROPHY, CLOACAL

Jason C. Fisher, MD
Harry P. Koo, MD, FAAP, FACS

ASSOCIATED CONDITIONS
- Upper gastrointestinal anomalies:
  - Unilateral renal agenesis (33%)
  - Pelvic kidney (33%)
  - Horseshoe kidney
  - Fusion anomalies
- Lower gastrointestinal anomalies:
  - Separation of or absence of distal ileum/colon
  - Unsegmented rectum/colonic/ileal hernias
  - Urinary and vaginal duplication anomalies
- Genitourinary anomalies:
  - Omphalocele (88–100%)
  - Short gut (20%; cause of major morbidity)
  - Intestinal malrotation
  - Intestinal duplication anomalies
- Skeletal anomalies:
  - Cerebral palsy
  - Increased intracranial pressure
  - Mental retardation
- Soft tissue anomalies:
  - Impaired continence, ambulation, erectile function
- Musculoskeletal anomalies:
  - Scoliosis
  - Hips subluxation and acetabular dysplasia
  - Lower limb anomalies
- Other anomalies:
  - Irritable bowel syndrome
  - Asthma

PATHOPHYSIOLOGY
- Disrupted cellular proliferation and apoptosis of dorsal cloacal wall and hindgut
- Disruption of the mesenchyme—this disrupts the renal tubules
- Diaphragm (82%)

PHYSICAL EXAM
- Classic collection of findings include:
  - Exstrophy of the bladder
  - Complete pelvic separation
  - Wide pubic diastasis
  - Cecal state varied between 2 hemibladders
  - Blind-ending hindgut; no well-formed colon
  - Omphalocele

TREATMENT
- Thorough assessment for associated anomalies (see “Associated Conditions”):
  - Spinal and vertebral defects
  - Lower extremity malformations
  - Renal and bladder anomalies
  - Presence of severely affected viscera
- Detailed exam of exstrophy
  - Marked: Divided corpus cavernosum and glans
  - Females: Divided clitoris, duplicated vagina
  - Additional müllerian anomalies
- Identification of external orifices: Two exstrophic hemibladders are on either side of the exstrophied intestinal segment. Each half usually drains the ipsilateral vertebral body
- Identification of intestinal orifices: Appendix, hindgut, jejunum (often prolapsed)

DIFFERENTIAL DIAGNOSIS
- Unique appearance makes it unlikely to confuse with other conditions
- Extends along EEC spectrum
- Consider associated bladder exstrophy, giant isolated omphalocele, large epispadias

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - CBC, basic metabolic panel
  - At risk for nonimmune metabolic acidosis due to absorption of urine chloride by intestinal mucosa
  - Type and cross blood for surgery
- Imaging:
  - Plain CXR, sacral and spinal x-rays
  - Ultrasound of abdomen, kidneys, head, spine
  - Consider MRI to detect occult spinal lesions if no obvious dysraphism and US nondiagnostic
- Skeletal and bony films of pelvis and lower extremities as needed

HISTORY (ANTENATAL)
- Major diagnostic criteria (210):
  - Nephromegaly (91%)
  - Large midline infraumbilical anterior abdominal wall defect or cystic anterior abdominal wall structure (82%)
  - Omphalocele (77%)
  - Lumbar myelomeningocele (68%)

PHYSICAL EXAM
- The classic collection of findings include:
  - Exstrophy of the bladder
  - Complete pelvic separation
  - Wide pubic diastasis
  - Cecal state varied between 2 hemibladders
  - Blind-ending hindgut; no well-formed colon
  - Omphalocele
Surgical pitfalls to avoid:

- Stage 3 involves procedures aimed at continence
- Multistage approach (3): Creates classic bladder exstrophy repair at 48–72 hrs of life if stable
- Open spinal anomaly: Prompt neurosurgical repair
- Generally not candidates for epidural anesthesia due
- IVF support: Adjust for fluid losses across
- – Primary perineal pull-through of the hindgut (can
- – Excising/discarding the hindgut even if short
- – Excising/discarding diminutive male phallic
- – Overaggressive closure of a large omphalocele
- – Gynecologic issues after onset of menarche
- – Ambulation impairments
- – Urinary continence: Rarely achieved; dependent
- – Important to avoid using any bowel for GU
- – 30–50% will have failure to thrive before age 5
- – Consider gastrostomy tube placement and/or
tunneled central line during initial repair if patient
appears at risk for short gut syndrome

Complementary & Alternative Therapies

- Multistage approach vs. single stage
- Single-stage approach (48): In highly select
patients, can proceed with bladder and abdominal
wall closure and phalic reconstruction which may
avoid ostomies, minimize bladder scarring. Otherwise,
Stage 2 is performed in late infancy, mirroring a classic bladder exstrophy repair:
- Mobilize bladder plate and posterior urethra
depth into perineum. Voids incontinent bladder.
- Orchiopexy with repair of inguinal hernias
- Reconstruct gender-based external genitalia
- Pubic reapproximation +/- pelvic bone osteotomies with fixation and traction for
4–6 wk

- Stage 3 involves procedures aimed at continence and genital cosmesis and is addressed in older
children, often involving bladder augmentation and catheterizable conduits
- Surgical pitfalls to avoid:
  - Injury to ureteral orifices. Place stents
  - Overaggressive closure of a large omphalocele
defect leading to compartment syndrome
  - Excising/discarding diminutive male phallic
remnants and assigning female gender. Coronal
wall and still occurs with unclear long-term
correlation.
  - Excising/discarding the hindgut even if short
  - Primary perineal pull-through of the hindgut (can
be performed in highly select patients)

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies
- Large omphalocele: Not amenable to primary
closure can be treated with Salameh-mediated
epithelialization of cut followed by delayed closure,
or by excision of sac and placement of a silo with
gradual staged reduction of sac
- Consider gastrostomy tube placement and/or
tunneled central line during initial repair if patient
appears at risk for short gut syndrome

Ongoing Care

PROGNOSIS
- Survival >95% over last 20 yr
- Nutrition and growth is the most important
determinant of early survival and mortality
- 30–50% will have failure to thrive before age 5
- Important to avoid using any bowel for GU
reconstruction procedures until child is thriving
- After 3 yr, quality-of-life issues outweigh nutritional
concerns
- Urinary continence: Rarely achieved; dependent
on a compliant reservoir and continent
catheterizable conduit
- Fecal continence: Usually managed by enema
regimen, rarely are perineal pull-through
performers associated with any continence
- Gender assignment and reconstruction, especially
for genetic males raised as females
- Ambulation impairments
- Gynecologic issues after onset of menarche
- Large urinary problems

Complications
- Infection and breakdown of repair
- Abdominal compartment syndrome
- Short gut syndrome
- Vasovagal reflex and hypotension
- Hypochromic-type enterocolitis in the dysmotile
hindgut, even after colostomy formation

Follow-up
- Requires a multidisciplinary team (see “Diagnosis”) to
coordinate regular follow-up through all stages of
surgical repair, with careful attention to nutrition and
growth in infancy, and both surgical and psychological
support for the multiple quality of life issues which
begin in childhood and persist into adulthood

Patient Resources
- Urology Care Foundation: http://www.urinaryhealth.org/urology/index.cfm?article=91

References
3. Stoler CH, Randolph JS, Flanigan IP. Cloacal
exstrophy: Individualized management through a
experience with cloacal exstrophy and gender

ADDITIONAL READING
exstrophy: Improving the quality of life: The Johns
exstrophy: Morbidity associated with abnormalities of
the genitourinary tract and spine. / Pediatr Surg.
- Reiner WG, Psychosocial development in genetic
males assigned females: The cloacal exstrophy
- Soffer TD, Rosen KG, Hong AH, et al. Cloacal
exstrophy: A unified management plan. / Pediatr

See Also (Topic, Algorithm, Media)
- Etiologies
- Urinary-Tract-Exstrophy Complex
- Urinary Bladder (Classic Exstrophy)
- Exstrophy, Cloacal Images

Codes
- ICD9 753.5 Exstrophy of urinary bladder
- ICD10 Q64.12 Cloacal exstrophy of urinary bladder
- ICD10 Q64.12 Cloacal exstrophy of urinary bladder

Clinical/Surgical Pearls
- Maternal ascertainment of associated anomalies can
prevent early clinical and surgical mishaps,
particularly with regard to spinal defects.
- A multidisciplinary team is critical to the short- and
long-term outcomes in these children.
- A staged surgical repair remains the preferred
approach for most children with cloacal exstrophy.
- Do not underestimate the impact of early gender
assignment. Avoid irreversible surgical resection of
structures that may be useful for genital
reconstruction.
- Save as much bowel as possible, especially the short
hindgut, to maximize nutritional capability.
FERTILITY AND CANCER THERAPY, UROLOGIC CONSIDERATIONS

James M. Hotaling, MD, MS
Craig S. Niederberger, MD, FACS

DESCRIPTION
• 2008 ASCO Guidelines recommend that all patients in their reproductive years undergoing cancer therapy be offered fertility preservation options (1).
• Majority of fertility preservation in men is referral to a reproductive specialist and sperm cryopreservation.
• Sperm cryopreservation is often not covered by insurance but Livestrong Foundation and Fertile Hope offer financial support (2).

EPIDEMIOLOGY
Incidence
• 1.4 million people are diagnosed with cancer every year.
• 10% of those diagnosed with cancer are <44 yr old (3).
• Testicular cancer is one of the most common cancers seen by men in their reproductive years and typically presents to urologists.

Prevalence
Advances in cancer treatment have led to increased survival rates of 75–80% for those diagnosed <50 yr old (4).

RISK FACTORS
Men with male factor infertility (azoospermia) are significantly more likely to develop testis cancer.

GENETICS
• Presence of Vas Deferens
• Longitudinal Testicular Axis
• Sexually Active?
• Nocturnal Emissions?

DIAGNOSIS
• Abnormal Reproductive History
• Gonadotropin Exposure?
• Degree of Consanguinity

BASICS
• For patients with testicular cancer, surgery is typically performed to remove the cancer and preserve fertility.

PHYSICAL EXAM
• Assessment of onset of puberty in adolescent males.
• Discussion of future fertility.
• Discussion of potential fertility preservation options.

DIAGNOSTIC TESTS & INTERPRETATION
• Laboratory evaluation (e.g., FSH, LH, estradiol, total testosterone, sex hormone binding globulin (SHBG), and albumin to calculate bioavailable T).

ASSOCIATED CONDITIONS
• Hematologic malignancies
• Whole-body radiation used before bone marrow transplant usually causes lifelong infertility.

GENERAL PREVENTION
• Radiation to the testes can cause permanent loss of sperm production.
• Unless the cancer is in the testicles, attempt to protect them from radiation by using a shield called a clam shell (5).

GENERAL MEASURES
• Sperm aspiration with cryopreservation of ejaculated sperm by a high-volume lab.

TREATMENT
• Patients should obtain from ejaculation for 2 days before banking sperm but not more than 3 days.
• Fertility preservation should only be done after a frank discussion with the patient regarding the ongoing costs of cryopreservation and methods for patient contact in the future is vital.

HOPE Foundation
• 4.5
• 155 ng/dL
• 15 million
• 39 million/mL
• 10:1
FERTILITY AND CANCER THERAPY, UROLOGIC CONSIDERATIONS

MEDICATION

First Line
• To convert a retrograde ejaculation to an antegrade ejaculation
  – In the United States, ephedrine is most often used
  – In Europe, imipramine is also used
• α-adrenergic agents (dosing highly variable)
  – Pseudoephedrine 60 mg
  – Ephedrine 25–50 mg
  – Imipramine 25–50 mg (may cause dizziness and nausea); commonly used in Europe
  – Frequency ranges from QD to QID
  – Duration ranges from 2 to 14 days
  – Side effects: HTN, tachycardia

Second Line
N/A

SURGERY/OTHER PROCEDURES
In men who are azoospermic, aspiration of seminiferous tubules from the testis, sperm from the epididymis or microTESE with extraction of sperm and cryopreservation is a viable option and should be offered

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PRONOSIS

Roughly 30% of men who receive gonadotoxic chemotherapy or radiotherapy will remain azoospermic permanently

COMPLICATIONS
N/A

FOLLOW-UP
Patient Monitoring
• Men should have a repeat interrogation of their male endocrine axis and another semen analysis by a reproductive health specialist when they desire paternity

• Some men may be hypogonadotropic after completion of treatment and referral to a reproductive health specialist is essential to ensure that they are offered medication other than testosterone for androgen replacement

Patient Resources
• Oncofertility Consortium: http://oncofertility.northwestern.edu
• NetFert: Hope: www.fertilehope.org
• ASRM Cancer and Fertility Preservation: http://www.asrm.org/Cancer_and_Fertility_Preservation/

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Kruger Strict Sperm Morphology
• Retrograde Ejaculation
• Semen Analysis, Abnormal Findings, and Terminology
• Semen Analysis, Technique, and Normal Values
• Tanner Stage

CODES

ICD9
• 186.9 Malignant neoplasm of other and unspecified testis
• 606.8 Infertility due to extratesticular causes
• 726.82 Encounter for fertility preservation procedure

ICD10
• C62.90 Malig neoplasm of unsp testis, unsp descended or undescended
• N46.024 Azoospermia due to radiation
• Z31.84 Encounter for fertility preservation procedure

CLINICAL/SURGICAL PEARLS

• < 10% of men who bank sperm retrieve it for use in assisted reproductive technologies.
• Referral to a reproductive specialist and sperm cryopreservation prior to initiation of gonadotoxic chemotherapy, radiation, or radical oncologic surgery is essential
• Cost of sperm cryopreservation typically ranges from $200 to $500 initially usually with an annual maintenance fee.
FILLING DEFECT, UPPER URINARY TRACT (RENAL PELVIS AND URETER)
Scott G. Hubosky, MD

BASES

DESCRIPTION
- Radiographic diagnosis of a radiolucent entity occupying the confines of the upper urinary tract including the intrarenal collecting system or ureter, as seen against contrast within the intraluminal space.
- The finding itself is non-specific but may represent malignant or benign processes.
- Histoscopic evaluation is the gold standard to establish definitive diagnosis.

PHYSIOLOGY
N/A

GENETICS
N/A

RISK FACTORS
- For UTUC:
  - History of smoking
  - History of urothelial carcinoma of the bladder
  - Gene carrier or family history of Lynch syndrome (hereditary nonpolyposis colorectal cancer)
  - Previous stone history
  - Chronic dehydration
  - Elevated sodium intake
  - Purine gluttony
  - For sloughed papilla:
    - MSAD disease
    - Sickle cell disease or trait
  - History of diabetes
  - For fungus ball:
    - Immunosuppression

DIAGNOSIS

HISTORY
- Flank pain or renal colic
- Hematuria
- Gross
  - Microscopic
  - Pre-existing malignancy
  - History or urinary diversion
  - Prior urinary tract manipulation (scent, stone treatment, etc.)
  - Intraluminal administration of contrast
  - Retrograde pyelogram
  - Antegrade nephrostogram
  - IVP
  - Intravenous injection of contrast
  - Intravenous urogram
  - CT urogram
  - MR urogram
  - Cystogram (if reflux present)

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis
- Urine culture including fungal cultures
- Serum creatinine/BUN
- Urine cytology may suggest malignancy
- Sediment analysis

Imaging
- Filling defects are found in imaging modalities which utilize contrast that fills the intrarenal collecting system
  - Intravenous urography
  - Secretory urogram
  - Intravenous injection of contrast
  - Retrograde pyelogram
  - Antegrade nephrostogram
  - Cystogram (if reflux present)
  - CT urogram
  - MR urogram
  - IVP
  - Intravenous injection of contrast

Pathologic Findings
Depends on underlying etiology

DIFFERENTIAL DIAGNOSIS
- Malignant lesions
  - UTUC
  - Rare primary cancers of the upper urinary tract
  - Squamous cell carcinoma (often associated with chronic untreated infected staghorn calculi)
  - Adenocarcinoma
  - Inverted papilloma (about 15% have malignant components)
  - Sarcoma
  - Leiomyosarcoma
  - Adenocarcinoma
  - Small cell carcinoma
  - Metastatic carcinoma
  - Renal cell carcinoma
  - Benign lesions
    - Ac: iatrogenic, infectious, fistula
    - Blood blister
    - Fibroepithelial polyp
    - Fungus ball
    - Hemangioma
    - Inflammatory lesions: Granuloma, malakoplakia, TB
    - Sloughed papilla
    - Calsies (usually radiolucent)
    - Malignant lesions: Leukemia, lymphoma, cholesterol, dystrophic compression of the ureter
    - Mucous (malignancy) or diverticula
    - Protein matrix
    - Urothelial or papillary cystica
    - Vascular impression
    - Fibroepithelial polyp
    - Papilla
    - Prominent papilla (ectopic or end on; normal anatomic variant)
    - Sloughed papilla (may cause obstruction or hematuria)
    - Foreign body
    - Stent fragment (retained)
    - Staple/clip (more likely with urinary diversion)

TREATMENT

GENERAL MEASURES
- If any doubt exists about the etiology of the filling defect then diagnostic uroscopy is indicated.
- Benign tumors may appear as filling defects, in the very peripheral aspect of renal calyces in an “end on” position.

MEDICATION
First Line
- For stones composed purely of uric acid manifesting as filling defects, alkalinization of the urine can be attempted and if pH of 6.5 or greater is achieved then uric acids may dissolve over time.
- Potassium citrate
- Sodium bicarbonate

Second Line
N/A
SURGERY/OTHER PROCEDURES

- **UTUC**
  - For low-grade UTUC which can be reached endoscopically and completely ablated, 5-yr survival is equal to radical nephroureterectomy (RNU).
  - After complete ablation, local recurrence can be seen in up to 75% of patients. If followed for at least 5 yr.
  - Progressive of low-grade to high-grade disease occurs in about 15% of cases.
  - These points should be stressed to patients when counseling on the management of UTUC.
  - For high-grade UTUC or very large volume low-grade UTUC, radical exstirpative surgery is considered the gold standard for cancer control.

- **Nephrolithiasis**
  - Ureteroscopy with laser lithotripsy.
  - Cross-sectional imaging (CT or MRI) is recommended to check for locally advancing disease.

- **Fibroepithelial polyp**
  - Can be removed with ureteroscopy using laser or grasper.
  - Avoid overuse of NSAIDs.

- **Sloughed papilla**
  - Can be removed with ureteroscopy using laser or grasper.

- **Ureteral grasper**
  - Cross-sectional imaging are also needed on a regular basis (NU), surveillance cystoscopy and cross-sectional imaging are also needed on a regular basis.

- **Antireflux surgery**

ADDITIONAL TREATMENT

- **Radiation Therapy**

Additional Therapies

- **UTUC**
  - Neoadjuvant chemotherapy is currently under investigation for suspected high-stage disease with preliminary data suggesting down-staging on pathologic specimens.

- **Complementary & Alternative Therapies**

ONGOING CARE

PROGNOSIS

- Depends on underlying etiology.

- Prognosis usually excellent for benign conditions.

- UTUC (prognosis depends on pathologic staging (pT)). TNM pathologic staging and prognosis is as follows:
  - pT0, pTa, and pTis have 95% and 89% cancer-specific survival at 5 and 10 yr.
  - pT1 has 91% and 89% cancer-specific survival at 5 and 10 yr.
  - pT2 has 75% and 70% cancer-specific survival at 5 and 10 yr.
  - pT3 has 54% and 45% cancer-specific survival at 5 and 10 yr.
  - pT4 has 12% and 6% cancer-specific survival at 5 and 10 yr.

COMPLICATIONS

NA.

FOLLOW-UP

Patient Monitoring

- **Ureteroscopy**

  - For those undergoing ureteroscopic conservative treatment, regular surveillance including cystoscopy and ureteroscopy is required given high chance of local recurrence.

  - Cross-sectional imaging (CT or MRI) is recommended to check for locally advancing disease.

  - For those undergoing radical nephroureterectomy (RNU), surveillance cystoscopy and cross-sectional imaging are also needed on a regular basis.

- **Nephrolithiasis**

- **Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)**

- **Fibroepithelial Polyp, Genitourinary**

- **Ureter and Renal Pelvic Tumors, General**

- **Ureter and Renal Pelvic Tumors, Nephromas**

- **Antireflux surgery**

ADDITIONAL READING


- See Also (Topic, Algorithm, Media)

  - **Philosophical Polyp, Cystinuria**

  - **Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter) Image**

  - **Fungal infections, Cystinuria**

- **Reference Tables: TNM, Renal Pelvis and Ureter Cancer**

- **Ureter and Renal Pelvis, Tumors, General Considerations**

- **Ureter and Renal Pelvis, Squamous Cell Carcinoma**

- **Ureter and Renal Pelvis, Urothelial Carcinoma**

- **Urolithiasis, General**

- **ICD9**

  - 189.1 Malignant neoplasm of renal pelvis.

  - 189.2 Malignant neoplasm of ureter.

- **ICD10**

  - C66.9 Malignant neoplasm of unspecified ureter.

  - C66.9 Malignant neoplasm of unspecified ureter.

- **ICD10-PCS**

  - B81.4 Abdominal findings on diagnostic imaging of urinary organs.

- **CLINICAL/SURGICAL PEARLS**

  - Up to 40% of patients with an upper tract urothelial carcinoma will develop urothelial carcinoma of the bladder.

  - Ureteroscopy can be both diagnostic and therapeutic.
FLANK PAIN, GENERAL

Taylor B. Vaughan, MD
James S. Rosoff, MD

DIAGNOSIS

HISTORY
- Age and sex of patient
- Past medical history
  - Congenital anomalies
  - Urologic disease
  - Prior surgery
  - Infections
- Familial and genetic history
- Personal history
  - Tobacco use
  - Alcohol use
  - Maternal history
- Medications
- Psychosocial factors
- Use of herbal medications
- Genetic testing

PHYSICAL EXAM
- Vital signs
  - Temperature
  - Heart rate
  - Respiratory rate
  - Blood pressure
- General appearance
  - Skin and orifices
  - Neurologic examination
- Localized findings
  - Flank pain
- Associated symptoms
  - Nausea, vomiting
  - Hematuria
- Radiation
  - Radiation to lower extremities
  - Radiation to back

DIAGNOSTIC TESTS & INTERPRETATION

Lab tests
- Complete blood count
  - White blood cell count
  - Hemoglobin
  - Hematocrit
- Liver function tests
- Creatinine
- Urea nitrogen
- Electrolytes
- Urinalysis

Radiology
- Ultrasound
- CT scan
- MRI
- Excretory urogram/IVP

BASICS

DESCRIPTION
- Flank pain refers to pain or discomfort in the side of the abdomen between the last rib and the hip.
- Sometimes referred to as loin pain, it is often associated with urologic conditions, although not exclusively.

EPIDEMIOLOGY

Incidence
- True incidence is difficult to ascertain, as it is a common symptom associated with many medical conditions.

Prevalence
- Many medical conditions can cause flank pain, the prevalence is high.
- Up to 12% of the adult US population will suffer from urinalithiasis at some point.

RISK FACTORS
- Risk factors are dependent upon etiology

GENETICS
- Flank pain caused by urolithiasis is usually due to a history of a familial or congenital disorder.
- Flank pain from renal inflammation may be due to a history of trauma or infection.

PATHOPHYSIOLOGY
- Flank pain from renal causes may be due to obstruction, infection, or renal cell carcinoma.
- Flank pain from chronic obstruction is generally less severe, or may be absent.

ASSOCIATED CONDITIONS
- Pregnancy Considerations:
  - Pregnancy alone may cause flank pain in up to 20% of women (more commonly on the right side).
- Flank pain may occur as a symptom of many medical conditions.

GENERAL PREVENTION
- Strategies for the prevention of urolithiasis or nephrolithiasis depend on the underlying metabolic abnormality.
- Diet modifications may be necessary depending on the underlying metabolic abnormality.
- Calcium reduction has not been shown to affect the likelihood of recurrent stone formation in most patients.
DIFFERENTIAL DIAGNOSIS

Pathologic Findings

There are many causes of flank pain. It is useful to differentiate between urologic and nonurologic causes. Renal/ureteral etiologies are the most common and those that usually require urologic intervention. Some of the most common causes are listed below (3):

• Urologic
  - Calculi: Mostly renal, however, renal pelvic and calyceal stones (obstructing infundibulum) can cause flank pain
  - Acute pyelonephritis
  - Acute papillary necrosis
  - Prune belly syndrome
  - Polycystic kidney disease
  - Acute tubular necrosis
  - Renal infarction (renal artery thrombus or dissection)
  - Renal cyst (especially hemorrhagic; benign cysts rarely cause flank pain)
  - Renal neoplasm
  - Renal trauma
  - Renal vein thrombosis
  - Retroperitoneal bleed or mass
  - Ureteropelvic junction obstruction
  - Cystic renal disease
  - Medullary sponge kidney
  - Other urothelial obstruction (extrinsic compression, blood clot, necrotic material, etc.)
  - Neoplastic:
    - Appendicitis
    - Abdominal aortic aneurysm
    - Diabetes
    - Diverticulitis
    - Hespos zoster
    - Macrocystic renal (muscle-sparing, costochondritis, strain)
    - Myocardial infarction
    - Diabetic torsion
    - Pancreatitis
    - Peripheral nerve compression or trauma
    - Peripheral neuropathy
    - Mumps
    - Tubal pregnancy
    - Ventral or spinal cord/neural entrapment
    - Perineal disc, sciatica, ventral body fracture, or colliqua

MEDIATION

First Line

• Acute pain control (NSAIDs, opioids)
• Anxiolitics, antispasitics, antibiotics as appropriate
• IV fluids if sepsis/hypovolemia. May also help with passage of stones

Second Line

• Anticoagulation and calcium channel blockers may help with expulsion of urinary stones

SURGERY/OTHER PROCEDURES

• Prior to any diagnostics or intervention, the patient must be stabilized.
• Surgical management may be required in some cases depending on the etiology and the patient’s medical condition.
• Examples of surgical management: If the collecting system is infected and obstructed or renal abscess is present, percutaneous drainage and antibiotics are the mainstays of treatment. If dealing with a ruptured AML, embolization should be considered. Ruptured tumor should be treated on an elective basis. Emergent nephrectomy for ruptured AML, or XGP/emphysematous pyelonephritis may be necessary.

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

Complementary & Alternative Therapies

N/A

ONGOING CARE

Follow-up for flank pain will also be dictated by the etiology and acuity of the clinical presentation. Repeat imaging or other lab studies may be required depending on response to initial therapy.

If clinical picture fails to improve or worsens, a change in therapy should be instituted (ie, different antibiotic, PCN, surgical intervention).

PROGNOSIS

In general, for nephrolithiasis, the prognosis is good but this may vary for other etiologies.

COMPLICATIONS

Longstanding ureteral obstruction can cause permanent loss of renal function.

FOLLOW-UP

Patient Monitoring

Periodic renal imaging, urinalysis, or 24-hr urine may be indicated for patients with stone disease. Follow-up may be more or less intensive based on etiology.

Patient Resources


REFERENCES


ADDITIONAL READING

N/A

See Also (Topic, Algorithm, Media)

• Calculifications, Abdominal and Pelvic
• Hydropnephrosis/Hydronephrosis (Dilated Ureters/Renal Pelvis)

CODES

ICD-10

• N23.9 Urinary calculus, unspecified
• 788.0 Renal colic
• 995.9-6 Abdominal pain, other specified site

ICD-19

• N23.9 Urinary calculus, unspecified
• N23 Unspecified renal colic
• R10.9 Urinary tract infection, unspecified

CLINICAL/SURGICAL PEARS

• Flank pain associated with fever and chills may represent urinary tract infection (pyelonephritis).
• Abdominal aortic aneurysm is a potentially life-threatening cause of flank pain.
**Foley Catheter Problems (Insertion and Removal)**

James Kearns, MD

### BASICS

**DESCRIPTION**
- The terms “urethral catheter” and “Foley catheter” are often used interchangeably. Urethral catheter is a general description of a tube that traverses the urethra whereas a Foley catheter refers to a urethral catheter with a retention balloon.

**Common types of urethral catheter include:**
- Foley: rounded tip with balloon
- Coudé: angulated distal tip to allow for navigating past large prostates or elevated bladder necks

- 2-way catheters have a drainage port and a balloon port.
- 3-way catheters have a drainage port, an infusion port, and a balloon port.

- Note: Drainage channel is larger in a 2-way catheter than 3-way catheter of the same size.

- Size measured in Charrière or French (Fr) scale
  - Fr = 3.5 × 10−3 mm
-Common sizes include 5–10 Fr in the pediatric population and 16–24 Fr in the adult population
-Common materials include latex and silicone
- Silicone is better for long-term or latex allergy
- Hydrophilic coatings may facilitate easier passage of catheter
- Problems can occur with insertion, drainage, or removal

### EPIDEMOLOGY

**Incidence**
- Unknown but very common in hospitalized patients

**Prevalence**
- N/A

### RISK FACTORS

- Hospitalized patients requiring strict documentation of urine output
- Bladder neck contracture, previous urethral or prostate surgery
- Trauma, immobility, obesity

**Genetics**
- N/A

### PATHOPHYSIOLOGY

Indications for urethral catheterization include need for bladder decompression, need for accurate monitoring of urine output, immobility during postoperative setting, diversion of urine from wounds, instillation of therapeutic agents, and facilitation of certain diagnostic studies (eg, urodynamics, VCGUS, cystogram)

### ASSOCIATED CONDITIONS

- BPH
- Balanitis xerotica obliterans (BXO)
- UTI
- Urinary retention
- Neoplastic bladder
- Liver failure, heart failure—edema

### GENERAL PREVENTION
- Minimization of unnecessary urethral catheterization
- Removal of urethral catheter as soon as clinically indicated
- Proper insertion technique prevents false passages and potential bladder neck or urethral strictures
- Catheter should always be placed without undue force, using copious lubrication
- Excess force may lead to false passage creation

### ALERT

- Do not inflate Foley balloon unless the catheter is confirmed in the bladder.
- Look for urine return and insert catheter until “hub” reaches urethral meatus.
- If no urine return with “hubbled” catheter, irrigate normal saline into the bladder with a catheter-tipped syringe; 120 mL is often necessary before fluid can be aspirated.
- Inflation in urethra or prostate may lead to significant hematuria or future urethral stricture as well as inability to place another catheter.
- Always inflate balloon with water as saline may crystallize and is usually not necessary to test balloon prior to insertion

### DIAGNOSIS

**HISTORY**
- Previous difficulty with catheterization
- Urethral instrumentation in the past
- Episodes of urethral catheterization
- Prior pelvic radiation or biotherapy
- History of urinary symptoms
  - Quality of urinary stream, urinary frequency, sensation of emptying, history of urinary retention
- Circumcision may lead to meatal stenosis

**PHYSICAL EXAM**
- Abdominal examination for palpable bladder, dullness to percussion over lower abdomen
- DRE feels for evidence of prostate cancer (nodularity or hardness), prostatic abscess (tender prostate), urethral disruption (high-riding or nonpalpable prostate)
- Bimanual examination to evaluate for bladder or pelvic masses
- Palpate penis for strictures
  - Both location and length of stricture important
- Blood at meatus suggests trauma/urethral disruption

### DIAGNOSTIC TESTS & INTERPRETATION

**Lab**
- Electrolytes and creatinine to evaluate for renal function
- Decreased renal function in an obstructed patient is risk factor for postobstructive diuresis

**Imaging**
- Generally unnecessary
- Retrograde urography can demonstrate urethral disruption, hydronephrosis, or stricture
- Cystourethroscopy, if needed

**Diagnostic Procedures/Surgery**
- Catheterization is both diagnostic and therapeutic
  - See treatment section

**Pathologic Findings**
- If performed in OR, may consider biopsy of strictures

### DIFFERENTIAL DIAGNOSIS

**General Measures**
- Assess need for urethral catheterization
- For difficult placement, start with an 16–18 Fr Foley and note location of difficulty
- If stricture suspected, attempt 1 pass with 12–16 Fr Foley
- If BPH suspected, attempt 1 pass with 18–22 Fr coudé
- Choose proper catheter size for pediatric population
- Newborns/neonates based on body weight (no retention balloon)
  - < 1000 gm: 3.5 Fr
  - 1000–1800 gm: 5 Fr
  - 1800–4000 gm: 6.5 Fr
  - ≥ 4000 gm: 8 Fr
- Children
  - Age 0–5 yr, 5–8 Fr
  - Age 5–10 yr, 8–10 Fr
  - Age 10–14 yr, 10 Fr
- Age > 14 yr, 12–14 Fr

### MEDICATION

**First Line**
- Intravesical lidocaine jelly may be useful in difficult catheter placement
**Second Line**
- Hyoscine

### SURGERY/OTHER PROCEDURES

**Urethral sphincter spasm**
- Provide reassurance and ask patient to relax and take slow, deep breaths
- Intravesical lidocaine jelly may not decrease pain (1)
- Instruct patient to attempt to void when encountering the sphincter
**BPH**
- Use a coudé catheter to help navigate the prostate
- Bend of catheter always facing up toward ceiling (often matches a raised area on balloon port)
- Larger (ie, 20–22 Fr) preferable because less likely to bend on itself
**FOLEY CATHETER PROBLEMS (INSERTION AND REMOVAL)**

- Urethral stricture/bladder neck contracture  
  - If unable to pass 14 Fr or larger catheter, dilation likely necessary  
  - General principle is to place catheter over a wire into the bladder using feeding technique  
  - Flexible cystoscopy is ideal  
  - Advance scope to level of stricture  
  - Pass 0.038” wire through stricture into bladder  
  - If cystoscope unavailable, consider filtration with followers, or blindly pass 0.038” soft-tip wire into bladder and confirm location of wire in bladder  
  - Portable pelvic x-ray  
  - Insert 5-F open-ended catheter over wire and aspirate; presence of urine indicates bladder location of wire

**ALERT**

Never dilate urethra unless wire in bladder.  
- Wire rigid enough to potentially undermine bladder neck or enter rectum:  
  - Dilate over wire using serial Amplatz-type renal dilators to 1 size larger than desired catheter (ie, 23 Fr for 20-Fr catheter)

- If dilators unavailable, serial silicone catheters may be rigid enough for dilation:  
  - Insert Council catheter over wire until return of urine and inflow balloon

- If Council unavailable, use 14-gauge Angiocath to thread wire into Foley.

- Urethral disruption  
  - Retrograde urethrogram generally necessary for diagnosis, but consider blind passage of catheter in trauma patient without pelvic fracture or signs of urethral injury (ie, blood at meatus, perineal hematoma, high-riding prostate) (2)  
  - Consider cystoscopically inserting catheter  
  - Use trocar for suprapubic catheter

- Urethral false passage  
  - False passage generally down, so use coude with tip pointed up  
  - If unable to pass coude, use cystoscope to place wire in bladder and place catheter over wire

- Phimosis  
  - Attempt to retract foreskin  
  - If able to visualize meatus, attempt to place Foley through meatus normally  
  - If unable to visualize meatus, perform dorsal slit in foreskin under local anesthesia  
  - Manual stenosis  
    - Inject lidocaine gel  
    - Serial dilations with Van Buren sounds  
    - Penile balanitis edema

- Manually compress edematous skin to minimize edema  
  - Place catheter once meatus visible

- Retracted female meatus  
  - Inserting a finger into the vagina may bring meatus forward

- Manually retract catheter into meatus

- Urethral stone or foreign body  
  - Cystoscopically remove stone/foreign body

- Clot retention with no catheter output  
  - Ensure at least 20-Fr 2-way catheter

- Manually irrigate catheter  
  - If urine does not remain clear after irrigation, consider placing 3-way catheter (02 or 24Fr) for continuous irrigation

**ALERT**

If catheter from catheter stops while on continuous bladder irrigation (CBI), immediately stop inflow.  
- Decreased catheter output from bladder debris:  
  - Manually irrigate

- Consider insertion of larger catheter  

- Inability to remove catheter:  
  - Place syringe on balloon port for 30 min

- Cut balloon port and wait for fluid output

- Insert stiff end of wire through balloon port to attempt to undo the port

- If still unable to remove catheter:  
  - Under US guidance, spinal needle may be inserted into balloon percutaneously

- In women, transvaginal US and needle placement may be preferable  
  - If balloon palpable in bulbar or pendulous urethra, transcervical placement of a22-gauge needle may decompress balloon  
  - If catheter situated in place and suture resorbable, consider waiting before removing catheter

- Open cystotomy with urethral removal is a final resort

**ADDITIONAL TREATMENT**

Radiation Therapy

Additional Therapies

- May be necessary for suprapubic catheterization

**Compilimentary & Alternative Therapies**

**ONGOING CARE**

**PROGNOSIS**

**COMPLICATIONS**

- False passage  
  - Hematuria  
  - Catheter-associated UTI  
  - Many catheters have antimicrobial coatings, which may not be beneficial (3)

**FOLLOW-UP**

Patient Monitoring  

- Before removing difficult Foley, ensure no febrile indication for reinsertion of catheter

- Consider removing catheters at midnight so a failed voiding trial can be managed early during the day

**Patient Resources**

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- Benign Prostatic Hyperplasia
  - Foley Catheter Problems (Insertion and Removal)

- Flexible cystoscopy is ideal

- General principle is to place catheter over a wire

- If unable to pass 14 Fr or larger catheter, dilation likely necessary

- Always confirm wire in bladder before dilating.

- Perform voiding trials at times that allow for reinsertion of difficult catheter at a convenient time.

- Suprapubic catheterization is a reliable method of bladder drainage, if needed.

- Remove catheter as soon as possible to reduce risk of catheter-associated UTI.

**ICD9**

- 996.64 Infection and inflammatory reaction due to indwelling urinary catheter

- 996.76 Other complications due to genitourinary device, implant, and graft

- 953.6 Fitting and adjustment of urinary device

**ICD10**

- T83.89XA Other specified complication of genitourinary prosthetic devices, implants and grafts, initial encounter

- C59.82 Infection and inflammatory reaction due to indwelling urinary catheter

- T83.89HA Other specified complication of genitourinary prosthetic devices, implants and grafts, initial encounter

**CODES**

- 157
FOURNIER GANGRENE
Brad Figler, MD
Bryan Voelzke, MD, MS

DESCRIPTION
FOURNIER GANGRENE is a urologic emergency, causing progressive tissue destruction with significant potential for soft tissue loss, septic shock, and death. Prompt debridement is mandatory.

RISK FACTORS
- Diabetes mellitus
- Genital skin trauma
- Impaired immunity
- Recent penile, perineal, or perirectal surgery
- IV drug abuse
- Male
- Most common in 5th and 6th decades of life
- Rates of spread as high as 2–3 cm/h have been reported
- Obliterative endarteritis leads to thrombosis, ischemia, and necrosis, which allows for further bacterial proliferation
- Pathogen differs from nonnecrotizing infection: Higher frequency of virulent organisms such as group A streptococcus, community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), and Clostridium spp
- Testicular torsion
- Vasculitis
- Epididymitis/epididymitis
- Intraabdominal sepsis
- Pyoderma gangrenosum
- Strangulated inguinal hernia
- Testicular torsion

ASSOCIATED CONDITIONS
- Perianal/perineal abscess
- Immunosuppression
- Obesity
- Urethral structure
- Paraplegia
- Malignancy
- Septic abortions, vulvar abscesses, and epistaxis (in women)

DIAGNOSIS
HISTORY
- Presentation is typically abrupt with severe pain in the perineum, abdominal wall and thighs, however a prodrome of several days of fever and lethargy can be seen
- Perineal or genital trauma (including bites)
- Urethral instrumentation
- Perianal/perineal abscess or wound
- Urinary tract infection or STD
- Urethral stricture disease
- Anal fissure, fistulae, or hemorrhoids
- Alcohol or IV drug abuse
- Malnourishment
- Diabetes mellitus
- Steroid use
- HIV

PHYSICAL EXAM
- Pain out of proportion with physical exam
- Tachycardia and tachypnea
- Fever or hypothermia
- Altered mental status
- Pain out of proportion with physical exam

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC: Lymphopenia/thrombocytopenia, anemia
- Serum chemistry: Metabolic acidosis
- Coagulopathy
- Glucosuria and pyuria
- Wound culture (aerobes, anaerobes, fungi)
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

Pathologic Findings
- Infection presumed present as far peripherally as dermis
- Incision should be extended until normal appearing tissue is encountered
- Coagulopathy
- Glucosuria and pyuria
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained
- Septic abortions, vulvar abscesses, and epistaxis (in women)

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC: Lymphopenia/thrombocytopenia, anemia
- Serum chemistry: Metabolic acidosis
- Coagulopathy
- Glucosuria and pyuria
- Wound culture (aerobes, anaerobes, fungi)
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

Pathologic Findings
- Infection presumed present as far peripherally as dermis
- Incision should be extended until normal appearing tissue is encountered
- Coagulopathy
- Glucosuria and pyuria
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

PATHOPHYSIOLOGY
- Primary insult is a breach in the integrity of the GI or urethral mucosal lining
- Infection is frequently polymicrobial (aerobic and anaerobic, gram-positive and gram-negative)
- Pathogen differs from nonnecrotizing infection: Higher frequency of virulent organisms such as group A streptococcus, community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), and Clostridium spp
- Obliterative endarteritis leads to thrombosis, ischemia, and necrosis, which allows for further bacterial proliferation
- Process extends along Dartos and Colles fascia, potentially involving perineum, abdomen, thighs, ischiosciatic fossa, and retroperitoneum
- Rates of spread as high as 2–3 cm/h have been reported
- Deep structure (corpus cavernosum, corpus spongiosum, and testicles) are typically not affected

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC: Lymphopenia/thrombocytopenia, anemia
- Serum chemistry: Metabolic acidosis
- Coagulopathy
- Glucosuria and pyuria
- Wound culture (aerobes, anaerobes, fungi)
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

Pathologic Findings
- Infection presumed present as far peripherally as dermis
- Incision should be extended until normal appearing tissue is encountered
- Coagulopathy
- Glucosuria and pyuria
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC: Lymphopenia/thrombocytopenia, anemia
- Serum chemistry: Metabolic acidosis
- Coagulopathy
- Glucosuria and pyuria
- Wound culture (aerobes, anaerobes, fungi)
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

Pathologic Findings
- Infection presumed present as far peripherally as dermis
- Incision should be extended until normal appearing tissue is encountered
- Coagulopathy
- Glucosuria and pyuria
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC: Lymphopenia/thrombocytopenia, anemia
- Serum chemistry: Metabolic acidosis
- Coagulopathy
- Glucosuria and pyuria
- Wound culture (aerobes, anaerobes, fungi)
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained

Pathologic Findings
- Infection presumed present as far peripherally as dermis
- Incision should be extended until normal appearing tissue is encountered
- Coagulopathy
- Glucosuria and pyuria
- Aspiration of subcutaneous skin at the point of demarcation for Gram stain and culture may be useful
- Deep tissue cultures at the time of surgery should be obtained
TREATMENT

GENERAL MEASURES
• Immediate and aggressive surgical therapy with debridement of necrotic tissue
• Aggressive fluid resuscitation (isotonic fluid)
• Intotopic support is frequently necessary
• Correct hypernatremia
• Quadruple antibiotics
• ICU support until clinically stable

MEDEICATION
First Line
• Antibiotics should include gram-positive, gram-negative, and anaerobic coverage in full therapeutic doses
• Modify antibiotics as needed, based on Gram stain, culture, and sensitivity
• Appropriate empiric therapy typically consists of:
  – Piperacillin/tazobactam
  – Ertapenem
  – Imipenem/cilastatin
  – Vancomycin 1 g IV BID (MRSA)
  – Clindamycin 600–1,200 mg/d, divided dose
  – Penicillin G 3–5 million international units IV q6h
  – Nutritional support (preferably enteral) should be instituted early to correct the negative nitrogen balance associated with profound sepsis

ADDITIONAL TREATMENT
• VAC may result in earlier wound granulation compared to simple wet-to-dry dressing changes, but may be difficult to apply to the perineum and genitalia
• A VAC should be placed with fine-mesh gauge sealed in normal saline
• Don’t perform cystoscopy if there is concern for urethral involvement
• Don’t perform cystoscopy if there is concern for urethral involvement
• Aggressive fluid resuscitation (isotonic fluid)
• Immediate and aggressive surgical therapy with proctoscopy under anesthesia is necessary extensivly involved

ONGOING CARE

PROGNOSIS
• Historically, fournier gangrene carried a >50% mortality rate
• Modern mortality rates average 5–20%, which is highly dependent on prompt diagnosis and right coordination of definitive care

COMPLICATIONS
• Coagulopathy
• Death from sepsis
• Disfiguring skin and soft tissue loss
• Infertility
• Multi system organ failure
• Renal failure
• Urinary incontinence

FOURNIER GANGRENE

REFERENCES

ADDITIONAL READING
2. See Also (Topic, Algorithm, Media)
• Diabetes Mellitus, Urologic Considerations
• Unexpanded (Septic) Wound
• Fournier Gangrene Images

CODES
ICD9-10
• 616.89 Other inflammatory disease of cervix, vagina and vulva

CLINICAL/SURGICAL
PEARLS
• Signs of local infection with pain out of proportion to physical exam is highly suspicious for a diagnosis of fournier gangrene.
• Prompt and radical debridement is mandatory.
• Infections are typically polymicrobial, so broad-spectrum antibiotics are critical.

FOLLOW-UP
Patient Monitoring
Prolonged critical care may be required.

Patient Resources
http://www.mayoclinic.com/health/gangrene/DS00993
FUNGAL INFECTIONS, GENITOURINARY

Michael A. Pontari, MD
Daniel C. Parker, MD

DESCRIPTION
Primary fungal infection of the genitourinary (GU) tract is common with Candida, but uncommon with other fungi.

Other fungal infections are found in the GU tract but are seen more commonly with immunocompromised patients or in setting of systemic disease.

EPIDEMIOLOGY
Incidence
- Difficult to determine because most cases are not reportable
- Estimated 1–2 new cases per 100,000 population per year involving the GU tract

Prevalence
- Difficult to estimate as cases are not reportable

RISK FACTORS
- Urinary tract drainage catheter
- Prior antibiotics
- Diabetes mellitus
- Uranuria
- Female sex
- Prior surgical procedures
- Immunocompromise

Genetics
- No heritable form of transmission

PATHOPHYSIOLOGY
- Funguria to funguria:
  - Can occur with obstruction, reflux, or instrumentation
- Fungi to funguria:
  - Disseminated disease seeds GU tract
  - Multiple microabscesses develop in the renal proximal tubules

ASSOCIATED CONDITIONS
- Immunocompromised state
  - Diabetes
  - AIDS
- Anatomic GU abnormalities
  - Strictures
  - Prostatic hypertrophy
  - Diverticula
  - Indwelling tubes
  - Stones

GENERAL PREVENTION
- Remove unnecessary catheters/tubes
- Narrow antibiotic coverage
- Improve nutritional status
- Control hyperglycemia

DIAGNOSIS
HISTORY
- Immunocompromised state:
  - Fungi are ubiquitous in the environment and can overwhelm those with weakened immune systems
- Those receiving chemotherapy, with AIDS, or affected with diabetes
- Recent antibiotic use:
  - Risk of candiduria is 6–10× after use of broad-spectrum antibiotics
- Indwelling GU tubes or prosthesis:
  - Risk of Candida 12× with catheterization
- GU tract abnormalities:
  - Risk of candiduria 6–10× with abnormalities (TIA)

- Occupation:
  - Exposure to aerosolized soil; spelunkers; bird handler
- Recent travel or recreation (see image):
  - Blastomycosis found in Ohio, Missouri, and Mississippi river basins; Great lakes, Canada
  - Coccidioidomycosis found in semiarid regions of the Western US, Mexico, Central and South America
  - Histoplasmosis found in Midwestern and Southern US in areas of high-nitrogen soil such as chicken coops and bat caves

- Immunocompromised state:
  - Risk of candiduria is 6–10× after use of broad-spectrum antibiotics

- Prior antibiotics:
  - Risk of candiduria is 12× after use of broad-spectrum antibiotics

- Recent antibiotic use:
  - Risk of candiduria in (3)[A]:
    - Asymptomatic patients
      - Urine culture
      - Symptomatic patients
      - Urine culture
      - Urine culture
      - Neutropenic patients
      - Patients who will have GU procedures
      - Infants with low birth weight

- Infectious Diseases Society of America recommends treatment of candiduria in (3)[A]:
  - Clotrimazole, miconazole, terconazole topical for 1 wk
  - Fluconazole 200 mg/d for 1–2 wk
  - Amphotericin B 1–1.5 mg/kg/d for 10 wk

- Blood clots in collecting system
- Cryptococcus
- GU TB
- Neutropenias
- Squamous cell carcinoma (SCC)
- Urothelial carcinoma (transitional cell carcinoma)

TREATMENT
GENERAL MEASURES
- Infected Diseases Society of America recommends treatment of candiduria in (3)[A]:
  - Infants with low birth weight
  - Patients who will have GU procedures
  - Neutropenic patients
  - Symptomatic patients
- Treat UTI symptoms empirically for funguria only if the patient is unable to vocalize or perceive symptoms
- Asymptomatic candiduria: Asins for risk factors (3)[A]

MEDICATION
First Line
- Aspergillosis:
  - Amphotericin B 1.5–3 mg/kg/day for 10 wk
- Blastomycosis:
  - Itraconazole 200 mg PO BID for 4–6–12 mo
- Candidiasis:
  - Clotrimazole, miconazole, terconazole, econazole topical for 1 wk
- Candidiasis:
  - Fluconazole 100 mg PO for 1–2 wk

SECOND LINE
- Aspergillosis:
  - Amphotericin B 1–1.5 mg/kg/day for 10 wk
- Blastomycosis:
  - Itraconazole 200 mg PO BID for 1 year
- Candidiasis:
  - Fluconazole 200 mg PO BID for 4–6–12 mo
- Cryptococcus:
  - Amphotericin B 0.5 mg/kg/day for 1 year
- Fusarium:
  - Fluconazole 100 mg PO BID for 1 year

DIFFERENTIAL DIAGNOSIS
- Blood clots in collecting system
- Cryptococcus
- GU TB
- Neutropenias
- Squamous cell carcinoma (SCC)
- Urothelial carcinoma (transitional cell carcinoma)
FUNGAL INFECTIONS, GENITOURINARY

ADDITIONAL TREATMENT

Radiation Therapy
None

Additional Therapies
• Irrigation may be necessary in infectious infections when systemic medication is not excreted into the urine.
  • Amphotericin B GU tract irrigation
    – 50 mg in 1,000 mL water at 40 mL/hr
    (over 24 hr) for 5–7 days
  • In children, renal irritation with 10–24 mg/dl
  • Removing catheter may eradicate funguria in 40% of cases

Complementary & Alternative Therapies
None

ONGOING CARE

PROGNOSIS
• Candiduria does not predict development of candidiasis in most people
  • Rates 1.3–10.5%
• No different in renal transplant population: 5%
• Aspergillosis mortality 40–90% with treatment
• Pyococcosis (necrotizing, hypernephric) mortality 90% if untreated, 24% with nephrectomy and amphotericin B

COMPICATIONS
• Renal failure
• Empyemathous pyelonephritis
• Obstruction, pyonephrosis, death
• Fibrillary necrosis
• Perinephric abscess
• Renal scarring

FOLLOW-UP

Patient Monitoring
• Surveillance cultures can be obtained to document clearance of infection.
• Fungal urine can be fungal reservoir for recurrent infection.

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Candidiasis, Cutaneous, External Genitalia
• Candidiasis, Genitourinary Image
• Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
• Fungal infections, Genitourinary Algorithm
• Fungal Infections, Genitourinary Image
• Histoplasmosis, Genitourinary
• Urinary Tract Infection (UTI), Adult Female
• Urinary Tract Infection (UTI), Adult Male
• Urinary Tract Infection (UTI), Pediatric

CODES

ICD9
• 116.1 Candidiasis of vulva and vagina
• 116.2 Candidiasis of other urogenital sites
• 116.0 Blastomycosis

ICD10
• B37.1 Candidiasis of vulva and vagina
• B37.4 Candidiasis of other urogenital sites
• B40.89 Other forms of blastomycosis

CLINICAL/SURGICAL PEARLS

• When fungal infections are found in the GU tract in patients without risk factors, a search for systemic disease is warranted.
• Disseminated fungal disease can seed the GU tract through the development of renal microabscesses.
• Fungal infections are encountered in various geographic locales based on type.
• Treat candiduria in infants with low birth weight, those undergoing GU procedures, neutropenic patients, and symptomatic patients.
• Surgical drainage of fungal infections is indicated in cases of urinary tract obstruction.

• Cryptococcosis:
  • Amphotericin 0.5–1 mg/kg/d IV + fluconazole 100 mg/kg/d PO for 2 wk
  • Then fluconazole 400 mg PO for 8 wk OR
  • Then itraconazole 200 mg PO BID for 8 wk
• For oropharyngeal suppression:
  • Fluconazole 200 mg PO OR
  • Amphotericin 0.5–1 mg/kg IV every week
• Histoplasmosis:
  • Itraconazole 200 mg PO BID for 6–18 mo
  • For histoplasmosis suppression:
    • Itraconazole 200 mg PO BID OR
    • Amphotericin 0.5–1 mg/kg IV every week
• Mucormycosis:
  • Amphotericin 8–1.5 mg/kg IV for 6–10 wk

Second Line
• Aspergillosis:
  • Voriconazole 6 mg/kg q12h for 2 days, then 4 mg/kg q12h IV or oral for 10 wk OR
  • Itraconazole 200 mg PO BID for 4 days, then 200 mg PO q12h for 12 days, then 200 mg PO BID for 10 wk OR
  • Itraconazole 200 mg PO TID for 9 days, then 200 mg PO BID for 10 wk
• Blastomycosis:
  • Amphotericin 0.5–1 mg/kg for 6–12 wk OR
  • Fluconazole 400–800 mg PO for 6–12 mo
• Candidiasis:
  • Fluconazole 150 mg q12h
  • Candida (until 2 wk after antibiotic and Cr negative):
    • Caspofungin 70 mg IV q12h, then 50 mg q12h OR
  • Amphotericin 8.5–10 mg/kg
• Cryptococcosis:
  • Amphotericin 8.0–3.5 mg/kg IV for 1–2 wk OR
  • Fluconazole 25 mg/kg PO for 1–2 wk
• Coccidioidomycosis:
  • Fluconazole 400–800 mg PO for 1 yr OR
  • Amphotericin 8.0–3.5 mg/kg IV for 1 yr
• Histoplasmosis:
  • Fluconazole 400–800 mg PO q6–8 h OR
  • Amphotericin 8.0–3.5 mg/kg IV for 10–12 wk

SURGERY/OTHER PROCEDURES
• Obstructions from fungal bezoars require drainage.
• Access to upper tract: can facilitate drainage, antifungal irrigation, and extraction if needed.
• Perinephric abscesses can be drained percutaneously, but may require operative drainage if multiple loculations are present.
• Severe aspergillus kidney infections may require nephrectomy.
• Treatment of fungal prostatitis may require surgical intervention for prostatic resection or drainage of abscess in addition to medical therapy (46E).

• When fungal infections are found in the GU tract in patients without risk factors, a search for systemic disease is warranted.
• Disseminated fungal disease can seed the GU tract through the development of renal microabscesses.
• Fungal infections are encountered in varying geographic locales based on type.
• Treat candiduria in infants with low birth weight, those undergoing GU procedures, neutropenic patients, and symptomatic patients.
• Surgical drainage of fungal infections is indicated in cases of urinary tract obstruction.

161
GLOMERULONEPHRITIS, ACUTE

Christopher E. Keel, DO
Raju Thomas, MD, MHA, FACS

DESCRIPTION
- Inflammation of the glomerulus mediated through humoral and cell-mediated immune mechanisms including immunoglobulin, complement, and circulating T cells usually in response to an infection (typically streptococcal).
- The inflammation and immunologic response results in immune deposits in the glomerulus.
- Once symptoms is usually acute and includes oliguria, hypertension, hematuria, proteinuria, and renal impairment.
- Poststreptococcal acute GN is the onset of GN after a preceding group A β-hemolytic streptococcal infection, most commonly of the pharynx or skin.
- Most common glomerulonephritis affecting children.
- Synonym(s): Acute nephritic syndrome; Poststreptococcal glomerulonephritis.

EPISTEMIOLOGY
Incidence
- Poststreptococcal GN, the most common form, occurs most frequently in children between 2 and 10 yr of age but can occur at any age with a slight predominance of males over females.
- 10% cases are in adults, >40 yr of age.
- 20,000,000 yr

Prevalence
- Most patients have a complete recovery, with resolution of clinical signs within a few weeks.
- The reported incidence of chronic renal insufficiency is 0–20%.

RISK FACTORS
- Occurs with infection of specific types of group A β-hemolytic streptococci, and these vary by site of infection. It occurs more commonly after pharyngitis than pyoderma.
- Pharyngitis is associated with types 1, 3, 4, 12, 25, 49 with the more common sporadic variety.
- Pyoderma is associated with types 2, 49, 55, 57, 60.

Genetics
N/A

PATHOPHYSIOLOGY
- Tends to occur with impetigo in the late summer and with streptococcal pharyngitis in the winter.
- Note that cases of poststreptococcal GN have also been reported from other bacteria (Pneumococcus, Staphylococcus, Menigococcus) and after viral infections (chickenpox, hepatitis).
- The exact mechanism of renal injury from poststreptococcal GN is not clear. IgG and C3 deposits are found at the capillary wall and in the mesangium. It is unclear if the inflammatory response is due to circulating immune complexes, complexes in situ, or both.
- If the antin or antigens activate the alternative complement pathway and result in renal damage.

ASSOCIATED CONDITIONS
- Pharyngitis
- Hematuria
- Hypertension
- UTI
- Acute renal failure
- Rapid decrease in renal function heralds the syndrome of rapidly progressive glomerulonephritis

GENERAL PREVENTION
No specific prevention measures; prompt treatment of strep infections may reduce risk.

DIAGNOSIS

HISTORY
- Recent episode of pharyngitis or skin infection.
- Pharyngitis usually precedes renal disease by 8–14 days.
- Time between purulent skin disease and acute nephritis is widely variable.
- Serology varies from asymptomatic microhematuria to acute renal failure.
- Gross hematuria occurs in 30–50%.
- Volume overload occurs in up to 2/3 of patients and may be severe enough to cause congestive heart failure and pulmonary edema.
- Hypertension occurs in up to 80%.
- Severity may not correlate with the degree of volume overload.
- Hypertensive encephalopathy (seizures, confusion, coma) is the presenting feature in 5%.
- Often patient has contact with individuals complaining of similar symptoms.

PHYSICAL EXAM
- Patients may have periorbital edema, peripheral edema, HTN
- Transient oliguria will be present in half of patients

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis (1):
  - Proteinuria may be microscopic or gross and is present in all cases.
  - Microscopic analysis shows dysmorphic red blood cells and red cell casts.
  - >30% of red blood cells having dyssmorphic features is a highly sensitive test for glomerular disease.
  - Red blood cell casts present after acute pharyngitis episode is pathognomonic for poststreptococcal GN.
- Proteinuria may also be present and is usually mild (no more than 2+ on dipsticks), but some may have proteinuria to the nephrotic range.

- Evaluate proteinuria with a spot urine protein-to-creatinine ratio:
  - Normal <0.2.
  - Nephrotic range proteinuria being >2.0.
- Basic chemistry profile may reveal elevated BUN and creatinine consistent with ARF.
- Urine can be raised disproportionately to creatinine.
- Mild normochromic, normocytic anemia due to hemodilution.
- Hyperuricemia may be present due to volume overload.
- Acidemia and hyperkalemia may occur in those with severely depressed renal function.
- ESR will be elevated.
- Serum complement levels, in particular, C3 will be depressed early in the disease in 90%.
- Normalizes 2–4 wk after onset.
- Prior penicillin therapy may attenuate the fall in C3.
- If C3 remains depressed beyond this interval, look for other causes.
- Antistreptococcal O and antihyalurondase titers may be obtained and may be elevated in poststreptococcal GN.
- Not all strains of streptococci will cause these elevations and site of infection may affect which is present.

Imaging
- No imaging is indicated to identify poststreptococcal GN.
- CXR may identify fluid overload.

Diagnostic Procedures/Surgery
- Renal biopsy is not indicated in poststreptococcal GN unless symptoms persist or renal function deteriorates due to progressive disease.
- Renal biopsy, thus, indicated if:
  - Persistently low C3 beyond 8 wk
  - Persistent heavy proteinuria after 6 mo
  - Persistently low C3 beyond 8 wk
  - An acute presentation—nephritic syndrome, severe acute renal failure with estimated GFR <30 mL/min/1.73 m²
  - Arterial course—failure of renal function to improve after initial improvement during the acute phase which usually lasts no more than 2 wk

PHYSICAL EXAM
- Patients may have perihilar edema, peripheral edema, HTN
- Transient oliguria will be present in half of patients
Erythromycin is substituted if penicillin allergic.

Patients should be treated with a 10-day course of antibiotics to prevent the spread of the offending organism. This will not alter the course of the disease.

Erythromycin is substituted if penicillin allergic.

Family members of patients with acute GN should be cultured for group A β-hemolytic streptococci and treated if positive.

Supportive care, recovery is usually rapid and complete with an excellent prognosis.

> Furosemide 2–4 mg/kg/dose IV

Title: ONGOING CARE

PROGNOSIS

- Most patients have a complete recovery, with resolution of clinical signs within a few weeks.
- The reported incidence of chronic renal insufficiency is 0–20%.
- Microscopic hematuria may persist for months up to 2 yr, and mild proteinuria may persist for years following an episode of poststreptococcal GN.

COMPlications

- Rarely does poststreptococcal GN progress to chronic or rapidly progressive GN resulting in ESRD. Most cases resolve with no sequelae. Chronic renal failure or marked decline in glomerular filtration rate is very rare.
- It is rare to result in severe HTN, seizures, anuria, hyperkalemia, or death.
- Hyperensive retinopathy or encephalopathy.
- Rapidly progressive glomerulonephritis.
- Systemic lupus erythematosus.

SURGERY/OTHER PROCEDURES

Renal biopsy if indicated (see evaluation)

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

N/A

Complementary & Alternative Therapies

N/A

GLOMERULONEPHRITIS, ACUTE

TREATMENT

GENERAL MEASURES

- Supportive care and reassurance.
- Monitor weight and serum sodium daily during acute phase.
- Bed rest does not influence rate of recovery.
- Antibiotics do not change the course of illness once established but should be given to reduce infection-related morbidity.
- Restrict protein until azotemia clears.

MEDICATION

First Line

- Treatment is supportive for this condition and directed at the effects of renal insufficiency and HTN.
- Sodium and water restriction is indicated in patients who show signs of fluid overload (400 mL/m2/d).
- Loop diuretics, calcium channel blockers, and vasodilators are mainstays in the treatment of resistant HTN.
- Furosemide 2–4 mg/kg/dose IV

Second Line

- Patients should be treated with a 10-day course of penicillin antibiotics to prevent the spread of the nephritogenic organisms. This will not alter the course of the disease.
- Erythromycin is substituted if penicillin allergic.
- Family members of patients with acute GN should be cultured for group A β-hemolytic streptococci and treated if positive.

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Acute Kidney Injury, Adult (Renal Failure, Acute)
- Acute Kidney Injury, Pediatric (Renal Failure, Acute)
- Glomerulonephritis, Chronic

CODES

ICD9

- 580.9 Acute glomerulonephritis with unspecified morphologic changes
- 580.4 Acute glomerulonephritis with lesion of basement membrane dise
- 580.0 Acute post-streptococcal glomerulonephritis
- 580.1 Acute focal and segmental glomerulosclerosis
- 580.2 Acute membranous glomerulonephritis
- 580.3 Acute proliferative glomerulonephritis
- 580.7 Acute glomerulonephritis of other specified type
- 580.8 Acute glomerulonephritis with unspecified type

ICD10

- N01.9 Rapidly progr nephritic syndrome w unsp
- N00.9 Acute nephritic syndrome with unsp
- M31.0 Hypersensitivity angiitis

OTHER

- http://www.kidney.org/atoz/content/glomerul.cfm

See Also (Topic, Algorithm, Media)

- Acute Kidney Injury, Adult (Renal Failure, Acute)
- Acute Kidney Injury, Pediatric (Renal Failure, Acute)
- Glomerulonephritis, Chronic

CLINICAL/SURGICAL PEARLS

- Dynamic IPI on microscopic urinalysis suggest the diagnosis.
- Prior penicillin- or skin infection suggests diagnosis of acute glomerulonephritis.
- With supportive care, recovery is usually rapid and complete with an excellent prognosis.
GLomerulonephritis, Chronic

Eric Langewisch, MD
John M. Barry, MD, FACS

DESCRIPTION
Chronic glomerulonephritis is the loss of renal function caused by damage to glomeruli.

PATHOPHYSIOLOGY (2)
• Damage to glomeruli, often mediated through immune/inflammatory mediators, leads to decreased filtering surface and nephron mass.
• Remaining glomeruli are subjected to increased filtration pressure. This results in hypertrophy or remaining glomeruli.
• Increased glomerular pressure causes progressive sclerosis of glomerular and interstitial fibrosis, and progressive loss of functioning glomeruli.

ASSOCIATED CONDITIONS
See Risk Factors

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Elevated plasma creatinine from loss of renal function (3)
• Prior plasma creatinine values may help determine rate of renal function deterioration

RISK FACTORS
• Family history of hereditary GN (Alport syndrome, thin COL4A5 syndrome)
• Some cases of hereditary GN or nephritis (Alport syndrome, thin COL4A5 syndrome)
• Increased glomerular pressure causes progressive sclerosis of glomerular and interstitial fibrosis, and progressive loss of functioning glomeruli.

DIAGNOSIS
BASICS
• Chronic glomerulonephritis is the loss of renal function caused by damage to glomeruli.
• Often mediated by inflammation and cellular proliferation.
• Frequently associated with hematuria and proteinuria.
• Many forms of glomerulonephritis (GN) present azotemia. Progression from acute to chronic GN is variable.
• IgA nephropathy is the most common type of GN.

RISK FACTORS
• Family history of hereditary GN (Alport syndrome, thin COL4A5 syndrome)
• Acute GN (focal segmental glomerulosclerosis, membranous GN, diabetic nephropathy, membranous GN)
• Other systemic diseases (diabetes mellitus, multiple myeloma, amyloidosis, Henoch–Schönlein purpura, polycystic kidneys, Wegener’s granulomatosis)
• Family history of hereditary GN (Alport syndrome, thin basement membrane disease)

GENETICS
Some cases of hereditary GN or nephritis (Alport syndrome caused by a mutation of COL4A5 gene, usually X-linked and more severe in men; thin basement membrane disease)

HISTORY
• Often asymptomatic
• Past acute kidney disease
• Signs of uremia

PHYSICAL EXAM
• May be unremarkable
• Weight loss
• Hypertension
• Volume overload
• Elevated jugular venous pressure, pulmonary rales, pedal edema
• Signs of anemia
• Acneiform
• Pericardial rub

IMAGING
• Renal ultrasound to assess kidney size and cortical volume
• Advanced disease is associated with decreased renal size, increased echogenicity, and cortical thinning
• Kidneys usually normal sized with diabet nephropathy

DIAGNOSTIC PROCEDURE/SURGERY
• Renal biopsy can potentially diagnose different glomerular diseases.
• Biopsy may not be helpful in advanced disease

PATHELOGIC FINDINGS
• Renal biopsy may determine type of glomerular disease by pattern of injury and immune complex staining.
• With advanced disease and small kidneys on ultrasound, biopsy frequently shows advanced sclerosis/scarring and may not be able to determine etiology.
GLOMERULONEPHRITIS, CHRONIC

DIFFERENTIAL DIAGNOSIS
- Arteriolosclerosis (for weight control)
- Chronic interstitial nephritis
- Diabetic nephrosclerosis
- Diuretic abuse
- Hypertensive nephrosclerosis
- Nephrotoxin exposure
- Obstructive uropathy
- Prerenal disease
- Renal artery stenosis

TREATMENT
GENERAL MEASURES
- See GENERAL PREVENTION
- Referral to nephrology
- Treat specific glomerular disease (eg, prednisone or other immunosuppressive agents)
- Control blood pressure
- Renal replacement therapy may be necessary long term

MEDICATION
First Line
- Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) slow the decline of the glomerular filtration rate (GFR) in patients with diabetic and nondiabetic proteinuric nephropathies
  - ACEIs: Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, quinapril, ramipril, others
  - ARB: Candesartan, eprosartan, irbesartan, losartan, telmisartan, valsartan
- Use may be limited by drug-induced hyperkalemia, increased plasma creatinine due to decreased glomerular pressure, or anemia

Second Line
- Diuretics to treat volume overload
- Additional antihypertensive agents to reach blood pressure goals
  - β-Blockers, calcium channel blockers, central α2-agonists (eg, clonidine), α1-antagonists, and direct vasodilators

SURGERY/OTHER PROCEDURES
- Access for dialysis
  - AV fistula or graft
- Hemodialysis access or peritoneal dialysis catheter
- Renal transplantation
- preemptive transplantation before dialysis results in better survival than transplantation after the initiation of dialysis

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
- Oral calcium supplements (1 g) and vitamin D (400–800 IU) for prophylaxis against osteoporosis
- Sodium bicarbonate has been shown to slow progressive kidney damage

COMPLICATIONS
- ESRD
  - Uremia
  - Volume overload
  - Hyperkalemia
  - Anemia
  - Acidosis
- Increased risk of cardiovascular disease
- Increased risk of mortality

FOLLOW-UP
Patient Monitoring
- Lab monitoring
  - Estimate glomerular filtration rate (GFR): BUN, plasma creatinine
  - Basic metabolic panel + phosphorous
  - Random urine protein/creatinine ratio
  - 24-hr urine protein
  - Blood pressure
  - Signs or symptoms of uremia

Patient Resources
- www.kidney.org/patients

REFERENCES

ADDITIONAL READING

CODES
ICD9
- 582.1 Chronic glomerulonephritis with lesion of membranous glomerulonephritis
- 582.89 Chronic glomerulonephritis with other specified pathological lesion in kidney
- 582.9 Chronic glomerulonephritis with unspecified pathological lesion in kidney

ICD10
- N03.2 Chronic glomerulonephritis w diffuse membranous glomerulonephritis
- N03.89 Chronic glomerulonephritis with other specified pathological lesion in kidney
- N11.9 Chronic tubulo-interstitial nephritis, unspecified
- N03.2 Chronic nephritic syndrome w diffuse membranous glomerulonephritis
- N03.89 Chronic nephritic syndrome with other specified pathological lesion in kidney
- N11.9 Chronic tubulo-interstitial nephritis, unspecified

CLINICAL/SURGICAL PEARLS
- Many cases of acute GN can progress to chronic GN
- ACEIs and ARBs can slow the decline of the GFR in patients with proteinuric nephropathies

See Also (Topic, Algorithm, Media)
GloboMerulonePhritis, Acute

N/A
GONORRHEA

Arpeet Shah, MD
Ahmer V. Farooq, DO

BASICS

DESCRIPTION
A sexually transmitted disease (STD) caused by the gram-negative diplococcal bacteria Neisseria gonorrhoeae.

EPIDEMIOLOGY
Incidence
- In the United States, gonorrhea remains the 2nd most commonly reported bacterial STD.
- The Center for Disease Control and Prevention (CDC) estimates 320,000 new cases per year with over half occurring in young adults aged 15–24.
- In 2011, CDC reported the rate of gonorrheal infections to be 104.2/100,000 persons, with over half occurring in young adults ages 15–24.
- Rates in the United States have drastically declined since the 1970s due to the public health measures.

RISK FACTORS
- Multiple sexual partners
- Unsafe sexual practices
- Alcohol and substance abuse
- Men who have 20–30% chance and women have a 70–80% chance after having 1 exposure

GENETICS
Individuals with inherited or acquired deficiency of complement components C3–C9 are more susceptible to localized and systemic gonococcal infections.

PATHOPHYSIOLOGY
- N. gonorrhoeae is not part of the normal flora of the genitourinary tract.
- Bacteria are introduced to the mucosal epithelial surface after direct contact with an infected individual.
- Attachment of the bacteria to the mucosal epithelium is mediated by pili (PilC1 and PilC2) and Opa proteins.
- Penetration of the organism into submucosal tissue usually takes 24–48 hr.
- Invasion of the epithelial triggers a strong response by neutrophils causing sloughing of epithelium, submucosal microabcesses, and purulent drainage.

ASSOCIATED CONDITIONS
- Always recommend testing for other STDs.
- Commonly associated with concomitant infection with Chlamydia trachomatis.

GENERAL PREVENTION
- Delaying onset of sexual activity and reducing the number of new partners.
- Conscientious condom use.

DIAGNOSIS

HISTORY
- Detailed history of sexual activity and partners.
- Incubation period of 3–14 days.
- Approximately 50% of infections in men are asymptomatic or mildly symptomatic; most common symptoms include dysuria and mucopurulent discharge.
- Approximately 50% of women have asymptomatic infection, most common symptoms include vaginal/cervical discharge, dysuria, urinary frequency, abdominal pain, and abnormal menstrual bleeding.
- Pregnancy does not change clinical presentation, but does lower incidence of pelvic inflammatory disease (PID).
- Anorectal infection is usually asymptomatic but can cause sore throat, pharyngitis and cervical adenitis.

PHYSICAL EXAM
- In men, mucopurulent urethral discharge may be seen; other signs include testicular/epididymal tenderness.
- In women, pelvic exam with speculum may demonstrate mucopurulent cervical discharge; other signs include cervical erythema, edema, and friability as well as cervical motion and adnexal tenderness.
- If suspecting anorectal infection, external inspection may reveal few or no signs of infection and anoscopy may be indicated with collection of specimens for culture.
- Pharyngeal cases may demonstrate exudative pharyngitis and cervical adenitis.
- Conjunctival cases demonstrate severe purulent discharge with crusting and lid edema.

DIAGNOSTIC TESTS & INTERPRETATION
Lab (2)
- Gram stain of urethral or endocervical discharge with a swab.
- Considered positive if neutrophils with intracellular gram-negative diplococci are visualized. Sensitivity and specificity of the Gram stain varies depending on the site of infection and the presence of symptoms.
- Culture has long been considered the gold standard for diagnosis.
- Advantages include high specificity and the ability to test for antibiotic sensitivity.
- Disadvantages include strict transport and storage requirements, specific environmental variables needed for growth (Thayer-Martin agar in CO2 incubator), and delays in obtaining results. Culture is the test of choice for extragenital sites of infection.
- Nucleic acid amplification test (NAAT) use molecular techniques to amplify specific DNA and RNA sequences.
- Advantages include higher sensitivity and comparable specificities of culture, minimal delay in results, noninvasive and self-collected samples, and identification of coinfections.
- Disadvantages include inability to screen for antimicrobial sensitivity. CDC now recommends NAAT as the 1st-line diagnostic test for uncomplicated urogenital gonorrheal infection.

Imaging
- Not indicated in uncomplicated cases.
- Computed tomography or pelvic ultrasonography if pelvic inflammatory disease (PID) or pelvic abscess suspected.
- Retrograde urogram if urethral stricture suspected.

Pathologic Findings
- Gram stain demonstrates gram-negative diplococci found inside of polymorphonuclear cells.

DIFFERENTIAL DIAGNOSIS (3)
- Other genitourinary infections including C. trachomatis, Trichomonas vaginalis, Mycoplasma genitalium, and Ureaplasma urealyticum, herpes simplex virus, bacterial vaginosis, and candidiasis.
- Also consider noninfectious sources such as foreign body, chemical irritation, allergic reaction, trauma, carcinoma, and leukоecytosis of pregnancy.
- For women who present with suspected PID, must rule out ectopic pregnancy and other intra-abdominal processes such as appendicitis.
**TREATMENT**

**GENERAL MEASURES**
- Patients with suspected active infection should abstain from sex until diagnosed and adequately treated.
- All sexual partners who have contacted the infected patient within 60 days of diagnosis should also be evaluated.
- Treatment with penicillin and tetracycline are not effective due to the high level of penicillinase-producing bacteria and poorly-mediated high-level tetracycline-resistant bacteria.

**Over the last decade, increasing mean minimum inhibitory concentrations of selective cephalosporins have indicated decreasing susceptibility and have impacted current treatment recommendations.**

- Macrolide resistance has also been reported.
- Fluoroquinolone resistance has impacted treatment options and is most prevalent in the states of California and Hawaii.
- Macrolide resistance has also been reported.

**MEDICATION**

**First Line (4)**
- For uncomplicated cases of urethral and endocervical gonorrheal infection, patients must also be treated for concomitant chlamydia infection unless diagnosed and adequately treated.
  - Ceftriaxone 250 mg IM in 1 dose PLUS azithromycin 1 g PO in 1 dose is the current gold standard.
  - Ceftriaxone 500 mg IM in 1 dose, cefotaxime 1 g IM in 1 dose, or cefuroxime 2 g IM with probenecid 1 g PO in 1 dose are alternatives for ceftriaxone.
  - If an injectable cephalosporin is not an option, alternatives include cefixime 400 mg PO in 1 dose or ceftazidime 400 mg PO in 1 dose. However, patients who receive these options should return in 1 week for microbiologic test of cure with culture.
  - Doxycycline 100 mg BID PO for 7 days is an alternative for ceftriaxone.

**Second Line**
- The management of those with a penicillin allergy depends on clinical suspicion of true allergy and the severity of the allergy.
- Most patients with documented penicillin allergy are not found to have an allergy after further testing and only 2% of those with a penicillin-positive skin test are true reactors.
  - Azithromycin 2 g PO in 1 dose monotherapy treats gonorrhea and syphilis, however, due to GI side effects and growing macrolide resistance, it is not a preferred regimen unless the patient has a severe penicillin allergy.
  - Spectromycin 2 g IM in 1 dose is a safe and effective alternative therapy for those with severe penicillin allergies, but is only available outside the United States.
  - Quinolones were once a 2nd line therapy, but due to drug resistance in 10–100% of strains depending on location, they are no longer recommended for the treatment of gonorrhea.

**SURGERY/OTHER PROCEDURES**
- Chronic gonorrhreal infection may lead to bulbar urethral strictures requiring urologic intervention.
- Gonorrhreal abscesses may require incision and drainage procedures.

**ADDITIONAL TREATMENT**
- Patient compliance regarding safe sex practices and abstinence for 7 days following treatment initiation.
- Patients should also be offered additional STD testing and pregnancy testing.

**Pregnancy considerations**
- Most common symptoms include mucopurulent discharge and dysuria. Especially in patients who are in their 20s.
- Maintain a high degree of suspicion for gonorrhea.
- In females, can cause PID leading to chronic pelvic pain, ectopic pregnancy, and infertility.
- Genital abscesses may occur in either sex requiring surgical intervention.
  - Fitz-Hugh-Curtis Syndrome – perihepatitis characterized by acute right or bilateral upper quadrant tenderness – may occur in either sex.
  - Urethral strictures requiring urologic intervention.

**COMPLICATIONS**
- Ocular infection with gonorrhea in adults may lead to corneal scarring and vision loss.
- Genital abscesses may occur in either sex requiring surgical intervention.
- Pelvic pain, Female
  - In females, can cause PID leading to chronic pelvic pain, ectopic pregnancy, and infertility.
  - Genital abscesses may occur in either sex requiring surgical intervention.

**ONGOING CARE**

**PROGNOSIS**
- 95% of uncomplicated genitourinary gonorrheal infections are cured by 1 course of treatment.

**CLINICAL/SURGICAL PEARLS**
- Maintain a high degree of suspicion for gonorrhea, especially in patients who are in their 20s.
- Most common symptoms include mucopurulent discharge and dysuria.
- Culture has been the gold standard for diagnosis, however, it is now being widely used as a 1st line diagnostic modality.
- 1st line treatment includes ceftriaxone 250 mg IM in 1 dose PLUS azithromycin 1 g PO in 1 dose.
- Antibiotic susceptibilities continue to change and vary by geographical location.
- Always counsel patients regarding safe sex practices.

**REFERENCES**


**ADDITIONAL READING**

www.cdc.gov/std/Gonorrhea/STDFact-gonorrea.htm
See Also (Topic, Algorithm, Media)
- Epidemiology
- Gonorrhea Image 4
- PID
- Gonorrhea Image 3
- Sexually Transmitted Infections (STIs) STDs, General
- Urethra, Discharge
- Urethritis

**CODES**

ICD-9
- 098.11 Gonococcal cystitis (acute)
- 098.12 Gonococcal prostatitis (acute)
- A54.01 Gonococcal cystitis and urethritis, unspecified
- A54.22 Gonococcal prostatitis

ICD-10
- A54.00 Gonococcal infection of lower genitourinary tract
- A54.01 Gonococcal cystitis and urethritis, unspecified
- A54.02 Gonococcal prostatitis

ICD-11
- Gonococcal infection of lower genitourinary tract

**PEARLS**
- Prevented by routine screening for endocervical infection during pregnancy and prophylactic use of erythromycin ophthalmic solution.

**GONORRHEA**
GROIN/INGUINAL MASS, MALE AND FEMALE
Edouard J. Trabulsi, MD, FACS

ASSOCIATED CONDITIONS
- Chronic increased intra-abdominal pressure.
- STIs associated with lymphadenopathy.
- Penile cancer.

GENERAL PREVENTION
- Avoid chronic increase in intra-abdominal pressure that may encourage hernia formation.
- Avoid STIs.

DIAGNOSIS

HISTORY
- Onset of the mass (age, activity) and any associated symptoms.
- Family history of cryptorchidism.
- History of presence or absence of testes in the scrotum.
- History of pain or absence of tests in the scrotum, combined with tests in the scrotum.
- Evidence of adenopathy elsewhere, to suggest related lymphadenopathy.

PHYSICAL EXAM
- Patient should be examined in standing position.
- A cough impulse usually suggests an inguinal hernia.
- Transillumination test, if positive, may suggest a hydrocele.
- Tender testis suggests epididymitis, testicular torsion, or appendicitis.
- Absent testis suggests undescended testes.
- Ulceration may suggest a sexually transmitted disease.
- Groin tenderness: Likely infection is the etiology.

DIFFERENTIAL DIAGNOSIS
- Cryptorchidism.
- Inguinal hernia.
- Lymphadenopathy.
- Neoplasms, Trauma, Infections, Vasculitis, Vasculitis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab:
- Blood tests:
  - Full blood count and ESR
  - Renal function tests and electrolytes
  - Syphilis serology, if indicated
  - HIV serology, if indicated
  - LSG (lymphangiography/wirework) serologic test, if suspected
- Swab and culture the base of any lesions to diagnose genital herpes, syphilitic ulcer, chancroid (Nesseriofila ducreyi).

Imaging (2):
- US can confirm hernia and help to see the tests within the inguinal canal. Not sensitive for intra-abdominal tests.
- Doppler US for vascular conditions (Valsava maneuver should be performed during exam).
- CTVUS can diagnose obscure hernias. Also can identify related lymphadenopathy.
- Arteriography may help diagnose femoral artery aneurysm.
- Viscoscopy or Doppler US will help diagnose saphenous veins.

Diagnostic Procedures/Surgery
- Laparoscopy: Can be diagnostic and therapeutic for hernia and intra-abdominal tests.
- Exploratory surgery is necessary in many cases for both diagnosis and treatment.
- Femoral nerve block or fine needle aspiration (FNA) for definitive diagnosis of lymphadenopathy.
- Chromosomal and hormonal analysis in relation to bilateral undescended testes.

Pathologic Findings
- Cryptorchidism:
  - Decreased number of Leydig and Sertoli cells
  - Failure to develop primary spermatocyte
- Peritubular fibrosis
- Lymphadenopathy:
  - Can be metastatic or inflammatory cause.

ACRONYMS
- MINT
- Viral hepatitis
- Mumps
- Clinical findings
- Nephrotic syndrome
- Trauma
- Viral hepatitis
- Mumps
- Nephrotic syndrome
- Trauma
- Sexual contact or endogenous
- Rape
- Vascular injury
- Etiological

RAINFALL
- Scrotal:
  - Spermatocele
  - Varicocele
- Femoral:
  - Femoral artery aneurysm
  - Femoral nerve block
  - Femoral hernia
  - Femoral vein thrombosis

REFERENCES


**TREATMENT**

**GENERAL MEASURES**  
Management is based on the cause of the mass and can vary from antibiotic therapy, biopsy, or further imaging for more extensive adenopathy.

**MEDICATION**

**First Line**  
- **Infectious:**  
  - Infection requires treatment with specific antibiotics.  
  - For STD-related adenopathy, see specific chapter.

**Second Line**  
- **Hydrocele:**  
  - Self-exam for testicular masses
  - Requires follow-up for fertility
  - Increased risk of trauma and torsion
  - Malignancy: Increased risk of malignancy in absence of treatment

**SURGERY/OTHER PROCEDURES**

- **Cryptorchidism:**  
  - Treatment varies based on testis location
  - Surgeon preference
  - Corrective surgery does not reduce the chances of malignancy

**COMPLICATIONS**

- **Hernia:**  
  - Congenital hernias are repaired by ligating the processus vaginalis
  - Testicular Torsion
  - Self-exam for testicular masses
  - Hernia, for recurrence

**COMPLICATIONS**

- **Lymphadenopathy:**  
  - Infection requires treatment with specific antibiotics
  - Biopsy: If the mass is reducible, strongly suggests a hernia

**PROGNOSIS**

- Depends on the etiology of the mass

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- N/A

**ADDITIONAL THERAPIES**

- Complementary & Alternative Therapies
  - N/A

**ONGOING CARE**

- **Lymphadenopathy:** Requires follow-up for chronic infection, response to treatment.

**CLINICAL/SURGICAL PEARLS**

- The differential diagnosis varies greatly by the age of the patient.
- If the mass is reducible, strongly suggests a hernia.

**TREATMENT**

**GENERAL MEASURES**

- Management is based on the cause of the mass and can vary from antibiotic therapy, biopsy, or further imaging for more extensive adenopathy.

**MEDICATION**

**First Line**

- **Infectious:**  
  - Infection requires treatment with specific antibiotics.
  - For STD-related adenopathy, see specific chapter.

**Second Line**

- **Hydrocele:**  
  - Self-exam for testicular masses
  - Requires follow-up for fertility
  - Increased risk of trauma and torsion
  - Malignancy: Increased risk of malignancy in absence of treatment

**SURGERY/OTHER PROCEDURES**

- **Cryptorchidism:**  
  - Treatment varies based on testis location
  - Surgeon preference
  - Corrective surgery does not reduce the chances of malignancy

**COMPLICATIONS**

- **Hernia:**  
  - Congenital hernias are repaired by ligating the processus vaginalis
  - Testicular Torsion
  - Self-exam for testicular masses
  - Hernia, for recurrence

**COMPLICATIONS**

- **Lymphadenopathy:** Infection requires treatment with specific antibiotics. Biopsy: If the mass is reducible, strongly suggests a hernia.

**PROGNOSIS**

- Depends on the etiology of the mass

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- N/A

**ADDITIONAL THERAPIES**

- Complementary & Alternative Therapies
  - N/A

**ONGOING CARE**

- **Lymphadenopathy:** Requires follow-up for chronic infection, response to treatment.

**CLINICAL/SURGICAL PEARLS**

- The differential diagnosis varies greatly by the age of the patient.
- If the mass is reducible, strongly suggests a hernia.

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- Cryptorchidism
- Groin Hernia
- Groin Inguinal Mass Image
- Penis Cancer, General
- Sexually Transmitted Infections (STIs) (Sexually Transmitted Diseases)
## GYNECOMASTIA

**Samuel Walker Nickles**

**James S. Rosoff, MD**

### BASICS

**DESCRIPTION**
- Gynecomastia (GM) is benign enlargement of the male breast due to proliferation of ductal elements.
- Pseudogynecomastia/aplasia is an increase in breast adipose tissue. This can be distinguished by careful physical exam of subareolar tissue and comparison to adjacent adipose tissue.

**EPIDEMIOLOGY**
- Incidence (1)
  - Approximately 2,000 cases of male breast cancer are diagnosed in the United States annually
  - Prevalence
    - 30–65% of men have palpable breast tissue and at autopsy 40–55% of men have histologic evidence of GM
  - Age related: Asymptomatic GM is 60–90% in neonates, 50–60% in adolescents, and up to 70% in men aged 50–69 yr

**RISK FACTORS**
- Alcoholism
- Endocrinopathies
- Medications
- Obesity
- Renal failure

**Genetics**
- Klinefelter syndrome (47, XXX) is strongly associated with GM
- An increased risk of male breast cancer has been reported in families with a BRCA2 mutation

**PATHOPHYSIOLOGY**
- Male breast tissue has both androgen and estrogen receptors.
- Androgens inhibit breast development and estrogens stimulate it. GM develops when there is an imbalance of these two influences (ie, androgen deficiency or excess estrogen) or lack of tissue response to them.

**ASSOCIATED CONDITIONS**
- Prostate cancer
- Testicular tumors
- Carcinoma
- Renal failure

**GENERAL PREVENTION**
- With hormonally induced GM, prophylactic breast insufflation may reduce GM

---

### DIAGNOSIS

**HISTORY**
- Age of patient and onset of symptoms (pubertal, GM of aging)
- Associated bruises or chills, breast trauma, nipple discharge
- Medical conditions (cirrhosis, chronic kidney disease, HIV, hyperthyroidism)
- Medications/drugs
- History of cryptorchidism
- Sexual history. Sexual maturation, changes in libido, erectile dysfunction, infertility

**PHYSICAL EXAM**
- General appearance, weight, amount of adipose tissue (contains aromatase capable of peripheral conversion of androgens to estrogen)
- Secondary sexual characteristics such as body hair distribution and phallic size
- Breast exam
  - Breast exam: Special attention should be paid to distinguish true GM from pseudogynecomastia (unilateral vs. bilateral) If unilateral should be concerned for potential male breast cancer), firm and mobile vs. fixed, skin dimpling, any nipple discharge, position of axillary lymph nodes
- Genitourinary exam with special attention to the testicular exam

**DIAGNOSTIC TESTS & INTERPRETATION**
- Lab
  - Basic studies: Creatinine, LFTs, thyroid function tests, serum testosterone
  - Further testing as needed
    - Serum estradiols (estradiol, estrogen)
    - LH, FSH, prolactin
    - Tumor markers: AFP, β-hCG
    - Adrenal androgens, serum DHEA, urinary 17-ketosteroids

**Imaging**
- Nuclear US if abnormal tumor markers
- CT of the abdomen and pelvis if abnormal levels of adrenal androgens
- Mammography if cancer suspected

**Diagnostic Procedures/Surgery**
- Breast biopsy for suspected breast cancer

**Pathologic Findings**
- Proliferation of ductules embedded in a connective tissue stroma
- Over about 12 months, the breast tissue evolves into a quiescent stage, in which the amount of stroma and fibrous increases and the ductules become less prominent. glandular acini are rare (2)

**DIFFERENTIAL DIAGNOSIS**
- Physiologic GM Normal in neonatal boys secondary to maternal estrogen exposure.
- Occurs in 60–90% of neonatal boys and resolves within several weeks after delivery.
- Pubertal GM results from the earlier rise in estrogens in early puberty. As the normal ratio of estrogen to testosterone is restored later in puberty the GM resolves.
- 50–70% of boys develop GM during puberty. 25% of men still have GM at 20 yr of age.

**GM of aging:**
- The hypothalamic–pituitary–testicular axis is variable in age-related decline. Some men have elevated gonadotropins while others will be normal.
- Adiposity increases with age which leads to increased peripheral conversion.
- Sex hormone–binding globulin (SHBG) levels rise with age and decreasing bioavailable testosterone.
- Medications may also play a part in GM in older men.

- Testosterone secreting tumors:
  - Leydig cell tumors are rare tumors of the testis; 85–90% are benign, most are nonpalpable. Some Leydig cell tumors can directly secrete estrogens. This increases estrogen levels and inhibits LH secretion, suppressing testicular production of testosterone.
  - Seminal cell tumor: Converts androgens to estrogens leading to a direct increase in circulating levels of estrogens.
  - Remaining adrenal cortical tumors are generally malignant and poorly differentiated. These cancers directly secrete estrogens as well as steroid precursors that may be aromatized to estrogens in peripheral tissues. Increased estrogen suppresses LH-mediated production of testosterone as well.

- HCG-secreting tumor such as choriocarcinoma stimulates Leydig cells to preferentially secrete estrogens. Many HCG-secreting tumors also will take up steroid precursors such as DHEA and convert them to active estrogens.

- Increased peripheral aromatization to estrogens:
  - Familial estrogen excess syndrome. The enzyme aromatase (P450 arom or CYP19A1) catalyzes the conversion of steroidal precursors to estrogens.
  - Estrogen receptor agonists:
    - Therapeutic administration of estrogens such as DES (diethylstilbestrol) may be used to treat men with prostate cancer and can lead to GM.
    - Estrogens may also be used to stimulate breast development in male-to-female transsexuals.
    - Unintentional exposure may occur transnationally by sexual intercourse with a partner that uses topical estrogens. Occupational exposure is also possible. Estrogens can be found in hair creams, embalming creams, and in the production of medicinal estrogen products.
  - Marijuana smoke, digoxin, testosterone, or other aromatizable androgens.

- Androgen deficiency or resistance:
  - Primary or secondary hypogonadism: Testicular failure from any cause may result in GM. Testosterone deficiency leads to elevated LH which increases extralateral production by remaining Leydig cells. Increased estrogens lead to elevated levels of SHBG, further decreasing free testosterone.
  - Klinefelter syndrome is the most common genetic disorder associated with hypogonadism and infertility in men. GM is present in 50–70% of cases. Klinefelter syndrome is the only cause of GM with an established risk of breast cancer (20-fold increase).

- Deficits in genes critical for testosterone production may also lead to decreased testosterone production.
Gynecomasia

• Androgen resistance disorders:
  – In both partial and complete androgen insensitivity syndrome, cellular response to androgens is inadequate (elevated gonadotropins and increased serum testosterone) due to lack of negative feedback.

• Refeeding associated GM:
  – Recognized after WW II when imprisoned men resumed normal diets and developed tender GM. Starvation is associated with hypogonadotropic hypogonadism. With resumption of a healthy diet and regaining weight the hypothalamic-pituitary-testes axis returns to normal, resulting in transient estrogen excess. May also explain GM associated with several chronic diseases.

• Renal failure:
  – Many men with chronic kidney disease develop GM upon initiation of hemodialysis. Before initiation of diuretics are often nauseaed, anorexic, and on protein-restricted diets. The pathogenesis is thought to be similar to refeeding GM.

• Cirrhosis:
  – Studies have shown that the prevalence of GM in cirrhosis is no different than hospitalized age-matched controls. Hormonal changes in cirrhotic liver disease may increase the risk of GM.

• With longstanding GM, or those that refuse medical therapy:
  – Removal of the offending drug or exogenous source of estrogen if possible
  – Adrenal tumors: Adrenalectomy
  – Testosterone replacement therapy in androgen-deficient men may result in partial regression of GM, especially if breast enlargement is of recent onset.

• Breast cancer:
  – Dose: 12 Gy in 2 fractions to 20 Gy in 5 fractions
  – Suspicious lesions should be biopsied.

• Hypothyroidism:
  – With longstanding GM, or those that refuse medical therapy:
  – Aromatase inhibitors such as testolactone and anastrozole have been used but not proven as effective as tamoxifen.
  – Tamoxifen, 10 and 20 mg/d, for 3–9 mo with 90% resolution. Additionally, raloxifene and clomiphene citrate have also been used.

• Breast cancer:
  – Increased serum prolactin: Antipsychotic agents, amphetamines, diazepam, antidepressants (tricyclics and SSRIs).

• Gastrointestinal:
  – PUD:
  – Radiation Therapy
  – Metoclopramide.

• Alcohol abuse:
  – Androgen receptor blocker: Flutamide, bicalutamide, raloxifene, tamoxifen, spironolactone.

• Medications:
  – Diabetes Mellitus:
  – HIV:
  – Hyperthyroidism:
  – Cirrhosis:
  – Renal failure:
  – Refeeding associated GM:

• Androgen receptor blocker: Flutamide, bicalutamide, raloxifene, tamoxifen.

• Increased serum prolactin: Antiproliferotic agents, oestrosapride.

• Possible: Refeeding GM, scrotalized, androgen insensitivity. Known as: HAART, human growth hormone, anabolic agents, anabolic agents, antiandrogens, antipsychotics, antidepressants (tricyclics and SSRIs).

• Breast cancer:
  – Rare in men, are similar to those of female breast cancer.
  – A hard fixed mass, ulceration, bloody nipple discharge, or lymphadenopathy should raise suspicion.

• Suspsicious lesions should be biopsied.

• Median age of onset is thought to be 50 yrs.

• Complementary & Alternative Medicine:
  – Glutamine, Probiotics, St. John’s Wort, CoQ10.

• Radiation Therapy
  – Prophylactic breast irradiation has been used prior to initiation of estrogens or androgen blockade for blockade for prostate cancer patients.

• Second Line
  – Aromatase inhibitors such as testolactone and anastrozole have been used but not proven as effective as tamoxifen.

• Testosterone replacement therapy in androgen-deficient men may result in partial regression of GM, especially if breast enlargement is of recent onset.

• SURGERY/OTHER PROCEDURES
  – With longstanding GM, or those that refuse medical treatment, cosmetic surgical excision and reconstruction may be performed

• Adrenal tumors: Adrenalectomy

• ADDITIONAL TREATMENT

• Radiation Therapy
  – Prophylactic breast irradiation has been used prior to initiation of estrogens or androgen blockade for blockade for prostate cancer patients.

• Additional Therapies
  – Radioactive oral ibutrol or propylthiouracil for hypothyroidism.

• Complementary & Alternative Therapies

• N/A

ONGOING CARE

PROGNOSIS

• Generally favorable prognosis.

• Patient main concerns: Ruling out breast cancer and cosmetic correction.

COMPLICATIONS

Psychological stress

FOLLOW-UP

Patient Monitoring

No regular follow-up is necessary for patients who have physiologic GM and are untroubled by their symptoms and do not have symptoms suggestive of malignancy.

Patient Resources

N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

• Gynecomasia Algorithm

• Gynecomastia Image ID

• Infertility Male Syndrome

• Testicular Leydig Cell Tumor

• Testosterone, Decreased (hypogonadism)

• XXY Syndrome (Klinefelter Syndrome)

CODES

ICD9

• 278.00 Obesity, unspecified

• 611.1 Hypertrophy of breast

• 758.7 Klinefelter’s syndrome

ICD10

• E66.8 Obesity, unspecified

• N82 Hypertrophy of breast

• Q88.4 Klinefelter syndrome, unspecified

CLINICAL/SURGICAL PEARLS

• Breast cancer is rare in males, representing ~1% of all cases of breast cancer.

• Klinefelter syndrome is the only cause of gynecomastia with an established risk of breast cancer.

171
Hematospermia

Robert L. Segal, MD, FRCS(C)
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION
- Hematospermia (sometimes referred to as hemospermia) as the presence of visible blood (foul or altered) in the ejaculate (not specified with regard to how many episodes or overall duration).
- Semen can be described as bright red, coffee-colored, rusty, or darkened; appearance may change as blood ages.
- May occur as a single episode or persist chronically.
- Usually a self-limited and benign condition.

EPIDEMIOLOGY
Incidence
- Accounts for 0.02% (1/5,000) new patient visits to a urology clinic; seen in 0.5% of men presenting for prostate cancer screening [1].
- Mean presenting age of 57 yr old.
- Mean duration is 1–24 mo.
- In men <40 yr old, cause is almost always due to an inflammatory or infectious process.
- Only 2.4–3.5% of cases of hematospermia result in the diagnosis of a malignancy, typically >40 yr old.

Prevalence
Not truly known

RISK FACTORS
- Recent genitourinary trauma, surgery (prostate biopsy), infection
- Prostatic, bacterial
- Prolonged abstinence from or frequent ejaculation
- Use of anticoagulant medication
- Systemic coagulopathy/bleeding disorder
- Use of anticoagulant medication
- Any cause of bleeding

Genetics
None

PATHOPHYSIOLOGY
- Often occurs in isolation
- Pathophysiologic causes include:
  - Inflammatory and infection
  - Ductal obstruction and cysts of the accessory sexual glands
  - Neoplasms
  - Vascular abnormalities
  - Systemic factors
  - Inherited factors

ASSOCIATED CONDITIONS
- Nonmalignant prostatic disease (26%)
- Hypertension (HTN) (15%)
- Genital tuberculosis (TB) (11%)
- Prostate cancer (1%)

GENERAL PREVENTION
None known

DIAGNOSIS

HISTORY
- Duration and amount of bleeding
- Sexual history/frequency
  - Sexual history/frequency
  - Sexual behavior: synchronous or diurnal
  - Isolated episodes or periods of abstinence or after frequent ejaculation
  - Associated voiding disorders
    - Hematuria
    - Dysuria
    - Urethral discharge
  - Fever
  - INR for patients on coumadin
  - Liver disease
  - Neurologic conditions
  - Fatigue
  - LUTS

PHYSICAL EXAM
- Assess blood pressure (BP)
- Abdominal exam for masses
- Perineal/rectal:
  - Proctoscopy
  - Rectal examination
- Surgical:
  - Axillae
  - Induration may indicate TB
- Abnormal stool:
  - Hematuria
  - Metastatic disease
  - Hemorrhoids

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- urine culture (for acid-fast bacilli and parasites if indicated)
- Serum white cell count and coagulation profile (international normalized ratio [INR])
- Complete blood count (CBC) if blood dyscrasia
- Suspected: stool for patients on coumadin
- Tuberculin skin test should be considered, particularly in patients with exposure history or if originate from or recent travel to endemic areas.
- Serum analysis can be used to confirm diagnosis of true hematospermia and, in case of schistosomiasis, eggs may be noted. If performed, semen culture should also be sent.
- Urine cultures/urine samples for the diagnosis of sexually transmitted infection if indicated.
- In patients >40 yr or with risk factors for prostate or bladder malignancy:
  - Prostate serum antigen (PSA)
  - Urine cytology
- Imaging
  - Transrectal ultrasound (TRUS) of the prostate:
    - To evaluate the prostate, seminal vesicles (SV’s), and possible Mullerian duct remnants
    - To evaluate the prostate, seminal vesicles (SV’s), and possible Mullerian duct remnants
  - Magnetic resonance imaging (MRI): facilitates diagnostic procedures such as biopsy, puncture
- Should be 1st imaging study for hematospermia
- Ultrasound:
- Renal ultrasound:
  - For the kidneys, ureters, and bladder:
  - Cross-sectional or endorectal coil MRI may be obtained
- Should be used if TRUS is not diagnostic or if TRUS is equivocal
- Cross-sectional or endorectal coil MRI may be obtained
- Diagnostic Procedures/Surgery
- Indicated for patients with evidence of tumor or infection
- Cystoscopy:
  - Allows visualization of urethral inflammation and opening of ejaculatory ducts
- Critical for ruling out urothelial carcinoma

Pathologic Findings

Risk

LABORATORY

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- urine culture (for acid-fast bacilli and parasites if indicated)
- Serum white cell count and coagulation profile (international normalized ratio [INR])
- Complete blood count (CBC) if blood dyscrasia
- Suspected: stool for patients on coumadin
- Tuberculin skin test should be considered, particularly in patients with exposure history or if originate from or recent travel to endemic areas.
- Serum analysis can be used to confirm diagnosis of true hematospermia and, in case of schistosomiasis, eggs may be noted. If performed, semen culture should also be sent.
- Urine cultures/urine samples for the diagnosis of sexually transmitted infection if indicated.
- In patients >40 yr or with risk factors for prostate or bladder malignancy:
  - Prostate serum antigen (PSA)
  - Urine cytology
- Imaging
  - Transrectal ultrasound (TRUS) of the prostate:
    - To evaluate the prostate, seminal vesicles (SV’s), and possible Mullerian duct remnants
    - Magnetic resonance imaging (MRI): facilitates diagnostic procedures such as biopsy, puncture
- Should be 1st imaging study for hematospermia
- Ultrasound:
  - Renal ultrasound:
    - For the kidneys, ureters, and bladder:
    - Cross-sectional or endorectal coil MRI may be obtained
- Should be used if TRUS is not diagnostic or if TRUS is equivocal
- Cross-sectional or endorectal coil MRI may be obtained
- Diagnostic Procedures/Surgery
- Indicated for patients with evidence of tumor or infection
- Cystoscopy:
  - Allows visualization of urethral inflammation and opening of ejaculatory ducts
  - Critical for ruling out urothelial carcinoma

Pathologic Findings

Risk
DIFFERENTIAL DIAGNOSIS

- Infections:
  - Caused by SVs, prostate, or urethra
  - Prostatitis
  - Urethritis
  - Proctitis
  - Urethral infections
  - Viral
  - Herpes simplex
  - Cytomegalovirus
  - Human papilloma virus/cytomeblyoma
  - Bacterial
  - TB
  - Chlamydial trachomatis
  - Gonorrhea
  - Syphilis
  - Parasitic
  - Chlamydia
  - Mycobacterial disease (Tuberculosis)
  - Ductal obstruction and ots of accessory glands:
    - Epididymal duct cysts
    - SV diverticulum
    - Urethral structure
    - Urethral ots
    - Wolffian duct ots
    - Prostatic ots
  - Neoplasms:
    - Benign
      - Prostatic cysts
      - Wolffian duct cysts
      - Utricular cysts
      - Urethral stricture
      - Ejaculatory duct cyst
    - Malignant
      - Prostatic adenocarcinoma
      - Prostatic ductal adenocarcinoma
      - Adenocarcinoma of the SV
      - Adenocarcinoma, sarcoma, stromal tumor, lymphoma, malakoplakia
      - SV adenocarcinoma, squamous cell carcinoma, malakoplakia, metastases to prostate or SVs (metastatic melanoma to the SVs or prostate, may result in melanospermia)
      - Urethra
      - Testes

- Epididymal Mesotheloma
- Vascular abnormalities
  - Arteriovenous malformations
  - Prostatic varicosities
  - Hemangiomata
- Systemic factors
  - Renal insufficiency conditions
  - Hemophila
  - Von Willebrand disease
  - HIV
  - Chronic liver disease
  - Amyloidosis of the SVs
- Iatrogenic causes
  - Prostate biopsy (most common)
  - Genitourinary (GU) instrumentation
  - Extraperitoneal shock wave lithotripsy (ESWL) of distal urotheal stones
  - Radiotherapy (occurs in 28% of seed cases)
  - Prostate radiation
  - MRI
  - Postbiopsy (vasoogenitum vasa)
  - Postrectotomy

TREATMENT

GENERAL MEASURES

- If an underlying cause is identified (ie, bleeding disorder, GU TB, chlamydia infection), initiate appropriate medical management.
- Patients should be made aware that this is very common after prostate biopsy
- Spontaneous hematospermia is rarely associated with malignancy
- Most commonly a benign condition that resolves spontaneously and reassurance is appropriate

MEDICATION

First Line

- In men ≤40 yr old without an obvious cause of hematospermia after workup (normal physical exam, negative urine studies):
  - Reassurance and expectant management
  - Empiric antibiotic therapy with doxycycline or fluoroquinolone
  - Trial of 5α-reductase inhibitor (finasteride, dutasteride) for 3 mo (3C)
- While a similar approach can be taken in men >40 yr old, diagnostic workup should be more exhaustive and prostate biopsy should be considered if PSA or DRE indicates.

Second Line

SURGERY/OTHER PROCEDURES

- Prostatic calculi: Transurethral resection
- Cystoscopic resection of any lesions seen on exam
- Prostatic calculi: Transurethral incision
- Epididymal mesothelium: Removal
- Urethral adenoma:
  - Transperineal or transurethral approaches
  - Interferon or surgery
- SVs or prostate, may result in melanospermia

Additional Treatment

RADIATION THERAPY

ADDITIONAL READING


SYMPTOMS

- Patients should be reassured, as should their partners.
- A significant number of cases remain idiopathic even after a full workup.
- Hematospermia following prostate biopsy may take several months to clear.

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostate Biopsy: Infections and Complications

FOLLOW-UP

Patient Monitoring

- Follow PSA in older patients, as per prostate cancer screening recommendations

Patient Resources

- N/A

CODES

- ICD9
  - 588.9 Other unspecified coagulation defects
  - 601.9 Prostatitis, unspecified
  - 608.82 Hematospermia

- ICD10
  - D48.9 Coagulation defect, unspecified
  - N41.9 Inflammatory disease of prostate, unspecified
  - R86.1 Hematospermia

- CLINICAL/SURGICAL

- Pearls

- Hematospermia is usually a benign and self-limited condition, particularly in men <40 yr old.
- It is often resolve spontaneously in all age groups.
- Work-up only indicated if persistent or if other associated symptoms (such as hematuria).
- Expected symptoms following prostate biopsy and can last for several weeks.
- Treatment should be directed toward underlying cause if identified.

- Outcomes

- N/A

- Prostate Biopsy: Infections and Complications
HEMATURIA, GROSS AND MICROSCOPIC, ADULT

Megan M. Merrill, DO
Surena F. Matin, MD, FACS

BASICS

DESCRIPTION
- Hematuria may be gross (GH) (visible) or microscopic (MH).

RISK FACTORS (5)
- Male gender
- Age
- History of irritative voiding symptoms
- Recent febrile illness
- Pelvic radiation

EPIDEMIOLOGY
Incidence
- Incidence of various disorders in patients who present with MH or GH: (3)
  - No diagnosis — 64.5%
  - UTI — 13%
  - Bladder cancer — 12%
  - Renal disease — 9.8%
  - Stone disease — 3.6%
  - Renal cancer — 0.6%
  - Prostate cancer — 0.4%
  - Upper tract cancer — 0.1%

Prevalence
- Prevalence of asymptomatic MH varies with age and gender, and ranges from 0.19–21% (4).

PATHOPHYSIOLOGY
- Macroscopically:
  - Blood clots that have a vermiform (worm-like) appearance suggest the origin of hematuria to be the upper tract.
  - Blood clots that are amorphous suggest the origin to be the lower urinary tract—bladder or prostate.
- On microscopic analysis:
  - RBCs in the urine that are isomorphic and have smooth, round membranes and uneven hemoglobin distribution suggests urologic disease.
  - RBCs that are dysmorphic with irregular shapes and uneven hemoglobin distribution suggests glomerular disease.

ASSOCIATED CONDITIONS
- Neoplasms
- UTI
- Glomerulonephritis
- Anatomic abnormalities of urinary tract (eg, UPJ obstruction)
- Benign prostatic enlargement

GENERAL PREVENTION
- Adequate fluid intake, especially for patients with history of calculi
- Smoking cessation
- Occasional/infrequent consumption of alcohol

DIAGNOSIS

HISTORY
- Age and sex: Age >35, bladder cancer is the most common cause of hematuria, urologic cancer is more common in males; females may have vaginal bleeding (4).
- Timing of GH during urinary stream:
  - Initial hematuria—anterior urethral pathology
  - Terminal hematuria—bladder neck, prostate, or urethra inflammation/pathology
  - Hematuria throughout—vesical or upper-tract origin

- Associated pain:
  - Painless hematuria suggests bladder cancer
  - Flank pain, GH, and abdominal mass is pathognomonic of renal cell carcinoma
  - Unilateral or bilateral pain can be caused by calculus (most common), tumor, or blood clot
  - Ureteral colic/flank pain can cause hematuria associated with dysuria, urgency, and frequency

- Presence of clot—indicates significant degree of hematuria and higher probability of significant pathology
  - Amorphous clots—bladder/prostate origin
  - Vermiform clots—upper tract origin
  - Lower urinary symptoms (frequency, urgency, etc.):—bladder can cause hematuria
  - Incomplete bladder emptying can predispose to bladder stones and infection
  - Straining to urinate or spaying of urinary stream can indicate a urethral stricture
  - Activity/exercise-induced hematuria should be excluded

- Trauma—significant crush injury or burn may result in myoglobinuria, abdominal or pelvic trauma may cause urinary tract injury
  - Recent upper respiratory infection—associated with GIN or immunoglobulin A (IgA) nephropathy
  - Medical or surgical history:
    - Renal or urologic disease or surgery
    - Recent urologic instrumentation (including catheterization)
    - Sexually transmitted diseases (STDs)
    - History of tuberculosis (TB)
  - History of pelvic radiation
  - History of autoimmune diseases and bleeding disorders
  - Current medications
    - Antiplatelets
    - Analgesic abuse
  - History of smoking tobacco
  - Menstrual history: Vaginal bleeding can be mistaken for hematuria

- Family history
  - Primary renal disease
  - Hypertension (HTN)
  - Adult polycystic kidney disease
  - Alport syndrome
  - Urothelial malignancy
  - Occupational risk factors
  - Exposures to chemicals or dyes (aromatic amines, benzene) in rubber, petroleum, and dye industries—risk of urothelial carcinoma
PHYSICAL EXAM

- Vital signs
  - Hypertensive evaluate for renal parenchymal disease, chronic kidney disease (CKD) or renal failure, renal cystic disease or renal vascular disease; may be hypertensive if hematuria present/urate stone
- Palpation
  - Abdomen or renal palpation
- Rectal examination (DRE)

Pelvic examination:

- Flank lacerations, contusions or rib fractures—underlying renal injury
- Flank tenderness:
  - Hematuria, gross and microscopic, adult
- Palpable abdominal or flank masses
- Heart murmurs: Subacute bacterial endocarditis
- Hearing loss: Alport syndrome
- Rashes
  - May indicate a systemic process
- Vital signs
  - Color
  - Nodularity suggest cancer
- Urinalysis: Must include standard urine dipstick and digital rectal exam (DRE)

- Pyuria – suggests infection
- Blood: Suggests recent or ongoing bleeding
- Proteinuria: Heavy (3–4+), indicates intrinsic renal disease
- Specific gravity: Poorly concentrated urine—low specific gravity (<1.005) suggests nephropathic with renal impairment or intrinsic renal disease
- Leukocyte esterase and/or nitrite positive – pyelonephritis, pyelitis, pyelonephritis (nephrotic analysis is negative)
- False-positive dipoles for blood: Cholesterol crystals (bile, bacterial peritoneal, myoglobinuria, hemoglobinuria (microscopic analysis is negative)
- False-negative dipoles for blood: Reducing agents (high dose vitamin C), urine pH >5.5
- Microscopic
  - Pyuria – suggests infection
  - Red cell casts – pathognomonic of glomerular bleeding
- Crystalluria – suggests urolithiasis

Phase-contrast microscopy or urinary sediment: Differentials: granular (renal) and nonglomerular bleeding based on the presence of distal RBC’s (80%) in glomerular bleeding, sensitivity of 95% and specificity 100% (2)

- Urine culture
  - If analysis suggests infection

Urinary cytology
- Recommended for all patients with risk factors or irritative voiding symptoms. Not recommended as part of routine evaluation for asymptomatic MH
- Sensitivity for detecting bladder cancer 40–76% (1) (Better at detecting high-grade urothelial carcinomas and CIS)
- Negative result does not rule out malignancy
- Physical cells can be seen with calculi or inflammation
- NMP22, IFA stat, and triixsys are alternatives; not considered standard of care but can be useful in some cases of bladder cancer

- Renal function tests (creatinine and BUN)
- CBC – anemia may be due to GH or chronic renal failure

Diagnostic Tests & Interpretation Lab

- Urinalysis: Must include standard urine dipstick and microscopic evaluation
  - MH is defined as ≥3 RBC/high-powered field (hpf) in urinary sediments from ≥2 of ≥3 properly obtained urine specimens (catheterized sample if vaginal contamination or phimosis) (2)
  - Color
    - Bright red: Suggests recent or ongoing bleeding with urologic/anatomic-urethral
    - Brown (tea-colored): Suggests old blood/cystitis or medical renal disease (GR)
  - Dipstick (4)
    - Specific gravity: Poorly concentrated urine—low specific gravity (<1.005) suggests nephropathic with renal impairment or intrinsic renal disease
    - Proteinuria: Heavy (3–4+) suggests GR or renal disease
    - Leukocyte esterase and/or nitrite positive – pyelonephritis, pyelitis, pyelonephritis (nephrotic analysis is negative)
    - False-positive dipoles for blood: Cholesterol crystals (bile, bacterial peritoneal, myoglobinuria, hemoglobinuria (microscopic analysis is negative)
    - False-negative dipoles for blood: Reducing agents (high dose vitamin C), urine pH >5.5
    - Microscopic
      - Pyuria – suggests infection
      - Red cell casts – pathognomonic of glomerular bleeding
      - Crystalluria – suggests urolithiasis

- Imaging
  - Plain abdominal imaging: Limited utility in initial evaluation of hematuria, gross and microscopic, adult
  - Myoglobinuria, hemoglobinuria (microscopic analysis is negative)
  - If hypertensive evaluate for renal parenchymal disease, chronic kidney disease (CKD) or renal failure, renal cystic disease or renal vascular disease; may be hypertensive if hematuria present/urate stone
  - Febrile UTI, concern for urologic malignancies
  - NMP22, IFA stat, and triixsys are alternatives; not considered standard of care but can be useful in some cases of bladder cancer

- Renal function tests (creatinine and BUN)
- CBC – anemia may be due to GH or chronic renal failure

Diagnostic Procedures/Surgery

- Cystoscopy (5)
  - Should be performed in all patients >35 yr old with MH or GR
  - Patients: <35 yr; cystoscopy performed if significant risk factors for urologic malignancies present: irritative voiding symptoms, tobacco history, chemical exposure, etc.
  - Retrograde pyelography (RPG), cystoscopy as clinically indicated

Pathologic Findings

Based on primary cause

HEMATURIA, GROSS AND MICROSCOPIC, ADULT

- MIBI
  - Alternative imaging modality when CT scanning is not advised (contrast allergy, renal insufficiency, metastatic implants)
  - Provides excellent visualization of small renal masses and arteriovenous malformations but has less utility for stones
  - Gadodiurnum contract in avoidance of patients with creatinine >2 mg/dL (71 mL/min), due to risk of progressive systemic fibrosis (hypertrophic systemic fibrosis [HSF])

- Renal US
  - Detects renal cystic disease, renal masses, hematuria
  - Less sensitive for detecting stone disease but useful in children and pregnancy, when radiation is contraindicated
  - Operator-dependent, large body habitus can limit utility

- Bladder US
  - Useful to assess posterior residuals, can detect larger bladder tumors, bladder calcification and diverticulum, although less sensitive than CT scan

- VCUG
  - Voiding cystourethrogram (VCUG), cystoscopy as clinically indicated

175
HEMORRHAGIC DISEASES OF THE URINARY TRACT

DIFFERENTIAL DIAGNOSIS

- Pseudohematuria
  - Drugs:
    - Reddish color: Pyridium, doxorubicin, phenytoin, salicylates, amin, others
    - Brown color: Cascara, iron supplements, riboflavin, other
  - Vegetables: Beets
  - Dyes or pigments
  - Myoglobin and free hemoglobin
  - Menstrual period contamination
  - Dysfunctional uterine bleeding
- Congenital/inherited:
  - Cystic renal disease
    - Polycystic kidney disease
    - Medullary sponge kidney
    - Medullary cystic disease
  - Benign familial hematuria or thin basement membrane nephropathy
  - Alport syndrome
  - Inherited renal tubular disorders that can lead to urolithiasis
    - Renal tubular acidosis type I
    - Cystinuria
    - Ocuprosis
  - Hemolytic-uremic abnormalities
    - Bleeding dyscrasias
  - Sickle hemoglobinopathies
- Anatomic causes
  - Urethral and ureteric strictures
  - Phimosis
  - Posterior urethral valves
  - Urethral caruncle
  - Diverticula
  - UPJ obstruction
  - Obstructive uropathy: Hydronephrosis
  - Venous outflow reflux
  - Vascular malformations: Hemangiomas
- Traumatic
  - Abdominal and pelvic injury
  - Degree of hematuria is a poor indicator of injury severity
  - Urterogent trauma after abdominal, pelvic, or urinary tract surgery
  - Exercise-induced hematuria
  - Foreign bodies: Catheters, stents, self-introduced, etc.
  - Inflammatory
    - Urinary tract and specific infections
    - Radiation: Radiation cystitis and nephritis
  - Metabolic
    - Uric crystalluria
    - Hypercalcuria
    - Hyperuricosuria
  - Neoplastic: Any benign or malignant GU lesion
  - Drug-induced
    - Nephritic or tubular damage
    - Analgesic abuse
  - Miscellaneous
    - Bladder stone
  - Arterial emboli or thrombosis
  - Renal vein thrombosis
  - Endometriosis of the urinary tract—female with cyclic hematuria
  - Benign essential hematuria

TREATMENT

GENERAL MEASURES

- The standard urologic evaluation should include urinalysis, urine culture, cystoscopy if risk factors, CTU and cytology as outlined above (see also “Hematuria Algorithm”)
- Treatment depends on etiology
  - Consider and rule out pseudohematuria or medical causes of hematuria based on presentation, history, lab data, or if evaluation for anatomic lesion is negative
- Gross hematuria
  - If patient is urinating without difficulty and has no blood clots can treat conservatively—increase oral fluid intake
  - For patients with ureteral retention: Place a large-bore 3-way Foley catheter (large-bore 2-way or rigid catheter may be more effective to clear clots) and hand irrigate out all clots, followed by continuous bladder irrigation (CBI) with sterile saline or water
  - More severe hematuria or hemodynamic instability may require surgery—cystoscopy with clot evacuation/fulguration
- Microscopic hematuria
  - Work-up can be done in the office setting and usually requires no immediate monitoring or treatment unless associated with trauma

MEDICATION

First Line

- Not treated primarily by medications
  - Aminocaproic acid (Amicar)—for intractable gross hematuria (6)
    - Inhibitor of fibrinolysis
    - Rare but serious side effects of thrombotic events and renal failure
  - Finasteride may be effective for prostatic hemorrhage

Second Line

- Transfuse RBCs if indicated for extreme acute blood loss
- Continuous bladder irrigation (CBI) with normal saline for persistent hematuria with clots
- Consider bladder irrigation with 1% Alum if GH persists
- Cystoscopy, clot evacuation, fulguration if conservative treatment fails
HEMATURIA, GROSS AND MICROSCOPIC, ADULT

ADDITIONAL TREATMENT

Radiation Therapy

- N/A

Additional Therapies

- N/A

Complementary & Alternative Therapies

- Hyperbaric oxygen therapy (HBO) has been shown to be effective in hematuria caused by radiation-induced cystitis if delivered within 6 mo of initiation of hematuria.

ONGOING CARE

PROGNOSIS

Based on etiology of the hematuria

COMPLICATIONS

Hypotension and anemia may result on degree and chronicity of blood loss

FOLLOW-UP

Patient Monitoring

- Monitor hemodynamic status if severe gross hematuria, especially if associated with trauma

Patient Resources

- Urinary Care Foundation, http://www.urinaryhealth.org/urine/index.cfm?article=113

REFERENCES


ADDITIONAL READING


CODES

ICD9
- 599.0 Urinary tract infection, site not specified
- 599.71 Gross hematuria
- 599.72 Microscopic hematuria

ICD10
- R31.0 Gross hematuria
- R31.2 Other microscopic hematuria
- N39.0 Urinary tract infection, site not specified

CLINICAL/SURGICAL PEARLS

- Gross or microscopic hematuria in any patient should be evaluated, especially when significant risk factors are present (age >35, smoking history, exposure to chemicals/dyes, irritative voiding symptoms).
- Risk of urologic malignancy is 5 times higher in patients who present with gross hematuria.
- Cytology is recommended for patients with risk factors; however, a negative result does not rule out malignancy.
- CTU is the imaging test of choice for evaluating hematuria from the upper tract.
- Cystoscopy should be performed on any patient >35 yr of age presenting with unexplained MH or GI.

See Also (Topic, Algorithm, Media)
- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Glomerulonephritis, Acute
- Glomerulonephritis, Chronic
- Hematuria, Adult Algorithm
- Hematuria, Gross and Microscopic, Pediatric
- Hematuria, Traumatic Algorithm
- Hematuria-Dysuria Syndrome
- Hematuria-Left Pain Syndrome
- Urine, Abnormal Color

ON SEVENTY SEVEN
HEMATURIA, GROSS AND MICROSCOPIC, PEDIATRIC

Douglas W. Storm, MD, FAAP, FACS
Christopher S. Cooper, MD, FAAP, FACS

ASSOCIATED CONDITIONS
Depends on the bleeding source

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Microscopic hematuria considered clinically significant if >5–10 RBCs/hpf
- Recommend that 2 of 3 urinalyses show microscopic hematuria over 2–3 wk before work-up initiated (1,2)[A]
- False-negative results occur with high urine specific gravity or with high ascorbic acid concentration
- False-positive results occur in presence of myoglobin, medications (eg, rifampin, pyridium, etc.), bile pigments, and oxidizing agents (eg, household bleaches)
- Urinalysis
  - Proteinuria
    - If 1+ or 2+ child should be evaluated for postural proteinuria
    - 2+ or greater proteinuria child should be evaluated for glomerulonephritis and nephrotic syndrome
  - RBC casts are highly specific for glomerulonephritis
  - Dysmorphic RBCs predict glomerular bleeding
  - Dysmorphic RBCs predict glomerular bleeding with a sensitivity of 93–95% and a specificity of 96–100%
  - WBCs, bacteria, leukocyte esterase, nitrites suggest UTI
  - Recommend urine culture to verify UTI and identify bacteria causing the infection
- Other urinary tract infections
  - Complete blood count CBC
  - Plasma IgA levels (may be increased with IgA nephropathy)
  - Urinalysis
    - Glycosuria (indicative of poststreptococcal GN)
    - Total hematuria suggests upper tract source
    - Initial or terminal hematuria suggests lower tract source
    - WBC casts are highly specific for glomerular bleeding
  - Urinalysis
    - Proteinuria
      - If 1+ or 2+ child should be evaluated for postural proteinuria
      - 2+ or greater proteinuria child should be evaluated for glomerulonephritis and nephrotic syndrome
    - RBC casts are highly specific for glomerulonephritis
    - Dysmorphic RBCs predict glomerular bleeding
    - Dysmorphic RBCs predict glomerular bleeding with a sensitivity of 93–95% and a specificity of 96–100%
    - WBCs, bacteria, leukocyte esterase, nitrites suggest UTI
    - Recommend urine culture to verify UTI and identify bacteria causing the infection
- Other blood tests
  - Serum creatinine, BUN, electrolytes (if renal insufficiency noted)
  - Complete blood count CBC
  - Anti-glomerular basement membrane (anti-GBM) (indicative of poststreptococcal GN)
  - CBC to evaluate for anemia
    - Hemoglobin, hematocrit
    - Erythrocyte sedimentation rate
    - Erythrocyte counts (can be elevated in cases of SLE and ON)
    - Plasma IgG levels (may be increased with IgG nephritis and HSP)
  - Other urine tests
    - Urine calcium to creatinine ratio varies by age, but generally <0.18; if >0.18 suggests high 24-hr excretion of calcium >4 mg/kg/day
  - Other lab tests
    - Uric acid (to rule out gouty arthritis)
  - Other imaging
    - Renal and bladder sonography
      - Evaluate for renal parenchymal disorders, stones, tumors, and anatomic abnormalities
      - Voiding cystourethrogram (VCU/G)
      - Not routinely performed in work-up of hematuria
      - May be done if hematuria is felt to be in conjunction with laboratory findings
      - Can be useful for evaluation of renal disease or anatomic abnormalities or after recent trauma
DIFFERENTIAL DIAGNOSIS
Dependent on the cause of the bleeding

Diagnostic Procedures/Surgery
- Cystoscopy
- Renal biopsy
- Cystoscopy
- Renal biopsy

Pathologic Findings
- Hematuria

DIAGNOSTIC PROCEDURES
- Cystoscopy
- Renal biopsy

COMPLICATIONS
- Unstable BP, renal insufficiency, fevers
- HTN, edema, oliguria, significant proteinuria, RBC casts

PROGNOSIS
Based on underlying cause of the hematuria and any interventions delivered

FOLLOW-UP

Patient Monitoring
- Current recommendation of American Academy of Pediatrics is screening urinalysis at age 5 yr
- Urinal measurements of height, weight, and BP measurements after age 3 yr

Patient Resources
- www.chop.edu/healthinfo/hematuria.html

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Hematuria-Loin Pain Syndrome
- Hematuria, Gross and Microscopic, Pediatric Images
- Hematuria, Pediatric Microscopic (Gross) Algorithm
- Hematuria, Gross and Microscopic, Adult
- Hematuria-Loin Pain Syndrome
- Urine, Abnormal Color

CODEx
- ICD9 599.72 Microscopic hematuria
- ICD10 R31.2 Other microscopic hematuria
HEMORRHAGE FOLLOWING TURP OR TURBT

Frank M. Nezu, MD
Mohamed T. Ismail, MD

**BASICS**

**DESCRIPTION**
Significant gross hematuria with or without clot retention that occurs following transurethral resection of the prostate (TURP) or transurethral resection of bladder tumor (TURBT).

**EPIDEMIOLOGY**
- Occurs in up to 11% of patients, typically within the 1st 3 mo after TURP (181B).
- TURP is associated with a 2.9% transfusion rate (181B).
- 2.2–3.3% of patients require recatheterization, clot evacuation, or return to OR for bleeding after TURP (118[A]).

**RISK FACTORS**
- Excessive bleeding/straining/constipation
- Inadequate hemostasis/coagulation of bleeding vessels
- Infection
- Medications: Warfarin, heparin, low molecular weight heparins, aspirin, thienopyridine (clopidogrel), etc.
- Trauma
- Undermining of bladder neck

**Genetics**
Patients with deficiencies in the clotting cascade (e.g., hemophilia) or other coagulopathies are more prone to hemorrhage.

**GENERAL PREVENTION**
- Obtain sufficient hemostasis intraoperatively
- Stop anticoagulants or other blood-thinning medications prior to surgery
- Delay starting anticoagulant medications postoperatively if possible, although this practice has been questioned (141B)
- Gentle postoperative catheter traction
- See reductive inhibitors, taken pre operatively, may reduce surgical blood loss intraoperatively (181A).
- See reductive inhibitors, do not decrease rates of postoperative clot retention (181A).

**PATHOPHYSIOLOGY**
- Anesthetic technique (regional or general) appears to have no impact on TURP related bleeding.
- Inadequate hemostasis/coagulation of bleeding vessels.
- Nausea may cause constipation and increased intra-abdominal pressure
- NSAIDs are not contraindicated after TURP, they do not increase risk of postoperative adverse events (181A).

**DIAGNOSIS**

**HISTORY**
- Color of urine, presence of clots
- Patient is not able to void (clot retention)
- History of TURP/TURBT—timing, complications, catheter removal
- Use of anticoagulation or similar medications
- Excessive straining or trauma, last bowel movement
- History of clotting disorder
- History of prostate cancer

**PHYSICAL EXAM**
- General: Pallor, dehydrated, acutely ill
- Vitals: Hypotensive or tachycardic
- Abdomen: Bladder distended or palpable
- Genitalia: Edematous, ecchymotic

**DIAGNOSTIC TESTS & INTERPRETATION**
- CBC to assess for anemia
- Creatinine level for obstruction
- Urinalysis, urine culture
- Coagulopathy screen (platelets, PT/PTT) particularly if there is suggestion of bleeding from other sites

**Imaging**
- Bladder US or pelvic CT to evaluate for large organized clot within bladder

**Differential Diagnosis**
- Bleeding from lower GU tract source: Urethra, prostate, bladder
- Bleeding from upper GU tract source: Ureter, renal pelvis, kidney

**TREATMENT**

**GENERAL MEASURES**
- Limit physical activity, encourage bed rest
- Limit fluids and avoid constipation through stool softeners
- Adequate hydration, IV fluid resuscitation
- Bladder drainage and clot evaluation with large-caliber hematuria catheter
- Continuous bladder irrigation (CBI) via 3-way Foley catheter to clear clots and prevent new clots from forming in the bladder
- Foley traction, additional inflation of Foley balloon
- Cessation of anticoagulants or blood-thinning medications
- Check CBC and coagulation profile
- MR CT transabdominal if necessary, vitamin K and/or FFP if coagulopathic
- CIB with intravesical alum or silver nitrate
- These are reported but rarely necessary.
  - Hyperbaric oxygen
  - Antimicrobial and (African) antibacterial
  - Hormonal manipulation: LHHR agonists
  - Urinary diversion with bilateral PCNs
  - Salvage radical prostatectomy
  - Selective arterial prostatic embolization (SAPED) (181A)
HEMORRHAGE FOLLOWING TURP OR TURBT

MEDICATION

First Line
- Antibiotics if infected
- Stool softeners
- 5α-reductase inhibitors such as finasteride or dutasteride (although will not have an acute effect)

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Transurethral clot evacuation with fulguration and cautery (laser or electrocautery) of prostate if bleeding does not subside within a reasonable timeframe
- Post-TURBT hemorrhage, more expeditious clot evacuation and fulguration

ONGOING CARE

PROGNOSIS
- The mortality rate for hemorrhage after TURP and TURBT is unknown
- Whether hemorrhage after TURP increases the risk of future prostatic bleeding has not been described in the literature
- Use of stool softeners and avoidance of constipation for several weeks after TURP and TURBT seems advisable

COMPLICATIONS
- Severe anemia and/or hypovolemic shock can lead to syncope and/or MI

FOLLOW-UP
- Patient Monitoring
- Can be managed on the floor setting with staff who are accustomed to managing catheters and CBI
- Serial CRs, blood transfusions as necessary
- Monitor coagulation profile, FFP if needed

Patient Resources
- N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Hematuria, Gross and Microscopic, Adult
- Hemorrhage, Postop, Urologic Considerations
- Hemorrhagic Cystitis
- Urine, Abnormal Color

CODES
- ICD9: 599.71 Gross hematuria
- 998.11 Hemorrhage complicating a procedure

ICD10
- N99.820 Postproc hemor/hematom of a GU sys org fol a GU sys procedure
- N99.820 Hemorrhage

CLINICAL/SURGICAL PEARLS
- Proper patient selection, identify patients at risk for bleeding with attention to medications.
- Attention to detail at the end of TURP/TURBT, complete hemostasis and evacuation of specimen.
- Avoid contamination postoperatively.
- In patient with clot retention a large-bore catheter is used to evacuate all clots and start continuous bladder irrigation (CBI) immediately.
**HERPES SIMPLEX, GENITAL**

Michael Perrotti, MD

### BASICS

**DESCRIPTION**
- Herpes simplex is a common sexually transmitted virus infection.
- Herpes simplex virus (HSV)
  - HSV-2 is the most common cause of genital herpes.
  - Can be caused by HSV-1 (oral sex during HSV-1 outbreak).
- An increasing proportion of anogenital herpetic infections in some populations has been attributed to HSV-2 infection.

**EPIEMIOLOGY**

- **Incidence**
  - 0.5–1 million new cases of genital herpes per year in US.
- **Prevalence**
  - ~45 million people in US have genital herpes.

**RISK FACTORS**

- Sexual contact with an infected person.
- Unprotected sexual intercourse.
- Multiple sexual partners.

**PATHOPHYSIOLOGY**

- Transmission can occur by anal, vaginal, or oral sex.
- Prophylactic and antiviral therapy may reduce transmission.
- Transmission can occur by anal, vaginal, or oral sex.
- Prophylactic and antiviral therapy may reduce transmission.
- HSV-2 infection is most frequent during the first 12 mo after acquiring HSV-2.

**ASSOCIATED CONDITIONS**

- HSV.
- Other STIs.

### GENERAL PREVENTION

- Monogamous seronegative partner.
- Condom use.
- Randomized trials have demonstrated that male circumcision (MC) reduces heterosexual acquisition of various STI/STD including HSV type 2, and it reduces genital ulcer disease among female partners.

### DIAGNOSIS

**HISTORY**

- Patients may experience prodrome before appearance of lesions.
- Tingling, pruritus, paresthesias.
- Fever.
- Headache.
- Painful genital lesions.
- Dysuria.

**PHYSICAL EXAM**

- Multiple shallow genital ulcers that may be vesicular.
- However, these classical painful multiple vesicular or ulcerative lesions may be absent in some.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- Polymerase chain reaction.
- Direct fluorescence antibody.
- Viral culture.

**Imaging**

- MRI in suspected CNS disease.

**Diagnostic Procedures/Surgery**

- Biopsy of vesicular or ulcerative lesions may be absent in some.
- Patient's history.
- Viral culture.
- Type-specific serology testing.
- Both lab-based assays and point-of-care tests that provide results for HSV-2 antibodies from capillary blood or serum.
- The sensitivities of these glycoprotein G type-specific tests for HSV-2 antibody vary from 85–98%, are false-negative at early stages of infection. The specificities are ≥96%.
- False-positive results can occur, especially in patients with a low likelihood of HSV infection.

**DIFFERENTIAL DIAGNOSIS**

- Acute UTI.
- Anogenital gonorrhea.
- TREPONEMA pallidum.
- Drug eruption.
- Behcet's disease.

### TREATMENT

**GENERAL MEASURES**

- No cure is available.
- Encourage safe sex practices to reduce transmission.
- Unprotected sexual intercourse.
- Multiple sexual partners.
- Avoidance of sexual activity during recurrences.
- Antiviral medications can prevent or shorten outbreaks.
- Daily suppressive therapy can reduce recurrences.
- Topical therapy with antiviral drugs offers minimal clinical benefit.
- Treatment guidelines based on most current CDC recommendations.

**MEDICATION**

**First Line**

- Acyclovir, valacyclovir, and famciclovir are safe for use in immunocompromised patients in the doses recommended for treatment of genital herpes.

**Second Line**

- Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in patients who have very frequent recurrences (≥10 episodes per year).
HERPES SIMPLEX, GENITAL

- Episodic therapy for recurrent genital herpes (2)
  - Requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks.
  - Provide patient with a supply of drug or a prescription for the medication with instructions to initiate treatment immediately when symptoms begin.
  - Acyclovir 400 mg TID for 5 days OR 800 mg PO TID for 2 days
  - Famciclovir 125 mg PO BID for 5 days OR 1,000 mg PO BID for 1 day OR 500 mg once, followed by 250 mg BID for 2 days
  - Valacyclovir 500 mg PO BID for 5 days OR 1 g PO QD for 5 days

SURGERY/OTHER PROCEDURES
- Sitz baths
- Foley catheter for retention of urine associated with sacral nerve root involvement

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies
- In complicated HSV infection (central nervous system disease, disseminated HSV), the Centers for Disease Control recommend intravenous acyclovir (5–10 mg/kg) every 8 hr for 2–7 days or until clinical improvement.
- Suppressive or episodic therapy with oral antiviral agents is effective in decreasing the clinical manifestations of HSV among HIV-positive persons.
- Complementary & Alternative Therapies
  - None noted to be effective

ONGOING CARE

PROGNOSIS
- Symptoms may last 2–4 wk if untreated
- Symptoms less severe in nonprimary compared to person without pre-existing HSV immunity
- Treatment during primary infection lessens symptoms less severe in nonprimary compared to person without pre-existing HSV immunity
- Patient Monitoring
  - Patient’s education concerning the natural history of the disease, potential for recurrent episodes, asymptomatic viral shedding, and the risks of sexual transmission.
  - At 1st episode of genital herpes, advise the patient that suppressive therapy is available and effective in preventing symptomatic recurrent episodes
  - Encourage patients to inform their current sex partners that they have genital herpes and to inform future partners before initiating a sexual relationship.
  - The risk for HSV-2 sexual transmission can be decreased by the daily use of valacyclovir by the infected person. Episodic therapy does not reduce the risk for transmission and its use should be discouraged for this purpose among persons whose partners might be at risk for HSV-2 acquisition (4).
  - Symptomatic sex partners should be evaluated and treated in the same manner as patients who have genital lesions. Asymptomatic sex partners of patients who have genital herpes should be questioned concerning histories of genital lesions and offered type-specific serologic testing for HSV infection.

Patient Resources
http://www.cdc.gov/STD/Herpes/

REFERENCES

ADDITIONAL READING


See Also (Topic, Algorithm, Media)
- Aphthous Ulcer, External Genitalia
- Genital ulcers
- Genital ulcers Algorithm
- Herpes Simplex, Genital Ulcers
- Herpes Simplex, Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers
- Genital Ulcers

CODES

ICD9
- 054.10 Genital herpes, unspecified
- 054.11 Herpetic vulvovaginitis
- 054.19 Other genital herpes

ICD10
- A60.00 Herpesviral infection of urogenital system, unspecified
- A60.04 Herpesviral vulvovaginitis
- A60.9 Azoogential herpesviral infection, unspecified

CLINICAL/SURGICAL PEARLS

- It is estimated that 1 in 5 adults in US is infected with HSV, but that many are asymptomatic and do not know that they are infected with the virus.
- Most infected individuals have recurrent episodes of painful genital ulcers.
- The 1st episode usually occurs a few weeks following initial infection with the virus and may last 2–3 wk.
- HSV recurrences generally decrease in frequency over time.
Adequate Treatment of LUTS

GENERAL PREVENTION

BPH and erectile dysfunction in men

PATHOPHYSIOLOGY

Risk Factors

Prevalence

Incidence

Epidemiology

Description

Akhil Das, MD, FACS

Patricia Lewandoski, MD

HESITANCY AND INTERMITTENCY

Introduction

Hesitancy and intermittency are commonly characterized as obstructive (emptying) symptoms. These symptom patterns also include:

- Protracted dribbling
- Straining to void
- Decreased force of stream
- Incomplete bladder emptying

Epidemiology

Incidence

Obstructive urinary symptoms and age are highly correlated.

Patient symptom reporting is influenced by sociodemographic and cultural factors.

Hesitancy and intermittency is primarily related to BPH and occurs mostly in men.

Prevalence

- Age-stratified prevalence of moderate to severe lower urinary tract symptoms (LUTS) in men:
  - 40–50 yr old: ∼20%
  - 50–60 yr old: ∼30%
  - 60–70 yr old: ∼40%
  - 70–80 yr old: ∼50%

Risk Factors

- Bladder outlet obstruction:
  - In men, primarily related to benign prostatic hyperplasia (BPH), bladder neck contracture, bladder stones, urethral valves, urethral stricture disease, and prostate cancer.
  - In women, primarily caused by pelvic floor prolapse, cystocele, bladder stones, urethral stricture disease (rarely)

- Detrusor underactivity:
  - Idiopathic
  - Neuropathic (Diabetes, Parkinson disease, etc.)
  - Non-neurogenic (Dysfunctional voiding)

- Obesity is associated with a higher incidence of LUTS

Genetics

N/A

Pathophysicsology

- Bladder outlet obstruction causes increased resistance to urinary flow due to various etiologies (BPH, bladder neck contracture, bladder stones, urethral valves, urethral stricture disease, and prostate cancer).

- In women, primarily caused by pelvic floor prolapse, cystocele, bladder stones, and urethral stricture disease (rarely)

- Detrusor underactivity:
  - Idiopathic
  - Neuropathic (Diabetes, Parkinson disease, etc.)
  - Non-neurogenic (Dysfunctional voiding)

- Obesity is associated with a higher incidence of LUTS

Associated Conditions

BPH and erectile dysfunction in men

General Prevention

Adequate treatment of LUTS

Diagnosis

History

- Quantification of lower urinary tract symptoms
  - AUA/IPSS symptom index should be used.
  - Other obstructive voiding symptoms should be assessed.
  - Consider voiding diary if history is unclear.
  - Assess for irritative voiding symptoms:
    - Cystitis/contamination: Can present with acute, severe obstructive symptoms.
  - History of hematuria:
    - Urethral stricture
    - Bladder/urethral stones
    - Bladder mass
  - Certain pelvic procedures can result in detrusor underactivity.
  - Other medical conditions:
    - Certain neurologic conditions and diabetes can cause detrusor underactivity.
  - Prior pelvic irradiation can affect bladder contractility.
  - History of STD may predispose patients to urethral stricture disease.
  - Medications:
    - Antimuscarinics may lead to obstructive symptoms.
    - Other obstructive voiding symptoms should be assessed.

- Other obstructive voiding symptoms:
  - Straining to void
  - Decreased force of stream
  - Bladder mass

- Bladder stones

- Urethral stricture disease

- Bladder neck contracture (ie, after prostate surgery)

- BPH—common cause of hesitancy and intermittency

- Lower urinary tract symptoms, such as hesitancy or intermittency, according to the AUA guidelines for BPH

Physical Exam

- Abdominal Exam: Palpate for a distended bladder.
- Digital Rectal Exam (DRE) should be performed:
  - Prostate size
  - Prostatic nodularity
  - Rectal tone
  - Prostatic nodularity

- Neurologic exam:
  - Sensory examination
  - Motor examination
  - Reflexes

- Urethral lesions should also be assessed.

- Prostatic nodularity

- Anal sphincter tone

- General mental status

- Certain neurologic conditions and diabetes can cause detrusor underactivity.

- Certain neurologic diseases and diabetes can cause detrusor underactivity.

- Bladder mass

- Bladder stones

- Urethral stricture

- Bladder neck contracture (ie, after prostate surgery)

- BPH—common cause of hesitancy and intermittency

- Lower urinary tract symptoms, such as hesitancy or intermittency, according to the AUA guidelines for BPH

Diagnostic Tests & Interpretation

- Lab:
  - Urinalysis by dipstick testing or microscopic exam of the sediment should be performed to screen for hematuria and UTI.
  - If UTI suspected: Urine culture.
  - Serum PSA should be assessed in men with at least a 10 yr life expectancy.
  - Renal function tests (BUN and creatinine) are NOT recommended as part of the initial work-up of hesitancy and intermittency unless warranted by history, exam, or lab evaluation.
  - If urethral stricture disease is suspected, retrograde urethrography (RUG) may be helpful.
  - Transrectal US should be reserved for patients with an increased suspicion of prostate cancer undergoing prostate needle biopsy

- Imaging:
  - Upper tract evaluation (CT scan, IVP, or US) is NOT recommended as part of the initial work-up of hesitancy and intermittency unless warranted by history, exam, or lab evaluation.

  - If urethral stricture disease is suspected, retrograde urethrography (RUG) may be helpful.
  - Transrectal US should be reserved for patients with an increased suspicion of prostate cancer undergoing prostate needle biopsy

- Diagnosing Procedures/Surgery

- Urinary flow rate should be considered:
  - May be helpful in patients with complex medical history.
  - Should be performed in patients who are to undergo invasive therapy, as this may predict response to surgery.

- Cystoscopy and/or transurethral resection

- Cystourethroscopy should be considered in patients with possible urethral stricture.

- Bladder mass

- Bladder stones

- Urethral stricture disease

- Bladder neck contracture (ie, after prostate surgery)

- BPH—common cause of hesitancy and intermittency

- Lower urinary tract symptoms, such as hesitancy or intermittency, according to the AUA guidelines for BPH

- Diagnosing Procedures/Surgery

- Urinary flow rate should be considered:
  - May be helpful in patients with complex medical history.
  - Should be performed in patients who are to undergo invasive therapy, as this may predict response to surgery.

- Cystoscopy and/or transurethral resection

- Cystourethroscopy should be considered in patients with possible urethral stricture.

- Bladder mass

- Bladder stones

- Urethral stricture disease

- Bladder neck contracture (ie, after prostate surgery)

- BPH—common cause of hesitancy and intermittency

- Lower urinary tract symptoms, such as hesitancy or intermittency, according to the AUA guidelines for BPH

- Differential Diagnosis

- Bladder outlet obstruction
  - BPH—common cause of hesitancy and intermittency in men
  - Bladder neck contracture (ie, after prostate surgery)

- Urethral stricture disease

- Bladder stones

- Foreign body

- Cancer (prostate, bladder, urethra)

- Prostatitis

- UTI

- Bladder neck dyssynergia
• Detrusor-sphincter dyssynergia
• Pelvic organ prolapse
• Detrusor underactivity (more common cause of hesitancy and intermittency in women):
  - Cholinergic dysfunction
  - Parkinson disease
  - Multiple sclerosis
  - Intervertebral disc
  - Radiation syndromes
  - Sexual and/or psychosocial dysfunction
  - Medications: Anticholinergic drugs are less likely to cause sexual dysfunction but more likely to cause urinary hesitancy

TREATMENT

GENERAL MEASURES
• When the effect of LUTS on quality of life was studied, most important factors for seeking treatment were the severity and degree of bother.
• Treatments are tailored to the degree of bother and the severity of the disease.
• Review medications (anticholinergics, sympathomimetics, and opioids) to determine if any are potential cause; consider alternatives.
• Micturition diary:
  - Limit fluid intake
  - Avoid diuretics
  - Avoid coffee, tea, alcohol which may irritate the bladder

MEDICATION (2)

First Line
• For patients with evidence of infection, appropriate antibiotic therapy should be initiated.
• For men with hesitancy and intermittency presumably due to BPH/BOO:
  - α1-adrenergic antagonists (alfuzosin, doxazosin, tamsulosin, terazosin, ubidesiride) reduce resistance at the bladder outlet and provide symptom relief.
  - At maximal doses, all agents are felt to be equally effective.
  - Side effect profiles may include orthostatic hypotension, retrograde ejaculation, asthenia, and nasal congestion.
• 5α-reductase inhibitors (5ARI) (finasteride 5 mg and dutasteride 0.5 mg) reduce prostate volume, prevent progression of BPH, and improve symptoms in clinical trials.
  - These drugs can cause decreased libido, sexual dysfunction, and reduce PSA by ~50% and are of little use in men without evidence of clinical BPH.
  - Combination therapy: MTPS study showed a 67% 5-yr risk reduction in BPH progression in men on combination therapy (doxazosin and finasteride) compared to placebo and better than either agent alone (39% and 34%, respectively).

Second Line
• Combination therapy combining an 5ARI with an α1-blocker may be useful
• If ED and BPH/BOO coccur daily tadalafil (2.5–5 mg PO QD) can be used

SURGERY/OTHER PROCEDURES
• Unilateral urethral disease and/or bladder neck contractures should be addressed using appropriate endoscopic or open procedures.
• Cyclosporine and/or pelvic floor relaxation in women should be addressed surgically if indicated.
• For men with hesitancy and intermittency presumably due to BPH/BOO who do not respond to medical management:
  - Transurethral resection of the prostate (TURP) remains the gold standard surgical approach in patients who do not respond to medical management to BPH.
  - Can be combined with various laser techniques to facilitate tissue hemostasis and removal.

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
• Behavioral interventions, such as timed voiding or double voiding

Complementary & Alternative Therapies
• Saw palmetto (Serenoa repens) has been reported to improve LUTS due to BPH/BOO. Randomized clinical studies have produced contradictory results.

ONGOING CARE
PROGNOSIS (3)
• 25% of untreated patients with moderate-to-severe LUTS presumably due to BPH/BOO experience clinical progression of symptoms within 5 yr.
• Randomized clinical trials of patients receiving α1-blocker therapy indicate that >75% will report a 25% improvement in symptoms within 3 mo of initiating treatment.
• 5–10% of men with moderate-to-severe LUTS will fail medical therapy and will require surgical intervention for their condition.

COMPLICATIONS
• Patients with disease progression who do not receive appropriate treatment may experience the following complications:
  - Renal insufficiency
  - UTI
  - Stone formation
  - Acute urinary retention
  - Secondary bladder dysfunction

FOLLOW-UP

Patient Monitoring
• After appropriate treatment has been initiated and patients report improvement, annual follow-up should include:
• History and physical exam, urinalysis, PSA
• – Uroflowmetry and postvoid residual urine as needed

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Bladder Outlet Obstruction (R40)
• Lower Urinary Tract Symptoms (LUTS)
• Prostate, Benign Hypertrophy
• Prostatitis, General

HESITANCY AND INTERMITTENCY

CRITICAL CODES
ICD10
• R39.19 Other difficulties with micturition
• R39.13 Splitting of urinary stream
• R39.14 Urinary retention
• R39.18 Other abnormality of urination

ICD9
• 788.69 Other abnormality of urination

CLINICAL/SURGICAL PEARLS
• Hesitancy and intermittency is often associated with BPH and generally represents LUTS associated with an obstruction.
• Increasing hesitancy may be seen before an episode of retention.
• In men, the incidence increases with age.
• Pressure flow studies are helpful in determining obstruction vs. detrusor underactivity.
HIV/AIDS, UROLOGIC CONSIDERATIONS
Daniel C. Parker, MD
Michael A. Pontari, MD

ALERT
The American Urological Association (AUA) policy statement now considers circumcision to be of a health benefit, citing a 50–60% risk reduction in HIV transmission in some African nations.

BASICS
DESCRIPTION
• HIV disease results from the acquired deficiency of cellular immunity caused by the human immunodeficiency virus (HIV).
  – Hallmarks:
    • Reduction of the helper T-lymphocytes in the blood and the lymph nodes
    • Development of opportunistic infections (Pneumocystis carinii pneumonia, cytomegalovirus infections, tuberculosis, candida infections, cytomegalo, others)
    • Development of malignant neoplasms (non-Hodgkin lymphoma and Kaposi sarcoma)

• A spectrum of HIV infections range from asymptomatic seropositivity to AIDS

• Urologic manifestations of HIV/AIDS:
  – Bacterial and nonbacterial infections
  – Voiding dysfunction
  – Renal impairment

EPIDEMIOLOGY
PREVALENCE
• 0.1% of US adults < 50 are infected
  – 2.6% of African American men and 1.5% of African American women were HIV positive from 1999 to 2006
  – 3.2 million people worldwide with HIV/AIDS
  – 2.1 million deaths due to HIV/AIDS in 2007

RISK FACTORS
• Unprotected intercourse, anal or oral sex
  – Fr drug abuse and needle sharing
  – Transmission of blood products
    – Consistent TID/ID
  – Uncircumcised phallus
  – Transmission of mother to infant at birth or via breast milk
  – Health care workers
    – Risk for HIV after percutaneous exposure to HIV-infected blood is 0.3%; after mucous membrane exposure 0.09%

GENETICS
• 3 groups of HIV viruses: M, N, and O
  – Most infections by class M
  – 9 subtypes of M exist
  – 15–20% genetic variation between viruses

PATHOPHYSIOLOGY
• HIV-1 infects cells expressing CD4, leading to decline in CD4 cells and immune function.
  – Immunosuppression allows opportunistic/sexual infections, demise; host defense against malignancy.

ASSOCIATED CONDITIONS
• UFT
  – Greater if CD4 count < 500/mm³
  – Associated with typical bacteria (Eubacterium coli, E. coli, enterococcus) and atypical pathogens such as fungi, mycobacteria, and viruses

• Epididymitis/orchitis
  – Chlamydia, gonorrhea, salmonella, toxoplasmosis

• Prostatectomy
  – Up to 16% in patients with AIDS
  – Greater risk in AIDS patients for developing postoperative abscess

• Urolithiasis
  – Risk with use of indinavir or from metabolic abnormalities

• Hepatitis B virus (HBV)
  – Malformations
    – Non-Hodgkin lymphoma
    – Usually B cell
    – May involve kidneys in 6–12% of AIDS patients
    – Kaposi sarcoma
    – Up to 20% of untreated patients
    – Testicular tumors
    – Usually seminoma
    – Up to 50% times more common
    – Renal cell carcinoma
    – Up to 8-fold increased risk vs. noninfected individual

• HIV associated nephropathy (HAN)
  – Prostatitis + > 3 g/d, edema, and HTN
  – Associated with focal segmental glomerulosclerosis (FSGS) on renal biopsy
  – Progression to dialysis in < 10 yrs.

• Voiding dysfunction
  – Can be retention, detrusor overactivity, and sphincter dyssynergia

GENERAL PREVENTION
• Barrier protection during sex (male and female condoms)
  – Mix well with any other HIV risk-reduction strategy
  – Available in 14 g/day

• Latex condoms
  – Can be retained, detrusor overactivity, and sphincter dyssynergia

• Screening HIV-1 antibody titers
  – If positive, need confirmation by Western blot or immunofluorescence.

• Need separate consent for HIV testing

• Lab
  – May show rectangular crystals from indinavir
  – Common bacterial pathogens in HIV-infected patients are E. coli, Enterobacter (enterococc), Pseudomonas aeruginosa, Proteus spp., Alcalivib, Acinetobacter, Staphylococcus aureus, group B streptococcus, Salmonella, and Salmonella spp.
  – If UTI suspected and C&S negative, consider atypical organisms: fungi, parasites, viruses

• U/Bladder stones
  – Specific testing for STD if urethral discharge present

IMAGING
• With flank pain: Noncontrast CT
  – Indium stones may not show on CT. Consider contrast study or intravenous pyelogram if renal impairment

• Social urinary tract infection
  – Prostatic abscess: CT scan

DIAGNOSIS
HISTORY
• Vaginal history (TTVA)
  – Dysuria
  – Frequency
  – Incontinence
  – Urinary discharge
  – Pelvic or testicular pain
  – Pain during
  – Proctologic history
  – Neurology
  – Gastroenterology
  – Social history
  – Sexual history

• IV drug use
  – Blood product transfusions

• Generalized symptoms: fever, weight loss, and chronic diarrhea are common symptoms.

• Review of systems (ROS): Constitutional symptoms, skin lesions, cough, oral ulceration

PHYSICAL EXAM
• General: Skin lesions, adenopathy
  – Neurologic exam: Numbness, alterations in sensation

• GU exam: Urethral discharge, testicular/penile/genital exam for masses, prostate exam for nodule or tenderness

• Perineal lesions of Kaposi sarcoma present as red/brown/purple nodules, macule, or papule
First Line

Highly active antiretroviral therapy (HAART)

– Combination therapy to combat the ability of HIV to generate drug-resistant mutants (DRMs)
– 10 million people now on antiretroviral therapy according to the WHO
– HAART therapy should be started in patients with:
  – AIDS
  – New WHO guidelines recommend starting therapy when CD4 count < 500/mm³ (previous guidelines were < 350/mm³)
– Pregnant women
– Patients with HIV nephropathy
– Confirmed with HIV regardless of CD4 count.

Second Line

– General urologic conditions such as UI, voiding symptoms, calcium stones treat as per general practice
– Salmonella epididymitis
– 2–4 wk of doxycycline 100 mg PO BID plus Cipro 500 mg PO BID
– If difficult to localize may need imaging suppression
– Kaposi sarcoma
– If focal, local radiation, cryosurgery, or radiotherapy
– For disseminated use chemotherapy (doxorubicin) or immunotherapy with interferons

SURGERY/OTHER PROCEDURES

– Indinavir and other protease inhibitor (PI) stones
  – Stop indinavir
  – Hydration
  – If necessary
  – Stones are soft and may pass after stenting.

ADDITIONAL TREATMENT

Radiation Therapy

Indicated in some cases of nodal Kaposi sarcoma

Additional Therapies

– For health care worker exposure
– Post-Exposure Prophylaxis (PEP)
  – Occupational PEP (OPEP): healthcare worker potentially exposed to material infected with HIV
  – Non-occupational PEP (NOPEP): someone is potentially exposed to HIV outside the workplace (eg, from sexual assault, unprotected sex, needle-sharing injection drug use)
  – begin within 72 hrs of exposure; 2–3 antiretroviral medications for 28 days

Pre-Exposure Prophylaxis (PrEP)

– For people who are HIV-negative and at substantial risk for HIV infection (relationship with HIV-infected partner, gay or bisexual man who has had sex without a condom or been diagnosed with a sexually transmitted infection within the past six months, others
– Along with other prevention methods like condoms, PrEP can offer good protection against HIV.

COMPLICATIONS

– Antiretroviral therapy
  – Risk of nephrotoxicity, crystal precipitation leading to stones, hypocalcemia
  – Erectile dysfunction and decreased libido (caused by increased estradiol) may be associated with HAART therapy

– Drugs used for the treatment of HIV-infected patients have become the most frequent cause of drug-containing urinary calculi.

– Among these agents, PI’s are well known to induce kidney stones, (indinavir, atazanavir, darunavir).

FOLLOW-UP

– CD4 counts
– Serum creatinine

Patient Monitoring

– CD4 counts

Patient Resources


REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

– HIV/AIDS, Urologic Considerations Image

– Kaposi Sarcoma, Urologic Considerations

– Sexually Transmitted Infections (STIs) (Sexually Transmitted Disease (STDs), General Treatment: A comparison of different regimen


HOT FLUSHES/VASOMOTOR INSTABILITY IN MALES

Tara K. Ortiz, MD
Judd W. Moul, MD, FACS

BASICS

DESCRIPTION

- Hot flushes are typically described as a feeling of intense heat with associated flushing, sweating, rapid heart rate, and anxiety.
- Sometimes called “hot flashes”.
- Common side effect of androgen ablation therapy in men with metastatic or locally advanced prostate cancer.
- Flushing can be associated with wide ranges of other conditions and medications.
- This section primarily discusses this condition in males.

EPIDEMIOLOGY

Incidence

- Occurs in 50–80% of men on androgen deprivation therapy.

Incidence

- Prevalence

TREATMENT

GENERAL MEASURES

- Reassure if symptoms mild.
- Attempt to identify and avoid lifestyle triggers.
- Keep environment cool.
- Ask about use of dosed acetaminophen, aspirin, or ibuprofen.
- Avoid tobacco, alcohol, and caffeine.
- Avoid hot baths or showers.
- Keep cool, dry bedding.

DIAGNOSIS

HISTORY

- Abrupt onset of warmth, frequently followed by profuse sweating requiring change of clothes.
- More likely to occur at night.
- Sensation typically affects the face and trunk.
- Duration is typically seen within the 1st yr after androgen ablation.
- Onset is typically seen within the 1st yr after androgen ablation.
- Episodes may be daily or occur intermittently.

PHYSICAL EXAM

- Rapid heart rate, and anxiety
- Profuse sweating
- Slight increase in oral and forehead temperature
- Perspiring frequently present
- During acute episode, facial flushing common

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No routine lab evaluation indicated.
- No pattern of characteristic changes in testosterone, follicle-stimulating hormone (FSH), or prolactin

Imaging

- No Imaging

Diagnostic Procedures/Surgery

- No Pathologic Findings

ASSOCIATED CONDITIONS

- Cholinergic syndrome
- Ectopic, parasympathetic reflexes
- Metabolic syndrome (insulin resistance, unfavorable lipid profile, increased fat mass)
- Gynecomastia
- Hormonal, normochromic anemia
- Fatigue

DIFFERENTIAL DIAGNOSIS

- Hypesthesia or hypohidrosis
- Emotional blushing
- Systemic illness:
- Cerebral syndrome
- Rheumatoid arthritis
- Metastatic thyroid tumors
- Paracrine/somatostatinomas
- Benign prostatic hyperplasia
- Ovarian disease
- Neurologic disorders
- Medications:
- Phosphodiesterase 5 inhibitors (sildenafil, tadalafil, avanafil)
- Any vasodilator agent (nitroglycerine, etc.)
- Nicotinic acid
- Calcium channel blockers most commonly nifedipine, diltiazem, amlodipine
- Opoids
- Antidepressants
- Antibiotics (saxopenycin, amphotericin B)
- Nonsteroidal anti-inflammatories
- Dietary
- Ethanol ingestion
- Monosodium glutamate or other food additives

TREATMENT

GENERAL MEASURES

- For flushing related to androgen deprivation therapy:

SYSTEMIC

- Antihypertensives (β-blockers, angiotensin-converting enzyme inhibitors, diuretics)
- Antidiabetics
- Antihistamines
- Antidepressants
- Antipsychotics
- Anticonvulsants
- Antithyroid medications
- Antiepileptics
- Anticoagulants
- Antibiotics (saxopenycin, amphotericin B)
- Nonsteroidal anti-inflammatories
- Dietary
- Ethanol ingestion
- Monosodium glutamate or other food additives

MEDITATION

First Line

- For androgen deprivation therapy related hot flushes most are hormonal agents:

- Megestrol acetate (Mepron 20 mg/d)
- Synthetic derivative of progesterone
- – 1 study demonstrated complete resolution of symptoms in 90% of patients, >90% improvement in 25% (10,38)
- Side effects include: weight gain, nausea, androgen/progesterone blockade

- Nifedipine, nisoldipine, amlodipine
- Calcium channel blockers most commonly nifedipine, diltiazem, amlodipine

- Nicotinic acid
- Any vasodilatory agent (nitroglycerine, etc.)
- Phosphodiesterase 5 inhibitors (sildenafil, tadalafil, avanafil)
- Rosacea
- Renal cell carcinoma
- Pancreatic islet cell tumors
- Medullary thyroid tumors
- Pheochromocytoma
- Carcinoid syndrome

- Monosodium glutamate or other food additives
- Nonsteroidal anti-inflammatories

DIFFERENTIAL DIAGNOSIS

- N/A
- Pathologic Findings

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No routine lab evaluation indicated.
- No pattern of characteristic changes in testosterone, follicle-stimulating hormone (FSH), or prolactin

Imaging

- No Imaging

Diagnostic Procedures/Surgery

- No Pathologic Findings

ASSOCIATED CONDITIONS

- Cholinergic syndrome
- Ectopic, parasympathetic reflexes
- Metabolic syndrome (insulin resistance, unfavorable lipid profile, increased fat mass)
- Gynecomastia
- Hormonal, normochromic anemia
- Fatigue

DIFFERENTIAL DIAGNOSIS

- Hypesthesia or hypohidrosis
- Emotional blushing
- Systemic illness:
- Cerebral syndrome
- Rheumatoid arthritis
- Metastatic thyroid tumors
- Paracrine/somatostatinomas
- Benign prostatic hyperplasia
- Ovarian disease
- Neurologic disorders
- Medications:
- Phosphodiesterase 5 inhibitors (sildenafil, tadalafil, avanafil)
- Any vasodilator agent (nitroglycerine, etc.)
- Nicotinic acid
- Calcium channel blockers most commonly nifedipine, diltiazem, amlodipine
- Opoids
- Antidepressants
- Antibiotics (saxopenycin, amphotericin B)
- Ni...
HOT FLUSHES/VASOMOTOR INSTABILITY IN MALES

• Denolad/hydrocortisone (DS): 0.1–1 mg/d:
  – 20–40% of men achieve excellent results [1]
  – Side effects include painless gynecomastia
  – At low doses, thromboembolic events are not a significant problem.
  – Generic drug, expensive though difficult to obtain in US

• Cyproterone Acetate (Androcur) 100 mg/d
  – Not approved for use in US
  – Peripheral antagonism, antigonadotropin with progestin-like activity
  – May interfere with ADT regimen
  – A study demonstrated resolution of symptoms in 84% of patients, 50% improvement in 37% (CBE)
  – Side effects include fatigue, increased risk of thrombosis, amenorrhea, potential hepatotoxicity, gynecomastia

Second Line (Nonhormonal Therapy)

• Venlafaxine (Effexor) 150–375 mg/d:
  – Antidepressant of the serotonin-norepinephrine reuptake inhibitor (SNRI) type
  – Median weekly hot flush scores decreased 54% from baseline after 1 mo (CBE)
  – Side effects include lack of sexual desire, delayed orgasm, and increase in suicidal ideation

• Paroxetine (Paxil-CR) 12.5–37.5 mg/d:
  – Antidepressant of the selective serotonin reuptake inhibitor (SSRI) class
  – In 1 study, daily hot flushes decreased from 6.2–2.5 (BHR)
  – Side effects include sexual dysfunction, constipation

• Ergotamine/baclofen/phenobarbital (EBP): 1 tablet PO BID:
  – Ergot used primarily to treat migraine headaches
  – Use with caution in patients with monosymptomatic headache disorders (MID), central nervous system (CNS) depressants, anticholinergic agents
  – Generally not recommended for the treatment of hot flashes in men

• Gabapentin (Neurontin) 900 mg/d (300 mg BID or TID):
  – Anticonvulsant treatment of neuropathic pain
  – Mosted 46% reduction in hot flush symptom score at target dose of 900 mg
  – Side effects include nausea, somnolence, dizziness, and constipation

• Clonidine (Catapres) 0.1–1 mg/d (PO or patch formulations):
  – Generally well tolerated with less of a fall in blood pressure
  – 13 of men will report a partial response although similar to placebo (13B)
  – Side effects include hypotension, dry mouth, skin irritation from patches

SURGERY/OTHER PROCEDURES

ADDITIONAL TREATMENT Radiation Therapy

Additional Therapies

• Acupuncture:
  – 1–2 wk twice weekly × 2 wk then once weekly × 8–10 wk
  – 43–78% reduction in frequency of flushes, average 9 mo duration of effect [13B]

• Vitamin E:
  – 30% reduction in 22% of women receiving placebo in 1 study (not studied in men)
  – May increase the risk of prostate cancer; unclear effect on existing cancer (10B)

• Soy products:
  – Contains phytoestrogens which might decrease severity of hot flushes (11C)
  – Also shown benefit with regard to cardiac and bone health
  – Black cohosh
  – Has been used in some postmenopausal women for treatment of hot flushes
  – Mechanism is unknown
  – In 1 trial, no difference found with men taking placebo (11C)

ONGOING CARE

PROGNOSIS

• Most men have symptom improvement with medical or complementary therapy
• 4–6 yr of treatment with ADT over 40% of men still have flushes
• In 1 study, 72% of patients noted that hot flashes interfered with sleep and 59% reported they interfered with the quality of life

COMPLICATIONS

Some men have side effects from medications taken to alleviate hot flushes (bloating, weight gain, rash, gynecomastia)

FOLLOW-UP

Patient Monitoring

• Ask patients on androgen deprivation therapy at each follow-up clinical evaluation about the presence and severity of hot flushes
• Requires a substantial side effect from therapy
• Immediate cessation of treatment can be used if side effects become bothersome
• May have positive effect on quality of life, but may decrease survival

Patient Resources

N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

• Andropause (Sex Hormone Hypothesis)
• Menopause, Urogynecologic Considerations
• Testosterone, Decreased (Hypogonadism)

CODES

ICD9

• 189.2 Syncope and collapse
• 780.8 Generalized hyperhidrosis
• 793.62 Flushing

ICD10

• B82.3.2 Flushing
• S83 Syncope and collapse
• R81.1 Generalized hyperhidrosis

CLINICAL/SURGICAL PEARLS

• Symptoms are usually reversible with cessation of ADT usually within 3–4 mo of stopping treatment.
• Most effective treatment is hormonal therapy with estrogen or progesterone derivatives
• There are limited data to support alternative/complementary therapies.
HYDROCELE, ADULT & PEDIATRIC
Costas D. Lallas, MD, FACS
Leonard G. Gomella, MD, FACS

DESCRIPTION
A hydrocele is a collection of serous fluid in some part of the processus vaginalis, usually in the tunica vaginalis. Can be congenital or acquired.

PATHOPHYSIOLOGY

ASSOCIATED CONDITIONS

ASSOCIATED CONDITIONS

PHYSICAL EXAM

Acquired: Can be primary or acquired secondary to disease of the testis. Secondary hydroceles may present acutely or chronically.
• The hydrocele of the canal of Nuck is comparable in infants/children to the hydrocele of the spermatic cord in adults.
• Changes in size of the swelling (eg, size varies throughout day).

DIAGNOSTIC TESTS & INTERPRETATION

DIFFERENTIAL DIAGNOSIS
• Cord lipoma
• Epididymo-orchitis
• Hydrocele of the spermatic cord
• Inguinal hernia
• Lymphedema of the external genitalia
• Neoplasms

PHYSICAL EXAM

• Transillumination test:
  – If transilluminates, favors simple hydrocele, but is not diagnostic.

RISK FACTORS

Lab

DIAGNOSIS

HISTORY

BASICS

No racial predilection

1% of adult males; prevalence: 1,000 in 100,000

• Prematurity, low birth weight are risk factors

GENETICS

• Hydrocele fluid characteristics:
  – Amber colored; specific gravity of 1.022–1.024
  – Components: water, inorganic salts, 6% albumin, and fibrinogen
  – Nonclotting, unless a drop of blood added
  – Chronic hydrocele: cholesterol-rich
  – Occasionally, tyrosine crystals are present

PREVALENCE

• No social prediction

PREVALENCE

• Migration of ventriculoperitoneal (VP) shunt
• Trauma with bleeding (technically a hematocele)
• Defective absorption of fluid by tunica vaginalis; known as congenital hydrocele
• Components: water, inorganic salts, 6% albumin, and fibrinogen
• Hydrocele of the canal of Nuck
• Hydrocele of the spermatic cord

DIAGNOSTIC TESTS & INTERPRETATION

– Hydrocele of the cord (PPV patent with obliteration of the peritoneal cavity)
– Congenital communicating (PPV communicates through the peritoneal cavity)
– Infantile (PPV around testis and cord)
– Exstrophy of the bladder
– Ehlers–Danlos syndrome
– Anasarca (protein-loosing enteropathy, cirrhosis)
– Nephrotic syndrome
– Retroperitoneal process with obstruction of the lymphatics (ie, multiple lymphatic filariasis)
– Nephritic syndrome
– Acartia (protein-losing enteropathy, cirrhosis)
– Spermatocele
TREATMENT

GENERAL MEASURES
- Adults:
  - No treatment is necessary unless the hydrocele causes discomfort or cosmetic concerns or there is a significant underlying cause present, such as a tumor.
  - Communicating hydroceles in older patients may have increased risk of incarceration.
- Children:
  - Most will resolve in 1st yr of life.
  - For newborns and children < 1 yr supportive care is indicated.
  - Persistence beyond age 1 suggests the presence of a patent indirect hernia sac that should be repaired.

MEDICATION

GENERAL MEASURES
- Adults: - Scrotal approach with drainage of the hydrocele
- In hydrocele of the cord, the sac can be completely closed
- High ligation of the processus vaginalis and division of the internal spermatic vessels
- Inguinal incision between internal and external spermatic vessels
- Persiste beyond age 1
- Children: - Persistence beyond age 1
- Suggests the presence of a patent indirect hernia sac that should be repaired.

COMPLEMENTARY & ALTERNATIVE THERAPIES
- Scrotal support may provide relief of discomfort.

ONGOING CARE

PROGNOSIS
- Many hydroceles do not enlarge and can be observed if confirmed that there is no underlying pathology.
- Follow-up (based on ultrasound confirmation).

COMPLICATIONS
- Rupture: Usually traumatic
- Nausea, vomiting, abdominal pain associated with damage to vascular supply to the testicle
- Postoperative:
  - Testicular atrophy or infarction after repair due to damage to vascular supply to the testicle
  - Recurrence

FOLLOW-UP

Patient Monitoring
- Periodic follow-up (baseline US) suggested if managed by observation; return for any change in symptoms.
- Patients of a resection with a hydrocele should be instructed in the natural history of the condition in children.
- Following surgical repair, edema may take several weeks to resolve.

ADDITIONAL TREATMENT

Radiation Therapy
N/A

ADDITIONAL THERAPIES
- Aspiration of the hydrocele, with or without the injection of sclerosing agents is not usually recommended.
- Noninfected hydrocele aspiration and sclerotherapy with doxycycline has been reported to have an 84% success rate with a single treatment.
- Aspiration may have a role in postoperative hydroceles such as after inguinal hernia repair.

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Canal of Nuck Hydrocele and Cyst (Female Hydrocele)
- Groin/Inguinal Mass, Male and Female
- HIV/AIDS, Urologic Considerations
- Image 9
- Hydrocele of the Spermatic Cord
- Spermatocele

CODES

ICD9
- 603.8 Other specified types of hydrocele
- 603.9 Hydrocele, unspecified
- 778.6 Congenital hydrocele

ICD10
- N43.2 Other hydrocele
- N43.3 Hydrocele, unspecified
- P83.5 Congenital hydrocele

CLINICAL/SURGICAL PEARLS
- Tenderness, fever, or other symptoms such as nausea, vomiting, abdominal pain associated with an acute hydrocele requires immediate evaluation to rule out other scrotal pathology.
- The inability to transilluminate a hydrocele could be due to a thick-walled or septated hydrocele, another cause of an enlarged scrotum such as tumor or hematoma or the presence of bowel in a large hemia defect.
HYDROCOLPOS AND HYDROMETROCOLPOS, PEDIATRIC
Sarah M. Lambert, MD
Pasquale Casale, MD, FACS

BASICS
DESCRIPTION
Hydrocolpos and hydrometrocolpos are congenital anomalies of the female reproductive tract due to an imperforate hymen or less commonly due to a transverse vaginal septum.
– Hydrocolpos: Gross distension of the vagina with fluid
– Hydrometrocolpos: Gross distension of vagina and uterus with fluid. May also be associated with vaginal or cervical atresia, stenosis, ureteral anomalies, or cloacal anomalies
– Hematocolpos: bloody fluid in vagina
– Hematometrocolpos: bloody fluid in vagina and uterus
– May be an infrequent cause of an abdominal mass in a newborn female

EPIDEMIOLOGY
Incidence
0.1–3.8% of live female births
Prevalence
N/A

RISK FACTORS
– Imperforate hymen
– High/low transverse vaginal septum
– Urogenital sinus/cloacal abnormality

Genetics (1)
– McKusick–Kaufman syndrome
  – Autosomal recessive multiple malformation syndrome
  – Characterized by vaginal atresia with hydrometrocolpos, polydactyly, congenital heart defects, nonimmune hydrops fetalis
– Bardet–Biedl syndrome
– Langer–Giedion syndrome
– Herlyn-Werner-Wunderlich (HWW) syndrome

PATHOPHYSIOLOGY
– Hydrocolpos: Congenital obstruction of the female genital tract leading to accumulation of vaginal secretions and distension of the vagina
– Hydrometrocolpos: Same as hydrocolpos but the pressure now is transmitted past the cervix into the uterus causing distention of both vagina and uterus.
– The most frequent cause of hydrometrocolpos is the presence of imperforate hymen due to failure of partial resorption of this membrane during the embryonic development
– Hymen fails to rupture during the 8th wk of gestation

ASSOCIATED CONDITIONS
– Vaginal atresia
– Urogenital anomalies
– Ureteral anomalies
– Other malformations, such as imperforate anus, bilateral cleft lips, polydactyly, oligo-or anhydrotic ectodermal dysplasia
– Pediatric considerations:
  – The diagnosis should be considered in the pubertal female with amenorrhea

GENERAL PREVENTION
Early diagnosis may prevent urinary retention, hydronephrosis, and upper urinary tract complications.

DIAGNOSIS
HISTORY
– Sonolucent mass on prenatal ultrasound (US)
– Stranguria due to bladder outlet obstruction
– Intestinal obstruction with larger mass
– Amenorrhea in pubertal females if the problem was not diagnosed before menarche. In these rare cases, chronic cyclic lower abdominal pain may be present.

PHYSICAL EXAM
– Imperforate hymen with bulging cystic vaginal introitus. The hue is typically bluish if there is trapped blood.
– Palpable suprapubic mass due to distended bladder if associated with outlet obstruction
– Lower extremity lymphedema due to decreased venous return
– Examine for stigmata of McKusick–Kaufman syndrome (see above)

DIAGNOSTIC TESTS & INTERPRETATION
Lab
– Electrolytes and creatinine if significant bilateral upper urinary tract dilation

Imaging
– Abdominal US:
  – Large constant cystic mass displacing bladder anteriorly and rectum posteriorly
  – May see layering of fluid
  – Hydronephrosis or ureteral ectasia may be present
– Prenatal sonogram can detect hydrocolpos as an antenatal diagnosis but usually cannot identify the etiology
  – IVU:
    – May see hydroureteronephrosis and a distended bladder
  – VCUG:
    – May see an anterolaterally displaced bladder
  – MRS/MRU:
    – May be useful for further delineation of pelvic anatomy when US is equivocal

Diagnostic Procedures/Surgery
N/A

Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS (2)
– Dermoid cyst
– Hydrometrocolpos:
  – Accumulation of menstrual blood products in vaginal and uterine cavity
– Mucocolpos
– Ovarian cyst
– Periurethral cyst:
  – Eccentric smooth mass displacing urethral meatus
– Prolapsed ureterocele:
  – May see necrotic tissue, asymmetric urethral meatus
– Prolapsed urethra:
  – Donut-shaped urethral meatus in the center of a normal vaginal introitus
– Rhabdomyosarcoma:
  – Cluster of grapelike masses protruding from vaginal introitus
TREATMENT

GENERAL MEASURES (2)
- Incision of the hymen if due to imperforate hymen. If an imperforate hymen is present and no mass or hydronephrosis is present, surgical correction is sometimes delayed until tissues become more estrogenized. However, the correction of the imperforate hymen must take place before there is development of hydrocolpos.
- Address vaginal or cervical issues as the anatomic pathology presents

MEDICATION
First Line
N/A
Second Line
N/A

SURGERY/OTHER PROCEDURES
- Simple incision of the imperforated hymen. A cruciate incision with resection of excess tissue tags as necessary
- Cloacal anomalies require a coordinated surgical team and planned intervention.
- Vaginal septum if present needs to be incised either endoscopically or through open surgery

ADDITIONAL TREATMENT
Radiation Therapy
N/A
Additional Therapies
N/A
Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
Excellent, especially with early diagnosis and treatment

COMPLICATIONS
- Renal compromise or acute kidney injury with severe hydronephrosis
- Abdominal ascites
- Urinary retention and voiding difficulty
- Reports of increasing rates of infertility based upon level of obstruction
- Respiratory compromise in neonates due to massive abdominal distension
- At menarche, retrograde flow may predispose patient to endometriosis

FOLLOW-UP
Patient Monitoring
Usually none necessary. Follow for resolution of hydronephrosis if present.
Patient Resources
N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Hydrocolpos and hydrometrocolpos Image
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal

CODES
ICD9
- 623.8 Other specified noninflammatory disorders of vagina
- 752.46 Imperforate hymen

ICD10
- N89.8 Other specified noninflammatory disorders of vagina
- Q52.3 Imperforate hymen
- Q52.11 Transverse vaginal septum

CLINICAL/SURGICAL PEARLS
The diagnosis should be considered in the pubertal female with amenorrhea.
HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), ADULT
Kelly A. Healy, MD
Demetrios H. Bagley, MD, FACS

BASICS

DESCRIPTION
- Hydronephrosis includes dilation of the renal pelvis and calyces while hydroureteronephrosis is dilation of the renal pelvis, calyces, and ureter.
- Both can result from obstructive and nonobstructive causes.
- Intrinsic and extrinsic obstructive processes can affect the entire urinary tract.

EPIEDEMOLOGY

Incidence
- Asymptomatic unilateral hydronephrosis occurs in ~3% of population.
- Prevalence
  - 3.1% prevalence in historic autopsy series of 59,000 patients
  - Age 20–40 more common in women, secondary to pregnancy/gynecologic conditions
  - Age >40 prostate obstruction more common in men
  - A similar 2.5% prevalence of asymptomatic unilateral hydronephrosis in radiologic series among potential renal donors
  - No association with potential donor age

Prevalence
- 60 yr obstruction more common in men

RISK FACTORS
- Unilateral is most common cause of upper urinary tract obstruction, prevalence between 10–15% by age 70 yr
- Ureteropelvic junction (UPJ) obstruction can occur from anatomic crossing vessel, high insertion, or secondary conditions (implanted stone)
- Lower urinary tract disorders can result in hydronephrosis, often bilateral
- Benign prostatic enlargement is the most common affecting 70% of men by age 70
- Hydronephrosis can develop with obstructive lesions at essentially any level.
- Kidney
  - Benign lesions including peripelvic cysts
  - Malpant neoplasms with renal cell carcinoma and urethelial carcinoma
  - Renal pelvic calculus
  - UPJ obstruction
  - Infection tuberculosis
  - Renal artery aneurysm
  - Hilar lymphadenopathy
- Ureter
  - Neoplasms: Benign papilloma, fibroepithelial polyp, ureteric strictures, malignant urethral carcinoma
  - Urinary calculi or stricture
  - Ureteroceles or congenital megoureter
  - Infection (tuberculosis, schistosomiasis)
  - Retroperitoneal lymphadenopathy (lymphoma, other malignancy)
  - Inflammation (nephropathy fibrosis and arterial aneurysms)
  - Genitourinary: Ovarian vein syndrome, endometriosis, GYN malignancy, pregnancy
  - Pelvic lymph node
  - Retrocaval ureter
  - Bladder diverticula
  - Müllerian neoplasms: eg, urethelial carcinoma
  - Locally advanced carcinoma of the prostate
  - Bladder neck contracture
  - Prune bellie syndrome
  - Detrusor dysfunction
  - Intravenous hypertension
  - Urinary tract infection, renal parenchymal disease

GENETICS
- Nonobstructive hydronephrosis occurs with several congenital syndromes, usually diagnosed in infancy (see “Hydronephrosis/Hydroureteronephrosis, Pediatric”).

PATHOPHYSIOLOGY

- Effective hydronephrosis on renal function depends on whether it is totally or partially obstructive and unilateral or bilateral.
- Effects of obstruction of the kidney are time dependent.
- Within several hours, changes are evident but (1) 1–2 wk—glomerular destruction, tubular atrophy, and interstitial fibrosis occur
- By 6–8 wk irreversible damage occurs

ASSOCIATED CONDITIONS
- Numerous causal conditions can be associated. See “Risk Factors” above.
- Acute obstruction can cause abdominal flank pain and/or back pain; may be associated with anemia, nausea, vomiting
- Gradual unilateral obstruction more typically presents with vague complaints or may be asymptomatic
- Acute obstruction of solitary kidney or bilateral can present with symptomatic obstructive uropathy or evidence of renal compromise
- Complete urinary history is essential
- Site of obstruction, upper vs. lower urinary tract may relate to presentation
- Upper urinary tract—back pain, costovertebral angle tenderness with acute obstruction
- Lower urinary tract maybe associated with obstructive voiding symptoms

PHYSICAL EXAM
- General condition—pain or localized symptoms
- Hypertension can be related to obstruction
- Abdominal, flank, or pelvic mass
- Reflex tenderness at site of obstruction
- No association with potential donor age
- Ureteral palpation
- Ureterocoele through urethra
- Digtal rectal exam
- Enlarged prostate, nodularity suggestive of prostate cancer

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis for hematuria, pyuria, crystalluria
- Urine culture
- Renal function studies:
  - BUN & creatinine
  - Serum prostatic-specific antigen (PSA)

CBC
- Anemia—associated with chronic renal insufficiency
- Elevated white blood cell count with infection

Imaging
- Several modalities are available. They differ in their degree of anatomic and functional information and may determine the presence and extent of obstruction.
- Renal ultrasound: inexpensive, widely available, no ionizing radiation, and no contrast
- Should include imaging through the bladder to assess for distal hydronephrosis, ureteral jets, bladder wall thickening, and postvoid residual
- Renal scans can be evaluated
- Color Doppler renal ultrasound
- Help distinguish obstructive vs. nonobstructive hydronephrosis

DIAGNOSIS

HISTORY
- Signs and symptoms vary dependent on the etiology and chronicity of the condition
- Acute obstruction can cause abdominal flank and/or back pain; may be associated with anemia, nausea, vomiting
- General and acute obstruction more typically presents with vague complaints or may be asymptomatic
- Acute obstruction of solitary kidney or bilateral can present with symptomatic obstructive uropathy or evidence of renal compromise
- Complete urinary history is essential
DIFFERENTIAL DIAGNOSIS

Pathologic Findings

- Chronic pyelonephritis
- Renal tuberculosis
- Tuberculosis (see above)

DIFFERENTIAL DIAGNOSIS

- Obstructive or nonobstructive hydronephrosis
- See also “Risk Factors”

TREATMENT

GENERAL MEASURES

- Management is highly dependent on underlying condition and the timing (acute vs. chronic)
- Urgent decompression is needed with:
  - Severe pain
  - Active urinary tract infection and acute kidney insufficiency
  - Retrograde ureteral or percutaneous nephrostomy can provide equally effective drainage
- Hydronephrosis lower urinary tract etiology is typically bilateral and patients may be asymptomatic
- May warrant catheter drainage or endoscopic treatment

MEDICATION

First Line

- Patients with infection and hydronephrosis require antibiotic therapy and drainage
- Renal failure and electrolyte abnormalities should be corrected in conjunction with drainage

Second Line

N/A

SURGERY/OTHER PROCEDURES

- Catheter drainage of obstructed system with percutaneous nephrostomy or ureteral stent is required
- Hydronephrosis and fever may be ominous signs requiring early drainage
- Other surgical procedures can be guided by the findings on imaging studies

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

N/A

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

Course varies

COMPLICATIONS

- Renal failure
- Re-infection
- Stricture formation
- Ureteral stricture
- Bilateral hydronephrosis

FOLLOW-UP

Patient Monitoring

- The timing for hydronephrosis will determine the appropriate surveilance regimen
- Consider renal ultrasound and renal scan at 3 mo after treatment
- Postoperative imaging may demonstrate the dilatation persists despite relief of obstruction

Patient Resources

N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Hydroureteronephrosis, Ural (Ureter/Renal Pelvis), Pediatric, Adult, Image 2. Hydronephrosis/Hydroureteronephrosis, Dilated Ureter/Renal Pelvis, Pediatric, Adult, Image 2
- Hydronephrosis/Hydroureteronephrosis, Dilated Ureter/Renal Pelvis, Pediatric, Adult, Image 2
- Hydronephrosis/Hydroureteronephrosis, (Dilated Ureter/Renal Pelvis), Adult
- Hydronephrosis/Hydroureteronephrosis, Adult
- Hydronephrosis/Hydroureteronephrosis, Adult

CODES

ICD9

- 591 Hydronephrosis
- 600.00 Hypertrophy (benign) of prostate without urinary obstruction
- 601 Hydronephrosis

ICD10

- N13.2 Hydronephrosis with renal and ureteral calculous obstruction
- N40.0 Enlarged prostate without lower urinary tract symptoms
- N03.0 Hypertrophy (benign) of prostate with urinary obstruction and other lower urinary tract symptoms (LUTS)

CLINICAL/SURGICAL PEARLS

- Hydronephrosis and fever especially sepsis may require immediate drainage.
- Hydronephrosis may be nonobstructive.
- Generally hydronephrosis in an adult can be considered a sign of a process that must be defined and possible treated.
**HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PEDIATRIC**

Ahmad H. Bani-Hani, MD, FAAP, FACS

---

### BASICS

#### DESCRIPTION
- Refers to dilation of any part of the collecting system, single or combined:
  - Pelvic (renal pelvis)
  - Calyceal (calyces)
  - Pyeloureteral (both renal pelvis and calyces)
  - Ureteral (ureter)
  - Hydroureteronephrosis (ureter-collecting system is dilated)
- Society of Fetal Urology (SFU) grading of infant hydronephrosis (1991)

#### EPIDEMIOLOGY
- Prenatal hydronephrosis is detected in about 1.4% of total prenatal ultrasound performed in US.
- The true incidence is difficult to determine secondary to many asymptomatic, undetected cases.

#### RISK FACTORS
- Family history of hydronephrosis, maternal type I diabetes mellitus (associated with infant sacral agenesis)
- Genetic syndromes: Downs, trisomy 13, trisomy 18, CHARGE, Ehlers–Danlos, Menkes, Prune belly, etc.
- Horseshoe kidney/pelvic kidney
- Duplication renal anomalies
- Neurogenic bladder secondary to tethered spinal cord, myelodysplasia, sacral agenesis

#### GENETICS
- No specific genetic abnormalities except if associated with specific genetic syndromes as outlined above.

#### ALERT
- Hydronephrosis is not a specific diagnosis but a finding or sign. The cause of the hydronephrosis is the diagnosis and indicates the appropriate treatment.

### PATHOPHYSIOLOGY
- **Physiologic hydronephrosis**: Unclear etiology but typically improves with serial renal ultrasound monitoring
- **Pathologic hydronephrosis**:
  - Vesicoureteral reflux: Reflux can be primary or secondary to conditions that raise the intravesical pressures (e.g., bladder outlet obstruction and neurogenic bladder)
  - Ureteropelvic junction (UPJ) obstruction (1991):
    - Defined as obstruction to the flow of urine from the renal pelvis to the proximal ureter
    - Considered to be the commonest cause of prenatal hydronephrosis
    - Obstruction can be caused by an intrinsic narrowing at the UPJ or by an extrinsic compression by a lower pole anteriorly crossing vessel
    - Examples of intrinsic obstruction can include: Narrow segment with musculomembranous obstruction, ureteral valves, musculature, fibrosis
  - Ureteral valves:
    - Primary: Called primary obstructive megareter.
    - The most common finding is a distal adenogenic ureteral segment that affects the flow of urine resulting in a functional obstruction
    - Secondary: Distal stone, hypertrophy of the distal ureter and trigone in neurogenic bladder or posterior urethral valves
    - Ureterocele:
      - Defines as cystic dilation of the distal ureteral segment
      - More common in females and can cause obstruction to the distal ureter flow
      - Often associated with duplication anomalies of the kidney, particularly involving the upper pole moiety
- Ectopic ureter:
  - Occurs when the distal opening of the ureter is not in the normal location at the urethro-trigonal junction
  - Ureter can enter the bladder neck, urethra, and, in females, the vestibule, vagina, and rarely the uterine cavity
  - Ectopic ureters opening outside the bladder or urethra tend to be obstructed and often associated with nonfunctioning renal moiety
  - Commonly involves the upper pole moiety in duplicated renal anomalies
  - Posterior urethral valves:
    - The most common cause of congenital lower urinary tract obstruction in males (1/4,000 to 1/7,500 births)
    - Values in severity and can result in deterioration of renal function, and progressive oligohydramnios, which may lead to pulmonary hypoplasia with a high risk of perinatal mortality and mortality
    - Other causes:
      - Abnormal urethral valves
      - Urethral atresia
      - Neurogenic neurogenic bladder (Hirman syndrome)

### ASSOCIATED CONDITIONS
- Hydronephrosis can be by physiologic or pathologic associated with many condition as noted above.

### DIAGNOSIS

#### HISTORY
- Detailed prenatal history of:
  - Timing of 1st detection of hydronephrosis in relation to gestational age
  - Ultrasound vs. bilateral
  - Gender of the baby
  - Maternal diabetes mellitus, particularly type I (associated with fetal sacral agenesis)
  - Family history of renal anomalies
  - Amniotic fluid volume
  - Prenatal allergy to penicillin
  - Detailed postnatal history:
    - Circumcision status
    - Birth weight
    - Jaundice
    - Urinary tract infections
    - Incontinence
    - Hypertension, failure to thrive

#### PHYSICAL EXAM
- Vital signs, particularly blood pressure
- Weight
- Jaundice
- Abdominal masses
- Is bladder palpable?
- Genital/anorectal exam
- Cutaneous manifestations of spina bifida occulta
- Is bladder palpable?
- Jaundice
- Birth weight
- Circumcision status
- Paternal allergy to penicillin
- Amniotic fluid volume
- Family history of renal anomalies
- Gender of the baby
- Unilateral vs. bilateral

#### DIAGNOSTIC TESTS & INTERPRETATION

**Lab**
- Basic metabolic panel
- Urine analysis and culture if indicated

**Imaging**
- Renal and bladder ultrasound (RUS)
- Should be 1st-line imaging study
- Will give excellent idea about the laterality and severity of hydronephrosis, associated bladder pathology such as ureteroceles, are ureters dilated too?
- Bladder pathology such as abnormal bladder wall thickness, key hole sign in posterior urethral valves
- Indirect way to assess overall renal function by looking at echogenicity and thickness of renal parenchyma

#### DIAGNOSIS
- Imaging
  - Renal and bladder ultrasound (RUS)
  - Should be 1st-line imaging study
  - Will give excellent idea about the laterality and severity of hydronephrosis, associated bladder pathology such as ureteroceles, are ureters dilated too?
  - Bladder pathology such as abnormal bladder wall thickness, key hole sign in posterior urethral valves
  - Indirect way to assess overall renal function by looking at echogenicity and thickness of renal parenchyma

---

**SUO grade** Pattern of renal sinus splitting on renal ultrasound

<table>
<thead>
<tr>
<th>Grade</th>
<th>Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No splitting</td>
</tr>
<tr>
<td>1</td>
<td>Urine fills partially splits sinus</td>
</tr>
<tr>
<td>2</td>
<td>Urine fills renal pelvis and/or urine fills anterior pelvis. Major calyces dilated</td>
</tr>
<tr>
<td>3</td>
<td>SFU Gr 2 and minor calyces uniformly dilated and parenchyma preserved</td>
</tr>
<tr>
<td>4</td>
<td>SFU Gr 3 and parenchyma thin</td>
</tr>
</tbody>
</table>

---

**Note:**
- Physiologic hydronephrosis: Unclear etiology but typically improves with serial renal ultrasound monitoring.
- Pathologic hydronephrosis:
  - Vesicoureteral reflux: Reflux can be primary or secondary to conditions that raise the intravesical pressures (e.g., bladder outlet obstruction and neurogenic bladder)
  - Ureteropelvic junction (UPJ) obstruction (1991):
    - Defined as obstruction to the flow of urine from the renal pelvis to the proximal ureter
    - Considered to be the commonest cause of prenatal hydronephrosis
    - Obstruction can be caused by an intrinsic narrowing at the UPJ or by an extrinsic compression by a lower pole anteriorly crossing vessel
    - Examples of intrinsic obstruction can include: Narrow segment with musculomembranous obstruction, ureteral valves, musculature, fibrosis
  - Ureteral valves:
    - Primary: Called primary obstructive megareter.
    - The most common finding is a distal adenogenic ureteral segment that affects the flow of urine resulting in a functional obstruction
    - Secondary: Distal stone, hypertrophy of the distal ureter and trigone in neurogenic bladder or posterior urethral valves
  - Ureterocele:
    - Defines as cystic dilation of the distal ureteral segment
    - More common in females and can cause obstruction to the distal ureter flow
    - Often associated with duplication anomalies of the kidney, particularly involving the upper pole moiety
  - Ectopic ureter:
    - Occurs when the distal opening of the ureter is not in the normal location at the urethro-trigonal junction
    - Ureter can enter the bladder neck, urethra, and, in females, the vestibule, vagina, and rarely the uterine cavity
    - Ectopic ureters opening outside the bladder or urethra tend to be obstructed and often associated with nonfunctioning renal moiety
    - Commonly involves the upper pole moiety in duplicated renal anomalies
  - Posterior urethral valves:
    - The most common cause of congenital lower urinary tract obstruction in males (1/4,000 to 1/7,500 births)
    - Values in severity and can result in deterioration of renal function, and progressive oligohydramnios, which may lead to pulmonary hypoplasia with a high risk of perinatal mortality and mortality
    - Other causes:
      - Abnormal urethral valves
      - Urethral atresia
      - Neurogenic neurogenic bladder (Hirman syndrome)
HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PEDIATRIC

**MEDICATION**

- **Anticholinergic drugs** in cases of an overactive bladder
- **β-blockers** in some cases of bladder outlet obstruction
- **β-Blockers in some cases of bladder outlet obstruction**

**DIAGNOSIS**

- **Cystoscopy and retrograde pyelogram** can be used to define the anatomy of the collecting system and placement of a drainage stent
- **Diuretic renal scan** (MAG-3 with Lasix): – Can provide useful information such as renal function and anatomic details when evaluating conditions such as ectopic ureter location
- **Voiding cystourethrogram**: – Can provide useful information such as renal function and anatomic details when evaluating conditions such as ectopic ureter location

**DIFFERENTIAL DIAGNOSIS**

- **Renal cysts**
- **Polycystic renal disease**
- **Multicystic dysplastic kidney**
- **Prominent extrarenal pelvis**

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- **Additional Therapies**: – **Clean intermittent catheterization** in cases of hydronephrosis and/or presence of reflux

**COMPLICATIONS**

- **Urinary incontinence**
- **Renal scarring**
- **Renal insufficiency**
- **Reflux**
- **Multiple UTIs**
- **Kidney/bladder stones**
- **Hypertension**

**FOLLOW-UP**

- **Patient Monitoring**: – **Patient need meticulous follow-up once hydronephrosis is diagnosed before and after treatment**

**TREATMENT**

- **Referral to pediatric urology/nephrology** for full assessment and treatment

**Ongoing Care**

- **National Kidney Foundation**: [http://www.kidney.org/ask/aboutHydronephrosis.cfm](http://www.kidney.org/ask/aboutHydronephrosis.cfm)

**REFERENCES**


**ADDITIONAL READING**


**See Also** (Topic, Algorithm, Media)

- **Hydronephrosis/Hydrourerteronephrosis, Adult: Ureter/Renal Pelvis**
- **Hydronephrosis/Hydrourerteronephrosis, (Dilated Ureter/Renal Pelvis), Prenatal**
- **Hydronephrosis/Hydroureteronephrosis, (Dilated Ureter/Renal Pelvis), Pediatric Images & Megacyste**: Ureter/Renal Pelvis
- **Posterior urethral valves**: Ureter/Renal Pelvis
- **Ureterocele**: Ureter/Renal Pelvis
- **Ureteroureterostomy, and partial nephrectomy**: Ureter/Renal Pelvis
- **Ureteropelvic junction obstruction**: Ureter/Renal Pelvis

**CODES**

- **ICD9**
  - 596.54 Neurogenic bladder NOS
  - 591 Hydronephrosis

- **ICD10**
  - N13.30 Unspecified hydronephrosis
  - N13.39 Obstructive hydronephrosis: Unspecified

**CLINICAL/SURGICAL PEARLS**

- **Hydronephrosis is not a diagnosis but a sign.**
- **Renal ultrasound, VCUG, and diuretic renal scan can establish the underlying etiology of hydronephrosis.**
HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PRENATAL

Bruce J. Schlomer, MD
Laurence S. Baskin, MD, FACS, FAAP

BASICS
DESCRIPTION
- May represent a normal developmental variant or a pathologic anomaly.
- Prenatal hydronephrosis (PH) may be observed early in pregnancy but the diagnosis usually cannot be made with certainty until 16 wk of gestation.
- Severe PH has a higher incidence of associated anomalies.
- Genetic counseling is recommended for all parents of a child with PH.

ASSOCIATED CONDITIONS
Congenital hydronephrosis is associated with many syndromes.

GENERAL PREVENTION
None.

DIAGNOSIS
HISTORY
- Timing of prenatal detection; earlier detection implies more severe condition.
- Presence of polyhydramnios and renal cortical thinning indicate more severe condition.
- Presence of cortical cysts may indicate dysplasia.
- Unilateral vs. bilateral renal involvement is a critical determination for diagnosis and prognosis.
- Change in dilation in relation to bladder filling may indicate vesicoureteral reflux.
- Presence of oligohydramnios important: Suggests severe renal function.
- Associated with severe obstructive pathology due to PUVs, congenital urethral stricture, or ureterocele obstructing bladder outlet.
- Associated with pulmonary hypoplasia and fetal or neonatal death.

PHYSICAL EXAM
- None.

DIAGNOSTIC TESTS & INTERPRETATION
- Urinalysis and urine culture as needed.
- Blood work:
  - Sodium: Interpretation depends on APD (affect renal function).
  - Chloride: Interpretation depends on APD (affect renal function).
  - Creatinine: Interpretation depends on APD (affect renal function).
  - Spot urine protein: Interpretation depends on APD (affect renal function).
- Postnatal US within 48–72 hr after birth may underestimate degree of hydronephrosis.
- Rare cases of pulmonary compromise from mass effect require emergent drainage.

Diagnostic Procedures/Surgery
- Postnatal evaluation: Controversial. Society of Fetal Urology (SFU) recommendations based on severity of PH (1)
  - Unilateral mild PH:
    - 1st postnatal US: 1–3 days after birth
    - VCUG: 1–7 days after birth
    - Consider diuretic nuclear renal scan (MAG-3) at 4 wk if hydro present on postnatal US
  - Unilateral moderate-severe PH:
    - 1st postnatal US: 1–3 days after birth
    - VCUG: 1–7 days after birth
    - Males: Early VCUG to rule out PUVs.
    - Consider diuretic nuclear renal scan (MAG-3) at 4 wk.
  - Bilateral moderate-severe PH:
    - Postnatal US: 1–3 days after birth
    - VCUG: 1–7 days after birth
    - Males: Early VCUG to rule out PUVs
    - Consider diuretic nuclear renal scan (MAG-3) at 4 wk.
- Special situations:
  - Bladder/urethral abnormalities, decreased amniotic fluid
  - Early evaluation similar to severe bilateral PH
  - Postnatal US within 48–72 hr after birth may underestimate degree of hydronephrosis.

Pathologic Findings
None.

DIFFERENTIAL DIAGNOSIS
- Urinary conditions:
  - Autosomal recessive polycystic kidney disease
  - Duplication anomalies
  - Ureteropelvic junction obstruction
  - Megacystis-microcolon intestinal hypoperistalsis syndrome
  - Autosomal recessive polycystic kidney disease
  - Autosomal recessive polycystic kidney disease
  - Prune belly syndrome
  - Urologic anomalies
  - Transient hydronephrosis
  - UPJ obstruction
  - Ureterocele
  - Vesicoureteral reflux
  - Intestinal disorders:
    - Intestinal atresia
    - Intestinal duplication
    - Meckel’s diverticulum
    - Gastrointestinal atresia
    - Persistent cloaca
    - Congenital nephrotic syndrome
    - Neuroblastoma

DIAGNOSIS
- N/A

DIFFERENTIAL DIAGNOSIS
- N/A

PATHOPHYSIOLOGY
- Genetics:
  - Most common is autosomal recessive.
  - Inheritance is autosomal dominant.
- Risk of clinically significant PH increases with severity.
  - Risk of undergoing surgery:
    - Severe: 2–13%
    - Moderate: 10–30%
    - Mild: 57–88%
- Incidence:
  - 1–5% of fetuses are observed to have PH (2).
- Prevalence:
  - In utero dilation of fetal renal collecting system made with certainty until 18 wk of gestation.
- Intrauterine severity.
  - Severe: >4 mm; moderate: 1–4 mm; mild: <1 mm.
- Postnatal severity:
  - Severe: >10 mm (2nd trimester); >7 mm (3rd trimester).
  - Moderate: 4–10 mm (2nd trimester); 7 to <10 mm (3rd trimester).
  - Mild: ≤4 mm (2nd trimester).

EPIDEMIOLOGY
- Associated with pulmonary hypoplasia and fetal/neonatal death.
- Additional prenatal US in 3rd trimester: Based upon severity of PH in 2nd trimester (1).
**HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PRENATAL**

**TREATMENT**

**GENERAL MEASURES**
- Pre-natal assessment: Measurement of hydronephrosis, oligohydramnios:
  - Unilateral cases: Serial prenatal US if severe; deliver at term
  - Bilateral cases:
    - No oligohydramnios: Observation, deliver at term
    - Oligohydramnios: Termination, early delivery, pre-natal treatment for pulmonary immaturity
- Post-natal management:
  - Pulmonary support if respiratory compromise
  - Antibiotic prophylaxis if moderate-severe unilateral or bilateral PN
  - Bladder/urethral abnormalities, dilated ureter, oligohydramnios (2)
  - Amoxicillin (20 mg/kg/d—1 dose per day)
  - Recommended by SFU with moderate-severe PN
  - Oligohydramnios: Termination, early delivery
  - No oligohydramnios: Observation, deliver at term

**ADDITIONAL TREATMENT**

**SURGERY/OTHER PROCEDURES**
- No specific antenatal medications exist
  - Prophylactic antibiotics controversial
  - Recommended by SFU with moderate-severe PN, bladder/urethral abnormalities, dilated ureter, oligohydramnios (2)
  - VCUG is not recommended for unilateral mild hydronephrosis
  - Tapping of fetal bladder
  - Frequent fetal interventions (cases with oligohydramnios only): Surfactant to assist lung function after birth with pulmonary hypoplasia

**MEDICATION**
- No specific antenatal medications exist
  - Prophylactic antibiotics controversial
  - Recommended by SFU with moderate-severe PN, bladder/urethral abnormalities, dilated ureter, oligohydramnios (2)
  - Amoxicillin (20 mg/kg/d—1 dose per day)
  - Surfactant to assist lung function after birth with pulmonary hypoplasia
  - Prophylactic antibiotics controversial.
  - No specific antenatal medications exist
  - Amoxicillin (20 mg/kg/d—1 dose per day)

**SECOND LINE**
- VA

**SURGERY/OTHER PROCEDURES**
- Fetal intervention (cases with oligohydramnios only):
  - Antibiotic prophylaxis if moderate-severe unilateral or bilateral PN
  - Bladder/urethral abnormalities, dilated ureter, oligohydramnios (2)
  - Amoxicillin (20 mg/kg/d—1 dose per day)
  - Surface to assist lung function after birth with pulmonary hypoplasia
- Surgery is seldom necessary in the neonatal period with the exception of severe bilateral obstruction due to bladder outlet obstruction or severe UPJ or UVJ obstruction.
- Need for post-natal surgery based upon diagnosis and correlated with severity of PN
  - Mild: ~10%
  - Severe: ~50%

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- VA

**Additional Therapies**
- VA

**Complementary & Alternative Therapies**
- VA

**ONGOING CARE**

**PROGNOSIS**
- Most neonates have an excellent prognosis.
- Prognosis depends on strategy of the dilated system and other associated anomalies.
- Severe bilateral hydronephrosis is associated with obstruction and oligohydramnios early in gestation predicts an adverse outcome.
- Resolves with bilateral hydronephrosis, a distorted bladder, and oligohydramnios are at highest risk of neonatal demise or pulmonary complications.
- Risk of UTI correlated with severity of PN
  - Mild: ~10%
  - Moderate-severe: ~30%

**COMPLICATIONS**
- Pulmonary hypoplasia with severe oligohydramnios
- Renal impairment
- UTIs

**FOLLOW-UP**

**Patient Monitoring**
- Based on initial evaluation, subsequent imaging may be necessary (3)
  - Most centres employ serial renal US every 3–6 mo for the 1st yr of life
  - If febrile UTI, consider VCUG and/or MAG-3 renal scan

**Patient Resources**
- http://urology.ucsf.edu/patient-care/children/hydronephrosis

**REFERENCES**

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
  - Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
  - Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric Image (5)
  - Megaureter, Congenital

**CODES**
- ICD9 753.03 Other obstructive defect of renal pelvis and ureter
- ICD10 O62.0 Congenital hydronephrosis
- O62.10 Congenital bladder neck obstruction
- O62.39 Other obstructive defects of renal pelvis and ureter

**CLINICAL/SURGICAL PEARLS**
- Majority of prenatal/fetal hydronephrosis (especially mild) is transient with no clinical significance.
- VCUG is not recommended for unilateral mild hydronephrosis.
- Prophylactic antibiotics have not been shown to be effective. Not recommended in mild cases.
- Emergent evaluation by urologist should occur with:
  - Severe bilateral prenatal hydronephrosis
  - Severe unilateral prenatal hydronephrosis in solitary kidney
  - Fetal hydronephrosis with dilated bladder consistent with posterior urethral valves
  - Severe prenatal hydronephrosis with pulmonary compromise from mass effect (pneumothorax)
HYPERALDOSTERONISM, PRIMARY (ALDOSTERONISM, CONN SYNDROME)

Mark W. Ball, MD
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION
- Primary hyperaldosteronism or Conn syndrome is characterized by HTN, hypokalemia, hypernatremia, alkalosis, and suppressed renin, due to excess production of aldosterone.
- It classically refers to an aldosterone-producing adenoma (APA) of the adrenal gland that is usually small (<1 cm), unilateral, and non-irremovable.
- APA subtype of primary hyperaldosteronism accounts for 30–40% of primary hyperaldosteronism.
- Secondary hyperaldosteronism is usually related to HTN and/or endocrine state disorders such as CHF, cirrhosis, and nephrotic syndrome.
- Pseudohyperaldosteronism can be due to ingestion of large amounts of licorice or situ hormone.

EPIDEMIOLOGY

Incidence
- Incidence data is lacking.

Prevalence
- 5–15% of hypertensive population (recent increased prevalence of primary aldosteronism due to improved diagnostic testing)
- Peak incidence during 4th and 5th decades
- 20% primary aldosteronism in resistant hypertensives (defined BP despite ≥3 antihypertensive medications)
- Adrenal adenoma is more common in women.

RISK FACTORS
- No known risk factors for primary hyperaldosteronism

Genetics
- Hereditary pattern for more common APAs unclear
- Gene for aldosterone synthase (CYP11B2) recently identified

PATHOPHYSIOLOGY
- The biochemical hallmark of the disease is increased aldosterone after sodium (Na) loading and low plasma renin activity (PRA) during Na depletion
- Autonomic aldosterone secretion leads to inappropriate Na and water reabsorption from the cortical collecting tubule.
- Electrolyte-patient crushed favors secretion of potassium (K), resulting in hypokalemia.
- Intracellular fluid volume (ECF) volume causes mild hypertension (HTN).
- Renal escape limits Na retention and prevents significant edema:
  - Occurs after ~1.5 kg of extracellular fluid (ECF) is aborbed, or a weight gain of ~3 kg.
  - Spontaneous diuresis then occurs, lowering the ECF.
- Increased atrial natriuretic peptide (ANP), decreased bradycardia-sensitive Na+ C+ transporter, and pressure natriuresis are factors that may contribute to renal escape.

ASSOCIATED CONDITIONS
- Adrenal cancer (rare)
- Essential HTN

GENERIC PREVENTION
- N/A

DIAGNOSIS

HISTORY
- HTN often refractory to medical therapy
- Headaches secondary to HTN
- Symptomatic hypokalemia:
  - Muscle cramps, paresthesias, tetany, nocturia, polyuria

PHYSICAL EXAM
- No specific findings
- NIDDM to moderate HTN, not usually distinguishable from essential HTN
- Malignant HTN rare
- Lack of edema

DIAGNOSTIC TESTS & INTERPRETATION
- Consider screening the following patients (1):
  - Family history of early HTN or stroke
  - Essential HTN
  - Adrenal cancer (rare)
  - Hypokalemia can be induced with oral Na loading.
  - 20% of patients with hyperaldosteronism are normokalemic; more often seen in adenomas.
  - Inappropriate kaliuresis on initiation of diuretics
  - Aldosterone and cortisol samples obtained from peripheral veins, IVC, right and left adrenal veins
  - Adrenal scintigraphy using 123I-iodomethyl-19-norcholesterol is rarely available in US. Cerenkov to perform, and depends heavily on the size of the adenoma.

Confirmatory studies:
- N/A loading test with:
  - Sodium infusion: PAC at baseline and 4 hr
  - Positive test (PAC > 10 ng/mL)
- Oral Na: 24-hr urine Na and aldosterone on days 3 and 4 (positive if aldosterone > 12 mg/dL and Na < 200 mEq/L)
- Fludrocortisone suppression
- All confirmatory tests should be used with care in patients with compromised left ventricular cardiac function.

Imaging
- CT with thin cuts through the adenals is the preferred normative test
- Used to identify surgically curable disease and differentiate the subtypes once primary aldosteronism is confirmed
- Aldosterone-producing adenomas (APA’s) usually uniform, mixed, and hypodense with Hounsfield unit ≤10
- 4–6% probability of identifying an adrenal mass on CT
- Lack’s overall accuracy to distinguish between unilateral and bilateral disease.
- Bypass adrenal vein sampling only if clear adrenal mass (<1 cm) is identified in the younger patient (<40) with highly suspicious biochemical findings.
- MRI is not more sensitive than CT
- Adrenal imaging using
  - Isotopic 131I-i-iodomethyl-19-norcholesterol is rarely available in US. Cerenkov to perform, and depends heavily on the size of the adenoma.

Diagnostic Procedures/Surgery
- Adrenal vein sampling (AVS) for aldosteronism is the gold standard in localizing the site of excess production:
  - Aldosterone and cortisol samples obtained from peripheral veins, IVC, right and left adrenal veins
  - 44% of patients with bilateral renal masses had a unilateral source of aldosterone secretion.
  - Cure also reported after adrenalectomy in patients with AVS proven unilateral despite normal aldosteronism on CT scan.
  - Postural tests, historically used to distinguish adenoma from bilateral hyperplasia have become less useful with the discovery of angiotensin-competitive ARAs.

Pathologic Findings
- Solid, well-demarcated mass with the typical mottled yellow color of adrenal cortex
- Without diffuse thickening of the zona glomerulosa or hyperplastic nodules
- May compress the nonneoplastic uninvolved adrenal gland

Histopathology: Foamy lipid-laden clear cells, in sheets or nests

200
Differential Diagnosis
- Other causes of HTN. In evolving disease, aldosterone and renin will both be low. In renal artery stenosis, there will be high renin and high aldosterone.
- Other causes of HTN and hypokalemia, such as:
  - Overproduction of hormone
  - Use of diuretics
  - Hypercalciuria/hyperparathyroidism
- Other causes of primary hyperaldosteronism:
  - Renal artery stenosis
  - Renal vein stenosis
  - Hypertension (HTN) type 1, autosomal dominant
  - Familial occurrence of APA or bilateral idiopathic hyperplasia
  - Adrenal cancer producing aldosterone: Extremely rare
- Liddle syndrome: Autosomal dominant disorder. Mimics hyperaldosteronism and involves problems with excess resorption of Na and loss of K.

Treatment
General Measures
- Treatment selected based on etiology of hyperaldosteronism
  - Control HTN

Medication
First Line (2)
- Mineralocorticoid receptor antagonist used in those with bilateral adrenal hyperplasia and unilateral hyperplasia or APA who are not surgical candidates
  - Spironolactone: Limited due to affinity for androgen and progesterone receptors. Causing gynecomastia, sexual dysfunction, menstrual irregularities
  - Eplerenone: No active metabolites, shorter half-life than spironolactone, 50–75% as potent as spironolactone but less adverse effects
  - Thiazide diuretics, ACE inhibitors, calcium channel blockers

Second Line
- Amiloride, a diuretic that blocks the Na channel and K-sparing diuretic, may also be used, especially if spironolactone or eplerenone are intolerable. More often used in conjunction with the above.

Surgery/Other Procedures
- Unilateral adrenalectomy is indicated in patients with hyperaldosteronism due to an adenoma.
- HTN is cured or improved significantly in up to 90% of such cases. Usually takes 3–6 mo to see an effect.
- Adequate control of BP (see “Medications”) for several weeks and correction of metabolic abnormalities should be done before surgery.
- Obtain PCC after surgery to confirm cure
- Monitor K closely postoperatively

Additional Treatment
Radiation Therapy
- Additional Therapies
Emerging therapies include developing drugs that inhibit actions of aldosterone synthase enzyme, encoded on the CYF11 gene.

Additional Reading
- See Also (Topic, Algorithm, Media)
  - Adrenal Mass
  - Aldosteronism (Hyperaldosteronism, Conn Syndrome) Algorithm
  - Hypertension, Urologic Considerations

Glossary
- Medical treatment of primary aldosteronism
- Therapy: Drugs used to stop or slow the progression of a disease
- Hypertension, Urologic Considerations
- Secondary aldosteronism
- Primary aldosteronism
- Signs and symptoms of primary aldosteronism
- Evaluation and diagnosis of aldosteronism
- Treatment of aldosteronism

Icd9
- 253.10 Hyperaldosteronism, unspecified
- 253.12 Conn’s syndrome
- 253.14 Other secondary aldosteronism
- 253.14 Other secondary aldosteronism

Icd10
- E26.09 Other primary hyperaldosteronism
- E26.10 Hyperaldosteronism, unspecified
- E26.11 Conn’s syndrome
- E26.12 Secondary hyperaldosteronism
- E26.09 Other primary hyperaldosteronism
- E26.09 Other primary hyperaldosteronism

Clinical/Surgical Pearls
- Hypertension (HTN) with serum K < 3 meq/L is highly suspicious of an aldosterone-producing adenoma (APA).
- Treatment selection is based on etiology of hyperaldosteronism
- Surgical excision provides excellent control of hypertension in aldosterone-producing adenoma (APA)
- Control of the adrenal vein is the most important step during adrenalectomy.

References
HYPERPROLACTINEMIA, UROLOGIC CONSIDERATIONS

Mark W. Ball, MD
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION
• Hyperprolactinemia (HPRL) refers to serum prolactin levels that exceed the normal range (<25 mg/L; 150-400 mg/L) in men.
• It is the most common endocrine abnormality due to hypothalamic-pituitary disorders.
• It may result in hypogonadism, erectile dysfunction, infertility, galactorrhea, and osteoporosis.
• Most common causes are pregnancy, medications, hyperthyroidism, and prolactin-secreting pituitary tumors (prolactinomas).

EPIEMIOLOGY
Incidence
• Peak incidence occurs in women of age 25–34, at 23.9/100,000/yr.
• Incidence data in men is lacking.

Prevalence
• Lifetime prevalence of prolactinoma is 30/100,000 in woman and 10/100,000 in men.
• Pituitary microadenomas are found in 10.9% of autopsies, with 44% prolactinomas.
• In men with sexual dysfunction, ~1% have HPRL.
• 90% of prolactinomas occur in women of reproductive age.
• 40% of pituitary adenomas are prolactinomas.

RISK FACTORS
• Female sex
• Pregnancy
• Prolactinomas
• Medications (antipsychotics, antidepressants, verapamil, opiates, GI motility drugs, estrogens)
• MEN-1 syndrome

Genetics
• Most prolactinomas are sporadic (1)
• Present in about 20% of adults with MEN-1, who have an autosomal dominant mutation in the MEN-1 tumor suppressor gene on chromosome 11
• Can rarely occur as part of familial isolated pituitary adenomas

PATHOPHYSIOLOGY
• Prolation is produced in the anterior pituitary
• Secretion is pulsatile and increases with stress and sleep
• Toniaically suppressed by dopamine via D2 receptors
• Medications that inhibit dopamine secretion raise prolactin levels
• Elevated prolactin suppresses GnRH, with subsequent reductions in LH, FSH, and sex steroid levels
• Low testosterone can cause decreased libido, erectile dysfunction, infertility, and gynecomastia in men
• Low estrogen can cause atrophy of bone, decreased libido, anovulation, and galactorrhea in women
• Increased bone mineral density can occur in both sexes secondary to low sex steroid levels.

• Prolactinomas: Pituitary microadenomas (<10 mm) and macroadenomas (>10 mm) can be seen in some patients as the cause of the elevated levels.
• Macroadenomas can have mass effect symptoms, including headache and visual disturbance by optic nerve compression.
• Rarely, chest wall injury can incrase prolactin levels.
• Macroprolactinemia is caused by an abnormal binding of the molecule to circulating IgG.

ASSOCIATED CONDITIONS
• Amenorrhea and/or galactorrhea in women
• Hypothalamic and/or ED in men
• Hypothyroidism: Increased thyroid-stimulating hormone can stimulate prolactin secretion.
• Renal failure can result in reduced clearance.
• Cirrhosis
• Herpes zoster (particularly involving the chest wall)

GENERAL PREVENTION
• Discontinuation of medication causing symptomatic HPRL (asymptomatic prolactin elevations need not be treated)

DIAGNOSIS
HISTORY
• Women: Often presents early in disease course.
• Infertility (including pregnancy history)
• Amenorrhea/menstrual irregularities
• Complaints of sexual dysfunction
• Deceased libido
• Erectile dysfunction (ED)
• Gynecomastia
• General
• Headache
• Visual field deficits
• Psychic history and antipsychotic medication use
• Alcohol abuse

MEDICATION USE
• Antipsychotics: Buptyrophene, haloperidol, chlorpromazine, thioridazine, risperidone, and others
• Nonsteroidal anti-inflammatory drugs, aspirin, ibuprofen, naproxen, methylprednisolone, opiate
• Others reported: Antihypertensives, cimetidine, ciprofloxacin, erythromycin, trimethoprim-sulfamethoxazole, verapamil

PHYSICAL EXAM
• Breast exam for gynecomastia, galactorrhea
• Evidence of chest wall trauma or hepatic lesions
• Signs of hypothyroidism
• Signs of hyperpituitarism
• Visual field abnormalities

DIAGNOSTIC TESTS & INTERPRETATION
LAB 2
• A single serum measurement > upper limit of normal makes the diagnosis of HPRL
• Serum PRL > 900 μg/L is diagnostic of a macroprolactinoma
• Women of reproductive age should have a pregnancy test
• In men presenting with ED, a testosterone level should be checked. If low, further evaluation of prolactin should be performed
• With medication-induced HPRL, prolactin levels are usually <50 mg/L and almost always <100 mg/L
• After stopping suspected medication, prolactin levels usually return to normal within 4 days

Imaging
• Pituitary MRI is the test of choice. Should be obtained in all cases where prolactin is persistently elevated and no cause is apparent.
• MRI scanning to evaluate for possible bone mineral density problems
• In women, pelvic US to assess for uterine or ovarian pathology

Diagnostic Procedures/Surgery
• Formal visual field assessment should be done in patients with macroadenomas.

PATHOLOGIC FINDINGS
• Prolactinomas: Glands composed of cuboidal cells. May be either eosinophilic or chromophobic.
• Pathologic findings
• Formally, prolactinomas appear hypercellular, with a monotonous population of cells

TREATMENT
• General measures: Do not treat women until pregnancy is excluded.
• Men: Often presents late in disease course.

DIFFERENTIAL DIAGNOSIS
• Hypothyroidism:
• Lab error or macroprolactinoma (abnormal prolactin molecule)
• Medication-induced
• Nonprolactin-secreting pituitary or hypothalamic tumors
• Polyglandular syndrome (FGOS)
• Pregnancy
• Prolactinoma
• Renal failure

ALERT
• Do not treat women until pregnancy is excluded.

GENERAL MEASURES (3)
• Women of reproductive age should have a pregnancy test 1st.
• Treat underlying cause or stop offending drug if possible
• Asymptomatic HPRL secondary to medication use does not require treatment.
HYPERPROLACTINEMIA, UROLOGIC CONSIDERATIONS

REFERENCES

ADDITIONAL READING

CODES
ICD9
• 254.1 Other and unspecified anterior pituitary dysfunction
• 256.39 Other ovarian failure
• 257.2 Other testicular dysfunction

ICD10
• E22.1 Hyperprolactinaemia
• E28.3 Other primary ovarian failure
• E29.1 Testicular dysfunction

CLINICAL/SURGICAL PEARLS
• Women present early in the disease course, while men present late.
• Dopamine agonists are the 1st-line treatment of prolactinomas.
• Surgical excision is reserved for refractory cases.
• All women should be screened for pregnancy before initiating treatment.

ON GOING CARE

PROGNOSIS
• 90–95% of prolactin-secreting pituitary microadenomas will not grow further, even without medical therapy.
• Medical therapy is usually successful in normalizing prolactin levels, normalizing menses, reducing or stopping galactorrhea, inducing ovulation, and shrinking pituitary tumors.
• ~90% of microadenomas do not grow significantly during pregnancy, even after medical therapy is stopped.
• Some microadenomas disappear with time (especially after menopause) or do not recur after medical therapy.
• Pituitary macroadenomas usually do not disappear completely with medical therapy and require continuous medical therapy.

COMPLICATIONS
• Dopamine agonists can worsen underlying psychiatric problems in patients taking psychotropic medications.
• Pituitary macroadenomas can secrete other hormones or become resistant to medical therapy.

FOLLOW-UP
Patient Monitoring
• Drug induced HPRL: Prolactin should normalize after switching medications and no further follow-up is needed.
• Microadenomas:
  • Some microadenomas resolve spontaneously.
  • Measure prolactin every 6–12 mo to ensure continued drug efficacy.
  • No need for repeat pituitary MRI unless prolactin increases markedly on therapy.
  • Consider stopping dopamine agonist after at least a year of successful therapy, some microadenomas do not recur.

• Macroadenomas:
  • If prolactin normalizes, repeat pituitary MRI after 3–6 mo to ensure tumor shrinkage and establish new baseline.
  • No consensus on frequency of further MRIs in patients whose prolactin is well-controlled medically.
  • Repeat prolactin measurements every 3–6 mo.
  • Follow visual fields in patients who have visual field defects at baseline.
  • Some macroadenomas resolve spontaneously.

Patient Resources
Patient guide to hyperprolactinemia is diagnosis and treatment. J Clin Endocrinol Metab. 2011;96:35A–36A.

PREGNANCY CONSIDERATIONS
• All women should be screened for pregnancy before initiating treatment.

FIRST LINE THERAPIES
• Cabergoline or bromocriptine (dopamine agonists): Usually will lower prolactin levels, regardless of cause, and shrink microadenomas.

SURGERY/OTHER PROCEDURES
• Cabergoline or bromocriptine (dopamine agonists): Usually better tolerated, more convenient, and more effective than bromocriptine, whereas bromocriptine is less expensive and has been used longer.
• Use dopamine agonists with caution in patients on psychotropic drugs that inhibit dopamine action.

Surgical excision is reserved for refractory cases.

ADDITIONAL TREATMENT
• Cabergoline dosing (0.5-mg tablets): Start with 0.25–0.5 mg once or twice weekly and increase the dose at monthly intervals until prolactin normalizes (> 3 mg/L is overly needed).
• Bromocriptine dosing (2.5-mg tablets): Start with 0.625 or 1.25 mg with food before bedtime and gradually increase at weekly intervals until prolactin level is controlled (usually 2.5 mg BID–TID).
• Surgical excision is reserved for refractory cases.

ADDITIONAL READING

MEDICATION

First Line
• Cabergoline or bromocriptine (dopamine agonists):
  • Usually will lower prolactin levels, regardless of cause, and shrink microadenomas.
  • In general, both cabergoline and bromocriptine are effective. Cabergoline is usually better tolerated, more convenient, and more effective than bromocriptine, whereas bromocriptine is less expensive and has been used longer.
  • Use dopamine agonists with caution in patients on psychotropic drugs that inhibit dopamine action.
• Cabergoline dosing (0.5-mg tablets): Start with 0.25–0.5 mg once or twice weekly and increase the dose at monthly intervals until prolactin normalizes (> 3 mg/L is overly needed).
• Bromocriptine dosing (2.5-mg tablets): Start with 0.625 or 1.25 mg with food before bedtime and gradually increase at weekly intervals until prolactin level is controlled (usually 2.5 mg BID–TID).
• Side effects include nausea and postural hypotension.
• Pregnancy considerations:
  • More experience with bromocriptine.
  • Neither bromocriptine nor cabergoline has been associated with teratogenicity.
• Nevertheless, either drug is usually stopped at the 1st evidence of pregnancy, except in patients with microadenomas in whom previous mass effects may recur if tumor enlarges.
• Significant enlargement of microadenomas is uncommon during pregnancy.
• Lactation: Dopamine agonists will inhibit lactation.
• Significant enlargement of microadenomas is uncommon during pregnancy.
• Lactation: Dopamine agonists will inhibit lactation.
• Significant enlargement of microadenomas is uncommon during pregnancy.
• Lactation: Dopamine agonists will inhibit lactation.

Second Line
N/A

SURGERY/OTHER PROCEDURES
• Often performed transphenoidally.
• For microadenomas, generally reserved for patients intolerant of drug therapy. Tumors may recur.
• Only indicated for pituitary microadenomas when medical therapy is ineffective, including persistent visual field abnormalities.
• Usually do not curative

ADDITIONAL TREATMENT

Radiation Therapy

Usually only indicated for pituitary microadenomas that have failed medical therapy, and where response to surgery is inadequate or surgery is contraindicated.

Additional Therapies
Men with ED or persistent hypogonadism may require additional therapies.

Complementary & Alternative Therapies

Vitex agnus-castus extract can be tried in cases of mild HPRL.
HYPOSPADIAS
Steve J. Hodges, MD
Anthony Atala, MD

DESCRIPTION
Common congenital disorder of male external genitalia characterized by a ventrally displaced urethral meatus.
- Associated conditions may include:
  - Ventral chordee
  - Incomplete foreskin with dorsal hood and ventral deficiency
- May be an isolated defect or may be associated with a significant underlying abnormality
- Classification:
  - Anterior (distal) 50%: Glandular, coronal, subcoronal, megameatus intact prepuce
  - Middle (midshifty) 30%
  - Posterior (proximal) 20%: Penoscrotal, crural, perineal

EPIDEMIOLOGY
Incidence
- 1 in 250–300 live male births
- 1 in 80–100 in family history of hypospadias
Prevalence
Prevalence in US for hypospadias ranges between 2.01 and 56.17 per 10,000.
Incidence
2–12% have upper tract anomalies (horseshoe kidney, renal ectopia, duplicated ureters, others)
5% of cases have genetic cause
- Genetics (see below)
- Examples include environmental chemicals such as bisphenol A (BPA) and hormones used during pregnancy such as progesterone.
- Not possible except by avoidance of environmental agents or medications with estrogenic effects by pregnant women (see “Risk factors”)

ASSOCIATED CONDITIONS
- Associated conditions may include:
  - Ventral chordee
  - Incomplete foreskin with dorsal hood and ventral deficiency
  - May be an isolated defect or may be associated with a significant underlying abnormality
  - Classification:
    - Anterior (distal) 50%: Glandular, coronal, subcoronal, megameatus intact prepuce
    - Middle (midshifty) 30%
    - Posterior (proximal) 20%: Penoscrotal, crural, perineal

PATHOPHYSIOLOGY
- Normal penile development:
  - Urogenital folds form on either side of the cloacal membrane, and fuse anteriorly at the genital tubercle
  - Lateral labioscrotal folds fuse posteriorly and separate the urogenital and anal membranes
  - Under influence of testosterone and DHT, phallus elongates and the genital folds fuse in the midline to enclose urethra proximally to distally
  - Canalization of the glans occurs distally, fusing with urethra
  - Process complete by 20th wk of gestation
- Glanular hypospadias likely represents failure of distal canalization
- Proximal hypospadias due to failure of fusion of genital folds
- Scrotal or perineal variants result inชาft occlusion

ASSOCIATED CONDITIONS
- Growth restriction (low birth weight and length, small head circumference) has been associated with hypospadias
- Associated anomalies are more common in cases of severe hypospadias:
  - Cryptorchidism (7–9%)
  - Inguinal hernia/hydrocele (9–16%)
  - Syndromes:
    - 49 described in which hypospadias is frequent or occasional (Anemia-Wilms tumor association, Beckwith-Wiedemann, Smith-Lemli-Opitz, Triosity syndromes, Apert, Saethre-Chotzen, TAR, VACTERL association, XX, Trisomy 13, 18, V-CAP-BL association, XX, Zellweger, and many others)
    - 78% of these have associated micrognathia, cryptorchidism, and/or crural anomaly
    - In presence of hypospadias and cryptorchidism must rule out intersex condition (15% with true hermaphroditism)
    - Mixed gonadal dysgenesis
    - Partial androgen insensitivity
    - True hermaphroditism

GENETIC TESTING
- Genetics (see above)
- <5% of cases have genetic cause (3)
- 5% incidence in IVF births compared to controls
- Environmental:
  - Because of increases in rates in certain areas an association with chemicals with estrogenic or antiandrogenic effects has been suggested
  - Examples include environmental chemicals such as bisphenol A (BPA) and hormones used during pregnancy such as progesterone.
  - Genetics
- In cases of proximal hypospadias associated with an undescended testicle differential should include:
  - Congenital adrenal hyperplasia
  - Mixed gonadal dysgenesis
  - Partial androgen insensitivity
  - True hermaphroditism

DIAGNOSIS
HISTORY
- Family history of hypospadias
- Any associated congenital anomalies
- Exposure of mother to hormonally active agents during pregnancy
- IVF may increase risk of hypospadias

PHYSICAL EXAM
- Determine location of urethral opening
- Evaluate for chordee
- Evaluate for cryptorchidism
- Evaluate presence of inguinal hernia, hydrocele, or cryptorchidism
- Severe proximal hypospadias may be associated with bifid scrotum and/or penoscrotal transposition
- Look for other congenital anomalies

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Karyotype and hormonal evaluation to rule out intersex condition
  - In cases of severe hypospadias and cryptorchidism

Imaging
- No routine imaging necessary for routine hypospadias evaluation
- In setting of intersex evaluation, genitogram or perineal US may be performed
- VCUG in proximal hypospadias may demonstrate prominent prostatic utricle

Diagnostic Procedures/Surgery
- Pathologic Findings
- N/A

DIFFERENTIAL DIAGNOSIS
- In cases of proximal hypospadias associated with an undescended testicle differential should include:
  - Congenital adrenal hyperplasia
  - Mixed gonadal dysgenesis
  - Partial androgen insensitivity
  - True hermaphroditism

ALERT
- Do not perform circumcision in the setting of hypospadias. Hypospadias in the presence of cryptorchidism may signal an intersex disorder.
HYPOSPADIAS

TREATMENT

GENERAL MEASURES (2)
The general tenets of repair are to move the urethral meatus to an orthotopic location, straighten the penis (repair chordee), and either remove or modify the foreskin to give the appearance of a normalcircumcised or uncircumcised penis.

MEDICATION

First Line
• There is no specific medical therapy for hypospadias.

Surgery/Other Procedures
• Indicators of repair (1):
  – Proximal hypospadias: 1 stage—Thiersch–Duplay,
  – Midshaft hypospadias: Tubularized incised plate
  – Distal hypospadias: MAGPI, Thiersch–Duplay,
  – Chordee should be repaired 1st (orthoplasty)
  – Techniques dictated by meatal location, degree of
  – Timing of repair is ideal at 4–6 mo of age,
  – Goals are to create a cosmetically normal
  – 25–50 mg of testosterone propionate given IM
  – However, although a preference for the use of

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
• Patient may need revisions for chordee, meatal issues, or recurrent chordee at later dates

Complementary & Alternative Therapies
Psychosocial support for patient and family if needed

ONGOING CARE

PROGNOSIS
Most patients have normal penile function for voiding, sexual performance, and infiltration.

COMPPLICATIONS
• Early
  – Bleeding/hemorrhage—treated with compression or surgical exploration; infection—treated with antibiotics or incision and drainage;
  – Skin/tissue—treated with appropriate antibiotics;
  – Wound dehiscence—requires respiration 6 mo
• Late
  – Residual/recurrent chordee—treated with
  – Meatal stenosis—treated with meatal dilation or
  – Urethral stricture—treated with dilation or
  – Meatal stenosis—treated with meatal dilation or
  – Urethral stenosis—treated with dilatation or
  – Urethral diverticulum—treated with excision and repair;
  – Meatal stenosis—treated with meatal dilation or
  – Urethral stricture—treated with dilatation or
  – Urethral strictures—treated with complete excision and
  – Wound dehiscence—requires respiration 6 mo
• Late
  – Residual/recurrent chordee—treated with
  – Meatal stenosis—treated with meatal dilation or
  – Urethral stricture—treated with dilation or
  – Meatal stenosis—treated with meatal dilation or
  – Urethral strictures—treated with complete excision and
  – Wound dehiscence—requires respiration 6 mo

FOLLOW-UP

Patient Monitoring
• Follow-up for observation of penile development and complications noted above
• Children may present after toilet training or even as late as adolescence with newly diagnosed complications from repair as an infant.

Patient Resources
Urology Care Foundation http://www.urologyhealth.org/urologyindex.cfm?artid=130

REFERENCES

ADDITIONAL READING
See Also (Topic, Algorithm, Media)
• BMD Section
• Disorder of Sexual Development (DSD)
• Hypospadias Image
• Penoscrotal Transposition

CODES

ICD9
• 752.61 Hypospadias
• 752.63 Congential chordee
• 752.69 Other penile anomalies

ICD10
• Q54.9 Hypospadias, unspecified

CLINICAL/SURGICAL PEARLS

• More severe cases (proximal) more likely to be associated with an intersex disorder
• All members of the health care team must clearly understand that circumcision should not be performed if hypospadias is present.
IMMUNOCOMPROMISED PATIENTS, UROLOGIC CONSIDERATIONS

Patrick J. Shenot, MD, FACS

Nathan Roberts, MD

BASICS

DESCRIPTION

Immunocompromised patients have attenuated immune responses caused by:

- Immunosuppressive drugs (chemotherapy)
- Radiation (bone marrow irradiation)
- Hematopoietic stem cell transplant
- Malnutrition
- Disease processes (HLA, lymphoma, congenital immune deficiencies, autoimmune disorders)

Immunocompromised patients are at risk for opportunistic infections:

- Hematopoietic stem cell transplant
- Need preparative regimen to prevent rejection of transplanted graft: Complete myeloablative, Nonmyeloablative or 1+ chemotherapy
- Miliary tuberculosis
- Hematogenous dissemination of Mycobacterium tuberculosis
- HIV infection is common, 38% with military TB patients also have HIV

EPIEMIOLOGY

Incidence

- HIV infections: 1.2 million Americans
- Hemorrhagic cystitis (HC) (1)
- Tuberculosis
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals

EPIDEMIOLOGY

- HIV/AIDS: 1.2 million Americans
- Hemorrhagic cystitis (HC) (1)
- Tuberculosis
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals

HIV/AIDS

- Increased degree of immunosuppression
- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- Donor–recipient gender mismatch
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB

PATHOPHYSIOLOGY

- Need for blood transfusions
- Graft versus host disease (GVHD)
- Allogenic HSCT transplant
- Donor–recipient gender mismatch
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB

ASSOCIATED CONDITIONS

- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- Donor–recipient gender mismatch
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB

HISTORY

- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- Donor–recipient gender mismatch
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB

DIAGNOSIS

- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- Donor–recipient gender mismatch
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB

ASSOCIATED CONDITIONS

- BK virus Hemorrhagic cystitis (HC)
- Early onset Hemorrhagic cystitis (HC)
- Conditioning regimen used for hematopoietic stem cell transplant (HSCT) with cyclophosphamide, busulfan, or with antithymocyte globulin (4)
- Donor–recipient gender mismatch
- Late onset Hemorrhagic cystitis (HC)
- Allogenic HSCT transplant
- Graft versus host disease (GVHD)
- Use of corticosteroids or cyclosporine for GVHD
- Use of T cell depleted grafts
- HIV/AIDS: Protection during sexual activity; universal precautions for healthcare professionals
- Military tuberculosis: Treatment of latent TB can prevent miliary TB
IMMUNOCOMPROMISED PATIENTS, UROLOGIC CONSIDERATIONS

PHYSICAL EXAM
- **HC**
  - May present with palpable bladder if in clot retention
- **HIV/AIDS**
  - Most common intrascrotal pathology in AIDS is testicular atrophy
    - Secondary to endocrine imbalances, febrile episodes, malnutrition, tubercular infections, and toxic effects of therapeutic agents
  - **Prostatitis**
    - Boggy prostate
    - Crystal swelling/needle pain
  - Epididymitis/testicular pain caused by common and uncommon organisms (Candida, CMV, toxoplasmosis)
  - **Voiding dysfunction**
    - May have enlarged prostate

**Miliary tuberculosis**
- Pulmonary: Course breath sounds on auscultation, may have lymphadenopathy
- Genitourinary involvement
  - Possible costovertebral angle tenderness
  - Epididymal/prostate tenderness

DIAGNOSTIC TESTS & INTERPRETATION

**Lab**
- **HIV/AIDS**
  - HIV ELISA for anti-HIV-1 and 2
    - >99% sensitivity; Western blot to exclude false-positive but also to confirm HIV diagnosis
  - Plasma HIV RNA
    - Detectable by day 12; antibodies detected day 21
    - Used to assess treatment response/failure
  - HIV-associated nephropathy: Proteinuria-increased creatinine
- **Tuberculosis**
  - PPD; may be false negative
  - Mycobacterial blood culture
  - Ultrasound: Stone pain, possible hematuria
  - Urine and fast bacillus (FAB) culture

**Imaging**
- **HC**
  - CT with and without contrast: Can show clot, filling defect, calculus
- **HIV/AIDS**
  - **Bilateral**
    - CT non contrast may be associated with minimal findings with indwelling calculus
  - Kidney infection
    - CT scan: Can see striated nephrogram in pyelonephritis, abscess
- **Tuberculosis**
  - Chest radiograph (miliary disease)
    - Pain, reticulonodular infiltrate distributed fairly uniformly throughout the lungs
  - ESR findings: QSP (similar to normal value. Larger may indicate caseous lesions or chronicity and fibrosis from autonephrectomy
    - Autonephrectomy: Diffuse, uniform, extensive parenchymal, putty-like calcification, a lobed cast of the kidney
    - Calcifications in 30–50% of cases
    - Calculi may also be seen in the collecting system or urinary tract due to stricture formation
    - Urethral calcifications are rare and are characterized by intraluminal calcifications
  - Bladder wall calcifications are not very common except in late cases of bladder infection
    - Calculi may also be seen in the collecting system or urinary tract due to stricture formation
    - Renal parenchymal masses and scarring
    - Thick urinary tract walls
    - Tuberculoma: Renal mass coalescing caseating granulomas
  - Can see hydroptysis
  - Sensitivity in seeing the calcifications
  - Contrast can evaluate function of the kidney
  - Ultrason: Limited in diagnosis, Can be used for monitoring disease progression

**Pathologic Findings**
- **Tuberculosis**
  - Granulomatous inflammation
  - Contains epithelial macrophages, Langhans giant cells, and lymphocytes
  - Contains caseation necrosis
  - Organisms may or may not be seen with acid-fast staining
  - **HIV**
  - HIV-associated nephropathy (HIVAN)
  - Collapsing form of focal segmental glomerulosclerosis
  - Dilated tubules and interstitial inflammation

**Differential Diagnosis**
- **HC**
  - Infectious source
  - Bacterial
  - Viral BK vs adenovirus, CMV, JC, and herpes
- **HIV**
  - **Voiding dysfunction**
  - Patient may have underlying neurologic opportunistic infection

**Diagnostic Procedures/Surgery**
- **HC**
  - Cystoscopy, possible ureteroscopy
- **HIV/AIDS**
  - Kidney biopsy: Help to diagnose HIV-associated nephropathy (HIVAN)
  - Voiding dysfunction
  - Mayo-want UDS, may uncover neurogenic voiding dysfunction
  - Post-void residuals, cystoscopy
  - **Tuberculosis**
    - Biopsy of the following can demonstrate granulomas and be used for culture: lung, bone marrow, lymph nodes, bones, joints, liver, brain, and other tissues
    - Cystoscopy/retrograde pyelograms
      - Limited in diagnosis: Stricture, acute UO inflammation, acute tubulobular ulce, Golf hole ulcer. Circumferential and often excessively lateral unusual orifice
Reduction of immunosuppression (if possible) can help to reduce clinical sequelae. HIV patients have higher risk of bladder infections than non-HIV patients. Salmonella is of particular concern due to high-risk fatal recurrence (may need chronic suppression).

**MEDICATION**

**First Line**
- **HC**
  - Increased hydration
  - Catheter placement with clot evacuation
  - Continuous bladder irrigation (CBI)
- **HIV/AIDS**
  - Antiretroviral therapy (ART)
  - Miliary TB (3)
    - Standard pulmonary therapy
    - Often directly observed therapy
    - Isoniazid (INH), rifamycin (rifampin), pyrazinamide, and ethambutol for 2 mo
    - Isoniazid and rifamycin for additional 4 mo

**Second Line**
- **HC**
  - Conjugated estrogens
    - Act by stabilization of microvasculature
    - Oral vs. intravenous administration
  - Intravesical instillation of Alum
    - An astringent precipitates protein over bleeding surface
  - E-aminocaproic acid
    - Inhibits fibrinolysis preventing activation of plasminogen to plasmin
  - Conjugated estrogens
    - Act by stabilization of microvasculature
  - Intravesical instillation of silver nitrate
    - Chemical caugetion and coagulation at bleeding sites
  - Intravesical instillation of formalin (40% formaldehyde)
    - Hydrolize proteins and coagulates tissue on superficial level
  - E-aminocaproic acid
    - Inhibits fibrinolysis preventing activation of plasminogen to plasmin

**Surgery**
- **HIV/AIDS**
  - Kidney infection abscess (Aspergillus and toxoplasma)
    - Percutaneous or open drainage
  - Prostatic abscess
    - Percutaneous (transrectal or transperineal)
  - Transurethral resection (TUR)
  - Testicular and epididymal infections
    - If intractable pain may warrant epididymectomy or orchectomy
- **Tuberculosis**
  - Often will proceed 3–6 wk after medications
  - Abscess drainage
  - Urethral or balloon catheter drainage
  - Percutaneous drainage
  - Nephrectomy
  - Prostatic abscess
    - Urinary tract infection (UTI)
    - Can treat with prolonged 3–10 day course of antibiotics
  - Epididymitis
    - Should be treated with antibiotics
    - Opportunistic infections should be suspected if not resolving
    - Vescicoureteral reflux
  - Partial nephrectomy
    - Caseating abscess that has not responded to medical therapy or firm swelling that has remained unchanged or increased in size with medical therapy
    - Augmentation cystoplasty (<100 cc capacity) vs. orthotopic bladder substitution (20 cc capacity)

**SURGERY/OTHER PROCEDURES**
- **HC**
  - Hyperbaric oxygen therapy
    - 100% oxygen in a hyperbaric chamber at 2.5 atmospheres absolute for 90 min 5 days a week.
  - Nephrectomy: If kidney is nonfunctioning, there is extensive disease involving the whole kidney, coexisting renal carcinoma
  - Partial nephrectomy
  - Epididymectomy: Caseating abscess that has not responded to medical therapy or firm swelling that has remained unchanged or increased in size with medical therapy
  - Augmentation cystoplasty (<100 cc capacity) vs. orthotopic bladder substitution (20 cc capacity)
IMMUNOCOMPROMISED PATIENTS, UROLOGIC CONSIDERATIONS

ADDITIONAL TREATMENT

**Additional Therapies**
- Oxazaphosphorine (cyclophosphamide)-induced HC
  - Mesna
  - Binds to acrolein and inactivates it
  - Supra hydration
  - Prophylactic Continuous bladder irrigation (CBI)
  - Often occurs within 72 hr

**ONGOING CARE**

**PROGNOSIS**
- HIV/AIDS
  - Greatly improved in the era of HAART therapy
  - CANCer
  - Rectal: 8-fold higher incidence
  - Testicular cancer: 2-fold increase in seminoma
- Miliary tuberculosis
  - Greatly improved with the introduction of antibiotics
  - Mortality previously 100% (pre-antibiotics) now 20%

**COMPLICATIONS**
- Increased risk for malignancy in immunosuppressed patients
- HIV/AIDS
  - 3.5% of HIV-infected patients will experience HIV-associated nephropathy
  - Caucasian patients: 12:1 risk
  - Intravenous drug use and men who have sex with men association
- Tuberculosis
  - Peritoneal nephrectomy (PCN)
  - Tuberculous fistula formation
  - Urinary stenting
  - Limit high-pressure contrast injection during retrograde pyelogram may disseminate infection

**FOLLOW-UP**

**Patient Monitoring**
- Hemorrhagic cystitis (HC)
  - Cyclophosphamide
  - 9-fold increase in urothelial carcinoma
  - 10-yr latency period

**REFERENCES**

**ADDITIONAL READING**

**CODES**

<table>
<thead>
<tr>
<th>ICD9</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>279.9</td>
<td>Unspecified disorder of immune mechanism</td>
</tr>
<tr>
<td>279.49</td>
<td>Autoimmune disease, not elsewhere classified</td>
</tr>
<tr>
<td>279.30</td>
<td>Graft-versus-host disease, unspecified</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD10</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D89.9</td>
<td>Disorder involving the immune mechanism, unspecified</td>
</tr>
<tr>
<td>D89.813</td>
<td>Graft-versus-host disease, unspecified</td>
</tr>
<tr>
<td>M35.9</td>
<td>Systemic involvement of connective tissue, unspecified</td>
</tr>
</tbody>
</table>

**CLINICAL/SURGICAL PEARLS**
- Recurrent UTI in the absence of infections in other organ systems, is not a typical presentation of an immunocompromised patient.
- Most common intrascrotal pathology in AIDS is testicular atrophy.
INCONTINENCE, URINARY, ADULT FEMALE
Debra L. Bronner, MD
Drew A. Freilich, MD

BASICS
DESCRIPTION
Incontinence is broadly defined as the loss of urine that is objectively demonstrable and is of social and hygienic concern.

PHYSIOLOGY
Stress urinary incontinence (SUI) occurs with increased intra-abdominal pressure without detrusor contraction.

RISK FACTORS
Advanced age, smoking, pregnancy, obesity, menopause, COPD, cognitive impairment, and advanced age.

EPIDEMIOLOGY
Incidence
Prevalence
Affects 30–50% of adult women
Stress urinary incontinence is the most common (40%), followed by mixed (20%) and urge (21%) incontinence.

Epidemiology

RISE PATHOPHYSIOLOGY
Stress incontinence occurs with increased intra-abdominal pressure without detrusor contraction.

Anatomy: Due to urethral hypermobility from lack of pelvic support.

Hammond theory: Normally, the suburethral support contributed by the endopelvic fascia and anterior vaginal wall provides a stable backboard against which the urethra is compressed while intra-abdominal pressure rises. When this suburethral support layer is lax and mobile, any effective compression is not achieved, causing leakage.

Intrinsic sphincter deficiency (ISD): Impairment of urethral mucosal seal and inherent closure from collagen, fibroelastic tissue, smooth and striped muscles. May be lost secondary to surgical scarring, radiation, or hormonal and menopausal changes

PATHOLOGY
Upper urinary tract anomalies may cause stress incontinence.

URGENCY INCONTINENCE: Detrusor overactivity (may be secondary to detrusor myopathy or neuropathy).

OK: Urinary retention (usually from lower motor paralytic, neurogenic bladder in women).

TOTAL INCONTINENCE: Constant loss of urine. Ectopic ureters in females usually open in the urethra distal to the sphincter or in the vagina, causing continuous leakage.

SUPPORT FIBROUS TUMOR (or intrapelvic leiomyoma) in history of radiation.

COTAL INCONTINENCE: Up to 60% of women who report incontinence appear to leak urine during intercourse.

ASSOCIATED CONDITIONS
Pelvic organ prolapse
Diabetes
Neurologic disease (e.g., multiple sclerosis, Parkinson’s disease)

GENERAL PREVENTION
Weight loss
Optimization of medical health (e.g., diabetes)
Smoking cessation

DIAGNOSIS
HISTORY
Part II: Weakness of the pelvic floor is more likely in multiparous women leading to SUI.

Amount and frequency of leakage
Continuous slow leakage in between regular voiding
Continuous leakage: Ectopic ureter, urinary fistulas, Nocturnal enuresis: Idiopathic, neurogenic, or iatrogenic

Urgency incontinence: Can be due to urinary tract, duplicated systems for ectopic ureters, and infection associated pathologies (indicated only when upper tract issues are suspected).

DIAGNOSTIC TESTS & INTERPRETATION
Lab
-Urine analysis
-Urine culture: Assess for infection

Imaging
-CSTogram: Determines status of upper urinary tract, duplicated systems for ectopic ureters, and infection associated pathologies (indicated only when upper tract issues are suspected).

Voiding cystourethrogram: Preferably done in combination with videourodynamics studies

Diagnostic Procedures/Surgery
-24-hr voiding diary to assess frequency, timing, volume of symptoms
-Cystoscopy: If concern for fistula or malignancy
-Urinal cytology: If hematuria and urgency (concern for carcinoma in situ)
-Urodynamic studies:

Pelvic suburethral support is bowel filling.

Assess Valsalva leak point pressure: Determines the intra-abdominal pressure at which leakage is observed at the meatus or by fluoroscopy. Low leak point pressure (< 60 cm H2O) implies ISD.

Assess detrusor leak point pressure: Increased detrusor pressure at which leakage of urine occurs in absence of detrusor contraction and increase abdominal pressure (> 40 cm H2O risk on renal deterioration).

Voiding cystometry: Pressure/volume relationship during micturition.

Assess urinary flow rate, postvoid residual, detrusor sphincter synergy.

Urodynamic studies: Combination of fluorourodynmenography and urodynmy studies mentioned above.

Most useful in patients at risk for neurogenic bladder to assess for detrusor sphincter dyssynergia which is risk for renal deterioration

Pathologic Findings

DIFFERENTIAL DIAGNOSIS
-Stress incontinence: Due to urethral hypermobility or ISD, although in the majority is mixed or due to both of the factors.

-Urgency incontinence: Can be due to urinary infection, interstitial cystitis, carcinoma in situ, bladder cancer, detrusor overactivity, or neurogenic detrusor overactivity. Most often idiopathic

-Nonspecific enuresis: Idiopathic, neurogenic, cardiogenic, or obstructive causes

-Corticosteroid therapy, interstitial cystitis, endometriosis-related complex

-Postcoital blushing: Urethral diverticulum, idiopathic or uretogenic

-Mobility or cognitive impairment post stroke

-Coronal or mixed incontinence
TREATMENT

GENERAL MEASURES (1)
- Non-surgical management (helps ~ 50–65% patients with milder symptoms)
- Treat constellate causes (iatrogenic, cardiovascular, diuretic, etc.)
- Encourage weight loss in obese patients
- Biofeedback and pelvic floor exercises (Kegel exercises) (2)
- Behavioral therapy: Voiding at progressively increasing predetermined intervals

MEDIATION

First Line (2)
- Stress urinary incontinence: Activation of urogenital straining increases the urethral resistance to urinary flow with symphysiophoric diap septum, estrogen, and tricyclic antidepressant medications have been used to treat this type of bladder symptoms.
- Mirabegron (25–50 mg/d) is a first-line agent for treatment of urge incontinence. When compared to anticholinergic medications, it has less dry mouth and constipation, but it is more expensive.

Second Line
- Anticholinergic, antispasmodic, and tricyclic antidepressant medications have been used to treat neurogenic bladder symptoms.
- α1 blockers used to treat overactive bladder symptoms
- ≤ 3-agonist for refractory UI

- Intravesical botulinum toxin for neurogenic overactive bladder (NDO/1)
- Percutaneous tibial nerve stimulation
- Sacral neuromodulation: Efficacy ∼ 80% in those refractory to other modalities (4)
- Catheter-related complications can result from long-term indwelling catheters, such as recurrent UTIs, skin infections, and urethral erosion.

FOLLOW-UP
- Initial postoperative assessment after midurethral slings: Evaluate voiding function with estimation of postvoid residual and need for intermittent catheterization.
- Periodic long-term follow-up with validated outcome-based questionnaire surveys

Ongoing Care
- Initial postoperative assessment after midurethral slings
- Catheter-related complications can result from long-term indwelling catheters, such as recurrent UTIs, skin infections, and urethral erosion.

ADDITIONAL TREATMENT

Radiation Therapy
- Radiotherapy overactive bladder

Additional Therapies
- Reducer or avoidance of spicy foods, citrus, or chocolate; limiting excessive fluid intake and caffeine can improve symptoms of urinary incontinence (especially if overactive bladder)
- Complementary & Alternative Therapies
- No high level data to support

ADDITIONAL READING

CODING
- ICD-10: N39.41 Urge incontinence
- N39.40 Stress incontinence
- 788.30 Urinary incontinence, unspecified
- 788.31 Urge incontinence
- 746.8 Stress incontinence, female
- R32 Unspecified urinary incontinence
- R32.5 Stress incontinence
- R32.3 Urge incontinence
- R32.41 Urge incontinence

CLINICAL/SURGICAL PEARLS
- Recent FDA alerts regarding vaginal mesh applies to prolapse repair and not midurethral slings. Mesh for stress incontinence has been supported in multiple randomized controlled trials.
- Consider reduction of pelvic organ prolapse as part of evaluation for incontinence.
- Consider referral to urologist in young patients with refractory idiopathic overactive bladder as 1st presenting symptom of multiple sclerosis or isolated urinary urgency in ~ 15%.
INCONTINENCE, URINARY, ADULT MALE
Michael J. Anvari, MD
Patrick J. Shenot, MD, FACS

DIAGNOSIS

HISTORY
- Voiding symptoms
  - Duration and characteristics of incontinence
  - Stress, urge, total
  - Precipitants and associated symptoms
  - Use of pads, briefs, diapers
  - Fluid intake
  - Alteration in bowel habits
  - Previous treatments and effect on incontinence
- Diabetes mellitus
- Associated conditions
- Neurologic disease
- Medication use
- Deinits
- Alcohol and drug use including caffeine
- Radical pelvic surgery or radiation
- Abdominoperineal resection
- Radical prostatectomy

PHYSICAL EXAM
- Abdominal exam
  - Sigmoidoscopy
  - Suggests retention
  - Proctoscopy
  - Suggests U/TI
  - Surgical scars suggesting pelvic surgery
  - Suprapubic tenderness
  - Skin lesions associated with neurologic disease
  - Vascular malformation, tuft of hair, or skin dimple on lower back
  - Cauda equina sign
  - Low, short gluteal cleft
  - Coccyx not palpable
  - Inspect muscle for atrophy
  - Coccyx not palpable
  - Rectal neurologic exam
  - Motor function
  - Posterior tibial (S1–S2): Ankle plantar flexion
  - Anterior tibial (L4–S1): Dorsiflexion of foot
  - tibialis anterior (L4–S1): Dorsiflexion of first metatarsal
  - Perineal tenderness

ASSOCIATED CONDITIONS
- Neurologic disease
- Pelvic disease, multiple sclerosis
- Pelvic trauma
- Bladder surgery

GENERAL PREVENTION
None

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Creatinine
- 8–11 mg/dl
- If significant retention suspected
- Urinalysis
- Glucosuria, infection

Imaging
- None usually indicated

Diagnostic Procedures/Surgery
- Urodynamics
- Useful for confirming bladder outlet obstruction as possible cause of detrusor overactivity

Pathologic Findings
- None

DIFFERENTIAL DIAGNOSIS
- Urge incontinence
- Loss of urine accompanied by urgency, often related to triggers such as sounds of running water, cold weather, passing a restroom
- Stress incontinence
- Urinary leakage associated with exertion, lifting, coughing, sneezing
- Mixed incontinence
- Urinary leakage associated with both stress and urge incontinence
- Low bladder compliance resulting in overflow incontinence
- Continuous urinary incontinence is the continuous loss of urine
- Post-obstructive detrusor dysfunction
- The involuntary loss of urine immediately after he has finished passing urine, usually after leaving the toilet
- Mobility or cognitive impairment post stroke

TREATMENT

GENERAL MEASURES
- Bladder diaries are invaluable
- Help patients understand patterns of incontinence
- Time voiding
- Avoids significant bladder distention
- For postradical prostatectomy incontinence see Section I: Incontinence, urinary following radical prostatectomy

MEDICATION

First Line
- Anticholinergics
  - Mirabegron (25–50 mg/d)
  - Fesoterodine (4–8 mg/d)
  - Oxybutynin (IR 7.5–20 mg/d, XL 5–30 mg/d)
  - Darifenacin (7.5–15 mg/d)
  - Golcisatan (5–10 mg/d)
  - Eltrombopag (50 mg/d)
  - Ureteral (7.5–20 mg/d), XL 5–30 mg/d (patch twice weekly)
  - Mirabegron (25–50 mg/d)
- Ph–alpha-methyldopa
- Anticholinergic agent: Promotes detrusor muscle relaxation


**Ongoing Care**

**Prognosis**

Continence can be improved in almost all patients.

**Complications**

- Caudal hematoma
- Bladder perforation
- Skin breakdown
- Dermatitis
- Edema
- Pain
- Urethral erosion
- Obstruction

**Follow-Up**

- Monitor post-void residual volume
- Monitor function of artificial urinary sphincter
- Monitor for complications

**Patient Monitoring**

- Urodynamic monitoring
- Symptom diaries
- Compliance with medications

**Patient Resources**


**References**

INCONTINENCE, URINARY, FOLLOWING RADICAL PROSTATECTOMY

Robert L. Segal, MD, FRCS(C)
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION
- Post-prostatectomy incontinence (PPI) is a well-recognized complication of radical prostatectomy (RP) whether performed open (perineal retroperitoneal) or laparoscopically with or without robotic assistance.
- The definition of continence following RP in the literature varies widely, with the strictest definition of continence being no pads used.

EPIDEMOLOGY
Incidence
- The incidence of PPI depends on the interval of time following surgery, the definition and methodology for assessing continence, and the experience of the surgeon.
- The overwhelming majority of men have some degree of PPI immediately after catheter removal.
- If PPI is defined as no pads/small protective pad or total control/occasional dribbling, experienced surgeons consistently report continence rates exceeding 95% at 1–2 yr after RP.
- Recent evidence suggests that PPI may improve after 2 yr.

Prevalence
- Approximately 6% of men will undergo a procedure for the management of PPI at a median of 20 mo after RP (1).

RISK FACTORS (2)
- RP (1)
- For the management of PPI at a median of 20 mo after RP.
- Approximately 6% of men will undergo a procedure for the management of PPI at a median of 20 mo after RP.
- Recent evidence suggests that PPI may improve after 2 yr.

PHYSICAL EXAM

- Observe caliber of urinary stream.
- Observe degree of pad saturation.
- Observe for skin excoriation secondary to PPI.
- Inquire if PPI is improving, stable, or deteriorating:
  - Assess the severity of LUTS.
  - Determine the severity of PPI by: Number of pads, degree of bother, and frequency of incontinence episodes.
  - Assess the severity of UTS.

DIAGNOSIS

HISTORY
- Assess the severity of UTS and incontinence preoperatively.
  - The International Prostate Symptom Score (IPSS).
- Inquire about the use of α-blockers because these agents may exacerbate PPI.

- Ascertain if the PPI is exacerbated by physical activity.
- Determine the severity of PPI by: Number of pads, degree of bother, and frequency of incontinence episodes.

PHYSICAL EXAM

- Observe degree of pad saturation.
- Observe degree of incontinence when transferring from the sitting to standing position.
- Observe caliber of urinary stream.

DIAGNOSTIC TESTS & INTERPRETATION (C)

- Lab
  - Urinalysis to exclude urinary tract infection

- Imaging
  - Sonographic post-void residual (PVR)
  - Uroflowmetry
  - Pressure flow study is useful for evaluating a possible obstructive anastomotic stenosis

DIFFERENTIAL DIAGNOSIS

- None

- Pathologic Findings

- General Measures

- Voiding before strenuous activity
- Limitation of fluid intake
- Avoid drugs that may cause urinary retention
- Encourage Kegel exercises—may accelerate continence recovery

MEDICATION

- First Line
  - α- Blockers generally not effective for SUI
- Inhibit α-blockers
  - Limitation of fluid intake
- Avoid drugs that may cause urinary retention
- Encourage Kegel exercises—may accelerate continence recovery

- Second Line
  - Oxybutynin, tolterodine, darifenacin, solifenacin, fesoterodine, trospium
  - Anticholinergic agents may improve PPI secondary to DI

- Associated Conditions
  - Detrusor instability (DI)/Overactive bladder (OAB)
  - Prevention
    - Detrusor instability (DI)/Overactive bladder (OAB)
    - Stress urinary incontinence
    - Overflow incontinence
    - Mixed incontinence

- Median

- Minimum

- Maximum

- Normal

- Pathologic Findings

- None

- Pathologic Findings

- General Measures

- Voiding before strenuous activity
- Limitation of fluid intake
- Avoid drugs that may cause urinary retention
- Encourage Kegel exercises—may accelerate continence recovery

- Medication

- First Line
  - α-Blockers generally not effective for SUI
- Inhibit α-blockers
  - Limitation of fluid intake
  - Typical off-label starting dose is 25–50 mg PO QHS
- Anticholinergic agents may improve PPI secondary to DI
  - Options include: Oxybutynin, trospium, darifenacin, solifenacin, fesoterodine, trospium
Periurethral bulking agents (buline–pseudaldehyde cross-linked collagen/polyethylene/polyanhydride) are costly; they require multiple injections and have limited durable success in this setting.

**Surgery/Others Procedures**
- Surgical intervention should not be pursued until at least 1 yr post-prostatectomy because of the temporal improvements in the condition.
- Surgical intervention should not be contemplated at 1–2 yr if there is evidence of progressive improvement.
- imperative to exclude anastomotic stricture and DI before embarking on surgical correction of SUI.
- Surgical options:
  - Fistulae surgical procedure is dictated by severity of PPI.
  - More severe cases best managed with an artificial urinary sphincter (AUS).
  - In many cases, surgery achieves marked improvement in PPI but some degree of SUI may persist.
  - Male slings.
  - Artificial urinary sphincter (AUS).

**ADDITIONAL TREATMENT**

**Radiation Therapy**
Although there is no role in the treatment of PPI, data suggest that radiation administered in the adjuvant setting following RP may limit resolution of continence particularly if the radiation is administered before continence returns.

**Additional Therapies**
- Unilateral dissection should be performed if evidence of bladder outlet obstruction and anastomotic stenosis.
- Transurethral excision of the stricture may be required if stricture recurs despite multiple dilation(s).
- In Europe duloxetine, a serotonin-norepinephrine reuptake inhibitor is approved for stress urinary incontinence (US approval is only for neuropathic pain and depression).

**Complementary & Alternative Therapies**
Biofeedback may have a role in selected patients in strengthening pelvic musculature.

**ONGOING CARE**

**PROGNOSIS**
- The overwhelming majority of men will spontaneously regain urinary continence following RP.
- The small subset of men with persistent SUI will improve, providing the appropriate surgical procedure is performed.
- The worst prognosis exists for cases with severe fixative anatomic structures (bladder neck contractures) who must be made totally continent with subsequent placement of an AUS.
- PPI secondary to DI likely to improve with anticholinergic agents.

**COMPLICATIONS**
- Sexual issues.
- Diminished self-esteem:
  - Limitation of physical activity.
  - Withdrawal from sexual activity.
  - Complications of treatment for PPI.

**FOLLOW-UP**

**Patient Monitoring**
- Pad use.
- Impact of PPI on quality of life.

**Patient Resources**
http://www.webmd.com/urinary-incontinence-
.

**REFERENCES**

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
  - Bulking Agents, Injectable
  - Incontinence, Urinary, Adult Male
  - Stress Urinary Incontinence, Male

**CODES**

**ICD9**
- 597.39 Other urinary incontinence.
- 997.5 Urinary complications, not elsewhere specified.

**ICD10**
- N39.498 Other specified urinary incontinence.
- N99.90 Other postprocedural complications and disorders of GU sip.

**CLINICAL/SURGICAL PEARLS**
- Post prostatectomy incontinence (PPI) is very common, with the vast majority (95%) resolving 6–12 mo postoperatively.
- Kegel exercises should be instituted immediately after catheter removal postoperatively.
- It is crucial to determine the exact pattern of urinary leakage.
- If conservative measures fail, treatment for both stress SUI requires surgery.
- Type of surgery is dictated by severity of SUI.
INCONTINENCE, URINARY, PEDIATRIC
Steve J. Hodges, MD
Anthony Atala, MD

DESCRIPTION
Normal urinary control occurs in stages:

- Constipation plays a major role in urinary continence
- Delayed voiding/defecation lead to bladder overactivity, constipation
- Bladder overactivity/constipation compounded by dyspnea of pelvic floor, with failure to relax pelvic floor completely with emptying

ASSOCIATED CONDITIONS
- Family history of enuresis
- Developmental delay
- Urinary tract anomalies
- Spinal dysraphism

Prevalence
- Day or night wetting occurs in up to 25% of 4–6 yr old children
- At 12 yr of age 4% of children are enuretic at least once a week, at 15 yr old it is 2%
- Enuresis is 3–4 times more common in boys than girls

HISTORY
- Child’s sex—bedwetting is more common in boys, daytime incontinence more common in girls
- Age at onset
- Interestingly, part of the time children get bedwetted because they have a low bladder capacity (60 cc at birth; 35 cc by 12 yr old)
- History of UTI; Functional constipation?

PHYSICAL EXAM
- Orifice rule out spina bifida, rule out occult infection

DIAGNOSIS
Incontinence in the presence of an abnormal back exam may signal a neurologic abnormality

GENERAL PREVENTION
- Aggressively prevent and treat constipation
- Ensure an environment where children are not delayed voiding/defecation lead to bladder overactivity, constipation
- Delayed voiding/defecation lead to bladder overactivity, constipation
- Bladder overactivity/constipation compounded by dyspnea of pelvic floor, with failure to relax pelvic floor completely with emptying

DIAGNOSTIC TESTS & INTERPRETATION
- Urinalysis
- Neutrophic glomerulonephritis
- Hypertension
- Microscopic hematuria
- Proteinuria
- Glucosuria
- If any of above discovered, require thorough evaluation and treatment
- Urine culture if UA shows signs of infection

Imaging
- KUB to rule out spina bifida, rule out occult infection
- Renal US to evaluate for normal GU anatomy
- VCUG only needed in the setting of palpable UI or any UI in boys, hydro-nephros allow evaluation of urethra in males
- MR urography may be needed when concerned for ectopic ureter
- Renogram rarely needed to evaluate for urinary obstruction, renal function

Pathologic Findings
- Urine—urine in vaginal vault or labial adhesions in girls
- Ecstatic perineal offsprings can be cause of constant wetness in girls
- Recanal exam to rule out rectal stool, evaluate normal sensation and tone
- Neurologic exam
- Measure or observe urinary stream for force, caliber, straining, duration (may obtain flow/PVR)

NOTES
GENERAL MEASURES

- Need KUB and renal/bladder US, urodynamics
  optional

- Other pediatric bladder disorders:
  - Lazy Bladder syndrome (incontinent voider)—rare
    voids, 2–3 + a day, may have infections, associated with constipation
  - Bladder overactivity—typically associated with delayed voiding and constipation, typified by
    unblended bladder contraction with no neurologic lesion

- Hinman-Allen syndrome—nonneurogenic
  neurogenic bladder, may be due to constipation as
  well

- Daytime frequency syndrome—frequent urination
  in a child with no other identifiable abnormalities, usually do have constipation on KUB

- Giggle Incontinence—rare form of incontinence
  where wetting only occurs with laughing, may be
  centrally mediated (brain), treated with Ritalin

DIFFERENTIAL DIAGNOSIS

- Structural Incontinence:
  - Ectopic ureter
  - Ectopic ureter
  - Spinal Dysraphism

- Neurogenic:
  - Anorectal malformation, caudal tumor
  - Intraventricular pterygium
  - Myelodysplasia
  - Occult dysplasia
  - Sacral agenesis, spinal cord trauma, myelitis
  - Tight retro peritoneal, distal syrinx
  - Isolated nocturnal enuresis: Constipation, sleep
    arousal disorder, nocturnal polyuria
  - Complicated incontinence:
    - Giggle Incontinence
    - Hinman-Allen syndrome
    - Lazy Bladder syndrome
    - Overactive Bladder

SUPPORTIVE MEASURES

- Perineal hygiene—voiding positioning
- Behavioral measures—timed voiding, constipation
- Drainage—physical therapy to relax external
  sphincter
- Des—avoid bladder irritant, caffeine
- Personal hygiene—voiding positioning

MEDICATION

First Line

- Treat UTI if present

- Overactive bladder
  - Anticholinergic medications
    - Oxybutynin: Safety and efficacy of oxybutynin
      chloride administration have been demonstrated
      for pediatric patients 5 yr of age and older
      - Tobsimone (off label in children)
    - Consider an antagonist (neurypage off label in
      children)
  - Constipation
    - PEG 3350, enemas or suppositories, Senna
      laxatives, fiber supplements

SURGERY/OTHER PROCEDURES

- Structural—alleviate structural cause of
  incontinence
  - Neurogenic: low compliance bladder may require
    enterocystoplasty, urethral dilation, neural
    stimulation, botulinum toxin injection
  - Overactive Bladder: may benefit from neural
    stimulation, botulinum toxin injection in bladder
    or sphincter, cysto urethral dilation

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

Aggressive constipation management for severe cases may require chronic enemas or antegrade continence
enema (ACE) creation

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

- Most patients do resolve over time as they grow, and gain more mature toileting habits
- Severe cases may lead to pelvic floor disorders (such as pelvic pain syndrome, dyspareunia in future, so
  aggressive therapy indicated

FOLLOW-UP

Patient Monitoring

- Follow-up for observation of progress, adjusting medications as needed
  - Structural and neurogenic causes need routine
    evaluations to rule out upper tract injury and
    monitor progress

Patient Resources

- National Kidney and Urologic Diseases
ASSOCIATED CONDITIONS

Pretesticular:
- Hypogonadotropic hypogonadism: Low follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone (T) with normal prolactin
- Hypothyroidism
- Medication use: See Risk Factors
- Elevated estradiol from moxibustion, tumors, or hepatic dysfunction
- Kallmann syndrome: X-linked, absent GnRH sensation, absent puberty, anosmia
- Pituitary or cranial trauma, infection, or tumor
- Hypogonadism: Prostatic inhibition of action on Leydig cells. Brain MRI to evaluate for macroprolactinemia (<1 cm)
- Macroprolactinemia: Refer for possible resection
- Microprolactinoma: May respond to dopamine agonist (11Tianeptine, Cabergoline, 2nd Biocytostatic)

Testicular:
- Varicocele: 15% of all men, 35–40% of men with primary infertility, 70–80% of men with secondary infertility
- Bilateral cryptorchidism, testicular injury, heavy alcohol use, recreational drugs (marijuana, cocaine), surgical history, medications, and other medical illnesses
- 46,XX with male phenotype: No spermatogenesis, donor sperm/adoption
- Androgenization disorders: Defects in synthesis of T, androgen receptor, and 5α-reductase
- Y microdeletions: AZFa, b and c: See Genetics
- 46,XY with male phenotype: Fertility factors: X-linked, autosomal, postpubertal mumps orchitis
- Sertoli-cell only syndrome: Absent germ cells
- Tuberculosis: Spermatozoa harbored at a certain stage

Genetic/chromosomal factors:
- Klinefelter: 47,XXY, small, firm testes; often azoospermic, however, spermatozoa (47,XY,46,XY) allows spermogenesis. Up to 60% have sperm found from TESA
- Noonan syndrome: AZFa (1–5% NOA) predicts TESA failure
- AZFa (1–5% NOA) predicts TESA failure
- AZFa (11% NOA) best prognosis, can be oligospermic, if azoospermic 2/3rd s have sperm on TESA

PATHOPHYSIOLOGY

3 categories:
- Pretesticular: Endocrine abnormality
- Testicular: Abnormal sperm production
- Posttesticular: Abnormal sperm transport
MEDICATION

DIFFERENTIAL DIAGNOSIS

Diagnostic Procedures/Surgery

 Pathologic Findings
  - Spermatozoa—Use in azoospermic patients with palpable vasa and low-volume ejaculate.
  - Seminal vesicle dilation (normal < 2 cm) indicative of EDO.
  - Scrotal ultrasound—only used in patients with NOA or severe oligospermia (< 5 million sperm/mL).
  - Consider 1 chromosome microdeletion testing if azoospermic

Imaging

  - Testicular ultrasonography—Use in azoospermic patients with palpable vasa and low-volume ejaculate.
  - Seminal vesicle dilation (normal < 2 cm) indicative of EDO.
  - Scrotal ultrasound—only used in patients with NOA or severe oligospermia (< 5 million sperm/mL).
  - Consider 1 chromosome microdeletion testing if azoospermic

TREATMENT

  - Assisted Reproductive Technologies (ARTs), Intrauterine insemination (IUI), In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI)
  - Additional Therapies
    - N/A
    - Counselling and CFTR mutation testing
    - Coenzyme Q10 is used
    - 20-30% pregnancy rates per cycle

ONGOING CARE

  - Pregnancy rates are highly dependent on the age of the female partner
  - MicroTESE for NOA: 67% sperm-retrieval rate
  - MicroTESE: Performed for NOA, superior to other sperm-retrieval techniques with 20-30% improvement in yield up to 67%

COMPLICATIONS

  - MicroTESE: Vasectomy, or vasectomy/lymphedema should be performed by microsurgical specialist.
  - OA, if patient does not desire reconstruction or it is not possible. TESAs, percutaneous or microsurgical epididymal sperm aspiration (PESA or MESA)
  - Varicocelectomy: Recommended for men with infertility, palpable varicocele, abnormal semen parameters, elevated FSH, and female partner with normal/potentially correctable infertility (A)[A]
  - Transurethral resection of ejaculatory ducts: For EDO
  - Neurostimulatory ejaculation: Men with spinal cord injury may be able to retrieve sperm via ejaculation with penile vibratory stimulation or, in the event of injury may be able to retrieve sperm via ejaculate

ADDITIONAL READING

  - See Also (Topic, Algorithm, Media)
    - Assisted Reproductive Technologies (ARTs)
    - Ejaculatory Disorders
    - Intrauterine insemination (IUI), In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI)

CLINICAL/SURGICAL PEARLS

  - Testis biopsy is rarely indicated in the evaluation of male infertility.
PATHOPHYSIOLOGY
- Population × prevalence greater than that of the general
- Adult female 1st-degree relatives of IC patients have a predisposition
- No known risk factors beyond a possible genetic

RISK FACTORS
- Ranges from 1.6 to 2,600 per 100,000 people
- Incidence
- Prevalence
- Incidence and prevalence vary widely

GENERAL PREVENTION
- Specific prevention strategies, although dietary changes and medical therapy may mitigate symptom
general/spinal anesthesia:
- Findings may include: Glomerulations (small foci
inflammation
- “Nonclassic”: No inflammatory lesions identified
- “Classic”: No inflammatory lesions identified upon
cystoscopy
- Median age of onset 30–40 yr
- Female: Male 5:1
- 5–10% of patients have Hunner lesions

DIAGNOSIS
- No definitive prevention strategies, although dietary
cystoscopy (formerly known as Hunner ulcer)
- “Nonclassic”: No inflammatory lesions identified
- Bimanual exam with palpation of bladder, urethra,
- Potassium sensitivity testing (KCl test):
- Cystoscopy with hydrodistention under
- Focused neurologic exam
- Bladder Pain/Interstitial Cystitis Symptom Score
- O’Leary-Sant Symptom and Problem Score
- Symptom evaluation with voiding diary
- PUF (Pelvic Pain & Urgency/Frequency)
- Visual analog scale (pain score)
- Urinary frequency, urgency, nocturia
- Urinary frequency based upon need to decrease
- Pain associated with bladder filling and/or emptying
- Promontory flare
- Abdominal/pelvis pubic pain
- Urinary frequency, urgency, nocturia
- Urinary frequency based upon need to decrease
- Bladder effects of chemotherapy
- Bladder outlet obstruction/urinary retention
- Increased sensitivity (pain) on filling and

PHYSICAL EXAM
- General: Abdominal exam to assess for supra-pubic
- Painful bladder syndrome
- Fibrinopyla
- Chronic fatigue syndrome
- Genital herpes
-外生殖器検査
- Digital rectal exam with palpation of prostate and
- External genitalia exam

ASSOCIATED CONDITIONS
- Multiple pelvic floor: Most commonly identified
comorbid condition
- Irritable bowel syndrome
- Fibromyalgia
- Chronic fatigue syndrome
- Multiple allergies
- Sjogren syndrome
- Chronic headaches
- Depression/neurogenic disorder
- In females: Vulvodynia, endometriosis
- In males: Chronic prostatitis/chronic pelvic pain
syndrome, BPH, prostate cancer

DIAGNOSTIC TESTS & INTERPRETATION
- Lab: Urinalysis and urine culture
- Urine cytology in high risk groups

Imaging
- No recommended imaging for the diagnosis of IC/PBS

Diagnostic Procedures/Surgery
- Urodynamics:
- Normal detrusor function on cystometry, may have
increased sensitivity (pain) on filling and
decreased capacity.
- Late stages of “classic” IC/PBS may be associated
with significant decrease in capacity and bladder
dyness.
- Cystoscopy:
- Used selectively to exclude other bladder
pathology and identify Hunner lesions
- Cystoscopy with hydrodistention under
general/spinal anesthesia:
- Findings may include: Glomerulations (small foci
inflammation
- Hunner lesions, decreased
anesthetic capacity, mucosal tears, low sensitivity
and specificity
- Hunner lesion (ulcer) is described as circumscript,
reddened area with small vessels radiating toward a
central scar. Fibrin deposit/coagulum can be
attached to this area. With bladder distention the
site ruptures with petechial blood oozing from the
lesion and mucosal margins (5)
- Potassium sensitivity testing (KCl test):
- Low sensitivity and specificity, positive result
provides pain
- Residual urination in males
Pathologic Findings
- Histologic findings can vary widely and are
truly pathognomonic:
- Bladder biopsy:
- Indicated only to rule out other disease processes
- Hunner lesions demonstrate pan-mural
inflammation

DIFFERENTIAL DIAGNOSIS
- Bacterial cystitis
- General bladder cancer (including CIS)
- Bladder effects of chemotherapy
- Bladder outlet obstruction/urinary retention
- Bladder/lower urinary tract
- Genital herpes

INTERSTITIAL CYSTITIS (IC)/PAINFUL BLADDER SYNDROME (PBS)
Nikhil Waingankar, MD
Sonia Bahmani, MD
Robert M. Moldwin, MD, FACS

BASICS
DESCRIPTION
- Interstitial cystitis (IC) or Painful Bladder Syndrome
(PBS) is an unpleasant sensation (pain, pressure,
discomfort) perceived to be related to the bladder,
associated with lower urinary tract symptoms (LUTS)
for more than 6 wk duration, and in the absence of
other identifiable causes (1,2)
- 90% of patients also complain of frequency
(>10–12 × daily), nocturia is common
- 8% complained of constipation/persistent urgency
- Dysuria & unusual:
- Symptoms can be associated with a wide range of
diseases (see “Differential Diagnosis”)
- Two forms of IC/PBS:
- “Classic”: Associated with Hunner lesions on
cystoscopy (formerly known as Hunner ulcer)
- “Nonclassic”: No inflammatory lesions identified
upon cystoscopy

Epidemiology (3)
- Incidence and prevalence vary widely

Incidence
- 0.6–1.6 per 100,000 people

Prevalence
- Ranges from 1.6 to 2,600 per 100,000 people

Risk Factors
- No known risk factors beyond a possible genetic
predisposition

Genetics
- Adult female: 1st-degree relatives of IC patients have a
prevalence 17× greater than that of the general
population

Pathophysiology
- Multifactoral etiology with a number of proposed
mechanisms:
- Epithelial permeability
- Antiproliferative factor
- Host cell activation
- Neurogenic inflammation
- Infectious
- Autoimmune
- Urinary abnormality: Toxic, allergic, immunologic

ASSOCIATED CONDITIONS
- Muscle of pelvic floor: Most commonly identified
comorbid condition
- Irritable bowel syndrome
- Fibrinopyla
- Chronic fatigue syndrome
- Multiple allergies
- Sjogren syndrome
- Chronic headaches
- Depression/neurogenic disorder
- In females: Vulvodynia, endometriosis
- In males: Chronic prostatitis/chronic pelvic pain
syndrome, BPH, prostate cancer

GENERAL PREVENTION
- No definitive prevention strategies, although dietary
changes and medical therapy may mitigate symptom
flares

DIAGNOSIS
HISTORY
- IC patients: 10× more likely to have childhood
bladder problems
- Symptoms unrelated to any identifiable cause
- “Classic” IC/PBS is an unpleasant sensation (pain,
pressure, discomfort) perceived to be related to the
bladder, associated with lower urinary tract symptoms
(LUTS) for more than 6 wk duration, and in the absence of
other identifiable causes (1,2)

Lab:
- Urinalysis and urine culture
- Urine cytology in high risk groups

Imaging
- No recommended imaging for the diagnosis of IC/PBS

Diagnostic Procedures/Surgery
- Urodynamics:
- Normal detrusor function on cystometry, may have
increased sensitivity (pain) on filling and
decreased capacity.
- Late stages of “classic” IC/PBS may be associated
with significant decrease in capacity and bladder
dyness.
- Cystoscopy:
- Used selectively to exclude other bladder
pathology and identify Hunner lesions
- Cystoscopy with hydrodistention under
general/spinal anesthesia:
- Findings may include: Glomerulations (small foci
inflammation
- Hunner lesions, decreased
anesthetic capacity, mucosal tears, low sensitivity
and specificity
- Hunner lesion (ulcer) is described as circumscript,
reddened area with small vessels radiating toward a
central scar. Fibrin deposit/coagulum can be
attached to this area. With bladder distention the
site ruptures with petechial blood oozing from the
lesion and mucosal margins (5)
- Potassium sensitivity testing (KCl test):
- Low sensitivity and specificity, positive result
provides pain
- Residual urination in males

Pathologic Findings
- Histologic findings can vary widely and are
truly pathognomonic:
- Bladder biopsy:
- Indicated only to rule out other disease processes
- Hunner lesions demonstrate pan-mural
inflammation

DIFFERENTIAL DIAGNOSIS
- Bacterial cystitis
- General bladder cancer (including CIS)
- Bladder effects of chemotherapy
- Bladder outlet obstruction/urinary retention
- Bladder/lower urinary tract
- Genital herpes
INTERSTITIAL CYSTITIS (IC)/PAINFUL BLADDER SYNDROME (PBS)

- Overactive bladder
- Pelvic floor muscle dysfunction
- Pelvic nerve entrapment
- Radiation cystitis
- Female:
  - Cervical/vaginal cancer
  - Urethral diverticulum
  - Pelvic organ prolapse
  - Endometriosis
  - Vaginal candidiasis
- Male:
  - BPH, prostate cancer, prostatitis

TREATMENT

GENERAL MEASURES
(Adapted from AUA guidelines 2011) (6)

- Patients should be aware that no single treatment has been found effective
- 1st line
  - Stress reduction
  - Exercise
  - Warm baths
  - Topical lidocaine
  - Biofeedback
  - Avoidance of spicy foods, caffeine, alcohol, artificial sweeteners, acidic beverages
- 2nd line
  - Pelvic floor physical therapy
  - Multimodal pain management
  - Amitriptyline
  - Clonidine
  - Hydroxyzine
  - Pentosan polysulfate
- 3rd line
  - Cystoscopy with hydrodistention (low pressure/short duration)
  - Fulguration of Hunner lesions
  - Submucosal injection of Hunner lesions with triamcinolone
  - Neurostimulation
  - Intravesical: 4% alkalinized lidocaine
  - Intravesical: 50% DMSO
  - Intravesical instillation: Author’s preferred
  - Intravesical “cocktail”: Lidocaine, gentamicin, heparin, artificial sweetener, acidic beverages

SURGERY/OTHER PROCEDURES

MEDICATION

First Line
See above

Second Line
See above

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
See General Measures

COMPLEMENTARY & ALTERNATIVE THERAPIES

Prognosis
Spontaneous remission rate of 50% at mean of 8 mos.

COMPICATIONS

N/A

ONGOING CARE

Patient Monitoring
See General Measures

FOLLOW-UP

Patient Resources
Interstitial Cystitis Association http://www.ichelp.org/

REFERENCES


ADDITIONAL READING


CODES

ICD9
- 598.31 Chronic interstitial cystitis
- 959.30 Hematuria, unspecified
- 768.41 Urinary frequency

ICD10
- N30.10 Interstitial cystitis (chronic) without hematuria
- N30.11 Interstitial cystitis (chronic) with hematuria
- R35.0 Frequency of micturition

CLINICAL/SURGICAL PEARLS

- IC/IC/PBS is more common in women than in men.
- This is primarily a clinical diagnosis based upon the presence of characteristic symptoms and the exclusion of other causes.

PEARLS

- Chronic interstitial cystitis/bladder pain syndrome is a chronic, refractory, distressing condition that requires an interdisciplinary approach.
LATEX ALLERGY, UROLOGIC CONSIDERATIONS

Ahmad H. Bani-Hani, MD, FAAP, FACS

RISK FACTORS

Prevalence

DESCRIPTION

- Localized or systemic reaction to latex, a natural substance from the sap of the rubber tree, Hevea brasiliensis (TA-A).
- Latex is a common ingredient in many medical and dental products (eg, bladder catheters, blood pressure cuffs, face masks, gloves, endotracheal tubes, IV infusion sets, etc.).
- Patients with spina bifida or congenital urogenital abnormalities have the highest risk.
- Mild forms include pruritus and swelling. The most severe form of allergic reaction is anaphylaxis. A severe, life-threatening, generalized or systemic hypersensitivity reaction characterized by rapidly developing life-threatening airway and/or breathing abnormalities may occur.

EXPOSURE TO MULTIPLE SURGERIES: 1/3–2/3 OF CHILDREN

ALERT

- Should report their allergies prior to any medical procedures.
- Should avoid latex-containing products.
- Should wear a medical alert bracelet indicating latex allergy.

GENETICS

- Genetic factor might be indicated.
- Latex allergy is less frequent in adults with spinal cord injury and multiple surgical procedures than in children with similar conditions.
- Interleukin-13 (IL-13) and IL-18 promoter polymorphisms more likely to be found in healthcare workers in comparison to nontoxic controls or patients with anorectal/urologic malformations.

PATHOPHYSIOLOGY

- Presentation with Hevea latex allergens is prerequisite to initiate an allergic response.
- A number of proteins found in the cytoplasm of H. brasiliensis are known potent allergens that can elicit human IgE antibody, leading to sensitization in exposed patients and a spectrum of allergic reactions upon subsequent exposure (4,24).
- Symptoms of delayed (type IV) hypersensitivity usually develop within 1–2 days of exposure. Immediate (type I) hypersensitivity causes symptoms within minutes of exposure.
- Immediate hypersensitivity reactions to latex (type I) are caused by cross-linking of latex protein-specific IgE antibody with mast cells and basophils.
- Cross-reactivity between various proteins is responsible for the clinical associations between latex allergy and allergic responses to a number of fruits and vegetables.
- Type I (1-today-mediated type), delayed hypersensitivity reaction can occur and usually manifest as contact dermatitis 24–96 hr after exposure.

GENERAL PREVENTION

- Facility:
  - Establishment of a latex-safe environment should be a priority for institutions by replacing all Hevea latex–containing products with non–Hevea-based synthetic products or powder-free latex products.
  - Synthetic alternatives to rubber include butyl rubber, a petrolatum-based product with no allergenic protein, neoprene, and copolymers of butadiene and acrylonitrile.
  - Non–Hevea source of natural rubber is the guayule plant (Ficus). Guayule-based products pose no risk to individuals allergic to Hevea latex and is approved by the Food and Drug Administration (FDA).
  - Individuals with latex allergy:
    - Should wear a medical alert bracelet indicating latex allergy.
    - Should be encouraged to have self-injectable epinephrine if they have a clinical history of systemic reaction to latex.
    - Should avoid latex-containing products.
    - Should report their allergies prior to any medical or surgical procedure

DIAGNOSIS

HISTORY

- Detailed clinical history of allergic reactions that are temporarily associated with exposure to Hevea latex–containing products (eg, prior history to anaphylaxis and/or intraoperative shock, itching, redness, or swelling following dental, sexual, or pelvic exam; itching or swelling with condoms, diapers, or latex sexual aids).
- Detailed history of associated risk factors: Healthcare workers, hair dressers, rubber handling, eczema/hay fever; multiple surgeries, food allergies, etc.
- 30–80% of patients with latex allergy also have food allergy.
- Allergic symptoms can include the following symptoms:
  - Angioedema
  - Dizziness
  - Pronus
  - Rhinitis
  - Tearing
  - Swelling at the site of contact
  - Abdominal cramps
- In the most extreme cases, anaphylaxis can develop

ALERT

- Use caution when examining any child for dysfunctional voiding especially if the child has neurologic symptoms or suspected spina bifida.

PHYSICAL EXAM

- Use nonlatex exam gloves.
- Use latex-free skin test if no history of previous latex exposure.
- Use nonlatex minocycline (eg, hydrocortisone).
- Use latex-free, neoprene, or nitrile latex-free gloves

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Routine urinalysis lab studies (blood, gas, etc.) if during acute anaphylaxis

IMAGING

- N/A

DIAGNOSTIC PROCEDURES/SURGERY

- These are performed on a routine basis and not during an acute event
- Pre-procedure skin test:
  - Skin prick test:
    - Extracts of Hevea latex, at least 3
    - Commercial extracts are available
    - Test involves performing a puncture with a lancet device through a drop of latex extract at sequential concentrations ranging from 0.001–1 mg/mL of protein
    - Results are read after 15 min and compared with the positive histamine and negative saline controls
  - Small risk of anaphylaxis

222
First Line

- **For the management of anaphylaxis**
  - **Removal latex source**
  - **Basic life support principles (Airway, Circulation, Breathing)**
  - **Injectable epinephrine in severe anaphylaxis:**
    - 0.3–0.5 mL of a 1:1000 solution \( \text{HCl} \) (adult)
    - 0.15–0.3 mL of a 1:1000 solution \( \text{HCl} \) (children)

- **EpiPen, Adrenaclick (0.3 mg) in adults**
- **Epinephrine autoinjectors:**
  - **Avoid foods with latex cross-reactivity:**
  - **Anaphylactic shock**
  - **Cardiogenic shock**

**Second Line**

**SURGERY OTHER PROCEDURES**

- **N/A**

**ADDITIONAL TREATMENT**

**Immunotherapy**

- **N/A**

**ADDITIONAL THERAPIES**

- **N/A**

**COMPLEMENTARY & ALTERNATIVE THERAPIES**

- **N/A**

**RISK FACTORS**

- **N/A**

**RADIATION THERAPY**

- **N/A**

**ADDITIONAL TREATMENT**

- **N/A**

**SURGERY/OTHER PROCEDURES**

- **N/A**

**REFERENCES**


**ADDITIONAL READING**


**CODES**

- **ICD9**
  - Z91.040 Latex allergy status
  - Q64.9 Congenital malformation of urinary system, unspecified
  - 753.9 Unspecified anomaly of urinary system
  - V15.07 Allergy to latex

- **ICD10**
  - N31.9 Haemorrhagic dysmenorrhoea of bladder, unspecified
  - O64.9 Congenital malformation of urinary system, unspecified
  - Z91.040 Latex allergy status

**CLINICAL/SURGICAL PEARLS**

- **Natural rubber latex allergy is caused by sensitization to proteins found in H. brasiliensis, the rubber tree.**

- **The highest prevalence of latex allergy (up to 68%) is in patients with spina bifida or congenital urogenital abnormalities.**

- **The mainstay of management of latex allergy is avoidance of latex products as there is no cure for latex allergy.**
LIBIDO, DIMINISHED, FEMALE
Sandip P. Vasavada, MD, FACS
Bradley C. Gill, MD, MS

LIBIDO, DIMINISHED, FEMALE

BASICS
DESCRIPTION
- Diminished libido, low sexual drive, or hyposexuality are defined by a lack of desire for sexual activity.
- Hypoactive sexual desire disorder or subjective sexual arousal disorder may be implicated.

EPIDEMIOLOGY
Incidence
- More common with advancing age and especially following menopause
- A congenital syndrome may be causative at a young age
Prevalence
- Estimated prevalence of 25–75% of women varies by study sample and assessment

RISK FACTORS (1)
- Low testosterone (physiologic or iatrogenic)
- Advanced age
- Menopause (physiologic or iatrogenic)
- Pelvic fluid disorder (incontinence or prolapse)
- Physical or psychological trauma (sexual assault, physical abuse, or verbal abuse)
- Pregnancy (multifactorial per hormonal, emotional, and physical changes)

Genetics
- Early menopause may be implicated

PATHOPHYSIOLOGY (2,3)
- Testosterone drops 50% from age 30 to 60 years
- Estrogen can increase sex hormone-binding globulin concentrations and lower free testosterone.
- Progesterone may lower mood and decrease sex drive as seen with some contraceptives.
- Full-time stimulating and leveling hormone reduction by contraceptives lowers androgen production.
- Sex steroid level alterations from certain antidepressants can decrease sex drive.

ASSOCIATED CONDITIONS
- Vaginal atrophy
- Congenital syndromes
- Posttraumatic stress disorder (prior physical or psychological trauma)

GENERAL PREVENTION
- Exercise, balanced diet, Healthy Lifestyle

DIAGNOSIS

HISTORY
- Details of low libido
  - Acquired or lifelong problem
  - Always or intermittently present
  - With or without sexual partners
  - After a new diagnosis or procedure
  - Following use of a new medication
  - Association with life events
  - Reproductive information
    - Age of menarche or onset of menstruation
    - Progesterones and deliveries
  - Contraception use and type
  - Infertility and treatment
  - Other sexual information
    - Sexually transmitted infection
    - Pain or discomfort with sexual activity
    - Problems with sexual function of the partner
  - Current or prior abuse
    - Sexual
    - Verbal or physical
  - Symptoms of androgen insufficiency
    - Decreased androgen
    - Decreased free testosterone or increased sex hormone–binding globulin concentrations
    - Signs of androgen insufficiency
  - Bone loss, decreased muscle mass, less strength
  - Memory changes and altered cognitive function
  - Other endocrine disorders
    - Hypothyroidism
    - Cushing syndrome
    - Diabetes
  - Urinary conditions
    - Urinary incontinence or fecal incontinence
  - Pelvic organ prolapse
  - Medications
    - Oral contraceptives, estrogens, progestins, gonadotropin-releasing hormone agonists
    - Antidepressants, anticonvulsants, antiepileptics, psychotropics
    - Alpha-blockers, antihypertensives, anticholinergics, antidiabetes, antihistamines
    - Statins, nectarin
  - Chronic medical conditions
    - Hypothyroidism
    - Substance abuse

PHYSICAL EXAM
- Assessment of congenital sexual characteristics
  - Breast development
  - Axillary hair
  - Signs of endocrinologic disorder
  - Cushingoid appearance
  - Hypothyroid skin and hair changes
  - Diabetic neuropathy
  - Visual inspection of the external genitalia
    - Distribution of pubic hair
  - Ulcerations, pustules, discharge, or bleeding
  - Prominence of urethra, vagina, or cervix
  - Speculum exam
    - Vaginal discharge, moisture, thinning, or erosion
  - Ulcerations, pustules, discharge, or bleeding
  - Cytoscopy, rectoscopy, or endoscopy
  - Vaginal wall masses
  - Palpation of the external genitalia, vaginal sidewalls, pelvic floor muscles, ovaries, and ovaries
  - Urethral or vaginal sidewall masses
  - Surgically placed foreign bodies
  - Pelvic floor muscle tension, spasm, or tenderness
  - Cervical motion, vacuum, or adnexal tenderness
  - Vaginal cut-out mass or tenderness

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Estrogens: Estradiol and estrene
  - Androgens: Dehydroepiandrosterone, androstenedione, testosterone, and dihydrotestosterone
  - Proteins: Sex hormone–binding globulin (SHBG)
  - Androgen: Free testosterone
  - Other tests: Gonadotropin-releasing hormone agonists
  - Imaging
    - Brain magnetic resonance imaging to assess the hypothalamus and pituitary gland

DIFFERENTIAL DIAGNOSIS
- Hypothalamic
  - Decreased free testosterone or increased sex hormone–binding globulin
  - Decreased estrogen
  - Hypogonadotropic hypogonadism
- Adrenal insufficiency or adrenal suppression
  - Adrenal suppression or glucocorticoid excess
  - Hypothyroidism or hyperthyroidism
LIBIDO, DIMINISHED, FEMALE

TREATMENT

GENERAL MEASURES (1)

- Psychological
  - Hypoactive sexual desire disorder, subjective sexual arousal disorder, sexual aversion disorder
  - Sexual dysfunction in a partner
- Iatrogenic
  - Medication side effect
- Gynecologic
  - Dyspareunia, pelvic organ prolapse, sexually transmitted infection
- Urologic
  - Urinary incontinence
- Congenital syndrome

MEDICATION

First Line

- Testosterone alone or in combination has been used off-label to increase drive
  - Postmenopausal women with decreased libido who are not receiving estrogen therapy have modest success using an experimental testosterone patch delivering 300 μg/d
  - If possible elimination or replacement of medications that may reduce libido
  - Adjunctive treatment of vaginal atrophy with topical estrogen can be helpful

Second Line

N/A

SURGERY/OTHER PROCEDURES

Appropriate treatment of possibly causative medical (ie, endocrine tumor) conditions

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS

- Results vary with etiology and treatment for many is long-term
- Multimodal approach to any etiology should be most beneficial

COMPLICATIONS

Use of libido can result in depression, infertility

FOLLOW-UP

Patient Monitoring

- Frequent follow-up with initiation of new therapy is best with regular lab work if hormones are used.
  - If using testosterone, monitor for signs of testosterone excess (acne, hirsutism, male pattern baldness, hyperlipidemia)

Patient Resources
N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Dyspareunia
- Female Hypoactive Sexual Desire Disorder
- Urinary incontinence
- Vaginal Atrophy

CODES

ICD9
- 799.81 Decreased libido
- 627.2 Symptomatic menopausal or female climacteric states
- 302.71 Hypoactive sexual desire disorder

ICD10
- T52.0 Hypoactive sexual desire disorder
- N85.1 Menopausal and female climacteric states
- R68.82 Decreased libido

CLINICAL/SURGICAL PEARLS

- A good social history is essential.
- Sexual dysfunction in partners can cause this.
- Overall physical health help maintain libido.
**LIBIDO, DIMINISHED, MALE**

Daniel Box, MD
Anish K. Shah, MD

---

**BASICS**

**DESCRIPTION**
- Diminished libido (hyposexuality) is the lack of desire to engage in sexual experience.
- Hypoactive sexual desire disorder is characterized by reduced libido and interest in sexual activity causing distress in women.
- This section primarily focuses on decreased libido in men.

**EPIDEMIOLOGY**

**Incidence**
- 10–15% of men
- 20–25% of women

**RISK FACTORS**
- Therapy for prostate cancer
- Congenital absence of the testicles
- Metabolic syndrome
- Surgical injury or removal of the testicles
- Inflammatory insults to the testicles
- Congenital absence of the testicles
- Therapy for prostate cancer
- Decreased bone density/osteoporosis

**GENETICS**
- Loss of libido may be associated with some of the genetic disorders/syndromes, listed below:
  - 17α-Hydroxylyase deficiency
  - Autoimmune polyendocrine syndrome
  - Klinefelter syndrome
  - Inactivation of the tubulinizing hormone (V-Ho-receptor gene
  - Mutations of steroid 5-α-reductase gene

**PATHOPHYSIOLOGY**
- Psychological causes of diminished libido
  - Libido (sexual drive) is mediated by the cerebral cortex.
  - Psychological disturbances of all degrees, from anxiety to major psychiatric disorders
  - May be secondary to medical conditions (ie, congenital anomaly, disfiguring injury, etc.)
  - Erectile dysfunction may cause loss of libido
- Hormonal causes of diminished libido
  - Hypogonadism: Androgen deficiency, particularly testosterone, whether primary (testicular defect) or secondary to hypothalamic-hypophysary dysfunction, Cushings syndrome
  - Hypothyroidism with or without pituitary lesion (TSH)
  - Thyroid: Both hyper- and hypothyroidism can lead to diminished sexual desire

**DIAGNOSIS**

**HISTORY**
- Sexual history
  - Frequency and level of sexual desire
  - Difficulty in achieving or maintaining an erection
  - Evidence of ejaculation disorder, overall satisfaction with sexual life
  - If semen volume is normal, it is unlikely that endocrine factors are responsible for loss of libido
  - Sexual Health Inventory of Men (SHIM) score
  - History of psychiatric illness
  - Symptoms to suggest decreased testosterone: ED, decreased bone density/osteoporosis
  - History of endocrine disorder
  - Therapy for prostate cancer
  - Chronic alcoholism may result in decreased serum testosterone, testicular atrophy, and decreased libido.

**DIFFERENTIAL DIAGNOSIS**
- Determine the cause and correct, if possible.
- Identify potential medications causing libido issues.
- Psychiatric consultation/sexual function therapist
- Endocrinology consultation

**TREATMENT**

**MEDICATION**

**First Line**
- Decreased testosterone (T)
  - Hormone supplementation. For replacement dosing, see chapter on "Testosterone, decreased (hypogonadism)".
  - Patients interested in sustaining fertility. Avoid exogenous testosterone; stimulate with human chorionic gonadotropin.
  - If sexual dysfunction is identified as the cause: Phosphodiesterase inhibitors (sildenafil, tadalafil, etc.) are potentially useful 1st-line therapies
  - Bromocriptine for prolactin-secreting tumors

**Second Line**

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Serum testosterone
- Serum prolactin
- If any disturbances of the above, then serum follicle-stimulating hormone and LH
- Serum-free T4 and TSH
- Serum GH and IGF-1 (primarily in children)
- Evlauation for increased cortisol if Cushing’s is suspected

**PHYSICAL EXAM**

**DESCRIPTION**
- Diminished libido (hyposexuality) is the lack of desire to engage in sexual experience.
- Hypoactive sexual desire disorder is characterized by reduced libido and interest in sexual activity causing distress in women.
- This section primarily focuses on decreased libido in men.

**GENERAL PREVENTION**

**GENERAL MEASURES**
- Avoid exogenous testosterone, stimlate with human chorionic gonadotropin.
- If sexual dysfunction is identified as the cause: Phosphodiesterase inhibitors (sildenafil, tadalafil, etc.) are potentially useful 1st-line therapies
- Bromocriptine for prolactin-secreting tumors

**ASSOCIATED CONDITIONS**
- Erectile dysfunction (ED) and infertility may be associated with loss of libido and vice versa (2).
- Hypothyroidism
- Alcoholism
- Syndromes, listed above in the Genetics section

**DIAGNOSIS**

**HISTORY**
- Sexual history
  - Frequency and level of sexual desire
  - Difficulty in achieving or maintaining an erection
  - Evidence of ejaculation disorder, overall satisfaction with sexual life
  - If semen volume is normal, it is unlikely that endocrine factors are responsible for loss of libido
  - Sexual Health Inventory of Men (SHIM) score
  - History of psychiatric illness
  - Symptoms to suggest decreased testosterone: ED, decreased bone density/osteoporosis
  - History of endocrine disorder
  - Therapy for prostate cancer
  - Chronic alcoholism may result in decreased serum testosterone, testicular atrophy, and decreased libido.

**DIFFERENTIAL DIAGNOSIS**
- Determine the cause and correct, if possible.
- Identify potential medications causing libido issues.
- Psychiatric consultation/sexual function therapist
- Endocrinology consultation

**TREATMENT**

**MEDICATION**

**First Line**
- Decreased testosterone (T)
  - Hormone supplementation. For replacement dosing, see chapter on "Testosterone, decreased (hypogonadism)".
  - Patients interested in sustaining fertility. Avoid exogenous testosterone; stimulate with human chorionic gonadotropin.
  - If sexual dysfunction is identified as the cause: Phosphodiesterase inhibitors (sildenafil, tadalafil, etc.) are potentially useful 1st-line therapies
  - Bromocriptine for prolactin-secreting tumors

**Second Line**

---

**MARKS & SYMPTOMS**

**DIAGNOSIS**

**HISTORY**
- Sexual history
  - Frequency and level of sexual desire
  - Difficulty in achieving or maintaining an erection
  - Evidence of ejaculation disorder, overall satisfaction with sexual life
  - If semen volume is normal, it is unlikely that endocrine factors are responsible for loss of libido
  - Sexual Health Inventory of Men (SHIM) score
  - History of psychiatric illness
  - Symptoms to suggest decreased testosterone: ED, decreased bone density/osteoporosis
  - History of endocrine disorder
  - Therapy for prostate cancer
  - Chronic alcoholism may result in decreased serum testosterone, testicular atrophy, and decreased libido.

**DIFFERENTIAL DIAGNOSIS**
- Determine the cause and correct, if possible.
- Identify potential medications causing libido issues.
- Psychiatric consultation/sexual function therapist
- Endocrinology consultation

**TREATMENT**

**MEDICATION**

**First Line**
- Decreased testosterone (T)
  - Hormone supplementation. For replacement dosing, see chapter on "Testosterone, decreased (hypogonadism)".
  - Patients interested in sustaining fertility. Avoid exogenous testosterone; stimulate with human chorionic gonadotropin.
  - If sexual dysfunction is identified as the cause: Phosphodiesterase inhibitors (sildenafil, tadalafil, etc.) are potentially useful 1st-line therapies
  - Bromocriptine for prolactin-secreting tumors

**Second Line**

---
LIBIDO, DIMINISHED, MALE

SURGERY/OTHER PROCEDURES
Only useful for pituitary adenomas causing hyperprolactinemia or in cases of Cushing’s disease.

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
L-arginine and yohimbine are touted but not proven

ONGOING CARE

PROGNOSIS
The prognosis is good when there is a treatable underlying cause for loss of libido. Otherwise it can be permanent.

COMPLICATIONS
Loss of libido can result in depression, infertility, and erectile dysfunction.

FOLLOW-UP
Patient Monitoring
Men treated with androgens should be followed closely with digital rectal exam and prostate-specific antigen every 6 mo.

Patient Resources
• http://www.merckmanuals.com/home/mens-health-issues/sexual-dysfunction/index.htm
• http://men.webmd.com/mens-libido-directory

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Andropause (Late Onset Male Hypogonadism)
• Erectile Dysfunction
• Female Hypoactive Sexual Desire Disorder
• Testosterone, Decreased (Hypogonadism)

CODES
ICD9
• 302.71 Hypoactive sexual desire disorder
• 752.89 Other specified anomalies of genital organs
• 799.81 Decreased libidos

ICD10
• F52.0 Hypoactive sexual desire disorder
• Q55.0 Absence and aplasia of testis
• R68.82 Decreased libido

CLINICAL/SURGICAL PEARLS
• Decreased libido can be from a number of causes (medications, hormonal or psychiatric disorders, etc.).
• A thorough history (including sexual history and SHIM score) and physical exam (assessment of secondary sex characteristics and testicular volume) are critical and can often point to a diagnosis.
• It is very important to distinguish decreased libido from other disorders of sexual function (arousal, erectile dysfunction, premature ejaculation, orgasm, and sexual pain disorders) but patients can often have multiple issues simultaneously.
• Surgery is usually designated for pituitary adenomas (ie, prolactinomas), which can be found on brain MRI.
LOWER URINARY TRACT SYMPTOMS
Matthew J. Resnick, MD
David F. Penson, MD, MPH

PATHOPHYSIOLOGY
- BOO results in generation of higher bladder pressures to overcome outlet resistance.
- Bladder "remodeling," secondary to longstanding outlet obstruction results in overactive bladder syndrome, storage symptoms, and over time, decreased contractility.
- LUTS may result from numerous conditions of the central and peripheral nervous systems.
- Result in either detrusor overactivity (storage symptoms) or detrusor hypertonia (urinary retention/hydronephrosis).

ASSOCIATED CONDITIONS
Erectile dysfunction

GENERAL PREVENTION
N/A

DIAGNOSIS

HISTORY
- Essential to quantify LUTS for both diagnosis and treatment planning.
- Use the validated AUA Symptom Score (AUASS) often referred to as the AUA symptom index (AUSI) or International Prostate Symptom Score (IPSS) (1–7 mild; 8–19 moderate; 20–35 severe).
- Attention should be paid to nature (obstructive/storage) and duration of LUTS.
- Consider voiding diary (frequency/volume charts) if the patient is unable to elaborate the nature of his or her symptoms.
- Elicit history of prior urinary tract infection or prostatitis.
- Elicit history of prior hematuria (gross or microscopic).
- Elicit history of prior urologic/pelvic surgery.
- Prior lower urinary tract intervention predisposes to stricture/bladder neck contracture.
- Disruption of pelvic floor with pelvic surgery may result in detrusor hyperreflexia.
- History of other medical conditions:
  - Neurologic disease—overactivity or bladder hypocontractility.
  - Diabetes—bladder hypertonia.
  - History of sexually transmitted infection(s)—urethral stricture disease.
  - History of pelvic radiation—urethral stricture disease or bladder hypertonicity.
- Elicit family history of genitourinary disease (BPH/LUTS, prostate cancer, prostatitis).
- Review medications as certain antihistamines, antimuscarinics, sympathomimetics, and bronchodilators may exacerbate LUTS.

PHYSICAL EXAM
- Abdominal exam to assess suprapubic region for bladder distension.
- Focused neurologic exam should be performed with particular attention to:
  - General mental status.
  - Ambulatory status.
  - Motor and sensory function of the lower extremities and perineum.
  - Anal sphincter tone.

In men:
- Inspection of the urethral meatus should be performed to rule out meatal stenosis.
- Digital rectal exam (DRE) should be performed to evaluate for:
  - Prostatic enlargement.
  - Nodularity or firmness suggestive of prostate cancer.
  - Regression or tenderness suggestive of prostatitis.
- Anorectal tone, abnormalities of which suggest neurologic disease.

In women:
- Speculum exam should be performed to evaluate for mass, prolapse, and urethral abnormalities.

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Urinalysis should be performed to evaluate for urinary tract infection or hematuria.
- Serum PSA should be considered as a diagnostic test (as opposed to a screening test).
- Serum creatinine is not recommended in the evaluation of routine LUTS associated with BPH.

IMAGING
- Imaging with CT or ultrasound (US) is not recommended as routine procedure.
- Upper tract imaging with either CT or US may be considered in the context of:
  - Acute symptom onset.
  - History of upper urinary tract infection or stone disease.
  - History of renal insufficiency.
  - Recent onset of nocturnal enuresis.
- Prostate imaging with transluminal US may provide information for treatment planning but is considered optional.

Diagnostic Procedures/Surgery
- Assessment of post-void residual urine with US imaging is recommended prior to intervention.
- Pressure flow urodynamic studies are not indicated in the evaluation of the uncomplicated patient with LUTS.
- Serum PSA should be considered as a diagnostic test (as opposed to a screening test).
- Assessment of urinary flow rate is optional that may predict response to invasive therapy.
- Immediate intervention for bladder function is optimal.
- Pressure flow urodynamic studies are not indicated in the evaluation of the uncomplicated patient with LUTS.
- May be useful in patients with mixed symptoms or neurologic disease to develop a therapeutic strategy.
- Cystoscopy is not recommended for the uncomplicated patient with LUTS.

Pathologic Findings
- Histopathology of BPH reveals proliferation of both stromal and glandular prostatic elements.

Risk Factors
- Increased risk of moderate-to-severe LUTS in men with a family history of BPH.
- The precise contribution of genetic and environmental factors to the development of LUTS remains largely unknown.
GENERAL MEASURES (1,2)

- Antimuscarinic agents can be used alone or in combination therapy (5) α–Side effects include decreased libido and sexual dysfunction.
- Finasteride or dutasteride α–Reductase inhibitors: reduce prostatic volume by 25%–30% in 1 year, reduce symptoms (I-PSS), reduce men’s likelihood of requiring intervention (5).
- Terazosin start 1 mg/d to max. 20 mg α–Side effects include syncope, orthostasis, retrograde ejaculation, asthenia, and nasal congestion.
- Tamsulosin start 0.4 mg to max. 0.8 mg α–Side effects include dizziness, orthostatic hypotension, headache, diarrhea.
- Silodosin 8 mg/d
- Doxazosin start 1 mg/d to max. 8 mg
- Alfuzosin 10 mg/d
- Proscar 5 mg
- Lotensin 2.5 mg

TREATMENT

**GENERAL MEASURES (1,2)**
- Treatment should be offered to men with moderate to severe symptoms (I-PSS ≥ 28) who are bothered enough to consider therapy.
- Men with demonstrable sequelae of BPH/BOO (renal failure secondary to obstruction, bladder calculi, etc.) should be counseled on benefits of treatment.
- Treatment is tailored to symptom type (obstructive, detrusor overactivity, etc.)
- Treatment should be offered to men with moderate to severe symptoms and prostatic enlargement.
- Combination therapy (α-adrenergic blocker + 5α-reductase inhibitor) should be considered in men with moderate to severe symptoms and prostatic enlargement.
- Saw palmetto is widely used to treat LUTS with little evidence of efficacy.

**MEDICATION**

**First Line**
- α-Adrenergic blockers: relax prostatic/bladder neck smooth muscle tone and improve symptoms (all appear to have equal effectiveness) –Adrenergic blocker + 5α-reductase inhibitor (5).

**Second Line**
N/A

SURGERY/OTHER PROCEDURES

- Urodynamics or direct visualized incision of urethral stricture (DVIU) should be considered for stricture/bladder neck contracture.
- Prostate repair should be considered for women with urinary symptoms and prolapse.
- Numerous surgical options exist for men with BPH/BOO (selective prostatectomy, transurethral resection of the prostate, transurethral microwave thermotherapy).

**FOLLOW-UP**

- Patient Monitoring: Monitoring with serial AUASS or IPSS to quantify symptom intensity and bother.
- Urinalysis, serum PSA, urinary flow rate, and postvoid residual as clinically indicated.

**COMPPLICATIONS**

- Complications of BPH/LUTS include:
  - Recurrent UTIs
  - Renal insufficiency
  - Bladder stone formation
  - Urinary retention
  - Secondary sterile pyelonephritis

**CLINICAL/SURGICAL PEARKS**

- Quantification of symptoms is paramount in the management of LUTS.
- Treatment should be offered to men with moderate to severe symptoms (AUASS ≥ 28).
- Treatment should be tailored to symptoms and prostate volume and may include behavioral intervention, medical management, or surgical intervention.

**REFERENCES**


**ADDITIONAL READING**

Lymphadenopathy, Inguinal

Michael E. Woods, MD
Ray S. Pruthi, MD, FACS

BASICS

DESCRIPTION
- Clinically evident inguinal lymphadenopathy can be secondary to infection, inflammation, or malignancy.
- Lymph nodes (LNs) are generally considered enlarged if > 1 cm.
- There is a > 1% annual incidence of unexplained peripheral (including inguinal) lymphadenopathy.
- 14% of all abnormal lymphadenopathy present in inguinal region

Epidemiology
Incidence
- Malignancy
  - Penile cancer (11A)
  - 0.4–0.64% of new cases in USA
  - Median age at diagnosis: 68 yr
  - 50% of enlarged LN secondary to cancer
- Lymphoma: ~80,000 cases/year in USA
- Infectious (STDS) (2A)
  - Approximately 15 million new Sexually Transmitted Infections (STIs)/year in USA
  - Chlamydia (Mannheimia haemolytica)–24 cases reported to the CDC in 2010
  - Herpes simplex: ~770,000 cases/year, 16% of 14–64 yr olds infected with HSV-2
  - Lymphogranuloma venereum (LGV)–relatively rare; rise in USA and UK associated with men who have sex with men and pierced with HIV
- Syphilis–In 2011, USA, men 82,100,000; women 1,100,000
- HIV–1.1 million people in USA infected
- Lymphogranuloma venereum (LGV)–relatively rare; increase in USA and UK associated with men who have sex with men and pierced with HIV
  - Syphilis–In 2011, USA, men 82,100,000; women 1,100,000
  - HIV–1.1 million people in USA infected
- Gonorrhea: 2nd commonest STI in USA

Risk Factors
- Penile Cancer
  - Circumcision (neonatal circumcision is protective)
  - Poor genital hygiene; phimosis
  - Number of sexual partners
  - Human papilloma virus (HPV) infection (type 16 and 18)
- Incidence of LN metastases related to grade, stage, and lymphovascular invasion
- 5% High-risk sexual practices (ie, nonuse of condom, multiple partners, men who have sex with men)

Pathophysiology
- Inguinal lymph nodes (ILNs) serve at the primary lymphatic drainage for the penis, scrotum, urethra, vulva, vagina, perineum, gluteal region, lower abdominal wall, lower arm, and lower extremities.
- ILNs lie within the femoral triangle (inguinal ligament, sartorius, and adductor longus) and are separated into superficial and deep groups by the fascial lata of thigh.
- Penile squamous cell carcinoma (SCCs) cancer spreads by a relatively reliable pattern: From superficial pelvic LNs to deep pelvic LNs

Associated Conditions
- Bacterial
  - Phimosis
- Additional sexually transmitted infections (STIs)

General Prevention
- Population screening is protective against penile cancer
- Good genital hygiene
- STD education and safe sexual practices
- Sun protection against melanoma
- HPV vaccination may reduce risk (unproven)

Diagnosis

History
- Constitutional symptoms: Weight loss, night sweats
- Age: Penile cancer is more likely in older individuals, STI more common in younger patients
- Sexual history: Number and sex of partners, condom use
- Travel: International travel is a common source of STI

Physical Exam
- Genital exam
  - Lower extremities bilaterally for lesions
- Abdominal exam
  - Cachexia: Suggests systemic illness
  - Generalized lymphadenopathy (neck, axilla)
  - HIV, lymphoma

Imaging
- Formal pelvic exam in women
- Excisional biopsy of abnormal LN or primary lesion
- Inguinal US: Evaluate solid vs. cystic lesions; identify perineal tumor
- CT abdomen/pelvis: Extent of disease
- CT chest/CXR: Staging in settings of malignancy

Diagnostic Procedures/Surgery
- Biopsy of abnormal LN or primary lesion
- Bone marrow biopsy (lymphoma workup)

Differential Diagnosis
- Nonmalignant (lymphadenitis)
  - Malignancy: In a historic study of over 200 patients the order of malignancy in inguinal lymphadenopathy was: Cutaneous malignancy of the trunk, testes, ovaries, and penile cancer.
  - Infectious
    - Soft-tissue infection of the lower extremity
    - Staphylococcus aureus
- Drug-induced: Treatment of primary lesion
  - Nonspecific lymphadenitis
  - Inguinal lymphadenopathy is reasonable if there are no other clinical findings.

Diagnostic Tests & Interpretation
- CBC, basic metabolic panel, liver function testing (LFTs)
- Infectious/STD (2)
  - Gonorrhea
    - Nucleic acid amplification testing (ie, polymerase chain reaction [PCR] of vaginal samples, urine, or anal samples–90% sensitive
    - Cultures–72–95% sensitive, perform if drug resistance is suspected
  - Syphilis
    - Darkfield microscopy of primary chancre, screen with nontreponemal test (RPR, VDRL) confirm with positive test confirmed via western blot assays
  - Herpes simplex
    - Viral culture of active lesion (50% sensitive)
    - PCR of specimen from genital ulcer
    - Direct fluorescent antibody of specimen
    - Serology for HSV-1/2 (90% and 95% sensitivity and specificity, respectively)
    - HSV–Culture, Chlamydia trachomatis from ulcers or ulcers
    - PCR–95% sensitive (specific: non-FDA approved)
  - LGV: Serology for LGV antibody to LGV-1 antigens

Treatment
- Generalized lymphadenopathy should be referred for general evaluation
- A period of observation for localized lymphadenopathy is reasonable if there is no other clinical findings
- Penile cancer requires treatment of primary lesion (based on size and location) followed by inguinal lymphadenectomy if indicated
- Infectious etiologies need to be accurately diagnosed so appropriate treatment can be initiated (see below)

Medications: Cephalosporins, others

References
- Raj S. Pruthi, MD, FACS
- Michael E. Woods, MD

230
**SURGERY/OTHER PROCEDURES**

**Perineal cancer (CEA)**
- Management of primary lesion (local excision, partial penectomy, total penectomy)
- Non-palpable LNs
- Up to 50% of all enlarged LNs are benign in patients with newly diagnosed perineal cancer. Treated with 6 wk of antibiotics (currently controversial) prior to consideration of inguinal lymph node dissection (ILND) or undergone a fine needle aspiration of the node in question if the primary tumor is low-risk.
- Occult metastasis ~25% without frozen section
- T1G1—surveillance
- T1G2—surveillance if LND or dynamic sentinel node biopsy (DSNB)
- T2 or greater—LND or DSNB
- Papillary ULC: Low risk—consider fine-needle aspiration to confirm malignancy; Intermediate/high risk—LND
- Inguinal lymphadenectomy techniques
  - Dynamic sentinel node biopsy (DSNB)
  - Use of blue dye + y-emission (radio nuclide tracer)
  - False-negative 5%, expert required
  - Superficial LND
  - Removal of LN above fascia lata
  - If lymph positive on frozen section, then complete LND widened
  - Option for prophylactic LND
  - Modified LND
  - Appropriate for prophylactic LND
  - Decreased morbidity
  - Limited template (lateral border femoral artery, vastus lateralis fascia)
  - Includes deep nodes medial to femoral vein
  - Smaller incision, preserve saphenous vein
  - Avoids transection of sartorius muscle
  - Positive on frozen, then standard LND
  - Radiation-treated LND
  - Indicated for patient with metastatic disease to the LND
- Larger template including fascia lata and limits transection of femoral artery and dissection to apex of the femoral triangle
- Routine dissection of saphenous vein and sartorius muscle for complete superficial LND
- Infectious etiology
  - Fine-needle aspiration for culture
  - Incision and drainage of abscess
- Lymphoma
  - Fractional biopsy of LN (may consider other site if generalized lymphadenopathy is present)

**ADDITIONAL TREATMENT**

**Infection Therapy**

- Perineal Cancer: Radiation of bulky, unresectable inguinal lymphadenopathy

**Additional Therapies**
- Perineal cancer
  - Patients with fixed LNs or pelvic ULC should receive cisplatin-based chemotherapy followed by consolidative surgery when appropriate (3CE)
  - Paclitaxel, ifosfamide, cisplatin—50% complete response (CR) or partial response (PR) and ~70% undetectable planned surgery

**ONGOING CARE**

**PROGNOSIS**

- Perineal Cancer
  - Node negative: 46–100% 5-yr survival (mean ~75%)
  - Node positive: 0–86% 5-yr survival based on nodal burden (average ~60%)

**COMPLICATIONS**

- LND
  - Severe, lymphatic, wound infection, skin necrosis
  - 25–50% risk

**FOLLOW-UP**

- **Patient Monitoring**
  - **Perineal Cancer (CEA)**
    - 
    - N0: 1-2 then N1: 3-5
    - 0: 1-2 then N1: 3-5
    - N2: 1-2 then N3: 1-2 then N4=MO: 0–6
    - Infectious (CEA)
      - Chancroid—7–14 days after initiating treatment
      - LGV—nucleic acid amplification at 6–12 months
      - Gonorrhea—treatment if symptoms resolve

**Patient Resources**

**ADDITIONAL READING**


**CLINICAL/SURGICAL PEARLS**

- Differentiate inguinal adenopathy from more generalized LR involvement
- The viability of the skin flaps developed during an inguinal dissection are based on the anatomic vessels within the superficial fatty layer of Camper’s fascia which course lateral to medial along the skin lines. This is a key anatomic dissection plane of the lymphatic drainage of the penis lies beneath Camper’s fascia allowing this superficial fatty layer to remain attached to the skin flaps.
- Use a modified technique in a clinically negative groin to decrease morbidity. The key components: Shorter incision (~10 cm), preserve saphenous vein, minimize dissection lateral to the femoral artery, and avoid transection of the sartorius muscle.

**ADDITIONAL DRUGS**

- Azithromycin 2 g PO × wk
- Zinc (1 or doxycycline 100 mg or ciprofloxacin 500 mg PO × wk)
- Acyclovir 200 mg PO TID × wk
- Valacyclovir 1 g PO BID × wk
- Ceftriaxone 250 mg IM × 7–10 days or azithromycin 1 g PO × wk
- Vancomycin 1 g PO × wk
- Surveillance

**REFERENCES**

**LYMPHADENOPATHY, PELVIC AND RETROPERITONEAL**

Carrie L. Fitzgerald, DO, MPH  
James A. Brown, MD, FACS

**BASICS**

**DESCRIPTION**
- Enlarged nodal tissue in the pelvis and retroperitoneum
- Can be regional or generalized
- Definitions vary, but include solitary node ≥ 1–1.5 cm in short axis, any rounded node ≥ 8 mm or multiple nodes > 1 cm (1).
- Pelvic lymph nodes (LN) are generally considered abnormal if ≥ 1.3 cm.
- Often discovered incidentally or with imaging performed for tumor staging.
- Usually nonspecific, but potentially life threatening.

**EPIDEMIOLOGY**
- Lymphadenitis: seen with inflammatory/infectious conditions of the pelvis
- Immunosuppression (HIV, autoimmune)
- Prostate cancer
- Tumor-associated syndromes:
  - Possibly Apert syndrome
  - Li–Fraumeni syndrome
  - SBLA syndrome (Sarcoma, Breast, Lung, Adrenal carcinoma)
  - Gardner syndrome
- Tuberous sclerosis complex (TSC)
  - Birt–Hogg–Dube (BHD)
  - Hereditary leiomyomatosis and renal cell cancer
  - Hereditary papillary renal carcinoma (HPRC)
  - Hereditary pheochromocytoma (HPP)
- Tuberculosis scrofula (TSC)
- Adrenal cancer:
  - Gardner syndrome
  - Birt–Hogg–Dube syndrome (associated with hemihypertrophy)
  - Multiple endocrine neoplasia type 1
- SBLA syndrome (Sarcoma, Breast, Lung, Adrenal carcinoma)
  - Le–Rounds syndrome
- Urothelial cancer:
  - Hereditary nephropathy colon cancer (HNCC)
  - Hereditary retinoblastoma
  - Cowden syndrome
  - Possibly Apert syndrome
- Prostate cancer:
  - Hereditary breast and ovarian syndrome (BRCA2)
  - Patients with primary tumors of GI, GU, and GYN tracts and associated risk factors for these malignancies
  - Smoking, age, family history, HPV
- Immunosuppression (HIV, autoimmune)
- Lymphadenitis seen with inflammatory/infectious conditions of the pelvis

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- CBC, ESR, exam of peripheral smear
- Creatinine (for imaging and to check renal function)

**Pathology**
- Urine cytology
- Urinalysis for hematuria
- Creatinine (for imaging and to check renal function)
- CBC, ESR, exam of peripheral smear
- PET: Evaluate fibrosis from metabolically active nodes, ie, postradiotherapy testicular cancer, seminoma (2), expanding role (3)
- Some studies show PET can define testicular relapse before CT
- SPECT: Advances in lymphoscintigraphy have advanced opportunity for TN injection in select GU malignancies (1)
- Bilateral lymphangiography largely replaced by CT and MRI

**Diagnostic Procedure/Surgery**
- Nodal tissue exam unless diagnosis is clear (ie, testicular or prostate tumor), then size or function and physiology becomes important (1).
- CT-guided biopsy best way to obtain nodal tissue.
  - Not always feasible (ie, proximity to major vessels), open/laparoscopic in select cases
  - CT-guided biopsy/SPECT imaging

**Pathologic Findings**
- Nodal, depends on cause (see below)

**DIFFERENTIAL DIAGNOSIS**
- Tumor:
  - Primary lymphatic: Lymphoma (non-Hodgkin, Hodgkin, others)
  - Secondary: Adrenal, renal, urothelial and nonurothelial bladder or upper tract cancer, prostate, urethral, penile, germ cell, ovarian, uterine, GI (carcinoid, lymphomas), colorectal, melanoma, Kaposi sarcoma
- Infections/inflammatory:
  - Granulomatous: TB, sarcoidosis, histoplasmosis, lymphogranuloma venereum, Castleman disease
  - Noninfectious: IL 1 receptor hyperactivity associated with HIV and human herpesvirus 8 (HHV-8)
  - Nongranulomatous: Viral, bacterial (Ab absence in local areas), sinus histiocytosis, retroperitoneal fibrosis
- Other:
  - Neoplastic, non-neoplastic, and cystic retroperitoneal masses (lymphocele, urinoma, hemorrhage) aneurysms
LYMPHADENOPATHY, PELVIC AND RETROPERITONEAL

TREATMENT

GENERAL MEASURES
- Wide variety, based on diagnosis of primary disease
- Image-guided needle biopsy, as a first-line investigation, is useful in the diagnosis of space-occupying lesions of the retroperitoneum
- Routine lymphadenectomy usually indicated for GU malignancy

MEDICATION
First Line
- Based on diagnosis of primary disease
Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Open or laparoscopic nodal sampling may be required in select cases
- Lymphadenectomy at time of organ-specific resection is indicated in many cases of GU, GYN, and GI malignancy

ADDITIONAL TREATMENT
- Underlying cause must be treated appropriately
- Benign reactive lymphadenopathy can be seen in the presence of malignancy and improves with appropriate treatment
- Radiation Therapy
  - For certain cases such as seminoma

ADDITIONAL THYERAPY
- In select cases, re-implanting for signs of growth or assessing therapeutic response, eg, hormonal therapy for prostate cancer, antibiotics for peritoneal cancer
- Notification of partner if HIV-positive [A]
- Complementary & Alternative Therapies
  - N/A

ONGOING CARE

PROGNOSIS
- Widely variable

COMPLICATIONS
- Severe lymphadenopathy can result in lower extremity edema, varicocele
- Potential surgical complications of retroperitoneal lymphadenectomy include vascular injury, lymphocele, chylous ascites, ejaculatory dysfunction, and GI complications (pancreatitis, bowel injury/infection)

FOLLOW-UP

Patient Monitoring
- Based on primary disease

Patient Resources
- N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Groin/Inguinal Mass
- Lymphadenopathy, Inguinal
- Lymphadenopathy, Pelvic and Retroperitoneal
- Retroperitoneal Mass and Cysts

CODES

ICD9
- 202.80 Other malignant lymphomas, unspecified site, extranodal and solid organ sites
- 567.9 Unspecified peritonitis
- 785.6 Enlargement of lymph nodes

ICD10
- C85.90 Non-Hodgkin lymphoma, unspecified, unspecified site
- K65.9 Peritonitis, unspecified
- R33.0 Localised enlarged lymph nodes

CLINICAL/SURGICAL PEARLS

- General malignancies (testis, penile) have predictable lymphadenopathy pattern of spread.
- Pelvic organ malignancies may have skip lesions to the retroperitoneum.
- Lymphadenectomy may be curative for many urologic and hematologic malignancies.
- Urinary, bowel, and vascular obstruction possible with advanced lymphadenopathy.
- Inflammatory and infectious conditions may lead to reactive lymphadenopathy.
LYMPHOCELE, PELVIC
Rafael E. Yanes, MD
Fernando J. Bianco, Jr, MD

ASSOCIATED CONDITIONS
- Bladder cancer
- Gynecologic malignancy
- Penile cancer
- Prostate cancer
- Renal cancer
- Renal insufficiency with transplantation
- Retropertitoneal metastasis

GENERAL PREVENTION
- Multicystic lymphadenopathy with clips on proximal end of lymphatic vessels.
- Monopolar electrosurgery may not adequately seal lymph channels.
- Bipolar or harmonic devices have been shown to be effective (bipolar devices created seals that were 10-fold stronger than the harmonic devices).
- These vessel-sealing devices (VSDs) may reduce risk.
- Use of Floseal or other hemostatic products after lymphadenectomy may reduce the number of symptomatic lymphoceles.
- Some reports that the use of anticoagulants (eg, subcutaneous heparin) postop may increase risk.
**TREATMENT**

**GENERAL MEASURES**
- Treat DVT if present.
- Foley catheter if the patient has significant voiding dysfunction.
- Asymptomatic small lymphoceles should be monitored (< 100–150 mL volume). Many will resolve spontaneously.

**MEDICATION**

**First Line**
- Lymphocele management is primarily interventional with limited role for medications unless associated with infection or sclerosis (see below) (2).
- Systemic antibiotics (with percutaneous drainage) if lymphocele is infected.

**Second Line**
- N/A

**SURGERY/OTHER PROCEDURES**
- Treatment of symptomatic or large lymphoceles is immediate percutaneous drainage (3).
- Reported success rates with aspiration and drainage tube are approaching 80%, with a mean drainage duration ranging from a few days to several months.
- Increased risk of infection, especially in immunocompromised (transplant) patients.
- Sclerosis therapy can be used to treat extraperitoneal lymphoceles:
  - Sclerotherapy (povidone–iodine, 95% ethanol, tetracycline 0.5–2 g in 50 mL NS, bleomycin 1 U/mL, fibrin glue):
    - Cavity is aspirated, then filled gently with a sclerosing agent.
  - Multiseptated lymphoceles: Drainage, lack of access to all chambers.
  - When the ureter is in close contact with a wall of the lymphocele (periureteral fibrosis, ureteral obstruction)
  - Incomplete lymphoceles should not be treated by sclerosis.
- Transperitoneal laparoscopic marsupialization (4)
  - If unsuccessful sclerosis or not amenable to percutaneous drainage.
  - Three transperitoneal ports provide access for excision of the peritoneal window and optional omental wick placement to keep peritoneal window open.
  - Success: 77–100%
- Open marsupialization (internal drainage) into the peritoneum is the historic gold standard:
  - A window of peritoneum is created, allowing the lymph to be reabsorbed by the peritoneum.
  - Infected lymphoceles require percutaneous or open surgical drainage.
  - Ureteral obstruction:
    - Placing a portion of omentum in the window decreases recurrence maintaining patency.
    - Success: 75–100%

**ONGOING CARE**

**PROGNOSIS**
- Most smaller asymptomatic lymphoceles resolve spontaneously.
- >90% success with marsupialization.

**COMPLICATIONS**
- DVT/PE
- Lymphostasis of the lower extremity
- Infection
- Ureteral obstruction
- Bowel obstruction

**FOLLOW-UP**
- Repeat imaging: Ultrasound or CT in 2–4 mo after treatment to detect recurrence.

**REFERENCES**

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
  - Edema, External Genitalia
  - Lymphocele, Pelvic Images
  - Urinoma (Perinephric Pseudocyst)

**CODES**

**ICD9**
457.8 Other noninfectious disorders of lymphatic channels

**ICD10**
B89.8 Other noninfectious disorders of lymphatic vessels and nodes

**CLINICAL/SURGICAL PEARLS**
- Use of clips on identifiable lymphatic channels can minimize the occurrence of postoperative lymphoceles.
- A transperitoneal approach for lymphadenectomy is not protective against the formation of a lymphocele because loculation of lymphatic fluid can still occur.
- Symptomatic lymphoceles may require percutaneous or laparoscopic drainage.
**MEDULLARY CYSTIC KIDNEY DISEASE (MCKD)**
Scott G. Hubosky, MD

**BASICS**

**DESCRIPTION**
- Medullary cystic kidney disease (MCKD) is a rare congenital, cystic disease of the kidneys which results in progressive renal deterioration and to eventual end-stage renal disease (ESRD).
- Symptoms develop insidiously and diagnosis is not common until renal insufficiency is detected and initiates evaluation.

**EPIDEMIOLOGY**
- **Incidence**: Less than 1:100,000
- **Prevalence**: N/A

**RISK FACTORS**
- Positive family history
- Genetics
  - Mode of inheritance is autosomal dominant (AD)
    - Medullary cystic kidney disease-1 (MCKD1)
      - Mutation in MCKD1 gene localized to chromosome 1q21
    - MCKD2
      - Mutation in MCKD2 gene localized to chromosome 16p12

**PATHOPHYSIOLOGY**
- Unlike other renal cystic diseases such as autosomal dominant polycystic kidney disease (ADPKD), there is no clear correlation between genetic mutation and identifiable protein product responsible for the MCKD phenotype.

**ASSOCIATED CONDITIONS**
- Hyperuricemia and gouty arthritis are associated with MCKD2
- In contrast to juvenile nephronophthisis, MCKD does not have many extrarenal manifestations

**GENERAL PREVENTION**
- N/A

**DIAGNOSIS**

**HISTORY**
- Polyuria
  - Usually the 1st clinical manifestation
  - Occurs due to reduced urinary concentrating ability of the kidney
- Polydipsia
- Family history of ESRD, or renal cysts

**PHYSICAL EXAM**
- Hypertension may be noted with disease progression

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urinalysis
  - Proteinuria and hematuria are usually absent
- CBC
  - Anemia present in advanced cases due to lack of erythropoietin
- Serum electrolytes
  - Elevated creatinine
  - Hyperkalemia or metabolic acidosis in later stages due to renal insufficiency

**Imaging**
- Renal ultrasound
  - Kidneys may be atrophic depending on stage of disease
  - Cysts may be visible at the corticomedullary junction in later disease but are usually not detectable in early stages due to renal insufficiency
- CT scan
  - Can detect cysts at the corticomedullary junction better than ultrasound
  - Need for IV contrast is suboptimal in patients with ESRD

**Differential Diagnosis**
- Juvenile nephronophthisis
  - Clinically and anatomically similar to MCKD
  - Autosomal recessive inheritance
  - ESRD usually manifests as early as age 13 yr
  - Extrarenal manifestations are common
    - Retinal disorders (retinitis pigmentosa)
    - Hepatic fibrosis
    - Bardet-Biedl syndrome (obesity, retinitis pigmentosa, mental retardation, polydactyly)
- Polycystic kidney disease
  - Autosomal recessive polycystic kidney disease (infantile form)
  - Autosomal dominant polycystic kidney disease (adult form)
- Multicystic dysplastic kidney
- Benign multicystic (cystic nephroma)
- Medullary sponge kidney
MEDULLARY CYSTIC KIDNEY DISEASE (MCKD)

TREATMENT

GENERAL MEASURES
- Same as for any patient with renal insufficiency
  - Control hypertension if present
  - Monitor fluid/balanced electrolyte intake
  - Monitor serum electrolytes

MEDICATION
First Line
- None for primary treatment
- Antihypertensive regimen may be necessary

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Transplantation when ESRD develops
  - Allograft is not affected by MCKD after transplantation

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS
- MCKD1 patients manifest with ESRD at median age of 62 yr
- MCKD2 patients manifest with ESRD at median age of 32 yr

COMPLICATIONS
Similar to any patient with renal insufficiency or ESRD

FOLLOW-UP
Patient Monitoring
Close nephrology follow-up is essential

Patient Resources
- National Kidney Foundation
  - www.kidney.org/patients

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Nephronophthisis (Juvenile, Infantile, and Adolescent)
- Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)
- Renal Mass

CODES
ICD9
- 585.6 End stage renal disease
- 753.16 Medullary cystic kidney
- 788.42 Polyuria

ICD10
- N18.6 End stage renal disease
- Q61.5 Medullary cystic kidney
- R35.8 Other polyuria

CLINICAL/SURGICAL PEARLS
- MCKD has an insidious disease onset.
- Symptoms generally not present until patient has renal insufficiency documented on serum testing.
- Polyuria is commonly the 1st clinical manifestation.
**BASICS**

**DESCRIPTION**

Medullary sponge kidney (MSK) consists of developmental abnormalities of the kidneys with ectatic or dilated terminal collecting ducts and associated medullary cysts.

**EPIDEMIOLOGY**

Incidence

N/A

**Prevalence**

• Estimated at 1 in 5,000–20,000 in the general population

• Occurs more frequently in stone formers ranging from 5 to 20%

• Identification and therefore recognized incidence of MSK may be decreasing since it depends on radiographic contrast studies to detect the dilated collecting ducts.

**RISK FACTORS**

N/A

**GENETICS**

Many cases may be sporadic:

• Increasing evidence suggests inheritability of the disorder, possibly of an autosomal dominance based on familial studies

• Mutations in glial cell–derived neurotropic factor (GDNF) account for roughly 12% of MSK cases

**PATHOPHYSIOLOGY**

• Dilated collecting ducts and medullary pyramidal cysts which may actually represent ectatic ducts

• Dilated ducts may be filled with calcium apatite crystal

• Distal renal tubular acidosis (DRTA) (33–40%)

• Hypercalcitria (9–100%)

• Hypo-citraturia (19–83%)

• Hypocalciuria (9–100%)

• Distal renal tubular acidosis (DRTA) (33–40%)

• Calcium phosphate predominate in 63–67%

• Calcium oxalate monohydrate 33% (pure) to 63% (mixed)

• Calcium oxalate dihydrate 10–40% (mixed)

• May show hypercalciuria (9–100%)

• 24-hr urine collections

• Serum electrolytes usually are normal except with episodes of pain

**ASSOCIATED CONDITIONS**

• Renal calculus

• Urinary tract infections (UTIs)

• Hypo-citraturia and hypercalcitria (as noted above)

• Reduced bone density (2)[B]

**GENERAL PREVENTION**

• This developmental condition cannot be prevented

• Secondary complications (infections, urolithiasis) can be prevented by appropriate measures

**DIAGNOSIS**

**HISTORY**

• Many patients are asymptomatic and are diagnosed incidentally on contrast studies

• Pain associated with renal/ureteral calculi

• Pain without associated obstructing calculi

• Hematuria, microscopic or gross

**PHYSICAL EXAM**

• May be normal without associated findings

• May have flank tenderness, especially among those with episodes of pain

**DIAGNOSTIC TESTS & INTERPRETATION**

**HISTORY**

• Many patients are asymptomatic and are diagnosed incidentally on contrast studies

• Pain associated with renal/ureteral calculi

• Pain without associated obstructing calculi

• Hematuria, microscopic or gross

• 24-hr urine collections

• Serum electrolytes usually are normal except with episodes of pain

**IMAGING**

• CT urogram (CTU) may be most useful imaging study

• After the injection of contrast for CTU, a blush of the involved papillae may be seen

**LAB**

• Urinalysis

• Microhematuria or pyuria

• 24 hr urine collections

• May show hypercalciuria (9–100%)

• May be normal without associated findings

• May have flank tenderness, especially among those with episodes of pain

**DIFFERENTIAL DIAGNOSIS**

• Dent disease

• Other rare abnormalities of calcium phosphate metabolism

• Primary hyperparathyroidism

• RTA

**TREATMENT**

• Noncontrast CT (NCCT) has largely replaced contrast studies (IVU, EXU) in the diagnosis urinary calculus disease

• May demonstrate multiple calcifications and possibly localize them to the renal pyramids (IVU)

• CT urogram (CTU) may be most useful imaging study

• After the injection of contrast for CTU, a blush of the involved papillae may be seen

**DIAGNOSTIC PROCEDURES/SURGERY**

• Endoscopy, specifically ureteroscopy differentiates intraluminal from intraparenchymal calcifications (IVU or EXU)

• 24-hr urine studies to identify metabolic abnormalities

**PATHOLOGIC FINDINGS**

• Typical sponge appearance of the medulla results from the dilated intrapapillary collecting ducts and small medullary cysts

• Calcifications may be found in the dilated collecting ducts

• May be used to detect obstruction in the symptomatic patient

**GENERAL MEASURES**

• Majority of asymptomatic patients can be observed

• General stone clinic measures including high fluid intake should be maintained

• Alkalization with potassium citrate appears to be of value

• Other abnormalities such as hypercalciuria which do not resolve should be treated specifically

• Treat UTIs as necessary
MEDULLARY SPONGE KIDNEY (MSK)

**MEDICATION**
- Potassium citrate is employed in patients with hypocitraturia (5).
- Thiazide diuretics are used in patients with stones and nonresponsive hypocitraturia.
- Specific antibiotics are indicated for the treatment of UTIs.
  - Suppressive antibiotics may be necessary in patients with persistent or multiply recurrent UTIs.

**SURGERY/OTHER PROCEDURES**
- Shock wave lithotripsy has been utilized for treatment of collecting duct stones that can be distinguished from nephrocalcinosis as well as symptomatic intratubular calculi.
- Endoscopy with ureteroscopy or occasionally percutaneous nephrostolithotomy can treat collecting system stones and unroof mucosa to remove obvious and accessible collecting duct stones.
- SWL and endoscopy have been advocated to reduce the frequency of symptomatic episodes but is unproven.

**ADDITIONAL TREATMENT**
- Radiation Therapy: N/A
- Additional Therapies: N/A
- Complementary & Alternative Therapies: N/A

**ONGOING CARE**

**PROGNOSIS**
- Urinary calculi are the most common risk but can be followed and also may be controlled with medical treatment.
- Recurrent UTIs can usually be treated.
- Development of renal failure is very uncommon.

**COMPLICATIONS**
- Stone formation and subsequent obstruction
- Recurrent/chronic flank pain
- UTI

**FOLLOW-UP**
- Imaging at every 6–12 mo in stone formers to evaluate for change in existing stones or appearance of new ones.
- In some patients, renal ultrasound (RUS) can be used to monitor stones and avoid sedation.
- 24-hr urine collections are used to monitor stone risk factors during treatment for urinary abnormalities.
- Serum studies are used to monitor changes related to medication.

**REFERENCES**

**ADDITIONAL READING**

**FOLLOW-UP**

**Patient Monitoring**
- Imaging at every 6–12 mo in stone formers to evaluate for change in existing stones or appearance of new ones.
- In some patients, renal ultrasound (RUS) can be used to monitor stones and avoid sedation.
- 24-hr urine collections are used to monitor stone risk factors during treatment for urinary abnormalities.
- Serum studies are used to monitor changes related to medication.

**Patient Resources**
- National Kidney and Urologic Diseases Information Clearinghouse (NCCD) [website]. Available at: http://kidney.niddk.nih.gov/kudiseases/pubs/medullaryspongekidney/

**CODES**
- ICD9
  - 588.89 Other specified disorders resulting from impaired renal function
  - 592.0 Calculus of kidney
- ICD10
  - N20.0 Calculus of kidney
  - N25.89 Oth disorders resulting from impaired renal tubular function
  - Q61.5 Medullary cystic kidney

**ICAL/SURGICAL PEARLS**
- Be suspicious of MSK in patients with multiple papillary calculi.
- Use contrast study for diagnosis.
- Search for metabolic defects.
- Treat metabolic factors in stone formers.
- Consider treatment of renal stones in patients with recurrent symptomatic stones.
- Significant benefit in endoscopic inspection and treatment.
MEGAURETER, CONGENITAL
Ahmad H. Bani-Hani, MD, FAAP, FACS

**BASICS**

**DESCRIPTION**
- Megaureters is a ureter that is dilated out of proportion to the rest of the urinary tract.
- Most consider ureters measuring ≥7 mm in diameter by ultrasound a megaureter.
- Four types of megaureter are described:
  - Refluxing megaureter
  - Obstructed megaureter
  - Restricting and obstructed megaureter
  - Nonrefluxing, nonobstructed megaureter
- Each of the above groups further categorized as either primary (defect lies in the ureter itself) or secondary (another disorder leading to megaureter such as urethral obstruction)
- Primary megaureter represents the 2nd most common cause of hydronephrosis in the newborn, with urethral outlet obstruction the most common cause.

**EPIDEMIOLOGY**

**Incidence**
- Varies depending on etiology
  - Vesicoureteral reflux (VUR): 0.4–1.8% in children
  - Primary obstructive megaureter (POM): 1 per 10,000 population
- VUR is more common in females
- POM is more common in males with predilection for the left kidney
- Bilateral involvement in up to 40%

**Prevalence**
- N/A

**RISK FACTORS**
- Pediatric urinary valves
- Neurogenic bladder
- Diabetes insipidus

**Genetics**
- No specific genetic factors can be identified in the majority of patients with megaureters
- VUR can be familial

**PATHOPHYSIOLOGY**

- Refluxing megaureter:
  - Caused by congenital abnormality of the intravesical ureter and secondary to abnormal insertion of the ureter into the bladder or the intravesical portion of the ureter is not long enough to enable closure of the ureter during bladder filling
- POM:
  - Exact etiology is unclear; however, the most common finding is a distal adynamic intravesical segment that affects the free eflux of urine resulting in a functional obstruction

- Refluxing, obstructed megaureter:
  - This paradox of pathology was 1st reported by Weiss and Lytton. The muscle cells in the intravesical and extravesical segments of the distal ureter are so lacking that they become incapable of adequate transmission of urine. On VCUG, delayed emptying of the refluxing contrast brokers cut-off distally is highly suggestive of the diagnosis

- Nonrefluxing, nonobstructed megaureter
  - Ureter are so lacking that they become incapable of adequate transmission of urine. On VCUG, delayed emptying of the refluxing contrast brokers cut-off distally is highly suggestive of the diagnosis

- Nonrefluxing, nonobstructed megaureter
  - Secondary to urethral valves if present
  - Can be combined with transurethral resection of urethral valves if present

**ASSOCIATED CONDITIONS**
- Prune belly syndrome

**DIAGNOSIS**

**HISTORY**

- Most megaureters are diagnosed currently prenatally with ultrasound or amniocentesis.
- For late diagnosis, patients may present with abdominal pain, UTIs, or kidney stones.

**PHYSICAL EXAM**

- Abdominal mass
- Abdominal pain and costovertebral angle tenderness with pyelonephritis

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urine analysis and culture if UTI is suspected
- Serum electrolytes, BUN, and creatinine
- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) for pyelonephritis

**Imaging**
- Normally best to perform ultrasound imaging several days after birth to allow relative newborn dephosphatation to equilibrate
- Renal and bladder ultrasound:
  - Establishes the diagnosis of megaureter, assesses renal parenchyma and may provide clues on possible etiology eg thickened bladder wall secondary to urethral valves
- Voiding cystourethrogram:
  - Will evaluate for the presence of VUR and urethral abnormalities such as anterior or posterior urethral valves
- Diuretic renal scan:
  - Will evaluate for the presence of VUR and urethral abnormalities such as anterior or posterior urethral valves
- Retrocaval/retroiliac ureter:
  - Will provide valuable information if diuretic renal scan is equivocal
- Endoscopy: Invasive test as it requires anesthesia.
  - Can be combined with transurethral resection of urethral valves if present

**Pathologic Findings**
- VUR with obstruction
- Electron microscopy, muscle population and collagen types I and III deposition

**DIFFERENTIAL DIAGNOSIS**
- Bowel segment misinterpreted as dilated ureter
- Horseshoe kidney
- Prune belly syndrome
- Renal and ureteral duplication
- Ureterovesical junction obstruction
- VUR
MEGAURETER, CONGENITAL

GENERAL MEASURES
-Serial renal and bladder ultrasounds to monitor progress/resolution of megaureter is important.
-Workup of megaureter to assess the presence or absence of reflux and/or obstruction will guide further treatment options.

Prenatally discovered megaureter
- Unilateral obstructed megaureter has a good prognosis.
- These patients can be followed expectantly in the prenatal period, without further intervention or early delivery.

Bilaterally obstructed megaureter findings require close monitoring for the development of oligohydramnios.

MEDICATION
First Line
- Treat active UTI with culture appropriate antibiotics.
- Consider prophylactic antibiotics in refluxing and obstructed megaureter variants (eg, Amoxicillin).

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Refluxing megaureters:
  - Antibiotic prophylaxis and monitor progress with renal ultrasound (RUS) and VCUG.
  - Ureteral reimplant in cases of breakthrough UTIs, renal scarring, or noncompliance with medications.

Primary obstructed megaureter
- Excision of the distal adynamic ureteral segment and ureteral reimplant. Ureteral tapering maybe required.

Refusing, obstructed megaureter:
- Excision of the distal ureteral segment and ureteral reimplant. Often requires ureteral tapering.

Nonrefluxing, nonobstructed megaureter:
- Observation with serial ultrasound is all that is needed.

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

ONOGH CARE
PROGNOSIS
- Depends on the baseline renal function.
- Surgical correction of obstructing megaureters carries a high success rate.
- Most nonobstructive, nonrefluxing megaureters will resolve with time.
- Outcomes can be poor with concomitant renal anomalies such as renal hypoplasia and dysplasia.

COMPLICATIONS
- UTIs
- Ureteral obstruction, mainly technical issues to details during ureteral reimplant that will cause either:
  - Ureteral kinking at the bladder insertion site.
  - Compromised blood supply to the distal ureter associated with excisional ureteral tapering.
- Nephrolithiasis

FOLLOW-UP
Patient Monitoring
- Serial RUS (3)[A]
- Serial serum chemistry to monitor renal function.

Patient Resources
- Urology Care Foundation http://www.urologyhealth.org/urology/index.cfm?article=3

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
- Hydronephrosis/Hydroureteronephrosis, Dilated Ureter/Renal Pelvis, Pediatric
- Hydronephrosis/Hydroureteronephrosis, Dilated Ureter/Renal Pelvis, Prenatal
- Megaureter, Congenital Image
- Pediatric Urinary Tract
- Prune Belly Syndrome
- Vesicoureteral Reflux

ICD9
753.22 Congenital obstruction of ureterovesical junction

ICD10
Q62.2 Congenital megaureter

Wee spread use of prenatal ultrasound helps identify patients with megaureters at an early stage, commonly prenatally.
- It is important to classify megaureters based on their refluxing and/or obstructing status with the aid of VCUG and diuresis renal scan.
- Long-term follow-up in patients with megaureter is important for best outcome.
MESOBlastic NEPHROMA, CONGENITAL (BOLANDE DISEASE)

Lauren N. Hendrix, MD
Stephen E. Strup, MD, FACS

**BASICS**

**DESCRIPTION**
- Congenital mesoblastic nephroma (CMN) is a renal tumor arising from nephrogenic mesenchyme
- Usually a solid lesion, but cystic varieties have been reported
- Majority are benign with a favorable prognosis
- First reported in 1967, referred to in older literature as Bolande’s tumor or Bolande disease

**Epidemiology**
- Incidence
  - Most common real tumor in children <6 mos of age, usually diagnosed prior to 3 mos
  - Accounts for 3–10% of all pediatric renal neoplasms
- Prevalence
  - N/A

**Risk Factors**
- Genetics
  - ETV6-NTRK3 gene fusion
    - Results from translocation t (12;15) (p13;q25)
    - Found only in the cellular variant
    - Also found in congenital fibrosarcoma

**Pathophysiology**
- Tumor classification
  - Stage I: Tumor limited to kidney without involvement of capsule or hilar vessels
  - Stage II: Tumor extends beyond capsule with invasion into perinephric fat or blood vessels, but margins of resection are negative
  - Stage III: Tumor not completely resectable, tumor spillage occurs at time of resection, or tumor was biopsied preoperatively
  - Stage IV: Hemorrhagic metastases or lymphatic spread outside of abdomen
  - Stage V: Bilateral tumors

**Associated Conditions**
- Polyhydramnios
- Hydrops fetalis

**DIAGNOSIS**

**History**
- History of prenatal ultrasound finding of unilateral renal mass
- History of polyhydramnios
- Neonate with abdominal mass
- Hematuria, jaundice, hypertension, anemia, hypercalcemia

**Physical Exam**
- Palpable abdominal mass
- Hematuria
- Jaundice

**Diagnostic Tests & Interpretation**
- Lab
  - Complete blood count
  - Basic metabolic panel
    - Serum creatinine
    - Serum calcium
  - Urinalysis
- Imaging
  - Abdominal ultrasound
    - Preferred modality
    - “Ring pattern”
    - Hypoechoic mass with hyperechoic rim signifying vessels at the tumor periphery
    - Seen only in the classic variant
  - CT
    - Homogeneous mass
    - May have peripheral enhancement or focal enhancement at sites of hemorrhage or necrosis
  - MRI
    - Signal similar to normal parenchyma with exception of areas of hemorrhage

**Diagnostic Procedures/Surgery**
- Biopsy
  - The role of biopsy in pediatric renal tumors is controversial as nephrectomy is the mainstay of treatment and preoperative biopsy upstages to stage III

**Pathologic Findings**
- Three histologic subtypes
  - Classic
    - 1/3 of cases
    - Similar macro- and microscopically to leiomyoma
    - Entrapped nephrons and blood vessels seen at the tumor periphery
    - Not associated with metastasis
  - Cellular
    - 2/3 of cases
    - More aggressive than classic with high mitotic index and atypical growth pattern
    - Associated with local invasion/recurrence and metastasis
    - Mixed (5)

**Differential Diagnosis**
- Solid renal mass
  - Wilms tumor
  - Rhabdoid tumor
  - Metanephric adenofibroma
  - Renal cell carcinoma
  - Angiomyolipoma
  - Clear cell sarcoma
  - Multilocular cystic nephroma
  - Autosomal recessive polycystic kidney disease
  - Cross fused ectopia
  - Renal vein thrombosis
  - Solitary kidney with compensatory hypertrophy
  - Beckwith-Wiedemann syndrome
  - Adrenal mass
  - Renal parenchymal mass (3)
MESOBLASTIC NEPHROMA, CONGENITAL (BOLANDE DISEASE)

**GENERAL MEASURES**
- Management of associated features
  - Hypertension
  - Hypercalcemia
  - Jaundice
  - Anemia
- Chemotherapy reserved for patients >3 mo with cellular variant, tumor spillage at resection, microvascular invasion, metastatic disease, and inoperable tumors

**MEDICATION**
- **First Line**
  - Vincristine, cyclophosphamide, and doxorubicin (VCD)
- **Second Line**
  - Isophosphamide, carboplatin, etoposide (ICE) – Has considerable nephrotoxicity (3)

**SURGERY/OTHER PROCEDURES**
- Radical nephrectomy – Gold standard – Allows for appropriate staging – Decreased risk of local recurrence
- Partial nephrectomy – Has been reported with success in Wilms tumors but not CMN

**ADDITIONAL TREATMENT**
- Radiation Therapy – No defined role
- Complementary & Alternative Therapies – N/A

**ONGOING CARE**

**PROGNOSIS**
- Radical nephrectomy generally curative
- Classic variant favorable
- Metastases and local recurrence possible with cellular type, but rare
- Risk factors for recurrence: Cellular variant, older patient age, tumor spillage during resection, and positive surgical margins (3)

**COMPLICATIONS**
- Prenatally
  - Polyhydramnios
  - Hydrops fetalis
  - Intrauterine fetal demise
- After birth
  - Hypertension
  - Hemodynamic instability
  - Respiratory distress

**FOLLOW-UP**
- Patient Monitoring
  - Regular abdominal ultrasound for 1 yr in classic variant and longer in cellular variant
  - Patient Resources
    - www.cancer.gov/cancertopics/pdq/treatment/wilms/Patient

**REFERENCES**

**ADDITIONAL READING**

**CLINICAL/SURGICAL PEARLS**
- Most common solid renal tumor <6 mo of age.
- Radical nephrectomy is generally curative.

**CODES**
- **ICD9**
  - 236.91 Neoplasm of uncertain behavior of kidney and ureter
- **ICD10**
  - D41.00 Neoplasm of uncertain behavior of unspecified kidney
  - D41.01 Neoplasm of uncertain behavior of right kidney
  - D41.02 Neoplasm of uncertain behavior of left kidney
MICROPENIS (MICROPHALLUS)
Bruce J. Schlomer, MD
Laurence S. Baskin, MD, FACS, FAAP

ASSOCIATED CONDITIONS
- Hypogonadal hypopituitarism
  - Most common cause of micropenis
  - Kallmann syndrome. Anosmia, defect in GnRH secretion, autosomal dominant
  - Prader–Willi syndrome. Short stature, hyperthermia, hypogonadism, behavior problems, hypothyroidism
  - Laurence–Moon–Biedl syndrome
  - Rud's syndrome
- Primary testicular failure: Gonadal dysgenesis
- Anorchia
- Klinefelter syndrome
- Luteinizing hormone (LH) receptor defects
- Defects in T steroidogenesis
- Noonan syndrome
- Rud's syndrome
- Laurence–Moon–Biedl syndrome
- Trisomy 18, 19, 18, and 21
- Defects in T action
- PAIS
- Sw-reductase deficiency
- Idiopathic form:
  - Normal hypothalamic–pituitary–testicular axis
  - Hypothesized to be due to delayed onset of fetal gonadotropin stimulation

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Pale suggestive of midline oral defect, mental retardation
  - Microcephaly, hypertelorism, low-set ears, small mouth, high-arched palate
  - Weight and body habitus. Prader–Willi syndrome, growth hormone abnormality
- Skin: Nails, ichthyosis
- Haring: Deafness
- Smell: Anosmia suggests Kallmann syndrome
- Family history: Germline mutations, hypoplasia, cryptorchidism, infertility, major congenital abnormalities
- Newborn:
  - Measure serum T and DHT levels on days 0 and 4.
  - If at day 4 > 500 ng/dL, response is normal. If no response, suggest primary testicular failure
  - Low prolactin suggests pituitary defect
  - Increased FSH ratio with hCG stimulation test or postpubertal suggests T-reductase deficiency
  - AR-gene mutation only found in 20% of PAIS

LAB
- Genetic testing if history consistent with known syndromes such as Prader–Willi or Kallmann
- Differentiate between hypogonadal and primary testicular failure
- Pituitary: Assesses ACTH, GH, TSH, LH, FSH.
- Low levels suggest hypogonadal hypopituitarism
- High prolactin suggests hypothalamic defect vs. low prolactin suggests pituitary defect
- Elevated levels of LH, FSH, and T are normal during 1st 6 mos of life. Low T during this time suggests testicular failure. Confirm with hCG stimulation test. LH, FSH should elevate but T will remain low in testicular failure
- hCG stimulation test. Assesses testicle for T biosynthesis. 1,000 U of hCG IV or IM thrice daily, measure serum T and DHT levels on days 0 and 4. If T at day 4 > 500 ng/dL, response is normal. If no response, suggest primary testicular failure
- From 6 mos to puberty, levels of LH, FSH, and T are low. LH, FSH elevate with hCG stimulation test but serum T low in testicular failure
- For patients who have undergone or started puberty, LH and FSH are normally elevated as may be serum T. LH, FSH, and T are usually low in micropenis. Do hCG stimulation test and look for response; assess pubertal changes to be sure it is not constitutional pubertal delay
- Anti-Müllerian hormone is produced by functional Sertoli cells and can be used to detect functional testis tissue
- Identifying defects in T action
  - LH, FSH, T, normal, or elevated with PAIS
  - PAIS diagnosis often given after excluding other diagnoses
  - Family history: Germline mutations, cryptorchidism, infertility, major congenital anomalies
- Newborn:
  - Measure serum T and DHT levels on days 0 and 4.
  - If at day 4 > 500 ng/dL, response is normal. If no response, suggest primary testicular failure
  - Low prolactin suggests pituitary defect
  - Increased FSH ratio with hCG stimulation test or postpubertal suggests T-reductase deficiency
  - AR-gene mutation only found in 20% of PAIS

IMAGING
- MRI of head: Assess hypothalamus, pituitary, brain, cerebellar anomalies, optic chiasm, 4th ventricle, corpus callosum
- Renal imaging: Assess kidneys and bladder, VCUG and MAMO renal scan if US suggest renal or bladder anomaly or ectopia

Diagnostic Procedures/Surgery
- Suspension to assess palpable undescended testicles, look for mullerian duct structures, biopsy any dysgenetic tissue
- Genitoectomy indicated if dysgenetic gonads, ovotestis, mullerian duct structures are found or if androgen insensitivity is suspected

PATHOPHYSIOLOGY
- Normal penile growth and development is both androgen dependent and independent
- 1st trimester: Maternal hCG stimulates testicle Leydig cells to produce testosterone (T). T is converted to dihydrotestosterone (DHT) by 5α-reductase in genital tubercle. Penis and urethra are completely formed by end of 1st trimester by influence of DHT.
- 2nd trimester: Fetal androgens and pituitary drive T production by fetal testes which causes penile growth
- Micropenis believed to be due to inadequate fetal T production or action after the 1st trimester (3).

EPIDEMIOLOGY
- Prevalence: ∼1.5/10,000
- Incidence: None

RISK FACTORS
- Maternal exposure to antiandrogen medications during pregnancy
- Advanced maternal age
- Fetal androgen exposure during molar pregnancy can lead to Down, Klinefelter syndromes, and polygony X syndromes

GENETICS
- X-linked recessive, autosomal recessive, autosomal dominant have all been identified
- Idiopathic spontaneous mutations noted
- Specific known genetic conditions:
  - Kallmann syndrome
  - Prader–Willi syndrome
  - Laurence–Moon–Biedl syndrome
  - Polygony X (Klinefelter)
  - Translocation, deletion, trisomy of chromosome 8, 18, 19, and 21
- Partial androgen insensitivity syndrome (PAIS)
- 5α-reductase deficiency
- Noonan syndrome
- Rud's syndrome

DIAGNOSIS

BASICS
- A micropenis refers to a stretched newborn penis that is <2.5 standard deviations below the normal mean in length (1)
- Full-term newborn micropenis would be <1.9 cm in length (1)
- Typical normal mean stretched penile length in a newborn is 5.5 cm
- The penis is normally formed but small, ie, no hypospadia (2)
- Scrotum usually normal but can be smaller
- Testicles usually descended but may not function normally
- A micropenis is generally not considered to be associated with ambiguous genitalia since the penis is normal and the testes are usually descended
- A micropenis is a finding with many causes

DESCRIPTION
- Micropenis believed to be due to inadequate fetal T production or action after the 1st trimester (3).
- Full-term newborn micropenis would be <1.9 cm in length (1)
- Typical normal mean stretched penile length in a newborn is 5.5 cm
- The penis is normally formed but small, ie, no hypospadia (2)
- Scrotum usually normal but can be smaller
- Testicles usually descended but may not function normally
- A micropenis is generally not considered to be associated with ambiguous genitalia since the penis is normal and the testes are usually descended
- A micropenis is a finding with many causes
Pathologic Findings
- Newborn penis is proportional but <1.5 cm
- Kallmann syndrome: Anosmia, GnRH deficiency
- 10% KALL: gene defect on 8p22.3, 10% KAL2 on 8p12, 7% autosomal dominant with no identified gene defect
- Pedlar-Wills syndrome: Short stature, hypothyroidism, mental retardation, diabetes, hypertension, behavioral problems; isolated expression of gene SNRPN or neulin on 15q of paternal origin
- Laurence-Moon-Biedl syndrome: Obesity, retinopathy, pigmentary retinopathy, polycystic kidney disease

DIFFERENTIAL DIAGNOSIS
- Concluded penis: Large suprapubic fat pad
- Webbed penis: Prominent penoscrotal web

Postinfection stenosis: Residual foreskin scarred above glans tip

Hypospadias with and without chordee

Chordee

Disorders of sexual differentiation:
- Female DSD: Congenital adrenal hyperplasia, genitoplasty not palpable in labia/crurum
- Male DSD
- Hypothalamic-pituitary axis dysfunction (50% of cases): Syndromes: Kallmann, Pedlar-Wills, Laurence-Moon-Biedl, Rud's
- Isolated hormone deficiency: Gigyn deficiency without Kallmann syndrome
- LH deficiency
- GH deficiency or growth hormone receptor defect (Laron dwarfism)

Primary testicular failure:
- Hypogonadotropic hypogonadism (25% of cases): Testicular dysgenesis, Klinefelter syndrome
- Laurence-Moon-Biedl syndrome
- Polygyn X syndrome
- Anorchia: Intradermal testicular tissue

Swiss-case deficiency: None

MAIS (Partial androgen insensitivity syndrome)

CHS abnormalities:
- Anorchia, congenital phallic aplasia, agenesis of corpus callosum, malformation of fourth ventricle

Chromosome defects:
- Polysomy X syndromes
- Translocation, deletion, and trisomy of chromosomes 8, 13, 18, and 21
- Rare syndromes: Rud, Robinow, Mortendsohn, Fanconi anemia, Smith-Lemli-Opitz syndromes

Hypospadias: Normal hypothalamic pituitary axis: Virilize normally at puberty

TREATMENT
GENERAL MEASURES
- Generally coordinated with an endocrinologist
- Correct any metabolic disturbances
- Specific treatment based on cause

Adrenal insufficiency: Treat with hydrocortisone supplementation and IV saline to correct hypovolemia

MEDICATION
First Line
- Testosterone therapy: Diagnostic and therapeutic
  - 25-50 mg testosterone enanthate IM Q monthly × 3 mo in infancy or prepuberty

Long-term cortisol replacement, growth hormone, and thyroid hormone if panhypopituitarism present

For gonadal deficiency: Induce puberty later in life with T injection or transdermal patch

For central deficiency: Administer HCG injection or GnRH therapy

Second Line
- None

SURGERY/OTHER PROCEDURES
- Manage cryptorchidism with orchiopexy or orchiectomy (if dysgenetic) as needed
- Manage micropenis: Effect of testosterone treatment on adult penis size—why sex reversal is not indicated.

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Androgen insensitivity syndrome (AIS), Androgen Resistance Syndrome, Complete (CAIS) and Partial (PAIS)
- Disorders of sexual differentiation (DSD)
- Micropenis (Microphallus)

ONGOING CARE
PROGNOSIS
- Overall good, but long-term effects depend on underlying cause
- Most will have stable male gender identity
- Generally good response to 3-mo course of T IM with 100% increases in length seen (3)
- Final adult penis size with treatment usually ≤normal, but within 2.5 standard deviations (3)

COMPLICATIONS
- Relate to endocrine abnormalities if present
- Side effects of testosterone:
  - Premature closure of epiphyseal plates; limits long bone growth
  - Behavioral changes: More aggressiveness
  - Early stimulation of penis growth does not affect ultimate penis length
- Psychosocial issues:
  - Most patients have a stable male gender identity but some dissatisfied with penis length
- Gender reassessment: Generally not done any more for micropenis and is of only historical interest

M

TREATMENT
GENERAL MEASURES
- Generally coordinated with an endocrinologist
- Correct any metabolic disturbances
- Specific treatment based on cause

Adrenal insufficiency: Treat with hydrocortisone supplementation and IV saline to correct hypovolemia

MEDICATION
First Line
- Testosterone therapy: Diagnostic and therapeutic
  - 25-50 mg testosterone enanthate IM Q monthly × 3 mo in infancy or prepuberty

Long-term cortisol replacement, growth hormone, and thyroid hormone if panhypopituitarism present

For gonadal deficiency: Induce puberty later in life with T injection or transdermal patch

For central deficiency: Administer HCG injection or GnRH therapy

Second Line
- None

SURGERY/OTHER PROCEDURES
- Manage cryptorchidism with orchiopexy or orchiectomy (if dysgenetic) as needed
- Manage micropenis: Effect of testosterone treatment on adult penis size—why sex reversal is not indicated.

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Androgen insensitivity syndrome (AIS), Androgen Resistance Syndrome, Complete (CAIS) and Partial (PAIS)
- Disorders of sexual differentiation (DSD)
- Micropenis (Microphallus)

ONGOING CARE
PROGNOSIS
- Overall good, but long-term effects depend on underlying cause
- Most will have stable male gender identity
- Generally good response to 3-mo course of T IM with 100% increases in length seen (3)
- Final adult penis size with treatment usually ≤normal, but within 2.5 standard deviations (3)

COMPLICATIONS
- Relate to endocrine abnormalities if present
- Side effects of testosterone:
  - Premature closure of epiphyseal plates; limits long bone growth
  - Behavioral changes: More aggressiveness
  - Early stimulation of penis growth does not affect ultimate penis length
- Psychosocial issues:
  - Most patients have a stable male gender identity but some dissatisfied with penis length

FOLLOW-UP
- Patient Monitoring
  - Psychological support and psychiatric therapy as needed
  - Measure concerns about penis size, function, gender, potency
  - Address behavioral and psychosocial problems

- Hormone biochemical monitoring:
  - Follow pubertal and gonadal hormone therapy

- Assess growth, vital signs, electrolytes, serum glucose, renal, ACTH, TSH, GH, and T.

- Physical monitoring: Serial penile measurements

PATIENT RESOURCES
- None

CODES
ICD9
752.64 Micropenis
ICD10
Q73.6 Hypoplasia of penis

CLINICAL/SURGICAL PEARLS
- Micropenis is a condition with many causes, most of which are either a form of hypogonadotropic hypogonadism or primary testicular failure
- Thought to be due to deficient 1 synthesis or action after the 1st trimester
- Watch out for large suprapubic fat pad leading to incorrect diagnosis
- Surgery generally not indicated except for associated cryptorchidism
MULTICYSTIC DYSPLASTIC KIDNEY

Daniel Wollin, MD
Ellen Shapiro, MD, FACS

ASSOCIATED CONDITIONS
- Premature hypertrophy of the contralateral kidney (24-46%)
- About 1/3 will have associated congenital anomalies of the heart and urinary tract (CAKUT)
- Contralateral vesicoureteral reflux (~20%) of those with reflux, 40% will have grades III-V
- Contralateral UPJ obstruction (3-12%) and UVJ obstruction (6%)
- Dilated nonobstructed contralateral renal pelvis (common)
- Anomalies of the ipsilateral internal duct structures (15%) including seminal vesicle cysts, Gartner’s cysts, distal ducts, or accessory ducts
- Congenital absence of the vas deferens
- Horseshoe kidney

DIAGNOSIS

HISTORY
At least 65% are detected prenatally

PHYSICAL EXAM
Abdominal mass palpable in 13%

DIAGNOSTIC TESTS & INTERPRETATION
- Urinalysis
- urine microscopy and culture
- Imaging
- US: Multiple noncommunicating cysts of variable size, scarring, or renal parenchymal thinning
- Renal scan: absence of function, or no function on contralateral side
- VCUG: to evaluate for contralateral reflux
- Renal ultrasonography

Pathologic Findings
- Acquired renal cysts
- Autosomal dominant kidney disease
- Cystic congenital mesoblastic nephroma
- Cystic Wilms tumor
- Cysts of the metanephros
- Neuroblastoma (calcifications)
- Renal cysts, scarring, or associated with syndromes (tuberous sclerosis, von Hippel-Lindau, etc.)
- Supernumerary duct junction obstruction (UPJO)
- Vescoureteral reflux (VUR)

TREATMENT

GENERAL MEASURES
- Educate parents about the signs and symptoms of UTI in infancy and childhood especially if reflux status unknown
- Use of nephrectomy to manage MCDK is controversial

MEDICATION
- First Line
- N/A
- Second Line
- N/A
MULTICYSTIC DYSPLASTIC KIDNEY

SURGERY/OTHER PROCEDURES

• Multiple congenital anomalies: May present with mild to severe anomalies of the kidney and urinary tract.

• MCDK occurs as a result of renal maldevelopment due to possible mutation(s) in genes responsible for ureteral bud formation.

• Large cysts of varying sizes present with no identifiable parenchyma; ureter usually atretic.

• Most involute or become significantly smaller; rare enlargement.

• As of 2012, the American Academy of Pediatrics states that contact sport participation is generally OK for children who have only one functional kidney. In a very large published series, none of the kidney injuries were catastrophic or needed surgery.

• Long-term follow-up for hypertension and microalbuminuria by informed pediatrician or family physician; referral to nephrology for renoprotective medications when indicated.

ADDITONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

N/A

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

• Usually excellent in unilateral disease.

• kidneys which remain large, increase in size, or show an increased amount of solid tissue (especially with function).

• May persist after nephrectomy depending on the patient age at onset of hypertension and the presence of CAKUT (see Prognosis).

ADDITIONAL READING


REFERENCES


See Also (Topic, Algorithm, Media)

• Multicystic Dysplastic Kidney Image

• Potter Syndrome/Potter Facies

• Renal Cysts

• Renal Dysplasia, Hypodysplasia, and Hypoplasia

ICD10

Q62.39 Other specified cystic kidney disease

CLINICAL/SURGICAL PEARLS

• MCDK occurs as a result of renal maldevelopment due to possible mutation(s) in genes responsible for ureteral bud formation.

• Large cysts of varying sizes present with no identifiable parenchyma; ureter usually atretic.

• Most involute or become significantly smaller, rare enlargement.

• Almost never require nephrectomy, consider for functioning solid component or increasing size.

• Not associated with increased risk of hypertension during childhood or Wilms tumor in large series.

• Long-term follow-up recommended for hypertension and microalbuminuria especially at puberty and in adulthood.

AS STM 247
MULTIPLE SCLEROSIS, UROLOGIC CONSIDERATIONS
Alana M. Murphy, MD

DESCRIPTION
- Multiple sclerosis (MS) is a neurologic disease causing focal demyelination of white matter in the brain and spinal cord that can impact urinary tract functioning.
- Plaques visible on magnetic resonance imaging (MRI) are inflammatory and often lead to scar tissue deposition. They interfere with conduction of electrical signals resulting in loss of central inhibition of reflex activity and dysfunctional conduction of sensory and motor signals.

EPIDEMIOLOGY
Incidence
- Most commonly presents between ages 20 and 50 yr old.
- Females have 1.5–3 times greater incidence than males.

Prevalence
- 1 in 250 lifetime risk of developing MS in USA
- More common in Caucasians and above 40

RISK FACTORS
- Genetics
  - Increased risk if MS is present in a 1st-degree relative
  - Primary relative with MS confers 20 times risk
  - Identical twin: 300 times increased risk if other twin develops MS
  - Unknown pattern of inheritance

PATHOPHYSIOLOGY (1)
- Spinal cord attack on the central nervous system (CNS) myelin:
  - Focal demyelination with relative axon sparing
  - Histopathology shows perivascular lymphocytic infiltrates, microglial within the white matter, gliosis, and scarring

- Urologic manifestations include urinary frequency, urgency incontinence, voiding symptoms, urinary retention, and sexual dysfunction.

- Detrusor sphincter dyssynergia (DSD) and detrusor overactivity (DO) are common dysfunctions noted on urodynamic studies (UDS).

DIAGNOSIS
HISTORY
- Presence of neurologic symptoms:
  - Vision changes, balance problems, discoordination, numbness, or paresthesia
  - Urologic history: All patients with MS should be screened for urologic problems:
  - Recurrent UTIs
  - Urinary frequency
  - Urgency incontinence
  - Voiding symptoms
  - Urinary retention

PHYSICAL EXAM
- Urologic exam:
  - Testicular and prostate exam in males to rule out neoplasm or infection
  - Pelvic exam in females to assess pelvic support and rule out uterine or vaginal pathology
  - Deep tendon reflexes, proprioception, Babinski nerves (absent in up to 30%)
  - Bulbocavernous reflex to assess function of sacral nerves
  - Pelvic exam in females to assess pelvic support and rule out urethral or vaginal pathology
  - Testicular and prostate exam in males to rule out neoplasm or infection

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CFS for initial MS diagnosis (oligoclonal IgG bands)

Imaging (2,3)
- MRI:
  - Most useful tool for diagnosing MS; diagnostic in 70–95% of cases
  - Increased signal intensity on T2-weighted images in areas of demyelination
  - Upper urinary tract imaging:
  - Rule out presence of hydronephrosis
  - Renal ultrasound (US) is a good screening test
  - Important in patients with known OUS or in patients with indwelling catheters

- Lower tract imaging less commonly performed:
  - Fluoroscopy during UDS can assess for bladder pathology (stones, trabeculation), vesicoureteral reflux, and DSD

ASSOCIATED CONDITIONS
- DSD leading to urinary retention, recurrent UTIs, and impairment in renal function
- Detrusor hyperreflexia due to urinary stasis from incomplete bladder emptying and recurrent UTIs

GENERAL PREVENTION
- No proven methods for prevention

GENERAL MEASURES
- Avoid stressors
- Disease-modifying medications specific to MS can reduce relapses and control some symptoms: biologic agents (natalizumab, and teriflunomide), β interferons, glatiramer acetate, fingolimod, mitoxantrone, and natalizumab
- Remissions can occur spontaneously, making management difficult

DIFFERENTIAL DIAGNOSIS
- Idiopathic overactive bladder
- DSD leading to urinary retention
- Urinary urgency

DIAGnostic Procedures/Surgery
- PVR
  - Urologic specialists to assess bladder capacity, compliance, detrusor function, continence, and detrusor–sphincter coordination
  - Routinely performed with fluoroscopy in MS patients

- Patients with indwelling catheters
  - Assess risk for upper tract deterioration (elevated storage and voiding pressures)
  - May suggest diagnosis of MS in patient with few other neurologic symptoms
  - Need follow-up UDS with change in clinical symptoms

Pathologic Findings
- Deterioration with trabeculation

TREATMENT
- Urologic overactive bladder
- Detrusor hyperreflexia
- Dysfunctional voiding
- Avoid stressors
- Detrusor underactivity or UCO with indwelling catheter

RECOMMENDATIONS
- Urologic examination at diagnosis
- Patients on antipsychotics may be at increased risk
- Lower tract symptoms in MS patients require prompt evaluation
- Patients with MS and indwelling catheters should have a thorough urologic examination

REFERENCES
**PROGNOSIS**

With proper urologic follow-up, renal function can be preserved in most patients.

**COMPLICATIONS**

- Hydrothorax and impairment in renal function due to elevated bladder pressure or voiding pressure
- Urolithiasis due to urinary stasis, indwelling catheters and infection
- Recurrent UTIs
- Urethral erosion from indwelling catheters

**FOLLOW-UP**

### Patient Monitoring

- Upper urinary tract screening is especially important in men, since men with MS often develop high bladder storage pressure and urinary stasis without developing overt urologic symptoms such as incontinence.

### Incontinence, especially in women, can become problematic as the severity of MS progresses.

- Patients with bladder dysfunction secondary to MS can be stratified into low- and high-risk patients:
  - Low-risk patients: Those with normal continence, no UTIs, and complete bladder emptying. These patients do not require frequent upper tract imaging.
  - High-risk patients: Incontinence, recurrent infections, DSD, elevated storage pressures >40 cm H2O, indwelling catheters

- Follow closely for upper tract deterioration, keep lines short, and avoid indwelling catheters.

### Providers’ Approach to Bladder Management in Multiple Sclerosis.


### Ongoing Care

- Stress reduction therapies and acupuncture have been associated with symptom reduction.

### Additional Reading


### Clincial/Surgical Pearls

- Medical therapy and behavioral modification remain the first line of treatment for urinary frequency and urgency incontinence.
- Indwelling injection of botulinum toxin should be used for refractory neurogenic detrusor overactivity.
- Adequate management of lower urinary tract function will lead to preservation of renal function.

### Codes

- ICD-9: 788.31 Urge incontinence
- ICD-10: N29.41 Urge incontinence
- R35.0 frequency of micturition

### References

Myasthenia Gravis, Urologic Considerations

Robert L. Segal, MD, FRCS(C)
Arthur L. Burnett, II, MD, MBA, FACS

BASICS

DESCRIPTION

- Myasthenia gravis (MG) is a chronic autoimmune disorder characterized by weakness and early fatigability of the skeletal muscles due to antibody-mediated loss of nicotinic acetylcholine (ACh) receptors (1,2).
- Involvement of the external urinary sphincter is rare but may be vulnerable to dysfunction after thymectomy or resection of the thymus (TURP), explaining the relatively high incidence of post-TURP incontinence in this group (1).
- Although smooth muscle is generally not affected, there are rare reports of detrusor areflexia (4).
- Urologic complaints are uncommon but may include incontinence, urgency, retention, or erectile dysfunction.

EPIDEMIOLOGY

Incidence

- Published estimates of 2–21 cases per million people per year (1,2).
- Prevalence:
  - In patients <40 yr:
    - Male > Female (1:3).
  - In the 5th decade, new cases of MG are evenly split between the genders.
  - After the 5th decade:
    - Male > Female (2:1, 1,2)

RISK FACTORS

- Thymic hyperplasia is observed in 65–75% of patients (1,2).
- MG has been described as a paraneoplastic syndrome related to renal cell carcinoma (RCC) (5), as well as other malignancies (thymoma, lymphoma, lung cancer, Kaposi's sarcoma) (6).

Genetics

- Congenital myasthenic syndromes, a subset of MG, stem from genetic mutations resulting in abnormal neuromuscular transmission (1,2).
- HLA types B8 and DR3 are associated with MG.

PATHOPHYSIOLOGY

- Autoantibodies develop against ACh nicotinic postjunctional receptors (1,2).
- The autoantibodies mechanically block the neuromuscular junction binding site and eventually destroy them.
- Cholinergic nerve conduction to striated skeletal muscle is thus impaired.
- Clinical symptoms begin to develop when the number of ACh receptors is reduced to ~30% of the normal level.

- Smooth and cardiac muscle are not affected.
- The role of the thymus in MG is unclear, but it is suspected to be a site of autoantibody formation.
- A majority of patients with MG have thymic hyperplasia or thymoma.

Many patients improve clinically following thymectomy.

ASSOCIATED CONDITIONS

- Neonatal MG is a transitory disorder resulting from passive maternal antibody transfer to the fetus.
- Congenital myasthenic syndromes result from genetic mutations that lead to abnormal neuromuscular transmission.
- Ocular MG refers to weakness limited to the extracocular muscles and eyelids.

GENERAL PREVENTION

None

DIAGNOSIS

HISTORY

- Reduced exercise tolerance that improves with rest and worsens with warm temperature (e.g., after a hot bath).
- The natural history of MG usually follows a characteristic pattern that initially involves weakness of eyelids and extracocular muscles.
- Difficulty climbing stairs is typical of generalized weakness in MG.
- Weakness is variable and fluctuating, but tends to be worse later in the day.

PHYSICAL EXAM

- Muscle fatigability can be tested for many muscles by repeated action: Ptosis, diplopia, dysphagia, and peripheral muscle weakness.
- “Dropped head syndrome”

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serology tests demonstrate anti-ACh receptor antibodies in ~90% of patients.
- ~30% of patients who test negative for anti-ACh receptor antibodies have antibodies against the MuSK protein.
- Urodynamics:
  - Complete urodynamic evaluation if urologic symptoms are present (4).
  - If bladder dysfunction present, resembles lower motor neuron pattern with variable areflexia or atonia.
- In one UDS series 63% failing to empty completely due to hypercontractile bladders and 6% had complete areflexia.

Pathologic Findings

- None

DIFFERENTIAL DIAGNOSIS

- Acute inflammatory demyelinating polyradiculoneuropathy
- Botulism
- Lambert–Eaton syndrome

TREATMENT

GENERAL MEASURES

- Immediate catheterization for rare cases of refractory detrusor areflexia (4).
- Adjust mealtimes to take advantage of daily periods of relative strength.
- Install railing in household places where it will be needed for support in rising, such as at the bathtub and toilet.
- Use electric toothbrushes and can openers to conserve strength.
- Generalized muscle weakness in the acute setting should prompt careful attention to the possibility of respiratory failure.
- Patients with MG have symptoms worsened by high core or ambient temperature; therefore, muscle strength will likely improve when a fever is treated with antipyretics.
- Urinary tract symptoms, if present, may respond favorably to therapy for MG.

Diagnostic Procedures/Surgery

- Diphenhydramine chloride test: Positive for MG if IV administration unequivocally yields improved strength.
- Repetitive nerve stimulation
- Single-fiber electromyography
- Complete urodynamic evaluation if urologic symptoms are present (4).

Imaging

- Chest computed tomography (CT) to rule out thymoma.
- If level of suspicion is high, CT abdomen to rule out RCC (5).

Urodynamics:

- If bladder dysfunction present, resembles lower motor neuron pattern with variable areflexia or atonia.
- In one UDS series 63% failing to empty completely due to hypercontractile bladders and 6% had complete areflexia.
MYASTHENIA GRAVIS, UROLOGIC CONSIDERATIONS

MEDICATION
First Line
- Cholinesterase inhibitors (neostigmine, pyridostigmine) provide temporary strength improvement in patients with MG.
- Corticosteroids can produce rapid improvements in MG but are associated with numerous dose-dependent side effects.

Second Line
- Plasmapheresis is reserved for short-term treatment in response to myasthenic exacerbations or crises.
- Intravenous immunoglobulin (IgG) also provides short-term improvements in strength during myasthenic exacerbations or crises as an alternative for patients who are poor plasmapheresis candidates because of vascular access issues.
- Immunosuppressive agents (azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, rituximab, tacrolimus) for steroid-sparing protocols, or for refractory disease.

SURGERY/OTHER PROCEDURES
- If surgical intervention for bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH) is being considered, some advocate suprapubic prostatectomy to reduce risk of incontinence.
- Thymectomy results in complete remission in 35% of cases and clinical improvement in 85% of patients.

OTHER TREATMENTS
- Radiation Therapy: N/A
- Additional Therapies: β-Agonist and anticholinergic bronchodilators can reduce bronchospasm and respiratory distress resulting from cholinergic medications.

Ongoing Care

PROGNOSIS
- Most (96%) of patients have normal lifespan when appropriate medical care involving cholinesterase inhibitors, plasmapheresis, and immunosuppressive agents is given.
- Thrombosis results in complete remission in about 1/3 of patients, but the postsurgical prognosis is otherwise highly variable.

COMPLICATIONS
- Post-TURP Incontinence
- Respiratory failure
- Cholinergic crisis from excessive use of cholinesterase inhibitors

FOLLOW-UP
- Patient Monitoring: Patients with MG should be followed by a neurologist with urology referral as needed.

ADDITIONAL TREATMENT
- Radiation Therapy: N/A
- Additional Therapies: β-Agonist and anticholinergic bronchodilators can reduce bronchospasm and respiratory distress resulting from cholinergic medications.

Complementary & Alternative Therapies: N/A

REFERENCES

ADDITIONAL READING

CODES
- ICD-9: 358.00 Myasthenia gravis without (acute) exacerbation
- 788.30 Urinary incontinence
- 788.63 Urgency of urination

- ICD-10: G70.00 Myasthenia gravis without (acute) exacerbation
- N39.41 Urge incontinence
- R32 Unspecified urinary incontinence

CLINICAL/SURGICAL PEARLS
- Patients with MG may develop voiding dysfunction, most commonly detrusor areflexia resulting in urinary retention.
- Urinary incontinence may develop after TURP.
- Urologic symptoms may be improved by systemic MG therapy, although specific therapy for urologic complications, such as urinary retention or incontinence, may need to be instituted.
**BASICS**

**DESCRIPTION**
- Myelodysplasia (spinal dysraphism, neural tube defect) is a very broad term encompassing a large heterogeneous group of congenital vertebral column defects that result from defects that occur during neural tube closure.
- Group of developmental abnormalities that can be open (meningocele, myelomeningocele, lipomyelomeningocele) or closed (spina bifida occulta, posterior meningocele, lipomyeloneuromuscular dysplasia).
- Primary functional defects can be lower limb paralysis and sensory loss, bladder and bowel dysfunction, and cognitive dysfunction.
- Affected children often have varying degrees of neurogenic bladder dysfunction.

**ALER T**
- Patients with myelodysplasia have a high incidence of latex allergies. From birth, parents need to be educated in latex precautions.

**EPIEDIOLOGY**

**Incidence**
- Spinal dysraphism: 1 per 1,000 births in USA previously.
- Spina bifida occulta: 5–10% of the general population; most cases are found incidentally.

**RISK FACTORS**
- Maternal folate deficiency during pregnancy.
- Family history: Incidence for mother with one affected child is 10–50/1,000 live births; also 2nd and 3rd degree affected relative.
- Poor pregnancy check or absence.
- Exposure to high temperatures in early pregnancy (fever or hot tub).
- Traumatic exposure to valproate or carbamazepine.
- Low vitamin 8-12 levels.
- Chromosomal anomalies (13 and 18, triploidy, and single-gene mutations).

**GENETICS**
- Genes involved in folate-homocysteine metabolism and transport (see Risk Factors).

**PATHOPHYSIOLOGY**
- Increased maternal blood AFP (α-fetoprotein) at 16 wk can indicate the presence of an NTD (neural tube defect).
- Spinal cord begins normal development on day 18 of gestation.
- The canal closes in a cephalocaudal direction; complete closure day 35 of gestation.
- Basis mechanism of dysraphism undifferentiated stem cells states can be subdivided:
  - Spina bifida occulta: The mildest form. No overt signs of spinal abnormality; may be associated with tethering of the spinal cord and often associated with a low-lying conus (below L2–L3) usually detected by plain x-ray, demonstrating open vertebral bodies.
  - Posterior meningocele, myelocystocele, and lipomyelomeningocele are closed defects associated with a skin-covered back mass.
  - Meningocele: The meninges or dural sac, but no significant neural elements, extend beyond the vertebral canal. Mostly normal lower extremity.
  - Myelomeningocele: The nerves and spinal cord are exposed through an opening in the spinal column, mengines, and skin. Significant neurologic defects (paraplegia, urinary incontinence) are usually associated.
  - Lipomyelomeningocele: Fatty tissue along with cord structures extend with protruding sac.

**ASSOCIATED CONDITIONS**
- Clinical anomalies: Local neurosurgical anomalies.
- Hydrocephalus/Arnold–Chiari malformation.
- Imperforate anus.
- Lipoma.
- Sacral agenesis.
- Urogenital anomalies (renal defects, renal agenesis, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb anomalies).

**GENERAL PREVENTION**
- Folic acid 0.4 mg/d in all women of childbearing age.
- Maternal folate deficiency during pregnancy.
- Begin 2 mo before planned conception or at time of pregnancy.

**DIAGNOSIS**

**HISTORY**
- Review medical and developmental history.
- Most patients now diagnosed prenatally.
- Older patients commonly present with urinary and bowel incontinence.
- Change in bowel habits or guilt, onset of leg or back pain, presence of seizures, or other neurologic symptoms may suggest subsequent spinal cord tethering.

**PHYSICAL EXAM**
- Abnormalities: size, body habitus, gait, dexterity, muscular, and neurologic development.
- Genitalia: Presence or absence of hypospadias, cryptorchidism, labial/abnormalities.
- Rectal exam: Perianal sensation, rectal tone, fecal impaction.
- Back exam: When present, spinal canal deformities, kyphoscoliosis, and scoliosis may be noted.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urodynamics, urine culture, basic metabolic panel with high-grade reflux or hydrocephrosis.

**Imaging**
- 15–20% of neonates have abnormality of upper tract: 1st studied.
- Plain abdominal x-rays:
  - May show structural urologic anomalies or evaluate for partial or complete sacral agenesis.
  - May visualize stones or fecal impaction.
- Renal US (abdominal):
  - Determine baseline of urinary tract should be performed shortly after birth. Important to repeat after back closure prior to discharge.
  - Assess for hydrocephrosis, hydronephrosis, and PVR.
  - Postvoid residual: If patient voids spontaneously.
  - Voiding cystourethrography (VCUG):
    - Assess for vesicoureteral reflux, bladder wall thickness, bladder capacity, and neurogenic bladder.
- Dimercaptosuccinic acid (DMSA) renal scan in select cases:
  - Including high-grade reflux, renal scarring, and solitary functioning kidney.
- Magnetic resonance imaging (MRI):
  - Assess spinal cord and vertebral anomalies in patients with suspected occult spinal dysraphism or a “closed” lesion.
  - Spinal sonogram useful in the diagnosis of occult spinal dysraphism.

**Diagnosis Procedure/Surgery**

**Uninduced studies (USS):** Fill rate based on average bladder capacity in milliliters (24.5 x age + 62) divided by 10 is the rate of filling the bladder with warm saline.
- Assess bladder capacity, volume, and pressure at abdominal and detrusor leak points (compliance), pressure when reflux, if present, is observed.
- Detrusor overactivity, detrusor spasticity, and epispadias.

**Pathologic Findings**
- See Pathophysiology.

**DIFFERENTIAL DIAGNOSIS**
- Other causes of neurogenic bladder (see Chapter on Neurogenic Bladder, general).
- Tethered cord syndrome.

**MYELODYSPLASIA (SPINAL DYSRAPHISM), UROLOGIC CONSIDERATIONS**

Blake A. Wynia, MD, MPH
Ellen Shapiro, MD, FACS

252
TREATMENT

GENERAL MEASURES (1,2,3)
- Urgent neurological intervention is critical for open defects, which may lead to hydrocephalus.
- Upper tract preservation is the primary goal with the achievement of continence at an appropriate age.
- Incontinence bladder emptying on significant upper tract hydroprostatic/hydronephrosis is not usually performed.
- Clean intermittent catheterization (CIC) for detrusor filling pressures >30-40 mm H2O. May often require the addition of anticholinergic therapy (see Medication).
- Colostomy, vesicostomy or urethral dilation to lower emptying pressures not usually performed.

MEDICATION

First Line
- Anticholinergics: Decrease detrusor overactivity, improve bladder compliance and functional capacity.
  - Oxybutynin 0.2 mg/kg BID; should be initiated early in life when indicated to prevent upper tract deterioration secondary to poor detrusor compliance and DDS.
  - Tolterodine 0.1 mg/kg BID to a maximum of 240 mg BID; avoid acting forms when older.
- Almost always used in conjunction with CIC.
- Side effects: Headaches, dry mouth, flushing of skin, abdominal discomfort, blurred vision.
- Prophylactic antibiotics considered for reflux.

Second Line
- α-sympathomimetic, α-sympatholytic, smooth muscle relaxants.
- Imipramine 0.7 mg/kg BID with maximum dosing of 2 α-sympathomimetic; consider prematurity EKG

SURGERY/OTHER PROCEDURES
- When pharmacotherapy and CIC do not result in favorable bladder dynamics and/or continence in older patients, consider:
  - Cystoscopy and botulinum A toxin injection.
  - Bladder augmentation usually with creation of continent catheterizable stoma since many of the children are wheelchair bound; wait until the child is 5-6 yr old for continence if upper tracts not deteriorating and bladder is not hostile.
  - Reflux surgery for high-grade reflux.
  - Bladder neck reconstructions.
  - Young-Owens-Leadbetter, Kropp, Papi-Salle modification, bladder neck closure.
  - Fecal diversion, antireflux and/or artificial urinary sphincters.
  - Bowel incontinence.
- If oral laxatives, enemas/irrigation, and rectal suppositories do not result in social bowel continence consider MAPE procedure selectively.

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
- Neurourologic evaluation of the bladder via intravesical electrical stimulation, sacral nerve stimulation, transcutaneous stimulation, and biofeedback. All of unknown efficacy.
- Tissue-engineered bladder augmentation (experimental).
- Artificial somatic-autonomic reflux pathway (experimental).

ONGOING CARE

PROGNOSIS
- Self-performance of CIC is likely in school-aged children with supervision.
- Regular monitoring for silent upper tract deterioration including renal isonogram and VUDs.
- Elective and prophylactic distention.
- Delivery concerns especially at the end of gestation in myeloblastosis patients with bladder or bladder neck reconstruction.

COMPlications
- Incisional wound infection requires the addition of skin ulceration due to ammonia burns; consider delaying circumcision until 1 year of age.
- Renal insufficiency.
- Symptomatic UTIs.
- Seizure disorders.
- Musculoskeletal problems (spina bifida, club foot, others).

FOLLOW-UP
- Patient Monitoring
  - Close follow-up with pediatric urology and neurology from infancy and throughout childhood is required to achieve urinary and bowel continence. Annul US and VUDs when continent with stable upper tracts.
- Patient Resources
  - Myelodysplasia Association.

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Latex allergy, Urologic Considerations.
- Myelodysplasia (Spinal Dysraphism), Urologic Considerations (Image 3).
- Neurogenic Bladder, General Considerations.
- Neurogenic Bladder, Urologic Considerations.

ICD9
- 788.30 Urinary incontinence, unspecified.
- 596.54 Neurogenic bladder NOS.
- 789.30 Urinary incontinence, unspecified.
- 238.75 Myelodysplastic syndrome, unspecified.
- 596.54 Neurogenic bladder NOS.
- 789.30 Urinary incontinence, unspecified.
- 441.20 Myelodysplastic syndrome, unspecified.
- 311.9 Neurovascular dysfunction of bladder, unspecified.
- 932 Unspecified urinary incontinence.

PEARLS
- Affects children often have varying degrees of neurogenic bladder and bowel dysfunction.
- First-line treatment consists of CIC for elevated PVR and anticholinergics when VUD testing suggests poor detrusor compliance and/or detrusor overactivity with or without upper tract deterioration.
- Botulinum A toxin injections, bladder augmentation, antireflux procedures and/or bladder neck procedures performed to protect upper tracts and achieve urinary continence.
NEPHROCALCINOSIS, ADULT

Jennifer E. Heckman, MD, MPH
Stephen Y. Nakada, MD, FACS

ASSOCIATED CONDITIONS

- Nephrolithiasis
- Hypercalciuric states:
  - Primary hyperparathyroidism (most common cause in adults)
  - Scurvy
  - Vitamin D intoxication
  - Multiple myeloma
  - Tuberculosis
- Hyperphosphaturic states:
  - Fanconi syndrome
  - Distal renal tubular acidosis
  - Medullary sponge kidney
  - Inherited tubular defects (eg, Bartter syndrome)
- Chronic pyelonephritis (eg, primary aldosteronism)
- Chronic immobilization
- Renal oxalosis
- Hyperuricosuria
- Other disorders:
  - Long-term suppressive antimicrobial therapy

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Used to identify underlying causative disorder
- Serum studies:
  - Calcium, phosphate, albumin
  - Electrolytes
  - BUN, Cr
  - Parathyroid hormone (PTH) levels
  - Thyroid stimulating hormone (TSH) levels
  - CBC
- Urine studies:
  - Urolithiasis with microscopy + i–j urine culture (if indicated)
  - 24 hr urine collection

Imaging
- Can be detected on:
  - Abdominal radiograph
    - Usually only if attenuation > 100 Hounsfield units and slice > 2 mm
  - Medullary nephrocalcinosis:
    - Stippled calcifications in renal pyramids
  - Cortical nephrocalcinosis:
    - Thin peripheral band with peripelvic extension; thin, peripheral calcific tracts, or diffuse punctuate calcifications
- Ultrasonography
  - Hyperdense areas with or without acoustic shadowing
- Computed tomography
  - Diffuse punctate calcifications diagnostic of CaPhos

DIAGNOSIS

HISTORY
- Most cases are asymptomatic ( incidental finding on imaging)
- Occasionally present with symptoms related to underlying cause or associated condition
  - Nausea, decreased appetite, abdominal pain, malaise, polydipsia, lethargy (hypercalcemia)
  - Fatigue, edema, mental status changes, anorexia (renal failure)
  - Renal colic, hematuria (nephrolithiasis)
- Review past medical history and medications

PHYSICAL EXAM
- Nonspecific; many patients are asymptomatic
- Physical findings otherwise a manifestation of underlying disorder

PATHOPHYSIOLOGY

- Increased urinary excretion of calcium, phosphate, and/or oxalate
- May occur with or without hypercalciuria
- Calcium oxalate (CaOx) and calcium phosphate (CaPhos) crystals result from urinary supersaturation
- CaOx and CaPhos crystals precipitate, aggregate, and move to interstitium
- May result in acute or chronic renal damage and/or lead to calculus formation
- Renal ischemia or injury may augment nucleation of CaOx or CaPhos crystals

ASSOCIATED CONDITIONS

- Nephrolithiasis
- Hypercalciuric states:
  - Primary hyperparathyroidism (most common cause in adults)
  - Scurvy
  - Vitamin D intoxication
  - Multiple myeloma
  - Tuberculosis
- Hyperphosphaturic states:
  - Fanconi syndrome
  - Distal renal tubular acidosis
  - Medullary sponge kidney
  - Inherited tubular defects (eg, Bartter syndrome)
- Chronic pyelonephritis (eg, primary aldosteronism)
- Chronic immobilization
- Renal oxalosis
- Hyperuricosuria
- Other disorders:
  - Long-term suppressive antimicrobial therapy

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Used to identify underlying causative disorder
- Serum studies:
  - Calcium, phosphate, albumin
  - Electrolytes
  - BUN, Cr
  - Parathyroid hormone (PTH) levels
  - Thyroid stimulating hormone (TSH) levels
  - CBC
- Urine studies:
  - Urolithiasis with microscopy + i–j urine culture (if indicated)
  - 24 hr urine collection

Imaging
- Can be detected on:
  - Abdominal radiograph
    - Usually only if attenuation > 100 Hounsfield units and slice > 2 mm
  - Medullary nephrocalcinosis:
    - Stippled calcifications in renal pyramids
  - Cortical nephrocalcinosis:
    - Thin peripheral band with peripelvic extension; thin, peripheral calcific tracts, or diffuse punctuate calcifications
- Ultrasonography
  - Hyperdense areas with or without acoustic shadowing
- Computed tomography
  - Diffuse punctate calcifications diagnostic of CaPhos

DIAGNOSIS

HISTORY
- Most cases are asymptomatic ( incidental finding on imaging)
- Occasionally present with symptoms related to underlying cause or associated condition
  - Nausea, decreased appetite, abdominal pain, malaise, polydipsia, lethargy (hypercalcemia)
  - Fatigue, edema, mental status changes, anorexia (renal failure)
  - Renal colic, hematuria (nephrolithiasis)
- Review past medical history and medications

PHYSICAL EXAM
- Nonspecific; many patients are asymptomatic
- Physical findings otherwise a manifestation of underlying disorder

PATHOPHYSIOLOGY

- Increased urinary excretion of calcium, phosphate, and/or oxalate
- May occur with or without hypercalciuria
- Calcium oxalate (CaOx) and calcium phosphate (CaPhos) crystals result from urinary supersaturation
- CaOx and CaPhos crystals precipitate, aggregate, and move to interstitium
- May result in acute or chronic renal damage and/or lead to calculus formation
- Renal ischemia or injury may augment nucleation of CaOx or CaPhos crystals
Nephrocalcinosis, Adult

Differential Diagnosis
- Nephrocalcinosis
  - Renal calculi, associated with:
    - Chronic ureteropelvic junction obstruction or urolithiasis
    - Renal infection
    - Renal trauma
  - Dystrophic calcifications, associated with:
    - Renal tuberculosis
    - Congenital cystic kidney
  - Renal artery calcifications
  - Calcification associated with spinal injury

Treatment

General Measures
- Treatment directed at underlying etiology
- No specific treatment prevents progression
- Early treatment of reversible causes of renal injury important
- Reduce urinary concentration and increase solubility of calcium, phosphate, and/or oxalate
- Increase fluid intake
- Goald urine output > 2 L
- If hypercalcemia:
  - Restrict animal protein intake (max 0.7 g/kg)
  - Restrict sodium intake (< 100 mEq/d)
  - If hypocalcemia and urine pH <7:
    - Potassium citrate (titrate to normal urinary citrate)

Medication

First Line
- Must be tailored to underlying etiology (eg, for hyperparathyroidism, resection of adenoma, treatment of renal tubular acidosis, etc.)

Second Line
- N/A

Surgery/Others Procedures
- Surgical intervention may be required, particularly if calcification obstructs collecting system
  - Endourologic management
  - May use in diagnosis (direct visual inspection)
  - May treat with flexible ureteroscopy/nephroscopy with laser or electrohydraulic lithotripsy (EHL)
  - Ununinvasive laser papillotomy may be safe and effective
  - Important to distinguish nephrocalcinosis from nephrolithiasis

Imaging if symptomatic
- Labs to monitor known metabolic abnormalities
- Imaging if symptomatic

Patient Resources
- http://www.nephron.com/article/000492.htm

References

ICD-9
- 275.42 Hypercalcemia
- 275.49 Other disorders of calcium metabolism

ICD-10
- N29 Other disorders of kidney and ureter in diseases classified elsewhere

Clinical/Surgical Pearls
- Important to distinguish nephrocalcinosis from nephrolithiasis
- Management directed at underlying cause of disorder
- Surgery is indicated in patients with chronic renal pain, sepsis, or failure to thrive

Ongoing Care
- Depends on underlying etiology
- Most do not progress to end-stage renal failure

Complications
- Nephrocalcinosis
- Obstructive urolithiasis
- May be associated with spondylolysis
- Renal infection
- Renal scarring
- Defects in renal tubular function
- Acute renal failure
- Chronic renal failure

Follow-Up
- Patient Monitoring
  - Urinalysis, 24-hr urine collection
  - Renal function testing
  - Serum Ca
  - Labs to monitor known metabolic abnormalities
  - Imaging if symptomatic

See also (Topic, Algorithm, Media)
- Calcium, Renal
- Hypercalcemia, Urologic Considerations
- Hyperparathyroidism, Urologic Considerations
- Hypernephroma, Urologic Considerations
- Hyperparathyroidism, Urologic Considerations
- Hypophosphatemia and Hypophosphatasia, Urologic Considerations
- Hypoparathyroidism
- Hypokalemia, Urologic Considerations
- Medullary Sponge Kidney
- Milk-alkali Syndrome
- Nephrocalcinosis, Adult Images
- Nephrocalcinosis, Neonatal
- Renal Tubular Acidosis
- Tumor Lysis Syndrome
- Unihithiasis, Adult, General Considerations
- Unihithiasis, Calcium Oxalate/Phosphate
- Unihithiasis, Pediatric, General Considerations

Additional Reading
Nephrotic Syndrome

Michael Pierotti, MD

**Basics**

**Description**
- Nephrotic syndrome refers to a specific renal disease with a distinct constellation of clinical and laboratory features:
  - Proteinuria (>3.5 g/dl)
  - Hypoalbuminemia (<3 g/dl)
  - Peripheral edema
  - Hypertension and thrombotic disease frequently seen
- Nephrotic syndrome (NS) can be caused by specific renal diseases or systemic diseases such as diabetes, lupus and others.

**Epidemiology**
- **Incidence**
  - **Children:** 2/100,000 new cases / year
  - **Adult:** 3/100,000 new cases / year
- **Prevalence** N/A

**Risk Factors**
- Primary renal disease (minimal change disease predominant cause in children)
- Underlying systemic disease in 30% of adults with NS including diabetes mellitus, amyloidosis, systemic lupus erythematosus
- Infection: Streptococcus, hepatitis, mononucleosis, syphilis, tuberculosis, HIV
- Medications: NSAIDs, interferons, bisphosphonates, lithium, gold, captopril, penicillamine, tyrosine kinase inhibitors
- Malnutrition

**Genetics**
- **Rare cause**
  - 2-8% of cases are familial
  - Finnish type congenital nephritic syndrome is inherited as autosomal recessive

**Pathophysiology**
- Severe proteinuria is due to abnormal permeability of the glomerular basement membrane (GBM) (1).
- FSBNs are seen as serum albumin falls below 2.5 g/dl.
- Proteinuria can be selective or nonselective.
- Edema results from primary salt retention and secondary decreased plasma oncotic pressure.
- Hypertension is secondary to increased hepatic synthesis from low oncotic pressure and urinary loss of regulatory proteins.
- Hypercoagulable state is likely due to loss of antithrombin III in urine.

**Associated Conditions**
- Membranous nephropathy (24%)
- Minimal change disease (11%)
- Lupus (14%)
- Focal segmental glomerulosclerosis (12%)
- Membranoproliferative glomerulonephritis (7%)
- Amyloidosis (8%)
- IgA nephropathy (8%)

**General Prevention**
- Avoidance of risk factors
- Treating conditions that may cause NS

**Diagnosis**

**History**
- Symptoms of fluid/sodium retention:
  - Dyspnea/orthopnea secondary to pleural effusion
  - Peripheral edema, especially at end of day
  - Periorbital edema, especially on awakening

**Physical Exam**
- Along with signs of fluid retention, patients may have signs of systemic disease causing NS
  - Fever
  - Rash (eg, butterfly rash of SLE), palmar, edema, lymphadenopathy
  - Ophthalmic exam: Uveitis in sarcoid, diabetic retinopathy
  - Skin exam: Rash (butterfly rash of SLE), palmar, edema, lymphadenopathy
  - Ophthalmic exam: Uveitis in sarcoid, diabetic retinopathy
  - Heartburn exam: Endocarditis, pleural effusion
  - Abdominal exam: Masses, ascites
  - Neurologic exam: Diabetic neuropathy, CNS lesion, mononeuritis multiplex

**Laboratory**
- Blood chemistry: BUN, Cr, comprehensive metabolic panel
- CBC
- **Albuminuria** detected by SSA; Protein is precipitated in urine by the addition of sulfosalicylic acid (SSA).

**Diff erential Diagnosis**
- Congestive heart failure
- Cirrhosis
- Malnutrition
- Protein-losing enteropathy

**Urinary Analysis and Microscopy**
- Marked proteinuria causes urine to foam.
- Albuminuria detected by dipstick, all proteinuria detected by SSA.

**Pathologic Findings**
- Minimal change glomerulopathy
- Membranous glomerulopathy
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis
- Diabetic glomerulosclerosis
- Fibrillary glomerulonephritis
- Light chain deposition disease

**Proteinuria (multiple myeloma)**
- Characteristic dipstick reading of 3+ to 4+ in NS patients
- Glycosuria: Suggests diabetes mellitus as possible cause of NS
- Hematuria common (usually microscopic)

**Imaging**
- Renal ultrasound: Increased echogenicity of renal parenchyma
- Screening for underlying malignancy with CT scan

**Differential Procedures/Surgery**
- Renal biopsy
TREATMENT

GENERAL MEASURES
- Sodium restriction (2-3 g/day)
- Protein restriction
- BF control
- Maintenance of fluid balance

MEDICATION
First Line
- ACE inhibitors (captopril, enalapril, ramipril, others) or Angiotensin II receptor blockers (losartan, irbesartan, telmisartan others)
- Should not be used concurrently due to risk of hypotension and worsening renal function
- Monitor for hypotension, hyperkalemia, or worsening renal function
- Common ACE-I side effects include cough, angioedema, or allergy

Second Line
- Statin therapy
  - Total LDL < 100 and triglyceride < 150
  - Side effects include myalgia, liver dysfunction, GI disturbance, and rash
- Corticosteroids for primary idiopathic or minimal change disease (3)

Second Line
- Cytotoxic agents (cyclophosphamide, chlorambucil, leflunomide)
- Second Line
- Cytotoxic agents (cyclophosphamide, chlorambucil, leflunomide)

ADDITIONAL TREATMENT
SURGERY/OTHER PROCEDURES
- Dialysis
- Renal transplantation

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
Anticoagulation for thrombosis

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Prognosis depends on age, race, pathology, presence of HTN, underlying systemic disease, degree of renal dysfunction, and degree of proteinuria.
- Minimal change disease in children has an excellent prognosis.
- Prognosis of the other glomerulopathies much more variable.
- Prognosis of secondary NS depends on the systemic diseases causing the NS.

COMPLICATIONS
- Acute kidney failure
- Atherosclerosis, hyperlipidemia, cardiovascular disease
- Chronic kidney disease
- Congestive heart failure
- Malnutrition
- Pneumococcal pneumonia and other infections
- Pulmonary edema
- Arterial and venous thrombosis (particularly deep vein and renal vein thrombosis)

Prognosis of secondary NS depends on the systemic diseases causing the NS.
Prognosis of the other glomerulopathies much more variable.
Minimal change disease in children has an excellent prognosis.
Prognosis depends on age, race, pathology, presence of HTN, underlying systemic disease, degree of renal dysfunction, and degree of proteinuria.
Minimal change disease in children has an excellent prognosis.
Prognosis of the other glomerulopathies much more variable.
Prognosis of secondary NS depends on the systemic diseases causing the NS.

See Also (Topic, Algorithm, Media)
- Chronic Kidney Disease, Adult (Renal Failure, Chronic)
- Chronic Kidney Disease, Pediatric (Renal Failure, Chronic)
- Glomerulonephritis, Acute
- Nephropathy, Membranous
- Nephropathy, Minimal Change
- Proteinuria

CODES
ICD9
- 250.40 Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled
- 250.41 Diabetes with renal manifestations, type I (juvenile type), not stated as uncontrolled
- 581.9 Nephrotic syndrome with unspecified pathological lesion in kidney

ICD10
- E10.21 Type 1 diabetes mellitus with diabetic nephropathy
- E11.21 Type 2 diabetes mellitus with diabetic nephropathy
- N04.9 Nephrotic syndrome with unspecified morphologic changes

REFERENCES

ADDITIONAL READING
NEUROBLASTOMA
Nilay M. Gandhi, MD
Arthur L. Burnett, II, MD, MBA, FACS

PATHOGENESIS
- Determined by tumor site origin, metasasis, and presence of pheochromocytoma syndromes
- Likely failure of persistent primitive ganglion cells to respond to normal signals
- Spinal cord, sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
  - Presence of metastasis:
    - Fever, lethargy, weight loss, bony pain, pallor
    - Bone metastasis (children and adults)
    - Liver metastasis (younger children)
- Active biochemical products:
  - 90% produce catecholamines
  - Paraganglionic hyperplasia (HTN), palpitation, flushing, headache
- Neuroblast: acid (NTA) in poorly differentiated tumors
- Vanillylmandelic acid (VMA) in well-differentiated tumors

ASSOCIATED CONDITIONS
- Other disorders of neural crest derived cells:
  - Hirschsprung disease
  - Neurofibromatosis type 1
- Congenital normal hypertension syndrome

GENERAL PREVENTION
- Screening with urinary catecholamines is not necessary
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)

IMAGING
- Paravertebral tumor compressing spinal cord
- Bone metastasis (costochondral, rib)
- Blurry hypodense subcutaneous nodules
- Skin metastasis, "blueberry muffin" spots
- Acute myeloid encephalopathy
- Raccoon’s eyes
  - Upper eyelid hemangiom (periorbital metastasis)
- Skull metastasis
- Familial neuroblastoma

DIAGNOSTIC TESTS & INTERPRETATION
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)
- 5% patients (catecholamines sequestered)

PATHOPHYSIOLOGY
- Determined by tumor site origin, metasasis, and presence of pheochromocytoma syndromes
- Likely failure of persistent primitive ganglion cells to respond to normal signals
- Spinal cord, sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
  - Presence of metastasis:
    - Fever, lethargy, weight loss, bony pain, pallor
    - Bone metastasis (children and adults)
    - Liver metastasis (younger children)
- Active biochemical products:
  - 90% produce catecholamines
  - Paraganglionic hyperplasia (HTN), palpitation, flushing, headache
- Neuroblastoma:
  - Acid (NTA) in poorly differentiated tumors
  - Vanillylmandelic acid (VMA) in well-differentiated tumors

ASSOCIATED CONDITIONS
- Other disorders of neural crest derived cells:
  - Hirschsprung disease
  - Neurofibromatosis type 1
- Congenital normal hypertension syndrome

GENERAL PREVENTION
- Screening with urinary catecholamines is not necessary
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)

IMAGING
- Paravertebral tumor compressing spinal cord
- Bone metastasis (costochondral, rib)
- Blurry hypodense subcutaneous nodules
- Skin metastasis, "blueberry muffin" spots
- Acute myeloid encephalopathy
- Raccoon’s eyes
  - Upper eyelid hemangiom (periorbital metastasis)
- Skull metastasis
- Familial neuroblastoma

DIAGNOSTIC TESTS & INTERPRETATION
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)
- 5% patients (catecholamines sequestered)

PATHOPHYSIOLOGY
- Determined by tumor site origin, metasasis, and presence of pheochromocytoma syndromes
- Likely failure of persistent primitive ganglion cells to respond to normal signals
- Spinal cord, sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
  - Presence of metastasis:
    - Fever, lethargy, weight loss, bony pain, pallor
    - Bone metastasis (children and adults)
    - Liver metastasis (younger children)
- Active biochemical products:
  - 90% produce catecholamines
  - Paraganglionic hyperplasia (HTN), palpitation, flushing, headache
- Neuroblastoma:
  - Acid (NTA) in poorly differentiated tumors
  - Vanillylmandelic acid (VMA) in well-differentiated tumors

ASSOCIATED CONDITIONS
- Other disorders of neural crest derived cells:
  - Hirschsprung disease
  - Neurofibromatosis type 1
- Congenital normal hypertension syndrome

GENERAL PREVENTION
- Screening with urinary catecholamines is not necessary
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)

IMAGING
- Paravertebral tumor compressing spinal cord
- Bone metastasis (costochondral, rib)
- Blurry hypodense subcutaneous nodules
- Skin metastasis, "blueberry muffin" spots
- Acute myeloid encephalopathy
- Raccoon’s eyes
  - Upper eyelid hemangiom (periorbital metastasis)
- Skull metastasis
- Familial neuroblastoma

DIAGNOSTIC TESTS & INTERPRETATION
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)
- 5% patients (catecholamines sequestered)

PATHOPHYSIOLOGY
- Determined by tumor site origin, metasasis, and presence of pheochromocytoma syndromes
- Likely failure of persistent primitive ganglion cells to respond to normal signals
- Spinal cord, sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
  - Presence of metastasis:
    - Fever, lethargy, weight loss, bony pain, pallor
    - Bone metastasis (children and adults)
    - Liver metastasis (younger children)
- Active biochemical products:
  - 90% produce catecholamines
  - Paraganglionic hyperplasia (HTN), palpitation, flushing, headache
- Neuroblastoma:
  - Acid (NTA) in poorly differentiated tumors
  - Vanillylmandelic acid (VMA) in well-differentiated tumors

ASSOCIATED CONDITIONS
- Other disorders of neural crest derived cells:
  - Hirschsprung disease
  - Neurofibromatosis type 1
- Congenital normal hypertension syndrome

GENERAL PREVENTION
- Screening with urinary catecholamines is not necessary
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)

IMAGING
- Paravertebral tumor compressing spinal cord
- Bone metastasis (costochondral, rib)
- Blurry hypodense subcutaneous nodules
- Skin metastasis, "blueberry muffin" spots
- Acute myeloid encephalopathy
- Raccoon’s eyes
  - Upper eyelid hemangiom (periorbital metastasis)
- Skull metastasis
- Familial neuroblastoma

DIAGNOSTIC TESTS & INTERPRETATION
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)
- 5% patients (catecholamines sequestered)

PATHOPHYSIOLOGY
- Determined by tumor site origin, metasasis, and presence of pheochromocytoma syndromes
- Likely failure of persistent primitive ganglion cells to respond to normal signals
- Spinal cord, sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
  - Presence of metastasis:
    - Fever, lethargy, weight loss, bony pain, pallor
    - Bone metastasis (children and adults)
    - Liver metastasis (younger children)
- Active biochemical products:
  - 90% produce catecholamines
  - Paraganglionic hyperplasia (HTN), palpitation, flushing, headache
- Neuroblastoma:
  - Acid (NTA) in poorly differentiated tumors
  - Vanillylmandelic acid (VMA) in well-differentiated tumors

ASSOCIATED CONDITIONS
- Other disorders of neural crest derived cells:
  - Hirschsprung disease
  - Neurofibromatosis type 1
- Congenital normal hypertension syndrome

GENERAL PREVENTION
- Screening with urinary catecholamines is not necessary
- 24-hr urinary VMA and NTA
- Elevated in 90–95% of patients
- CBC: Anemia suggests bone marrow involvement
- Ferritin: Elevation suggests liver involvement
- PENT: Elevation in advanced disease
- 40–50% of patients (must be > 3 standard deviations)

IMAGING
- Paravertebral tumor compressing spinal cord
- Bone metastasis (costochondral, rib)
- Blurry hypodense subcutaneous nodules
- Skin metastasis, "blueberry muffin" spots
- Acute myeloid encephalopathy
- Raccoon’s eyes
  - Upper eyelid hemangiom (periorbital metastasis)
- Skull metastasis
- Familial neuroblastoma
Pathologic Findings
- Gross: Solid/cystic vascular, poorly encapsulated purple mass
- Histology:
  - Small round blue cells
  - Mitosis-Karyorrhexis index is prognostic
  - Homer-Wright pseudorosettes
- Histopathologic markers:
  - N-MYC
  - DNA ploidy
  - Shimada classification (stroma poor/rich)
  - S-stage (based on age, histologic maturation, mitotic rate)
  - Stroma-rich (nodular, intermediate, well differentiated)
- Neurop-specific enolase (NSE) staining is specific for neuroblastoma
- Periodic acid-Schiff (PAS) staining can distinguish gangliocytic

DIFFERENTIAL DIAGNOSIS
- Ganglioneuroma (benign form)
- Ganglioneuroblastoma (intermediate between ganglioneuroma and neuroblastoma)
- Extra-abdominal mass in childhood:
  - Wilms tumor
  - Phaeochromocytoma
  - Rhabdomyosarcoma
  - Synovial sarcoma
  - Teratoma
  - Intra-abdominal mass in childhood:
    - Ganglioneuroma and neuroblastoma
    - Histopathologic markers:
      - Histology:
        - Gross: Solid/cystic vascular, poorly encapsulated purple mass
        - S-stage (based on age, histologic maturation, mitotic rate)
      - Shimada classification
      - Histopathologic markers:
      - S-stage (based on age, histologic maturation, mitotic rate)

TREATMENT

GENERAL MEASURES
- Multimodal treatment approach including surgery, chemotherapy, radiotherapy, and/or bone marrow or stem cell transplantation
- Nearly all stage 4s patients spontaneously resolve (observation)
- INSS surgical stage and more recently the International Neuroblastoma Risk Group (INRG) risk assessment system dictates treatment (3)

MEDICATION

First Line (4)
- Low risk: favored surgical failure
  - Cyclophosphamide, Adriamycin, and Cisplatin/VM-26 in low-dose cycles
- Intermediate risk: Induction with Cyclophosphamide and Adriamycin with or without radiotherapy
  - High risk: CsA, CsA, Adriamycin, VM-26, Doxorubicin, Cisplatin, Etoposide in various combinations
- Second Line
  - Intermediate risk: Cisplatin/VM-26
  - High risk: Alternative use of above listed combinations

SURGERY/OTHER PROCEDURES
- Low stage stages 1, 2, or 4 with age <1 yr or >1 yr with favorable pathology:
  - Surgery or resection
  - Chemotherapy indicated if recurrence, N-MYC amplification, or unfavorable histology
- Intermediate risk (stage 1a: <1 yr or >1 yr with favorable pathology, or stage 4: <1 yr):
  - Surgery + Multimodality chemotherapy
- High risk (stage 2 with age >1 yr with unfavorable histopathology, or stage 3, 4, 4v with N-MYC amplification regardless of age):
  - Intensive chemotherapy with or without bone marrow ablation and repaired surgery

ADDITIONAL TREATMENT

Radiation Therapy
- Reserved for primary or secondary chemotherapy failures in low-risk patients
- Indicated for local control in bulky stage 3 or advanced stage 4
  - Avoid if spinal cord compression due to adverse effects on spine growth
- Intermittent radiation therapy not better than external beam irradiation

Additional Therapies
- Bone marrow transplantation
- Complementary & Alternative Therapies (5)
  - 13-cis-retinoic acid improves 5-yr overall survival (OS) in children with advanced stage disease after transplantation or intensive chemotherapy
  - Epothilone B: MIBG targeted delivery for metastatic disease
  - Anti-GD2 antibodies (research pending)

ONGOING CARE

PROGNOSIS
- Dependent on risk status
  - Low risk: Resection is curative, >97% 5-yr OS
  - Intermediate risk: neoadjuvant chemo followed by >50% resection, 70–90% 5-yr OS
  - High risk: Neoadjuvant chemo 4 cycles (vastage after 2 cycles), >50% resection, radiation, peripheral stem cell transplant, nononstrosis, 20–40% 5-yr OS
  - Better survival in nonadrenal primary tumors
  - Shimada classification
    - S-stage: <10% survival

COMPLICATIONS
- Dumbbell neuroblastoma with spinal cord compression
  - Best treated with chemotherapy
- Neurosurgical intervention only for emergent decompression
- Associated with tumor presentation and with treatment modalities

FOLLOW-UP

Patient Monitoring
- Low risk:
  - Imaging + lab markers 1–2 mo after therapy, every 6 mo for 5 yr, then annually after 5 yr
  - Intermediate risk:
  - Imaging + lab markers 1–2 mo after therapy, every 1–3 mo for 1st yr, then every 4–6 mo for 2–5 yr, then annually after 5 yr
  - High risk:
  - Imaging + lab markers 1–2 mo after therapy, every 1–3 mo for 5 yr, every 6 mo after 5 yr

Patient Resources
- National Cancer Institute (http://www.cancer.gov/cancerTopics/types/neuroblastoma)

REFERENCES

ADDITIONAL READING
NEUROGENIC BLADDER, GENERAL CONSIDERATIONS
Alana M. Murphy, MD

BASICS

DESCRIPTION
Neurogenic bladder (NGB) is a general term used to describe dysfunction of the urinary bladder due to disease of the central nervous system (CNS) or peripheral nerves involved in the control of urine storage and evacuation.

Epidemiology
Incidence
Difficult to determine incidence due to multiple etiologies.

Prevalence
- Prevalence of voiding dysfunction by specific disease of the central nervous system (CNS) or neurogenic bladder (NGB) is a general term used to describe dysfunction of the urinary bladder due to CNS lesions (1):
  - Transverse myelitis
  - Spinal cord injury
  - Parkinson disease
  - Normal-pressure hydrocephalus
  - Multiple sclerosis
  - Cerebrovascular accident
  - Impaired sphincteric function
  - Impaired bladder sensation
  - Detrusor underactivity
  - Suprapontine: Lesions between pontine and sacral micturition centers:
  - Function: Coordinates sphincter relaxation during bladder contraction
  - Interruption of sacral reflex arc; no detrusor contraction
  - Detrusor underactivity or acontractility

Pathophysiology
- CNS lesions (1):
  - Suprapontine:
    - Function: Inhibits sacral micturition center
  - Detrusor overactivity (DO) due to loss of inhibition of sacral micturition center
  - Pontine micturition center:
    - Function: Coordinates sphincter relaxation during bladder contraction
  - Lesions between pontine and sacral micturition centers are associated with DO and detrusor sphincter dyssynergia (DSD)
- Sacral micturition center:
  - Function: Mediates reflex and voluntary bladder contractions
  - Detrusor underactivity or incontinence

Associated conditions
- CNS lesions (1):
  - Variable voiding dysfunction
  - Detrusor overactivity
  - Impaired bladder sensation
  - Impaired sphincteric function

Diagnosis
History
- Neurologic disease: Onset, duration
- Diabetes mellitus
- Congenital disorders:
  - Neonatal or newborn: Neonatal or newborn
  - Secondary damage: Pressure, infection, urolithiasis
  - Loss of CNS inhibition neurogenic lower urinary tract dysfunction

Urodynamics (UDS): Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction.

Digital rectal exam:
- Prostate size: BPH may coexist with NGB
- See neurologic exam

Laboratory
- Evaluate for sacral abnormalities:
  - Sacral dimple, skin tag, discoloration or tuft of hair may suggest occult spinal dysraphism
- Sacral agenesis
- Focused neurologic exam:
  - Sacral root
  - Perianal sensation
- Anal tone, sphincter control

Imaging
- Imaging is most important in patients with risk factors for upper tract compromise:
  - DSD (especially males who void reflexively)
  - Impaired bladder compliance
  - Renal ultrasound (US): To screen for calculus, hydronephrosis, or mass
  - Excretory urography:
    - Delayed excretion of contrast with high urinary storage pressures
    - Hydronephrosis
    - Marked elevation of intravesical pressure or calculi

Focused neurologic exam:
- Evaluate for sacral abnormalities:
  - Sacral agenesis
  - Sacral dimple, skin tag, discoloration or tuft of hair

Digital rectal exam:
- Prostate size: BPH may coexist with NGB
- See neurologic exam

Urodynamics (UDS): Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction.

Neurogenic DO (DSD):
- Loss of CNS inhibition

Diagnosis Procedures/Surgery
- Diagnostics and procedures necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction.

Neurogenic DO (DSD):
- Loss of CNS inhibition

Diagnosis Procedures/Surgery
- Urodynamics (UDS): Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction.

Neurogenic DO (DSD):
- Loss of CNS inhibition

Diagnosis Procedures/Surgery
- Urodynamics (UDS): Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction.

Neurogenic DO (DSD):
- Loss of CNS inhibition
Pathologic Findings
Bladder wall thickening with fibrosis and trabeculation

DIFFERENTIAL DIAGNOSIS
- Idiopathic overactive bladder
- Dysfunctional voiding

TREATMENT
GENERAL MEASURES (2)
- UDS is essential to determine lower urinary tract function/dysfunction and to plan urologic management.
- Maintaining low intravesical pressure protects upper urinary tracts
- Urinary drainage: Intermittent catheterization or external collection appliance
- Indwelling catheterization: Associated with recurrent UTIs, urethral erosion, and voiding dysfunction
- Interim self-catheterization: Most effective treatment; requires low storage pressure
- Surgical intervention is indicated when other therapies fail to protect the upper urinary tract or provide continence.

MEDICATION First Line
- Anticholinergics aimed at decreasing urinary storage pressure and reducing NDO. Most common side effects include dry mouth and constipation
  - Neostigmine 4–8 mg OD
  - Procyclidine extended release 0.375 mg BID
  - Oxybutynin 5 mg BID-TID
  - Oxybutynin transdermal patch 3.9 mg/day
  - Oxybutynin, topical gel 10% apply 1 sachet QD to dry area
  - Solifenacin 1–5 mg BID
  - Tolterodine LA 1.2 mg BID
  - Trospium CR 60 mg/day
  - f3 antagonist: Most common side effects include an increase in blood pressure and palpitations
- Adrenergic blockers: Decrease internal sphincter resistance, lower voiding pressure, ineffective for OAB
  - Alfuzosin 10 mg/day
  - Doxazosin start 1 mg/day to max 8 mg
  - Silodosin 8 mg/day
  - Terazosin start 0.4 mg to max 0.8 mg/day
  - Tamsulosin start 0.4 mg to max 0.8 mg/day
- α2 Agonist: Most common side effects include an increase in blood pressure and palpitations
  - Mirabegron 25 mg/day increase to 50 mg/day after 3-wk PRN

Second Line
- Botulinum toxin type A (onabotulinumtoxinA) injection into the external sphincter for OAB
  - Short-leaf, requires repeat injections
- Botulinum toxin injection into the detrusor for NDO
  - Duration of action is 3–9 mo
  - Requires repeated injections

SURGERY/OTHER PROCEDURES
- Endoscopic sphincterotomy or stenting
  - Only makes with UDS; requires condom catheter
- Augmentation cystoplasty using an intestinal segment to enlarge the bladder
  - Goal is to increase bladder volume and decrease bladder pressure
- Interstitial cystitis: Consideration for urinary drainage
- Limited dietary mandates: construction of a continent catheterizable stoma for the urinary reservoir, especially in females
- Revesicoectomy
  - Useful for those unable to perform self-catheterization (ie, quadriplegia)
- Cybertherapy with continent urinary reservoir
  - Neol or colost pouch, continent catheterizable stoma (appendix or tapered ileum)
- Cyproheptadine with ileal conduit

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
Neuromodulation, sacral nerve stimulation and posterior tibial nerve stimulation are not FDA-approved for the treatment of NDO but may have some benefit.

Complementary & Alternative Therapies
Acupuncture has been reported to improve symptoms of neurogenic bladder.

ONGOING CARE
PROGNOSIS
Proper urologic management greatly improves quality of life in patients with NGB dysfunction.

COMPlications
- Recurrent UTS
- Urinary retention
- Hydroceles
- Neoplastic transformation: Associated with chronic catheter
- Urethral erosion

FOLLOW-UP
Patient Monitoring
- Annual evaluation in high-risk patients may include UDS
  - EUS:
  - Imaging: Typically renal US
  - Serum creatinine

Patient Resources
- http://www.nationalkidney.org
- http://www.sphinctor.org
- http://www.parkevin.org

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Bladder Areflexia (Detrusor Areflexia)
- Detrusor Overactivity
- Detrusor Sphincter Dysynergia (DSD)
- Incontinence, Urinary, Adult Female
- Incontinence, Urinary, Adult Male
- Incontinence, Urinary, Pediatric
- Neurogenic Detrusor Overactivity (NDO)
- Overactive Bladder
- Spinal Cord Injury, Urologic Considerations
- Stroke (CVA), Urologic Considerations

CODES
ICD9
- 596.3 Hyper trophy of bladder
- 596.54 Neurogenic bladder NOS
- 596.59 Other functional disorder of bladder

ICD10
- N31.8 Other neuro muscular dysfunction of bladder
- N31.9 Neuro muscular dysfunction of bladder, unspecified
- N32.81 Overactive bladder

CLINICAL/SURGICAL PEARLS
- Adequate management of lower urinary tract function is essential to avoid upper urinary tract compromise and preservation of renal function.
**NOCTURIA**

Garjoe D. Lavien, MD
Michael J. Naslund, MD

### BASICS

**DESCRIPTION**
- Nocturia is a symptom describing an individual who awakens at night one or more times to void. Each void is preceded and followed by sleep.
- Can negatively impact quality of life.
- Can be associated with depression, daytime fatigue, and increased orthopedic morbidity among the elderly.

**PATHOPHYSIOLOGY**

- **Risk Factors (1)**
  - **Prevalence**
    - Higher prevalence in men among young adults
    - Higher prevalence in men than women among elderly population groups
  - **Epidemiology**
    - The incidence of nocturia and total number of voiding episodes increases with age
  - **Obesity**
  - **Depression**
  - **Psychogenic polydipsia**
  - **Diabetes mellitus**
  - **Bladder outlet obstruction**
  - **Nephrogenic polyuria**

**ASSOCIATED CONDITIONS**

- **Obstructive: BPH, urethral stricture**
- **Psychogenic polyuria**

### DIAGNOSIS

**HISTORY**

- **Number of times getting up at night to urinate from time of going to bed until time of waking in the morning**
- **Degree of bother assessment**
- **Differentiate between awakening due to the urge to void vs. awakening due to other sleep disturbances**
- **Fluid intake habits**
- **Timing, volume**
- **Caffeine and alcohol consumption**
- **Previous pelvic surgery or radiation**
- **Daytime fatigue and depression**
- **Review of medications known to contribute to nocturia: such as diuretics, excessive calcium supplementation, antidepressants, or lithium.**
- **Swelling of lower extremities**

**PHYSICAL EXAM**

- Global or local neurologic deficits
- Digital rectal: Assess tone, prostate exam in men
- Pelvic exam in women: Anterior prolapse causing retention, urethral diverticulum, atrophic vaginitis causing irritative urinary symptoms
- Lung auscultation for rales, crackles
- Dependent edema, pedal edema
- Suprapubic distension consistent with urinary retention
- Obesity and a wide neck circumference raises the possibility of sleep apnea

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- Uricalysis: Low specific gravity (polyuria), RBCs (rule out stones, bladder cancer, foreign body, etc.), granulocyturia (nephrotic syndrome), glycosuria (diabetes mellitus), pyuria (UTI)
- Urine culture: UTI
- Urine osmolality: Dilute low values suggest inappropriate excretion of ADH or excess intake of water
- PSA if indicated
- Serum electrolytes: Hyperkalemia with impaired contractility

**Imaging**

- Bladder US with PVR volume for suspected urinary retention, especially if considering antimuscarinics
- Renal US may demonstrate hydronephrosis in cases of urinary retention or poorly compliant bladders
Diagnostic Procedures/Surgery

• Voiding diary:
  – All voiding episodes and volumes should be recorded for a 24-hr period; the time the patient actually goes to sleep and wakes for the day should also be noted.
  – Nocturnal urine volume (NUV) is the total volume of urine voided during the night (the first morning void is included in this sum since it represents urine excreted during sleep hours).
  – Nocturnal polyuria index (NPI): NPI divided by the total volume voided over the 24-hr period.
  – NPI >33% = nocturnal polyuria.
  – Nocturnal Bladder Capacity Index (NBC):
    – NBC = NPI/Maximum volume per void–1
    – NBC >1.0 suggests that the nocturnal bladder capacity cannot store the amount of urine made at night.
  – Urodynamic:
    – Helpful when empiric treatment for overactive bladder (OAB) or bladder outlet obstruction has failed to improve nocturia.
  – Urodynamic and sleep studies: Differentiate between sleep disorder and true nocturia.

Pathologic Findings

Nocturnal polyuria may be caused by several conditions including: 

1. Polydipsia
2. Hypercalcemia
3. Drugs, autonomic dysfunction

A voiding diary is extremely helpful to determine the cause of nocturia.

DIFFERENTIAL DIAGNOSIS

• Sleep disorders:
  – Most patients awaken due to the sleep disturbance, but recall this as an awakening to void.
  – May need polysomnography

• Urodynamics:
  – Bladder outlet obstruction, OAB, incomplete bladder emptying.
  – Neuropathic:
    – Neurogenic: idiopathic nocturnal polyuria, diabetes mellitus, central diabetes insipidus, nephrogenic diabetes insipidus, primary polydipsia, hypereosinophilia, drugs, autonomic failure, obstructive sleep-apnea.

TREATMENT

GENERAL MEASURES

• Nocturnal polyuria secondary to diabetics:
  – Change to afternoon dosing to induce an early evening diuresis rather than a nocturnal diuresis.
  – Treatment of underlying condition associated with nocturia.

MEDICATION

First Line

• Antimuscarinics are appropriate for reduced voided volumes.
  – Men only (α-blocker alone or combined with a 5α-reductase inhibitor likely modulated benefit) (C2A).

Second Line

• DDAVP for nocturia associated with nocturnal polyuria (IIb)– Dosing 0.01 mg PO, titrate up to 0.04 mg.
  – DDAVP has a high risk of hyponatremia.
  – Greatest risk seen in men >65 yr old.

SURGERY/OTHER PROCEDURES

Sacral neuromodulation for nocturia secondary to reduced voided volumes is associated with refractory daytime frequency and urgency (IIIb).

ADDITIONAL TREATMENT

• Radiation Therapy
  – N/A

• Additional Therapies
  – Behavioral training:
    – Pelvic floor muscle exercises, scheduled fluid feedback:
      – More effective than both drug therapy and placebo in treatment of nocturia associated with daytime urgency and urge incontinence (C5A) and CRP for obstructive sleep-apnea.

• Complementary & Alternative Therapies
  – None

ONGOING CARE

PROGNOSIS

Although it is often difficult to completely eliminate episodes of nocturia, characterizing nocturia according to cause-specific etiologies allows for cause-specific treatment.

COMPLICATIONS

• Traumatic falling accidents, including hip fractures, falling from sleep to urine.

• Urinary retention secondary to antimuscarinics

FOLLOW-UP

• Patient Monitoring
  – Bladder sonography with PVR as needed.
  – Repeat 24-hr voiding diaries.
  – Urinary retention secondary to antimuscarinics.

• Patient Resources
  – Medline Plus: Excessive Urination at Night

CODES

ICD9

• 596.59 Other functional disorder of bladder

ICD10

• N32.9 Neurohumoral dysfunction of bladder unspecified

• R35.1 Nocturia

• R35.8 Other polyuria

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

• Bladder Outlet Obstruction
• Diabetes Mellitus
• Incontinence, Adult Female
• Incontinence, Adult Male
• Neurogenic Bladder
• Nocturia Algorithm
• Nocturnal Polyuria
• Overactive Bladder
• Urgency, Urinary (Frequency and Urgency)
• Urinary Retention
• Urodynamic Syndrome

• Emptying Diaries (see Section VII: Reference Tables)

CLINICAL/SURGICAL PEARLS

• The etiology of nocturia is not prostate or bladder related in the majority of men. Poor sleep pattern and fluid consumption/mobilization need to be considered.

• A voiding diary is extremely helpful to determine the cause of nocturia.
RISK FACTORS

- Prevalence
  - Incidence: 4 out of 5 cases occur in prepubertal males (<10 years old) prior to widespread use of MMR vaccine
  - Recent increase in incidence in postpubertal males corresponding to mumps outbreaks following national shortages of MMR vaccine as well as controversy related to MMR vaccine itself

- Immunocompromised states
- Bacterial orchitis even more rare and usually associated with concurrent epididymitis

- Prevalence
  - ~20% postpubertal males with mumps develop orchitis
  - Recent case reports of postpubertal mumps vaccinated males with mumps developing orchitis in outbreaks

PATHOPHYSIOLOGY

- Most commonly caused by hematogenous spread of mumps virus directly attacking testicular tissue resulting in parenchymal edema, congestion of seminiferous tubules, and perivascular infiltration of lymphocytes
- Rare case reports of other viruses causing orchitis (mononucleosis, coxsackievirus, others)
- Cases of bacterial orchitis usually result from local spread from the ipsilateral epididymis
- Truly noninfectious orchitis is usually idiopathic, trauma-related, or possibly autoimmune
- Orchitis is unilateral in 70% of cases
- Contrast-enhanced CT scan is indicated when there is clinical concern for a mass lesion

- ASSOCIATED CONDITIONS
  - Mumps
  - Epididymitis
  - STD in sexually active men
  - History of recent scrotal trauma
  - History of intravesical BCG therapy, may result in granulomatous orchitis

- GENERAL PREVENTION
  - Vaccination against mumps virus limits mumps orchitis
  - Protection from STD
  - Treatment of epididymitis prior to progression to epididymo-orchitis

- DIAGNOSIS

- HISTORY
  - Testicular pain and swelling
    - Mumps discomfort to severe pain
    - Onset of testicular pain and edema is acute
    - History of recent mumps infection
    - Systemic symptoms
      - Fever
      - Malaise
      - Myalgias
      - Nausea, vomiting
      - Headache
      - Obtain vaccination history

- Laboratory Tests
  - Mumps: serum immunofluorescence antibody assay
  - Urethral cultures if concern for urethritis
  - Urinalysis and urine culture
  - Evidence or history of immunocompromise
  - History of BPH
  - Evidence of past history of intravesical BCG therapy

- Imaging
  - Transrectal color Doppler ultrasonography
  - CT scan of pelvis

- DIAGNOSTIC TESTS & INTERPRETATION

- Lab
  - Uricalysis and urine culture
  - Urethral cultures if concern for urethritis
  - Mumps: serum immunofluorescence antibody assay

- Imaging
  - Transrectal color Doppler ultrasound is considered required by many clinicians:
    - Can rule out testicular torsion or malignancy
    - Additional imaging is unnecessary (i.e., CT scan or MRI)

- Diagnostic Procedures/Surgery
  - Usually not necessary

- Pathologic Findings
  - With viral infection, destruction of germ cells, edema and extensive inflammatory cell infiltrate is noted
  - Later seminiferous tubules can experience necrosis from increased pressure and edema, with subsequent interstitial fibrosis.
Differential Diagnosis
- Epididymitis
- Granulomatous orchitis, infectious and noninfectious
- Reactive hydrocele
- Sclerotic plaque
- Testicular malakoplakia
- Testicular torsion
- Torsion of testicular appendage
- Testicular tumor

Treatment

General Measures
- Supportive in nature
  - Bed rest
  - Hot or cold packs for analgesia
    - Applied for 10–15 min q 4 h or until pain subsides
  - Scrotal elevation and support with tight-fitting underwear or athletic support
  - Nonsteroidal anti-inflammatory drugs (NSAID)
  - Antimicrobics
  - Counsel patient on safe sex practices if STD suspected

Medication

First Line
- There are no targeted medications indicated in the treatment of viral orchitis. Supportive care is essential
- Bacterial orchitis requires coverage with appropriate antibiotic for suspected pathogen(s)
  - 35 years old, or epididymo-orchitis secondary to UTI
  - Additional gram-negative coverage with a fluoroquinolone or trimethoprim-sulfamethoxazole (TMP-SMX)
  - Tailor antibiotic prescription to local resistance patterns of most common UTI pathogens

Second Line
- NSA

Surgery/Others Procedures
- Surgical intervention is generally not indicated in the treatment of acute or chronic orchitis
- Associated scrotal pain or symptomatic hydrocele may require surgery
- Orchidectomy for chronic orchitis refractory to supportive measures is an option, but patients must be counseled surgery may not alleviate pain
- Consider microsurgical denervation of cord for chronic refractory orchalgia following favorable response to percutaneous cord block
- Consider in-office epididymectomy

Additional Treatment

Radiation Therapy
- There is no role for radiation therapy in the treatment of orchitis

Additional Therapies
- Interferon-2b has been investigated in bilateral mumps orchitis, given that the mumps virus replicates with a virus-associated transcriptase

Complementary & Alternative Therapies
- Patient-specific referral for psychologic evaluation and support for chronic refractory orchitis

Ongoing Care

Prognosis
- Most cases of mumps orchitis are self-limited, resolving within 3–10 days
- With appropriate antibiotic coverage, most cases of bacterial orchitis resolve without complication

Complications
- Unilateral testicular atrophy in up to 60% with mumps orchitis
- Bilateral testicular atrophy in up to 60% with mumps orchitis
- Sterility is rarely a sequel of unilateral orchitis with history of orchitis

Follow-Up

Patient Monitoring
- Most patients can be safely monitored in an outpatient setting
- A patient with a STD as the cause of orchitis should be tested for other STDs including Human immune deficiency virus (HIV)

Patient Resources
- http://www.nysayhealth.org
- http://www.nysayhealth.org

Additional Reading

See Also (Topic, Algorithm, Media)
- Acute Scrotum
- Orchitis
  - Orchitis, Granulomatous
  - Orchitis, Testicular
  - Orchitis, Testicular, Adult
  - Orchitis, Testicular, Adolescent

Codes

ICD-9
- 604.90 Orchitis and epididymitis, unspecified
- 604.91 Orchitis and epididymitis in diseases classified elsewhere
- 604.99 Other orchitis, epididymitis, and epididymo-orchitis, without mention of abscess

ICD-10
- N45.1 Epididymitis
- N45.2 Orchitis
- N45.3 Epididymo-orchitis

Clinical/Surgical Pearls
- Most cases of orchitis are viral in nature and self-limited, other cases are bacterial and most commonly associated with epididymitis.
- Physical exam findings include testes, scrotal tenderness with associated erythema of the scrotum with or without fever.
- Testicular ultrasonography is important to rule out torsion and malignancy.
- Medical therapy for orchitis is largely supportive; antibiotic coverage should be targeted to cover STDs in the young and sexually active and UTIs in the elderly.
- The role for surgical management of orchitis is limited.
OSTEITIS PUBIS, UROLOGIC CONSIDERATIONS

Patrick T. Gomella, MD, MPH
Leonard G. Gomella, MD, FACS

BASICS

DESCRIPTION

Osteitis pubis is a painful sterile inflammatory condition affecting the pubic symphysis. It is most commonly seen in athletes.

First described with suprapubic surgery and remains a potential complication of pelvic procedures.

EPIDEMIOLOGY

Incidence

Overall incidence in nonathlete populations unknown.

0.16% in procedures using bone anchors.

Prevalence

Overall prevalence in nonathlete populations unknown.

RISK FACTORS

- Invasive pelvic procedures
  - Several urologic procedures implicated
    - Radical prostatectomy
    - Prostate cryotherapy
    - TRUS Bx of prostate
    - TURP
    - Retropubic urethropexy: Specifically, Marshall–Marchetti–Krantz procedure
    - Sling procedures
    - Pelvic radiation

- Trauma

- Rheumatic disorders

- Pregnancy/parturition

- Overuse syndrome in athletes

- Genetics

No known genetic predisposition.

PATHOPHYSIOLOGY

Symphysis pubis is a nonsynovial amphiarthrodial joint at the confluence of the two pubic bones, consisting of an intrapubic fibrocartilaginous disc between thin layers of hyaline cartilage.

- Etiology unknown but may be related to periosteal trauma.

ASSOCIATED CONDITIONS

- Ankylosing spondylitis

- Rheumatoid arthritis

GENERAL PREVENTION

N/A

DIAGNOSIS

HISTORY

- Inciting event such as a pelvic procedure or trauma
- Insidious onset of suprapubic pain
- Pain radiating to thigh adductors, lower abdomen, perineum
- Pain worse when walking or when rising from a seated position

PHYSICAL EXAM

- Point tenderness over pubic symphysis
- Waddling gait
- Low-grade fever
- Increased pain with coughing or Valsalva
- Painful hip abduction

DIAGNOSTIC TESTS & INTERPRETATION

ALERT

Must rule out osteomyelitis, especially in postoperative patients.

Lab

- Not generally required to make diagnosis

- May see moderate leukocytosis and an increased erythrocyte sedimentation rate (ESR), raised levels of acute phase proteins (fibrinogen, C-reactive protein), and increased ESR are more suggestive of osteomyelitis.

Imaging

- Pelvic radiograph
  - Typically normal in acute phase
  - Articular surface erosion, sclerosis, osteophyte formation

- Scintigraphy
  - Increased uptake around pubic symphysis

- Symphysogram of joint
  - Pain on injection of contrast diagnostic

- Magnetic resonance imaging (MRI) most sensitive and considered gold standard
  - Acute (<6 mo): Bone marrow edema, fluid in joint, periarticular edema
  - Chronic (>6 mo): Subchondral sclerosis, bony margin irregularities, osteophytes (3)

Diagnostic Procedures/Surgery

- Symphysogram of joint
  - Pain on injection of contrast diagnostic

- Generally replaced by MRI.

- Aerobic/anaerobic culture of joint aspirate to rule out infection if clinically indicated.

Pathologic Findings

Scientific changes in bone architecture and degeneration of hyaline cartilage with normal periosteum (3).

DIFFERENTIAL DIAGNOSIS

- Osteomyelitis (the most critical)

- Neoplasia of pelvic rami

- Bony metastases

- Pubic osteolysis

- Sports hernia (athletic pubalgia, sportsman’s hernia)

- Adductor strain

- Muscle tears

- Avulsion injuries

- Stress fractures

- Tears of acetabular labrum

TREATMENT

GENERAL MEASURES

- Rest, heat, or ice

- Physical therapy to strengthen pelvic girdle can be considered.

MEDICATION

First Line

- Nonsteroidal anti-inflammatory
  - Ibuprofen 200–800 mg 2–4 ×/d (max dose 2.4 g/d)
  - Naproxen 250–500 mg 2 ×/d (max dose 1.5 g/d for limited time)

- Cyclooxygenase-2 (COX-2) inhibitor
  - Celecoxib 100–200 mg 1–2 ×/d
  - Use lowest effective dose for shortest duration possible.

Second Line

- Oral glucocorticoids such as prednisone if local glucocorticoid injections fail
  - Typical short course (ie, 60 mg for 5 days)

- Can use a taper dose.

266
OSTEITIS PUBIS, UROLOGIC CONSIDERATIONS

SURGERY/OTHER PROCEDURES
- Glucocorticoid injection in joint may be useful for cases refractory to rest and NSAIDs (4)
  - Any steroid preparation can be used based on provider preference
    - Include an adjuvant anesthetic
  - Various surgical techniques can be used for cases refractory to medical management
    - Curettage
    - Wedge resection
    - Wide resection
    - Arthrodesis
  - If bone anchors are in place, their removal may be necessary

ADDITIONAL TREATMENT
- Radiation Therapy
  - Has been attempted in the past with mixed results, but not recommended due to risk of neoplasia
- Additional Therapies
  - Cryotherapy, ultrasound therapy, laser therapy, and electric stimulation have been used with variable success in athletic osteitis pubis
    - No data on success of these modalities for nonathlete populations
  - Anticoagulant therapy with heparin has been suggested as a possible treatment in a postoperative setting with some minimal success

COMPLEMENTARY & ALTERNATIVE THERAPIES
- Physical therapy

ONGOING CARE

PROGNOSIS
- Typically a drawn out and variable clinical course
  - Symptoms can last several months to several years
  - Operative procedures may be needed in 5–10% of cases

COMPLICATIONS
- Wedge or wide resection of pubic symphysis—risk of posterior instability of pelvic girdle leading to damage to sacroiliac joints
- Arthrodesis—risk of nonunion or death of bone graft site requiring additional surgery

FOLLOW-UP
- Patient Monitoring
  - Follow-up depends on patient symptomatology and procedures obtained
- Patient Resources
  - N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Suprapubic Pain, General Considerations
- Sports Hernia (Athletic Pubalgia, Sportsman’s Hernia)
- Osteitis Pubis Images

CODES
- ICD-9 733.5 Osteitis condensans
- ICD-10 M85.38 Osteitis condensans, other site

CLINICAL/SURGICAL PEARLS
- Osteitis pubis pain and osteomyelitis pain worse when walking or when rising from a seated position.
- Essential to rule out osteomyelitis as a more significant cause.
- Rarely osteitis pubis and osteomyelitis of the pubis can coexist.
- To distinguish between osteomyelitis and osteitis pubis, a biopsy and culture of the affected area are necessary.
- Suspect the condition in a urologic patient where the pubic symphysis has been involved in urologic surgical intervention such as bone anchors or sling procedures.
OVERACTIVE BLADDER (OAB)

Nima Baradaran, MD
Samuel Walker Nickles
Eric S. Rozen, MD, FACS

BASICS

DESCRIPTION
• OAB is defined as a symptom syndrome consisting of urinary urgency, with or without incontinence, usually with urinary frequency and nocturia in the absence of causative factors or other identified pathologic conditions causing such symptoms.
• Urinary urgency is the key symptom.

ALERT
• OAB is not synonymous with detrusor overactivity (DO, strictly a urodynamic term) and should be distinguished from bladder pain syndrome.

EPIDEMIOLOGY
Incidence
Overall: 10.2–17.4% in adult males and 7.7–31.3% in adult females.
• Prevalence
  ≈16% of men and women over 40 suffer from OAB; the prevalence increases to 31% and 42%, respectively in patients >75 yr. OAB is more common in females.

RISK FACTORS
• Neurourologic: Stroke, Parkinson disease, multiple sclerosis, spinal injury, etc.
• Neuroendocrine: Cauterian, insulin-dependent diabetes mellitus, female gender, Depression, Aging associated with estrogen deficiency, Overactive bladder, Arthritis, Increased BMI.

GENETICS
For OAB, a definite genetic link is not well established.

PATHOPHYSIOLOGY
• Not well established or understood.
• DO is found in some but not all patients with OAB.
• Urthelial: afferent and efferent innervation, connective tissue, smooth muscle, pharmacologic (receptors, neurotransmitters, peptides, etc.), hormones, and other factors may contribute to OAB in individual patients.
• Ultimately, OAB results from either an afferent mechanism (underlying urgency), or a neurogenic or myogenic source or a combination of these.

ASSOCIATED CONDITIONS
• Post-void dribble
• BS
• High caffeine intake
• Depression/anxiety
• OB
• Smoking
• ADHD
• Obesity

GENERAL PREVENTION
Currently there are no known preventative measures to reduce the potential for development of OAB.

DIAGNOSIS

HISTORY
• Duration of symptoms
• Quantitative assessment of urinary frequency, nocturia, and incontinence (pad use)
• Documentation of urgency
• Quantitation of daily fluid intake
• Aggravating factors (caffeine, stress, etc.)
• Presence of dysuria, hematuria
• Response to prior therapy

ALERT
• GU history including childhood voiding dysfunction, prior surgery (BPH, urothelial stricture, stricture, etc.)
• History should include assessment of the impact of the disorder on daily life (OQL-1 and ICIQ-1 for urinary incontinence and OAB-q (3) for men and women with OAB specifically).

Medical/surgical/urogyn history (especially if associated with the initial symptom onset):
• Prior pelvic surgery: Pelvis, hysterectomy, anti-incontinence surgery. History of radiation therapy, etc.
• Pregnancy especially vaginal delivery/episiotomy
• Urinary especially vaginal delivery/episiotomy
• BOW (frequency, urgency, dysuria)
• Bowel function: Constipation

Neurologic:
• Neurologic history or events (eg, CVA/TIA, MS, Parkinson disease, trauma, back surgery, etc.)
• Neurologic exam including perineal sensation, bulbocavernous reflex, anal wink, resting, and volitional sphincter tone, mental status/cognitive function
• Abdominal masses, bladder distention
• Medical comorbidities: Congestive heart failure (CHF), diabetes, obesity, wiuos sufficiency, BPH, sleep apnea, etc.
• Medications (diabetes, prescription, OTC)
• Menopausal status and hormonal replacement: Contributes to atrophic vaginitis/urethritis
• Use of tobacco, alcohol, fluid intake, caffeine, etc.

PHYSICAL EXAM
General exam:
• Abdominal masses, bladder distention
• Mental status/cognitive function
• Neurologic exam including perinatal sensation, anal wink, resting, and volitional sphincter tone, bulbocavernous reflex
• Kneeling deep tendon reflexes:Sacral nerve compromise/injury

Pelvic exam:
• Condition of vaginal mucosa: Atrophy (thinning, pallor), narrowing of introitus, inflammation
• Kegel/bulbocavernous (BC) reflex

Urinalysis, urine cultures:
• Urinalysis, urine cultures: Possible diabetes, Hematuria: Possible kidney/bladder pathology, Proteines: Kidney/Chronic disease, Cytology: Atypia, urothelial carcinoma

Urinary urgency is the key symptom. OAB is not synonymous with detrusor overactivity (DO, strictly a urodynamic term) and should be distinguished from bladder pain syndrome.

DIFFERENTIAL DIAGNOSIS

Bladder Outlet Obstruction
Bladder cancer/carcinoma in situ
Bladder outlet obstruction/prostatitis hypertrophy
Congenital heart failure
Dysmenorrheal/vaginal endometriosis
Dysuria
Interstitial cystitis/painful bladder syndrome
Pelvic pain syndrome
Medications
Neurogenic bladder
Pelvic organ prolapse
Nutritional deficiencies
Sexually transmitted infection
Stress incontinence
Urethral diverticulum
Urinary tract infection

DIAGNOSTIC TESTS & INTERPRETATION

Urinalysis, urine cultures:
• Urinalysis, urine cultures: Possible diabetes, Hematuria: Possible kidney/bladder pathology, Proteines: Kidney/Chronic disease, Cytology: Atypia, urothelial carcinoma
• Response to prior therapy

GU history including childhood voiding dysfunction, prior surgery (BPH, urothelial stricture, stricture, etc.)
• History should include assessment of the impact of the disorder on daily life (OQL-1 and ICIQ-1 for urinary incontinence and OAB-q (3) for men and women with OAB specifically).

Medical/surgical/urogyn history (especially if associated with the initial symptom onset):
• Prior pelvic surgery: Pelvis, hysterectomy, anti-incontinence surgery. History of radiation therapy, etc.
• Pregnancy especially vaginal delivery/episiotomy
• Urinary especially vaginal delivery/episiotomy
• BOW (frequency, urgency, dysuria)
• Bowel function: Constipation

Neurologic:
• Neurologic history or events (eg, CVA/TIA, MS, Parkinson disease, trauma, back surgery, etc.)
• Neurologic exam including perineal sensation, bulbocavernous reflex, anal wink, resting, and volitional sphincter tone, mental status/cognitive function
• Abdominal masses, bladder distention
• Medical comorbidities: Congestive heart failure (CHF), diabetes, obesity, wiuos sufficiency, BPH, sleep apnea, etc.
• Medications (diabetes, prescription, OTC)
• Menopausal status and hormonal replacement: Contributes to atrophic vaginitis/urethritis
• Use of tobacco, alcohol, fluid intake, caffeine, etc.

PHYSICAL EXAM
General exam:
• Abdominal masses, bladder distention
• Mental status/cognitive function
• Neurologic exam including perinatal sensation, anal wink, resting, and volitional sphincter tone, bulbocavernous reflex

Pelvic exam:
• Condition of vaginal mucosa: Atrophy (thinning, pallor), narrowing of introitus, inflammation
• Kegel/bulbocavernous (BC) reflex

Urinalysis, urine cultures:
• Urinalysis, urine cultures: Possible diabetes, Hematuria: Possible kidney/bladder pathology, Proteines: Kidney/Chronic disease, Cytology: Atypia, urothelial carcinoma

Urinary urgency is the key symptom. OAB is not synonymous with detrusor overactivity (DO, strictly a urodynamic term) and should be distinguished from bladder pain syndrome.
Ongoing Care

Patient Monitoring
Depending on treatment modality dose follow-up with urologist or primary care physician is necessary

Follow-Up

Prognosis

Varies according to severity of disorder and compliance of the patient
50–80% of patients respond to combination of behavioral modification, pelvic floor therapy, and pharmacotherapy

Complications

Antimuscarinic agents are contraindicated in narrow angle glaucoma and patients should be aware of side effects (dry mouth, constipation, etc.)

Augmentation cystoplasty may lead to metabolic abnormalities and short bowel syndrome.

SNS implant site complications include infection and pain.

Botulinum toxin is associated with UTI and urinary retention

Surgical/Other Procedures (4)

Augmentation enteropyeloplasty: Using a portion of GI tract to increase bladder capacity. Usually involves use of balloon

Auto-augmentation: Incision of detrusor muscle creating a pseudodiverticulum (most commonly performed in pediatric age group)

Urinary diversion such as Birkh bilateral ureteroileostomy, rarely needed

Clinical use of endoscopic bladder transection, bladder shaveotomy, or transurethral phenol injection is no longer recommended for nonneurogenic OAB

Additional Treatment

Radiation Therapy

Additional Therapies

- Non-OAB approved
  - Ergonomics for females (topical or oral)
  - Tricyclic antidepressants (imipramine, etc.)
  - For intractable OAB, options are appliances, catheters (urethral), and pads with careful attention to skin care

Complementary & Alternative Therapies

- Acupuncture
  - Cognitive therapy

References


5. 1 evidence.

ADDISONAL READING


2. Acupuncture


ADDITIONAL MEASURES

- Lifestyle modifications and bladder/pelvic floor training in conjunction with pharmacotherapy is 1st-line therapy and may mandate of treatment
- Behavioral therapy:
  - Dietary and lifestyle modifications (weight loss, reduce caffeine intake, EtOH, and nicotine cessation)
  - Bladder retraining (education, diaries, self-monitoring)
- Pelvic floor physiotherapy: To reestablish inhibitory control over bladder storage
- Pelvic floor exercises (Kegel)
- Adjunctive measures include biofeedback, electrical stimulation, vaginal weights/cream, magnetic therapy, etc.

Medication

First Line

- Antimuscarinics: Inhibits the effect of acetylcholine at postjuncional muscarinic receptors on detrusor muscle cells. All used to treat OAB and all have Level 1 evidence.
  - Tolftepine (1–2 mg)
  - Trospium ER (20 mg)
  - Darifenacin (7.5–15 mg)
  - Oxybutynin (8–10 mg; XL 5–30 mg; patch every weekly)
  - Methadone (4–8 mg)
- β-3-adrenergic agonist agent: Promotes detrusor muscle relaxation
  - Mirabegron (25–50 mg)

Second Line

- Urgent PC (PTNS): Tibial nerve stimulation
  - Repeat procedure every 4–12 mo
- Interstim (sacral neuromodulation); Implantation of sacral nerves: Modulates activities of bladder, sphincter, and pelvic floor muscles
- Intravesical botulinum toxin (onabotulinumtoxinA) injection
- Address both motor efferent innervation and sensory afferent nerves that contribute to OAB. It is a transient effect requiring periodic retreatment at intervals of 4–12 mo.
- Anticholinergic and /or α-antagonists
- Bladder retraining (education, diaries, self-monitoring)

Surgery/other procedures (4)

- Augmentation enteropyeloplasty: Using a portion of GI tract to increase bladder capacity. Usually involves use of balloon
- Auto-augmentation: Incision of detrusor muscle creating a pseudodiverticulum (most commonly performed in pediatric age group)
- Urinary diversion such as Birkh bilateral ureteroileostomy, rarely needed
- Clinical use of endoscopic bladder transection, bladder shaveotomy, or transurethral phenol injection is no longer recommended for nonneurogenic OAB

TREATMENT

General measures

- Lifestyle modifications and bladder/pelvic floor training in conjunction with pharmacotherapy is 1st-line therapy and may mandate of treatment
- Behavioral therapy:
  - Dietary and lifestyle modifications (weight loss, reduce caffeine intake, EtOH, and nicotine cessation)
  - Bladder retraining (education, diaries, self-monitoring)
- Pelvic floor physiotherapy: To reestablish inhibitory control over bladder storage
- Pelvic floor exercises (Kegel)
- Adjunctive measures include biofeedback, electrical stimulation, vaginal weights/cream, magnetic therapy, etc.

Medication

First Line

- Antimuscarinics: Inhibits the effect of acetylcholine at postjuncional muscarinic receptors on detrusor muscle cells. All used to treat OAB and all have Level 1 evidence.
  - Tolftepine (1–2 mg)
  - Trospium ER (20 mg)
  - Darifenacin (7.5–15 mg)
  - Oxybutynin (8–10 mg; XL 5–30 mg; patch every weekly)
  - Methadone (4–8 mg)
- β-3-adrenergic agonist agent: Promotes detrusor muscle relaxation
  - Mirabegron (25–50 mg)

Second Line

- Urgent PC (PTNS): Tibial nerve stimulation
  - Repeat procedure every 4–12 mo
- Interstim (sacral neuromodulation); Implantation of sacral nerves: Modulates activities of bladder, sphincter, and pelvic floor muscles
- Intravesical botulinum toxin (onabotulinumtoxinA) injection
- Address both motor efferent innervation and sensory afferent nerves that contribute to OAB. It is a transient effect requiring periodic retreatment at intervals of 4–12 mo.
- Anticholinergic and /or α-antagonists
- Bladder retraining (education, diaries, self-monitoring)
PAPILLARY NECROSIS, RENAL
Demetrius H. Bagley, MD, FACS
Kelly A. Healy, MD

PATHOPHYSIOLOGY
- The renal papilla normally exists in the state of hypoxia because of the blood flow in the vasa recta which can be affected further with conditions that reduce blood flow
- Perfusion compromise in diabetes mellitus
- Diminution in blood flow because of stenosing of blood cells (sickle cell disease)
- Infection that causes infarction of the interstitium can lead to compression of the medullary vasculature
- Analgesic use causes COX inhibition and decreased prostaglandin production. This leads to decreased vascular perfusion, vasoconstriction and can cause ischemic necrosis
- Some medications can cause direct interstitial cell necrosis and decrease in prostaglandin production
- The necrotic, soft tissue can cause unilateral or bilateral ureteral obstruction

ASSOCIATED CONDITIONS
- Analgesic abuse
- Diabetic mellitus
- Pyelonephritis
- Sickle cell disease
- Urinary tract obstruction

GENERAL PREVENTION
- Treatment of underlying disorders including diabetes or sickle disease
- Avoidance of analgesic use

DIAGNOSIS

HISTORY
- May present with hematuria or obstruction or flank pain (2)
- With infection, fever, chills, dysuria, frequency, urgency, flank pain, and renal colic can occur
- Rarely, bilateral ureteral obstruction with necrotic tissue can present as acute oliguric renal failure

PHYSICAL EXAM
- Costovertebral angle tenderness
- Fever

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis and urine culture
- Proteinuria, glycosuria, and low urine-specific gravity
- Epithelial cells and casts may be present
- CBC may demonstrate leukocytosis
- Metabolic panel can demonstrate azotemia and elevated creatinine

Imaging
- CT has become the imaging modality of choice
  - Contrast images show:
    - Ring shadows in the medulla
    - Contrast filled defects
    - Retrograde pyelogram:
      - Useful in patients with azotemia, contrast sensitivity, or other situations where intravenous contrast is contraindicated
      - Findings may reveal a club-shaped calyx or a filling defect in the ureter

Diagnostic Procedures/Surgery
Patient presenting with hematuria needs a full urologic work-up even if papillary necrosis is confirmed.

Pathologic Findings
- The common features depressed areas of cortical atrophy (3)
- Papilla shows various stages of necrosis, dequamation, and sloughing
- Focal necrosis: Involves only the tip of the papilla
- Diffuse necrosis: The entire papilla and portions of the medulla are involved
- Microscopically, changes of papilla may be a patchy appearance or complete coagulative necrosis
- Glimmer are typically unchanged

DIFFERENTIAL DIAGNOSIS
- Acute tubular necrosis
- Neoplastic process
- Carcinoma of the ureter or bladder
- NSAID abuse and/or overuse
- Pyelonephritis
- Renal trauma
- TB
- Unilateral stone disease

DESCRIPTION
- Renal papillary necrosis is ischemic necrosis of the papillae and occasionally the medullary pyramids
- The clinical course may be acute and rapidly progressive or chronic
  - Acute forms are symptomatic and may present with pyrexia, pyelonephritis, and hematuria
  - Typically chronic forms are asymptomatic and discovered incidentally on radiographic studies

RISK FACTORS
- Acute presenting symptoms include hematuria, flank or abdominal pain, and fever and chills

EPIDEMIOLOGY
Incidence
Most cases occur after the 6th decade of life and papillary necrosis is uncommon in patients <40 yr
- Female > Male (1.1:1.0) [1]

Prevalence
N/A

ASSOCIATED CONDITIONS
- Diabetes mellitus
- Sickle cell trait or disease
- Pyelonephritis
- Urinary tract obstruction of any cause
- Antiretroviral treatment

GENETICS
N/A
PAPILLARY NECROSIS, RENAL

TREATMENT

GENERAL MEASURES
- Hydration, oral or intravenous
- Glycemic control, if diabetic
- Definition and treatment of sickle disease

MEDICATION

First Line
- Cessation of any associated/causative medications including analgesics
- Treatment of underlying cause of ischemia
- Broad-spectrum antibiotics, if associated with pyelonephritis

Second Line
N/A

SURGERY/OTHER PROCEDURES
- When a patient presents with acute urinary obstruction, drainage is indicated with percutaneous nephrostomy, ureteral stent placement, or endoscopic/ureteroscopic removal of obstructing sloughed tissue
- In the nonacute case, renal pelvic or ureteral filling defect can be electively evaluated with ureteroscopy
- Nephrectomy is rarely warranted

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
Depends on the basis for the ischemia, the complicating factors, and the amount of necrosis

COMPLICATIONS
- Infection may develop in the desquamated necrotic papilla
- Calculi can develop on the base of the sloughed papilla
- Obstruction can develop along the ureter from multiple sloughed papillae

FOLLOW-UP

Patient Monitoring
- Monitoring includes the kidney itself for further necrosis and for changes in function
- Causes of ischemia should be closely monitored

Patient Resources
http://www.scripps.org/articles/1151-renal-papillary-necrosis

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Diabetes Mellitus, Urologic Considerations
- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Hematuria, Gross and Microscopic, Adult
- Nephropathy, Analgesic
- Papillary Necrosis, Renal Image
- Sickle Cell Disease, Urologic Considerations

CODES

ICD9
- 594.7 Acute kidney failure with lesion of renal medullary (papillary) necrosis
- 590.80 Pyelonephritis, unspecified
- 591 Hydronephrosis

ICD10
- N19.7 Acute kidney failure with lesion of renal medullary (papillary) necrosis
- N19.80 Pyelonephritis, unspecified
- N91 Hydronephrosis

CLINICAL/SURGICAL PEARLS
- Gross hematuria in a patient with sickle cell disease suggests papillary necrosis.
PARATESTICULAR TUMORS
Mohamed T. Ismail, MD
Sallyanne M. Fisher, MSN, FNP-C, CUNP

BASICS

DESCRIPTION
- Intratesticular tumors involving the testicular tunic, epididymis, or cord structures. Can be benign (~70%) or malignant (~30%).
- The paratesticular region includes: contents of the spermatic cord, testicular tumors, epididymis, and vesicovaginal remnant (appendages testis and epididymis).
- 50% of extratesticular tumors are found within the spermatic cord.
- Of these, 10% are malignant.
- The majority represent benign lipomas.
- Mesenchymal tumors of the spermatic cord include rhabdomyosarcoma, leiomyosarcoma, liposarcoma, lipoma, fibrosarcoma, and myxochondrosarcoma.
- The most common paratesticular tumor in children is rhabdomyosarcoma, which accounts for ~24-40% of all paratesticular tumors.
- Adenomatoid tumor accounts for 30% of epididymis tumors and is a benign:
- Typically seen in 3rd and 4th decades of life.
- Rarely arises in testicular tunica or spermatic cord (1%).
- Leiomyosarcoma is the most common type of paratesticular sarcoma in adults:
- Incidence peaks in the 6th and 7th decades.
- Can be bilateral.
- May accompany a hydrocele or hernia.
- Cytoplasm is a benign tumor that involves the epididymis in young adults:
- Ven-Hill and Hill syndrome (2%)
- Typically bilateral.
- Malignant mesothelioma presents in older patients (55–75) and usually presents in association with a hydrocele.
- Malignant lymphoma: Cord structures are frequently invaded by testicular lymphoma, but primary lymphomas do occur rarely.
- Epidermoid cysts occur in up to 40% of men.
- 70% of these are true cysts and contain lymphatic fluid (1%).

EPIDEMIOLOGY

Incidence
- The exact incidence of paratesticular soft tissue neoplasms is difficult to estimate.
- Rhabdomyosarcoma:
- Occurs primarily in children and adolescents during the 1st 2 decades of life.
- Racial differential: White (3:1), Black (3:1)
- Leiomyosarcoma: Incidence varies, ~110 reported cases in the literature.

Prevalence
- Primary malignancies of the epididymis or paratesticular structures in adults are extremely rare.
- Rhabdomyosarcoma accounts for a large proportion of the paratesticular tumors in the pediatric population.

RISK FACTORS
- Marijuana and cocaine use in the parents is associated with rhabdomyosarcoma.
- Von-Hippel-Lindau syndrome is associated with epithelioid sarcomas.
- Equine semen is prone to scrotal injury with up to 77% evidence of scrotal pathology (1%).

GENETICS
- Partial monosomy of chromosome 11 often leads to embryonal rhabdomyosarcoma.
- Alveolar rhabdomyosarcoma is characterized by translocations t(2;13)(q35;q14) or t(1;13)(p36;q14); this subtype carries a poor prognosis.

PATHOPHYSIOLOGY
- Electron microscopy is very helpful in differentiating the type of sarcoma.
- Subtypes of sarcoma include rhabdomyosarcoma, leiomyosarcoma, liposarcoma, fibrosarcoma, malignant fibrous histiocytoma, and desmoplastic round cell tumor.
- Soft tissue sarcomas tend to infiltrate local tissues and are not limited to the testis.
- Delays in presentation due to embarrassment.
- Testicular vs. paratesticular:
- Solid vs. cystic (2%).
- Solid lesions almost always require exploration.
- Simple cystic lesions are mostly benign.
- Computed tomography (CT) of the abdomen and pelvis with and without contrast for staging.
- Paratesticular tumors may spread to retroperitoneal lymph nodes or hematogenously depending on the histology of the primary tumor.
- Chest radiograph.
- CT abdomen or pelvic metastases are seen.
- Clinical staging of retroperitoneal lymph nodes.
- Radioscopy bone scan.
- Especially for elevated alkaline phosphatase or symptoms with rhabdomyosarcoma.

DIAGNOSIS

HISTORY
- Patient complains of mass within his scrotum, distinct from the testicle:
- Typically painless.
- Delays in presentation due to embarrassment.
- Occult complete history to include accompanying symptoms, duration, and constitutional changes (2%).

PHYSICAL EXAM
- Palpation of the testes, epididymis, and cord structures bilaterally including the inguinal region:
- Rhabdomyosarcoma reveals a firm mass that is usually distinct from the testis.
- Adenomatoid tumor appears clinically as small solid lumps and is most commonly found at the head of the epididymis, testicular tunics, or spermatic cord.
- Cystadenoma presents as asymptomatic cystic lumps and are bilateral in up to 1/3 of cases.
- Leiomyosarcoma normally presents as a discrete nodular mass, frequently near the spermatic cord and entirely separate from the testicle.
- Liposarcoma usually presents in an older patient as a large fatty-applying mass.
- Lymphoma presents as a hard, tender mass, separate from the testis; seen in young adults.
- Electron microscopy suggests a fluid-filled lesion such as a hydrocele.
- Cervical exam of the groin is necessary to rule out hernia and to evaluate for lymphadenopathy.
- Masculine are occasionally accompanied by hydrocele.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Ultrasonography (midstream) and culture if epididymitis is suspected (1%).
- Tumor markers to include α-fetoprotein (AFP), or human chorionic gonadotropin (hCG), α-fetoprotein (AFP), or lactate dehydrogenase (LDH) should be sent if the origin of the tumor is in question.

Imaging
- Gold standard: Scrotal ultrasound (US)/CT (1%)
- To evaluate location and characteristics of the lesion within the scrotum.
- Testicular vs. paratesticular.
- Solid vs. cystic (2%).
- Solid lesions almost always require exploration.
- Simple cystic lesions are mostly benign.
- Computed tomography (CT) of the abdomen and pelvis with and without contrast for staging.
- Paratesticular tumors may spread to retroperitoneal lymph nodes or hematogenously depending on the histology of the primary tumor.
- Chest radiograph.
- CT abdomen or pelvic metastases are seen.
- Clinical staging of retroperitoneal lymph nodes.
- Radioscopy bone scan.
- Especially for elevated alkaline phosphatase or symptoms with rhabdomyosarcoma.

Diagnostic Procedures/Surgery
- Surgery is often diagnostic and therapeutic.

ALERT
- Pericapsular biopsies are contraindicated due to the documented risk of seeding in the scrotal wall with malignancy.
- Bone marrow aspirate:
- Routine part of staging at a time of diagnosis for rhabdomyosarcoma.

Pathologic Findings
- Electron microscopy can help differentiate between the different types of sarcomas; these differences can be quite subtle.
- Leiomyosarcoma spreads 1st by lymphatics, then hematogenously, and last by local extension.

DIFFERENTIAL DIAGNOSIS
- Adenomatoid tumors:
- Most common benign paratesticular tumor.
- Angiomylipoblastoma.
- Cystadenoma of the epididymis.
- Epithelioid cyst.
- Liposarcoma.
- Fibrous pseudotumor of testicular tunic.
- Rhabdomyosarcoma.
- Leiomyosarcoma.
- Lipoma of the spermatic cord.
- Leiomyosarcoma.
- Malignant fibrous histiocytoma.
- Mesotheloma, benign, testicular tunic.
- Mesotheloma, malignant, testicular vaginismus.
- Associated with asbestos exposure.
Surgery/Other Procedures

- Testicular or paratesticular lesions suspected to be malignant should be removed by radical inguinal orchietomy with high ligation of the spermatic cord.
- Early clamping of the cord limits hematogenous spread in leiomyosarcoma.
- Rhabdomyosarcoma: Consider hemiscrotectomy for any degree of scrotal wall involvement.
- The Intergroup rhabdomyosarcoma study group (IRSG) recommended radical inguinal orchietomy and routine RPLND in all males >10 yr and in boys <10 with metastasis noted on imaging.
- Complete surgical excision with a negative margin has significant impact on local recurrence and overall survival in soft tissue sarcomas.

Additional Treatment Radiation Therapy

- Rhabdomyosarcoma: -4,000-6,000 cGy of radiation (15 Gy) over 5 wk.
- Dose and port size determined by the tumor’s primary site, patient age, and tumor burden.

Additional Therapies

- Complementary & Alternative Therapies
- Radiation Therapy
- Chemotherapy for malignant rhabdomyosarcoma
- Vincristine, cyclophosphamide, and actinomycin D-based chemotherapy in patients with gross or microscopic residual disease
- Radical inguinal orchiectomy with high ligation of the spermatic cord for any degree of scrotal wall involvement.

Complications

- Disease associated death in ~10% of malignant cases.
- Treatment associated:
  - Metastasis and/or incomplete primary resection lead to poorer overall prognosis.
  - Adjuvant treatment via radiation is warranted.

Follow-up

- Serial US for equivocal lesions, especially in the epididymis.
- Biopsy is recommended for uncertain or indeterminate lesions.
- Surveillance after local recurrence.

- Additional Therapies
- Complementary & Alternative Therapies
- Radiation Therapy
- Chemotherapy for malignant rhabdomyosarcoma
- Vincristine, cyclophosphamide, and actinomycin D-based chemotherapy in patients with gross or microscopic residual disease
- Radical inguinal orchiectomy with high ligation of the spermatic cord for any degree of scrotal wall involvement.
- The Intergroup rhabdomyosarcoma study group (IRSG) recommended radical inguinal orchietomy and routine RPLND in all males >10 yr and in boys <10 with metastasis noted on imaging.
- Complete surgical excision with a negative margin has significant impact on local recurrence and overall survival in soft tissue sarcomas.

Additional Reading


See Also (Topic, Algorithm, Media)

- Adenomatous Tumors (Testis/Unspecified)
- Epididymis, Mass (Epididymal Tumor and Cysts)
- Epididymis, Cystadenoma
- Fibrous Pseudotumor of Testicular Tunic
- Hydrocele of the Spermatic Cord
- IRS (Intergroup Rhabdomyosarcoma Study) Clinical Classification
- Mesothelioma, Benign, Testicular Tunic
- Mesothelioma, Malignant, Testicular Tunic
- Paratesticular Tumors Image (T)
- Rhabdomyosarcoma, Pediatric
- Scrotum and Testicle, Mass
- Spermatic Cord Mass and Tumors

Codes

- ICD9: 171.9 Malignant neoplasm of other specified sites of male genital organs;
- 222.8 Benign neoplasm of other specified sites of male genital organs;
- 239.3 Neoplasm of unspecified nature of other genital organs.

- ICD10: C63.7 Malignant neoplasm of other specified male genital organs;
- D29.8 Benign neoplasm of other specified male genital organs;
- E44.5 Neoplasm of unspecified behavior of other genital organs.

Clinical/Surgical Pearls

- It is impossible to distinguish a benign from a malignant tumor based on physical exam.
- Can be indistinguishable from testicular masses.
- Penetrating biopsies contraindicated due to documented seeding in scrotal wall with malignancy.


PARKINSON DISEASE, UROLOGIC CONSIDERATIONS

Robert C. Flanigan, MD, FACS
Sam J. Brancato, MD

BASICS

DESCRIPTION
Parkinson disease (PD), also called paralysis agitans, is a neurodegenerative disorder associated with loss of dopaminergic neurons.

• Three cardinal features are rest tremor, rigidity, and bradykinesia.
• Postural instability, sometimes deemed a cardinal feature, is nonspecific and usually absent in early disease.
• Autonomic dysfunction is manifested by urinary urgency and frequency, constipation, and orthostatic hypotension. Retention can also be seen.

EPIDEMIOLOGY

Incidence
• PD incidence increases with age, from 17.4 cases per 100,000 persons per year between 50–59 yr of age to 93.1 in 100,000 persons per year between 70–79 yr of age.
• Life risk of developing PD is 1.5%.
• Voiding dysfunction occurs in 40–70% of patients with PD.

Prevalence
N/A

RISK FACTORS

• Men are about 1.5 times more likely than women to develop PD.
• The median age of onset is 65 yr and the mean duration of the disease from diagnosis to death is 15 yr.
• Young-onset PD affects 5–10% of patients with the initial symptom arising before the age of 50 yr.

Genetics

• About 10% of patients with PD have a 10-q degree relative with the disease, typically without a clear mode of inheritance.
• Mutations in two genes cause autosomal dominant forms of PD:
  – α-Synuclein gene (SNCA): Located on chromosome 4q (rarely prominent early in the course of PD) (constipation) and sexual dysfunction
  – Leucine-rich repeat kinase 2 (LRRK2): located on chromosome 12q (often prominent early in the course of PD).
• To date, approximately 16 risk loci have been known to contain disease-causing mutations.

PATHOPHYSIOLOGY (1)

• The net effect of the basal ganglia on micturition is inhibitory, which is abolished due to cell loss in the substantia nigra.
  – The bladder detrusor can thus become unstable and result in urgency and frequency with urge incontinence.
  – The smooth sphincter is synergic, however pseudosynergism, as well as delay in striated sphincter relaxation (bradykinesia) leading to urinary retention (2).
• PD can be also associated with bowel dysfunction (constipation) and sexual dysfunction.

• Urinary symptoms tend to become worse in the course of the disease. Early on other reversible causes such as benign prostatic enlargement in men can cause similar symptoms.
• Centrally acting anticholinergic drugs such as trihexyphenidyl and benztropine have been used to treat PD and can cause urinary retention.

ASSOCIATED CONDITIONS

• Dementia
• Depression
• Erectile dysfunction
• Sleep disturbance
• Autonomic dysfunction
• Parkinson disease

GENERAL PREVENTION

N/A

DIAGNOSIS

HISTORY

• Urinary symptoms usually appear after the onset of neurologic symptoms.
• Assess for LUTS:
  – Storage symptoms: Most common, include nocturia, urgency, frequency, and incontinence.
  – Voiding symptoms: Difficult initiating stream, weak FOS/prolonged urination, and straining.
• Elevated PVRs are uncommon in PD patients.
• Assess for concurrent urologic conditions:
  – BPH in men and SUI in women.
• Assess for polypharmacy:
  – Central acting anticholinergics listed below can be used in younger patients in whom tremor is the major symptom but may exacerbate incomplete emptying and urinary retention.
  – Benzhexol meylrate (Cogentin), trihexyphenidyl (Artane), biperiden (Akineton), orphenadrine (Norflex, Flexerin)

PHYSICAL EXAM

• Cardiac features are rest tremor, rigidity, and bradykinesia.
• Slow, pill-rolling tremor of the hands (4–6 cycles/s) seen primarily at rest.
• Abolished by use of the affected hand.
• Agitated by stress and cold weather.
• Facial expressions can be immobile or rigid and speech slowed.
• Slow, shuffling gait with loss of normal arm swing (usually prominent early in the course of PD).

• Assessment of pelvic floor reflexes, motor and sensory.
  – Dystonic postural tremor.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• No diagnostic test exists for PD as the diagnosis is clinical.
• Standard urologic evaluation (UA, CBC) based on initial symptoms.

Imaging

• Brain MRI is reserved for patients suspected of having PD who fail to respond to therapeutic doses of L-dopa administered to exclude rare secondary causes.
• Routine urologic imaging is not required.

Diagnostic Procedures/Surgery

• PD is a clinical diagnosis, although the definition of PD is a postmortem finding based on the neuropathologic examination.

Uradyaynics

• Deterioration overactivity is the most common symptom.
• Sphincteric instability in the striated sphincter during involuntary bladder contraction is common, however, this does not cause obstruction.
• Pseudodysuria may occur, as well as delay in striated sphincter (bradykinesia) relaxation at the onset of voluntary micturition, both of which can be misinterpreted as true dyskinesia.
• Detrusor voiding relatively rare in PD and when present it is often be due to anticholinergic medications.

• Detrusor is a useful tool for investigating concomitant obstruction secondary to BPH.
Pathologic Findings

Irrespective Lewy bodies and Lewy neurites are the pathologic hallmarks of PD.

Differential Diagnosis

- Parkinson
  - Multiple system atrophy
  - Normal aging
  - Vascular parkinsonism (multiple infarcts within the basal ganglia and subcortical white matter)
  - Parkinson plus syndromes
  - Voiding dysfunction

General Measures

- For urologic symptoms of frequency, urgency, and incontinence, clinicians should offer behavioral therapies (eg, fluid management, clean intermittent catheterization) as 1st-line therapy.
- Evaluate medications that may result in urinary symptoms (such as retention/obstruction) with anticholinergic drugs such as trihexyphenidyl and benztropine used to treat some patients with PD.
- Assess for elevated PVRs, specifically if taking anticholinergics.
- Anticholinergic drugs such as trihexyphenidyl and benztropine may contribute to cognitive decline.
- Urinary incontinence due to detrusor overactivity may decrease urinary symptoms

Medication

First Line

- For urologic symptoms of frequency, urgency, and incontinence, anticholinergics are commonly used but should be monitored closely in elderly as they may contribute to cognitive decline.
  - oxybutynin 5 mg PO TID
  - Tolterodine 4 mg PO daily
  - Others (solifenacin, fesoterodine, darifenacin, trospium)

- β-3-Adrenergic agonist agent: Promotes detrusor muscle relaxation and can also be considered for obstructive bladder symptoms
  - Mirabegron (25–50 mg)

Second Line

- β-3-Adrenergic agonist agent: Promotes detrusor muscle relaxation and can also be considered for obstructive bladder symptoms
  - While not specifically approved for PD, is approved for treatment of urinary incontinence
  - Tolterodine LA 4 mg PO BID
  - Selective serotonin-norepinephrine reuptake inhibitors (SSNRI's): Duloxetine 20–40 mg PO BID
  - Selective serotonin reuptake inhibitors (SSRI's): Citalopram 20 mg PO BID
  - Tricyclic antidepressants (TCA): Imipramine 10–25 mg PO BID–TID

Surgery/Other Procedures

- Bladder outlet obstruction found on urodynamic testing

Additional Therapies

- Incontinence aids may be necessary and are primarily chosen by the degree of abscessing required and the ease of use. During the night, high absorbency pads are usually required.

Complementary & Alternative Therapies

- Dietary fiber, laxatives, and prokinetic drugs (such as serotonergic agonists) are used to treat PD-related bowel dysfunction.
- Ongoing Care

Prognosis

- PD is a progressive neurodegenerative disorder.
- Despite a variable disease course, the overall prognosis is poor with a mean duration of the disease from diagnosis to death of 15 y.

Complications

- Urinary incontinence
- Urinary retention

Follow-Up

- Assess for elevated PVRs, specifically if taking anticholinergics

Patient Monitoring

- Assess for elevated PVRs, specifically if taking anticholinergics

Patient Resources


References


Additional Reading


See Also (Topic, Algorithm, Media)

- Incontinence, Adult Males
- Incontinence, Adult Females
- Neurogenic Bladder, General

ICD Codes

- ICD-9 350.2 Paralyses of sphincters
- 788.41 Urinary frequency
- 788.63 Urgency of urination

ICD-10

- G30 Parkinson’s disease
- N39.41 Urge incontinence
- R55.9 Frequency of urination

Clinical/Surgical Pearls

- Cardiac features are rest tremor, rigidity, and bradykinesia.
- Urinary incontinence is a common feature of PD due to symptoms of obstructive bladder.
PELVIC ORGAN PROLAPSE (CYSTOCELE AND ENTEROCELE)

W. Stuart Reynolds, MD, MPH
Roger R. Dmochowski, MD, MMHC, FACS

BASICS

DESCRIPTION

Pelvic organ prolapse (POP): The descent of one or more of the anterior vaginal wall, posterior vaginal wall, uterosacral, or area of vagina (bilateral vault or cuff after hysterectomy)

Cystocele: Anatomic defect of the anterior vaginal wall in which bladder prolapses into the vagina

Enterocoele: Anatomic defect of the vaginal apex typically, small rectovaginal prolapse into the vagina

Rectocoele: Anatomic defect of the posterior vagina; the rectum prolapses into the vagina

Defects in any or many vaginal compartments (anterior, posterior, apex) may occur together

PREVALENCE

- 2% of US women report symptoms of vaginal bulging
- 40% of US women have POP on exam
- Women have an 11% lifetime risk of undergoing surgery for POP and/or UI by age 80

ASSOCIATED CONDITIONS

- Pelvic strain (high impact activity or work)
- Menopause
- Obesity
- Parity
- Race/ethnicity (Hispanic > White > African American)

RISK FACTORS

- Age
- Racemiethnicity (Hispanic > White > African American)
- Parity
- Obesity
- Menopause
- Prior POP surgery
- Menopause
- Pelvic strain (high impact activity or work)

GENETICS

- Inherited familial risk (sisters and mothers)
- 2-3 times more common if positive family history for POP
- Inherited collagen disorders (eg, Ehlers–Danlos syndrome)
- Genome-wide studies ongoing with several potential candidate genes identified, most related to elastic and collagen metabolism (eg, LAMC-1)

PATHOPHYSIOLOGY

- Integrated mander to the bony pelvic through the endopelvic fascial structure, suspensory ligaments, levator ani muscles, and pelvic organs help maintain the pelvic organs in the proper anatomic position in the pelvis.
- Classically, three levels of vaginal support are described:
  - Level I: Uterosacral and cardinal ligaments support upper 1/2 of vagina, cervix, and uterus.
  - Level II: Pubocervical and rectovaginal fascia attach laterally to the arcus tendineus fascia pelvis to support midportion of vagina
  - Level III: Direct attachment of vagina to urethra, perineal body, and levator ani muscles

DIAGNOSIS

HISTORY

- Assess for prolapse symptoms
  - Vaginal bulging, including visualization or palpation of a "bulge" in the vagina
  - Pelvic pressure, heaviness, or dragging sensation
  - Vaginal mucosal irritation, bleeding, discharge, and/or infection
- Provocative maneuvers (cough and Valsalva) to demonstrate urethral leakage; repeated with defecation
- Low backache, temporally associated with POP
- Splinting/digitation: Applying manual pressure to vagina or rectum to assist with voiding or defecation
- Vaginal mucosal irritation, bleeding, discharge, and/or infection
- Vaginal bulging, including visualization or palpation of a "bulge" in the vagina
- Vaginal pressure, heaviness, or dragging sensation
- Vaginal mucosal irritation, bleeding, discharge, and/or infection
- Abnormal examination findings:
  - Estrogen alone in postmenopausal with after menopause

PHYSICAL EXAM

- Useful to employ POP staging
  - POP quantification system (POPS)
    - Stage II: The prolapse is demonstrated
      - Stage I: Most distal portion of the prolapse is >1 cm above the level of the hymen
      - Stage II: Most distal portion of the prolapse is ≤1 cm below the hymen
    - Stage III: Complete eversion of the total length of the lower genital tract is demonstrated
  - Assessment of urinary incontinence
    - Provocative maneuvers (cough and Valsalva) to demonstrate urethral leakage, repeated with prolapse reduced to detect occult SUI

DIFFERENTIAL DIAGNOSIS

- Urethral diverticulum
- Cystocele
- Enterocele
- Rectocele
- Soft tissue vaginal mass
- Urinary incontinence

LAB

- Urinalysis and urine culture, as indicated

DIAGNOSTIC TESTS & INTERPRETATION

- Urethral function tests (leak point pressure, urethral pressure profilometry) assess urethral function and degree of SUI, if any

IMAGING

- Routine imaging is not indicated; imaging may supplement exam with complex cases
- Differentials:
  - Assess defecatory dysfunction, including degree of rectocele and rectal emptying
  - Voiding cystourethrogram
  - Urodynamic testing

- Allows dynamic assessment of pelvic organs and bladder volume
- Magnetic resonance imaging (MRI)
  - Allows dynamic imaging of functional relationships among the pelvic floor viscera and supporting structures, and assess pelvic pathology
- Expensive; clinical utility over exam alone not established

PATHOPHYSIOLOGY

- Relationships among the pelvic floor viscera and supporting structures
- Allows dynamic assessment of pelvic organs and bladder volume
- Magnetic resonance imaging (MRI)
  - Allows dynamic imaging of functional relationships among the pelvic floor viscera and supporting structures, and assess pelvic pathology
- Expensive; clinical utility over exam alone not established

TREATMENT

- General measures
  - Management is generally surgical
  - Bowel regimen for constipation
  - Hormone replacement, typical vaginal, for atrophic vaginitis
  - Estrogen alone in postmenopausal with after hysterectomy: estrogen and progesterone if uterus present, even if postmenopausal

MEDICATION

- First Line
- Second Line

276
**SURGERY/OTHER PROCEDURES**

**Additional Therapies**

**Radiation Therapy**

- Concomitant anti-incontinence procedure
  - Anterior colporrhaphy and paravaginal repair
  - Vaginal pessary: Supportive and space-occupying
- Vaginal apex fixation to the presacral fascia at S3–S4 using biologic or synthetic material
  - Transvaginal approach
  - Abdominal approach
- Colpocleisis
  - Partial colpocleisis (De La Fort colpocleisis)
- Uterosacral ligament fixation
  - Vaginal intercourse

- Mesh material complications occur in 10% of women;
- Requires routine maintenance and care (removal, cleaning, vaginal inspection)
- Synthetic mesh materials, if used in POP surgery, if anti-incontinence procedure not performed
- Perioperative complications of bleeding, pelvic organ injury, bladder dysfunction, infection
- Postoperative complications include vaginal and pelvic pain, vaginal shortening or narrowing, dyspareunia

**CLINICAL/SURGICAL PEARLS**

- Complete assessment of all vaginal compartments and symptoms, best with supervision of a physical therapist
- Requires routine maintenance and care (removal, cleaning, vaginal inspection)

**ADDITIONAL READING**


**CODES**

- ICD9: 618.6 Vaginal enterocele, congenital or acquired
- ICD10: N81.5 Vaginal enterocele

**REFERENCES**

2. Diwadker GB, Barber MD, Feiner B, et al. Prophylactic, synthetic MUS at time of vaginal POP surgery reduces need for additional surgery in women at 12 mo (OR 0.48, 95% CI 0.21–0.77 [46A])
3. Urethrocele
**PELVIC PAIN, FEMALE**
Kai-Wen Chuang, MD
Robert M. Moldwin, MD, FACS

**DIAGNOSIS**

**HISTORY**
- History of present illness
  - Urinary or rectal symptoms
  - Pain with defecation
  - Pain with bladder distension
  - Menstrual history
  - Past medical history
  - Family history

**PHYSICAL EXAM**
- Vital signs
- Head and neck exam
- Cardiovascular exam
- Respiratory exam
- Abdominal exam
- Pelvic exam
- Rectal exam
- Vaginal exam

**DIAGNOSTIC TESTS & INTERPRETATION**

**IMAGING**
- Ultrasound
- CT scan
- MRI
- Nuclear medicine
- Radiation therapy

**Pathologic Findings**
Based on diagnosis

**DIFFERENTIAL DIAGNOSIS**
- Gynecologic: Acute or chronic pelvic pain
- Urinary: UTI, bladder stones
- Gastrointestinal: Diverticulitis, appendicitis
- Musculoskeletal: Pelvic fracture, sacroiliac joint pain

**GENERAL PREVENTION**
- Prevent infection
- Safe sex practices

**RISK FACTORS**
- Prior pelvic inflammatory disease (PID)
- Prior sexually transmitted infections (STIs)
- Substance dependence
- Personal history of abuse
- Depression, anxiety

**GENETICS**
- Twin studies and familial clustering do suggest a genetic basis for increased nociception
- No established inheritance pattern

**PATHOPHYSIOLOGY**
- Exact mechanism unknown
- Complex and multifactorial, combining, biologic, psychological, and social factors

**ASSOCIATED CONDITIONS**
- Endometriosis, pelvic inflammatory, ovarian cysts, adhesions
- Urinary tract infections (UTIs), STIs, and PID
- Irritable bowel syndrome (IBS)
- Interstitial cystitis (IC)

**BASICS**
- Chronic pelvic pain (CPP) is defined as discomfort below the umbilicus lasting ≥6 mo
- Etiology often unknown and symptom severity often out of proportion to objective findings
- Bears impact on physical, mental, emotional, and sexual well-being

**Epidemiology**
- Prevalence: 1 in 7 women
- No established inheritance pattern
- Twin studies and familial clustering do suggest an increased risk

**Risk Factors**
- Substance dependence
- Personal history of abuse
- Depression, anxiety

**Etiology**
- Complex and multifactorial, combining, biologic, psychological, and social factors
- Exact mechanism unknown
Chronic Pelvic Pain Syndrome (CPP) In Females

**ON-GOING CARE**

**PROGNOSIS**

Variable and dependent on underlying etiology and treatment modalities.

**COMPICATIONS**

- Risk of pharmacologic dependence, tolerance, and abuse associated with long-term angesic therapy.
- Surgical complications such as bleeding and infections are procedure specific.

**FOLLOW-UP**

- Patient Monitoring
  - CPP is typically managed in outpatient setting.
  - Monitor serum hepatic/renal function and electrocardiogram when using antidepresants.

**Patient Resources**

- The International Pelvic Pain Society
  - www.pelvicpain.org

**REFERENCES**


**ADDITIONAL READING**


- See Also (Topic, Algorithm, Media)

- Chronic Pelvic Pain Syndrome (CPP) In Females

- Inflammatory Bowel Disease (Ulcerative Colitis and Crohn Disease), Urologic Considerations

- Neurological啪CTitis (ICP/Plaflate Bladder Syndrome)

- Prostatect, Chronic, Nodular. Inflammatory and Noninflammatory (NI-CP/CPS III A and B)

**CODES**

- ICD9 - 338.29 Other chronic pain
- ICD10 - 617.8 Endometriosis, site unspecified
- ICD10 - 625.9 Unspecified symptom associated with female genital organs

**CLINICAL/SURGICAL PEARLS**

- The pathophysiology of CPP is multifactorial, and the treatment for it is multidisciplinary.
- Initial evaluation for CPP aims to identify Ne- or organ-threatening conditions and rule out anatomic or structural abnormalities.
- Subsequent management of CPP focuses on symptom control and consistent care.
- Treatment may take time, and cure may not be possible. Therefore, it is important to set patient-centered yet realistic goals of care.
P1: OSO/OVY

P2: OSO/OVY

LWBK1391-SEC-P

QC: OSO/OVY

LWBK1391-Gomella

T1: OSO

ch138.xml

September 19, 2014

18:44

PENILE PROSTHESIS PROBLEMS (INFECTION/EXTRUSION/MALFUNCTION)
Nelson Bennett Jr., MD

BASICS
DESCRIPTION

r While generally very reliable, penile prostesis can
become infected, undergo extrusion and suffer form
mechanical failure.
r 2 types of penile prosthesis, malleable (semirigid,
noninflatable, nonhydraulic) and inflatable.
Inflatables consist of 2-piece (pump and cylinders)
and 3-piece (pump, cylinders, and reservoir).
r Implanted via suprapubic or penoscrotal approach.
r Meticulous sterility is required.
r Infections of any or all parts of the device
components require removal of the entire device.
r Extrusion/erosion of the device may occur into or
through the urethra, penile glans, proximal crura,
bladder or bowel, or adjacent vascular structures.
r Mechanical breakdown may manifest as inability to
inflate/deflate device, abnormal erectile morphology,
or auto inflation.

EPIDEMIOLOGY
Incidence
N/A

Prevalence

r Overall infection rate: 1–8%
r Prosthesis revision infection rate: 10–13%
r Prosthesis revision through infected field infection
rate: 18%
r Mechanical failure rate 2-piece: 5% @ 5 yr
r Mechanical failure rate 3-piece: 18% @ 15 yr

RISK FACTORS

r Infection: Diabetes, spinal cord injury, previous
penile prosthesis, immunocompromised state, h/o
UTI, obesity
r Extrusion/erosion: Previous surgery, previous pelvic
radiation, penile fibrosis, aggressive dilation, lack of
surgical experience, Peyronie disease, previous
penile prosthesis, upsizing of cylinders
r Mechanical failure: Inadequate dilation of reservoir
space

Genetics
N/A

PATHOPHYSIOLOGY

r Infection
– 1–8% this percentage increases with number of
revision surgeries
– Most common bacteria – Staphylococcus
epidermidis
– Other bacteria: MRSA, Pseudomonas,
Enterococcus, Prevotella, Morganella
– Gram-negative bacteria may be associated with
rapid infection
– Biofilm plays important role in bacterial adherence
and infection
r Extrusion/erosion
– Erosion through skin is inherently infected
– Pre-existing infection may hasten erosion
– Iatrogenic-facilitated erosion may result from
overaggressive dilation

280

r Malfunction
– Mechanical failure rates are 15% at 5 yr and 30%
at 10 yr
– Common reasons include aneurysm, tubing
breakage, reservoir leakage, and connector failure
– Auto inflation is usually due to improperly
positioned reservoir

HISTORY

ASSOCIATED CONDITIONS

PHYSICAL EXAM

r Conditions associated with erectile dysfunction
– Adrenal disorders
– AIDS-associated neuropathy
– Alzheimer’s
– Cardiac arterial disease
– CNS infections
– CNS tumors
– Diabetes mellitus (Type I and II)
– History of kidney or liver transplant
– History of myocardial infarction
– History of prostatectomy, cystectomy, or colectomy
– Hyperprolactinemia
– Hypertension
– Hyperthyroidism
– Hypogonadism
– Hypothyroidism
– Liver failure
– Multiple sclerosis
– Peripheral vascular disease
– Renal failure

GENERAL PREVENTION

r The preoperative assessment should include issues
such as the patients’ needs and expectations of the
device (1,2)
– Issues such as complications and the irreversibility
of the procedure should be exhaustively discussed
and documented through informed consent
r Infection
– Ensure UTI or infectious skin rash is absent
– Tight control of serum glucose and HbA1C
– Preoperative parenteral antibiotic of vancomycin
+ aminoglycoside or imipenem
– Meticulous adherence to sterile technique
– Limit OR traffic
– 10-min scrub of operative area
– 10-min scrub for OR staff
– Use of alcohol-based solution for final prep
– Avoid having prosthesis contact skin
– Use antibiotic-coated/antibiotic dripped
prosthesis (3)
◦ Postoperative oral antibiotics 7–10 days
postoperatively
r Extrusion/erosion
– Avoid aggressive corporal dilation
– Avoid upsizing of cylinders
– Avoid early/premature inflation of device
r Malfunction
– Place corporotomy closing sutures before device
insertion to avoid iatrogenic puncture
– Demonstrate proper function and placement of
the device prior to conclusion of surgery

DIAGNOSIS
Assess for fever, chills, pain, lethargy, fatigue, change
in bowel or bladder function, dysuria, frequency,
urethral discharge.
r Assess penis/scrotum for erythema, edema,
induration, pain in palpation of penis/scrotum,
presence of wound drainage, adherence of
prosthesis components to skin.
r Erosion/extrusion of device through glans, urethral
meatus, scrotal skin, or perineum.
r Assess functionality of device by
inflation/deflation—if suboptimally rigid or deflated
pump, consider fluid leak.
r Assess penile contour/morphology upon inflation:
– Buckling of cylinder or S-shaped deformity
suggests oversizing of cylinders.
– Floppy glans (SST deformity) suggests undersized
cylinders or inadequate corporal dilation.

DIAGNOSTIC TESTS & INTERPRETATION
Lab
r Urinalysis
r Urine culture and sensitivity
r CBC with differential
r Metabolic profile
r Erythrocyte sedimentation rate

Imaging

r Usually not necessary
r Ultrasound scrotum—may reveal abscess
r MRI (with device inflated)—useful in assessment of
corporal abnormalities.

Diagnostic Procedures/Surgery
Cystourethroscopy may reveal urethral erosion of
cylinders or erosion of device component into bladder.

Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS

r Intraoperative complications (4)
– During corporal body dilation: Urethral
perforation, cross over perforation of opposite
crura during dilation
– Reservoir position: Bladder perforation or
improper positioning during the implant procedure
– Component failure: Check device function before
implantation; careful technique to avoid cylinder
injury during corporal body closure
r Postoperative complications:
– Infection
– Erosion (oversized cylinder): Often associated with
pain and buckling
– Undersized cylinder (“concorde deformity” or
“floppy glans”) whereby there is excess mobility
of the glans
– Cylinder aneurysm
– Fluid leak
– Auto inflation/inability to deflate or inflate


TREATMENT
GENERAL MEASURES
- Broad-spectrum antibiotic should be started if infection is suspected.
- If sepsis is present, resuscitation is indicated prior to explanation of prosthesis.

MEDICATION
First Line
- AUA guidelines recommend the following antibiotic prophylaxis at the time of implantation (See Additional Reading):
  - Ampicillin/Tranxactin (or aztreonam with renal insufficiency) plus
  - 1st/2nd generation cephalosporin or vancomycin
- Alternative regimens include:
  - Ampicillin/Tranxactin
  - Tranxactin/Clavulanate
  - Piperacillin/Tazobactam

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Infection
  - Removal of prosthesis may be completed on a semiurgent basis (within 24 hr)
  - Immediate prosthesis salvage (replacement) may be possible in absence of frank pusulence, erosion, necrotic tissue, poorly controlled diabetes, immunosuppression
  - Mucosal protocol for prosthesis salvage (6):
    - 1. Antibiotic solution (1 g vancomycin and 80 mg gentamicin in 1 L of normal saline)
    - 2. 1/2 strength hydrogen peroxide
    - 3. 1/2 strength betadine
    - 4. Pressure washing with 1 g vancomycin and 80 mg gentamicin in 1 L of normal saline
    - 5. 1/2 strength betadine
    - 6. 1/2 strength hydrogen peroxide
    - 7. Antibiotic solution
    - 8. Change instruments, gowns, drapes, and gloves immediately before prosthesis insertion
  - Extrusion/erosion
    - Prolonged extrusion/erosion managed by affixing RTS to the interior, proximal corpora with permanent suture
    - Alternatively, placing a purse-string suture in the corpora at tubule exit site
  - Delayed extrusion/erosion (periathal) is best managed by immediately removing offending cylinder and prolonged Foley drainage. If contralateral cylinder has been placed, it may remain in place
  - Malfunction
    - Floppy glans
      - Perform corporeoplasty to reposition glans or dilate distal corpora
    - Fluid leak
      - Replace device
    - Autinflation
      - Reposition, incise fibrotic capsule, or replace reservoir

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

ONGOING CARE
PROGNOSIS
- Prosthesis satisfaction rates approach 95% for patients and partners
- Satisfaction rates for revision surgery is ~40%
- Infection rates have decreased with antibiotic coated or antibiotic-dipped prosthetics

COMPLICATIONS
- Revision surgery may result in infection, extrusion/erosion, or malfunction
- Delay replacement of device may result in corporal fibrosis

FOLLOW-UP
Patient Monitoring
- In case of revision surgery, prolonged antibiotic treatment may be required
- Biweekly follow-up is indicated until patient is cleared to use the device

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Erectile Dysfunction (ED)
- Penile Prosthesis, Models and Descriptions
- Penile Prosthesis Problems (Infection/Extrusion/Malfunction) Images & Illustrations

CODES
ICD9
- 996.39 Other mechanical complication of genitourinary device, implant, and graft
- 996.69 Infection and inflammatory reaction due to other internal prosthetic device, implant, and graft
- 996.76 Other complications due to genitourinary device, implant, and graft

ICD10
- T83.40XA Infection/infest d/f pt prosth-dev in genit ltr, init
- T83.6XXA Infect/inflm react d/t prosth dev/grft in genitrct, init
- T83.89XA Other specified complication of genitourinary prosthetic devices, implants and grafts, initial encounter
- T83.424A Displacement of penile (implanted) prosthesis, initial encounter

CLINICAL/SURGICAL PEARLS
- Metabolic stability is required during the implant in the operating room.
- Infections of any or all parts of the device components require removal of the entire device.
- Extrusion/erosion of the device may occur into or through the urethra, penile glans, proximal crus, bladder or bowel, or adjacent vascular structures.
- Mechanical breakdown may manifest as inability to inflate/prolong device, abnormal erectile morphology, or auto inflation.

PENILE PROSTHESIS PROBLEMS (INFECTION/EXTRUSION/MALFUNCTION)
PATHOPHYSIOLOGY
E-cadherin (16q22) immunoreactivity correlates with Viral genes E6 & E7 expressed on high-risk HPV, Prevalence Incidence
- In 2014 in the United States, the American Cancer Society estimates that about 1,640 new cases of penile cancer will be diagnosed and 325 will die of penile cancer
- In the United States:
  - Hispanics (8.6 per million)
  - Blacks (4.0 per million)
  - White (3.8 per million)
Prevalence
- Race in developed countries
- Most common genitourinary malignancy in Uganda
  - In Brazil 6–14/100,000 males (1)
  - Whites (3.9 per million)
  - Blacks (4.0 per million)
  - In the United States
  - 1st line is surgical excision of lesion on penis.
  - Zoon balanitis
  - Ulcer from STD
  - Seborrheic keratosis
  - Lichen sclerosis
  - Bowenoid papulosis (multiple flat, warty lesions, BXO
  - Erythroplasia of Queyrat; shiny red patches on skin of the penis typically penile shaft)
DIAGNOSTIC TESTS & INTERPRETATION
LAB
- CBC, urinalysis, urine culture
PHYSICAL EXAM
- Persistent induration, erythema, nodularity of propude and/or glans. Usually has been treated with several agents, lesions
- Growth or sore on the penis that doesn’t heal within 4 wk
- Patients often denies or ignores lesions and present at later stages
- Bleeding ulcer
- Penile pain—infected
  - New onset of priapism with a mass suggests metastatic corporeal body lesion (eg, melanoma)
DIAGNOSIS
HISTORY
- Persistent irritation, erythema, nodularity of propude and/or glans.
  - Bleeding ulcer
  - Food smell with purulence
  - Phimosis
  - Inflamed adenopathy
ASSOCIATED CONDITIONS
- Phimosis
- Balanitis
- Sexually transmitted infections (STIs/STDs)
GENERAL PREVENTION
- Good hygiene, avoid smear accumulation
- Newborn circumcision more protective than circumcision later in life
- HPV vaccines may reduce the risk of HPV and, consequently, penile cancer (unproven)
ALERT
- Presentation at advanced stage is not uncommon due to denial and poor hygiene.
Diagnosis
- SCCs are graded using the Broders System:
  - Grade IV: Cells deeply invasive, marked nuclear atypia, increased mitotic activity, dermal keratin pearls
  - Grade III: Cells deeply invasive, marked nuclear pleomorphism, nuclear mitoses, necrosis, lymphatic and perineural invasion, no keratin pearls
DIFFERENTIAL DIAGNOSIS
- BKD
  - Erythroplasia of Queyrat: shiny red patches on mucosal surfaces (glans and prepuce if uncircumcised)
  - Bowen disease (red, scaly patches on the keratinized skin of the penis typically penile shaft)
  - Bowenoid papulosis (multiple flat, warty lesions, sometimes pigmented)
  - Condyloma acuminsata: increased risk of nodal metastases
  - Giant condylomata
  - Epidermodysplasia Verruciformis disease: Adenocarcinoma of the penis
  - Accumulation of pigmented keratinous material: perianal disease
  - Acrodermatitis enteropathica
  - Condyloma lata: lichen sclerosis
  - Bowenoid papulosis
  - Seborrheic keratosis
  - Ulcer from STD
  - Zoon balanitis
Pathologic Findings
- Most malignancies involve the epithelial surface of the penis.
  - CIS (erythroplasia of Queyrat, Bowen disease of the penis, low-grade papillomas)
  - Viral genes E6 & E7 expressed on high-risk HPV
  - Viral genes E6 & E7 expressed on high-risk HPV
  - HPV types 16, 18, and 33 or HIV
  - Presence of foreskin and/or phimosis
  - Invasive cancer:
    - 95% are SCCs
    - Torres of invasive atypical keratinoepithelium with multiple mitosis inside the lamina propria or deeper. Sites with foci of aberrant and atypical keratinization called squamous pearls
    - SCCs are graded using the Broders System:
      - Grade I: Well-differentiated, keratin pearls, prominent papillar bridges
      - Grade II: Greater nuclear atypia, increased mitotic activity, dermal keratin pearls
      - Grade III: Cells deeply invasive, marked nuclear pleomorphism, nuclear mitoses, necrosis, lymphatic and perineural invasion, no keratin pearls
  - Simply malignant involve the epithelial surface of the penis.
  - CIS (erythroplasia of Queyrat, Bowen disease of the penis, low-grade papillomas)
  - Presence of foreskin and/or phimosis
  - HPV types 16, 18, and 33 or HIV
  - Presence of foreskin and/or phimosis
  - Invasive cancer:
    - 95% are SCCs
    - Torres of invasive atypical keratinoepithelium with multiple mitosis inside the lamina propria or deeper. Sites with foci of aberrant and atypical keratinization called squamous pearls
    - SCCs are graded using the Broders System:
      - Grade I: Well-differentiated, keratin pearls, prominent papillar bridges
      - Grade II: Greater nuclear atypia, increased mitotic activity, dermal keratin pearls
      - Grade III: Cells deeply invasive, marked nuclear pleomorphism, nuclear mitoses, necrosis, lymphatic and perineural invasion, no keratin pearls
DIFFERENTIAL DIAGNOSIS
- BKD
  - Bowen disease (red, scaly patches on the keratinized skin of the penis typically penile shaft)
  - Bowenoid papulosis (multiple flat, warty lesions, sometimes pigmented)
  - Condyloma acuminsata: increased risk of nodal metastases
  - Giant condylomata
  - Epidermodysplasia Verruciformis disease: Adenocarcinoma of the penis
  - Accumulation of pigmented keratinous material: perianal disease
  - Acrodermatitis enteropathica
  - Condyloma lata: lichen sclerosis
  - Bowenoid papulosis
  - Seborrheic keratosis
  - Ulcer from STD
  - Zoon balanitis
GENERAL MEASURES
- 1st line is surgical excision of lesion on penis.
- Wound care issues are paramount after excision of the primary and after inguinal node dissections.
Grossly should be taken to minimize the complications of penile deformity and/or mental stress after excision the primary and diligent attention to avoiding infection, hematoma, and lymphocele after inguinal node dissection is necessary.
- Treatment based on extent of disease and specific tumor type. Recommendations below are for invasive SCC (B). For other tumor types, see specific sections.
**PROGNOSIS**

- Depends on T-stage and nodal status
- ARCC staging:
  - Stage I: Cancer is moderately or well-differentiated and only affects the subepithelial connective tissue
  - Stage II: Cancer is poorly differentiated, affects lymphatics, or invades the corpus or urethra
  - Stage III: Deep invasion into the penis and metastasis into one lymph node
  - Stage IV: The cancer has invaded into structures adjacent to the penis, metastasized to pelvic nodes, or distant metastasis is present

- 5-yr overall survival for men with node-negative disease is 80–90%.
- 5-yr survival for N+ is max 30–40%.
- Married or previously married men have better prognosis
- African Americans tend to present with more advanced disease and have a poorer prognosis

**COMPLICATIONS**

- Infections
  - Erosion of lymphadenopathy into femoral artery
  - After radiation or brachytherapy urethral fistula, erosion of lymphadenopathy into femoral artery
- Infections
  - Radical penectomy may be required

**FOLLOW-UP**

- Patient Monitoring
  - Close inspection for local recurrence usually every 3 mo for 5 yr
  - Consider imaging for ambiguous findings on physical exam

**Patient Resources**


**CLINICAL/SURGICAL PEARLS**

- A painless lesion on the penis is the most common presentation.
- 40% of cases of penile cancer in the United States derive from HPV infections.
- 2-cm surgical margin is critical for a successful partial penectomy.
- Historically 6 wk of antibiotics are required to appropriate assessment of inguinal region adenopathy, consideration can also be given to early fine-needle biopsy.

---

**ICD9**

- 187.2 Malignant neoplasm of glans penis
- 187.3 Malignant neoplasm of body of penis
- 187.4 Malignant neoplasm of penis, part unspecified

**ICD10**

- C60.9 Malignant neoplasm of penis, unspecified
- C60.2 Malignant neoplasm of glans penis
- C60.9 Malignant neoplasm of penis, unspecified
retinoblastoma (RB) tumor suppressor proteins through interactions with tumor protein 53 (p53) and HPV contributes to the development of penile cancer.

**Genetics**
- HPV contributes to the development of penile cancer through interactions with tumor protein 53 (p53) and retinoblastoma (RB) tumor suppressor proteins.

**Pathophysiology**
- Inguinal LNs serve at the primary lymphatic drainage for the penis, scrotum, urethra, vulva, vagina, perineum, gluteal region, lower abdominal wall, lower extremities, and lower extremities.
- Inguinal LNs lie within the femoral triangle (inguinal ligament, sartorius, and adductor longus) and are separated into superficial and deep groups by the fascia lata of thigh.

**ASSOCIATED CONDITIONS**
- Balanitis
- Phimosis
- STDs

**DIAGNOSIS**

**History**
- Circumcision
- PHIS: infection
- Penile condylomata
- Genital warts
- Sexual History (multiple partners, early age of initial intercourse)
- Smoking History
- Viral warts
- Laser treatment
- Treatment with topical and ultraviolet A phototherapy.

**Imaging**
- No imaging studies are currently utilized extensively for staging.
- Ultrasound and PET-CT can be used to detect recurrences.
- Chest x-ray and CT abdomen/pelvis can be used for follow-up.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- No tissue parameters, including HPV and p53 status, are predictive of LN involvement.

**TREATMENT**

**General Considerations**
- Pelvic LNs are palpable in 60% of presenting patients.
- Pelvic nodes should only be offered in experienced centers.
- Palpable inguinal nodes are predictive of LN involvement.
- Palpable inguinal nodes are present in 60% of presenting patients.

**DIAGNOSIS**

**Histology**
- If FNAC is positive, bilateral inguinal and pelvic LAD should involve at least 8 LNs, as this improves long-term survival.
- If contralateral frozen section is positive, deep inguinal or pelvic LAD and chemotherapy is warranted.
- If FNAC is negative, no resolution with antibiotics, excisional biopsy or inguinal LAD.
- If contralateral frozen section is negative, surveillance.
- If pelvic LNs are palpable, inguinal and pelvic LAD and contralateral superficial or modified inguinal LAD.
- T3-T4 primary tumors should undergo bilateral superficial inguinal or OSN.
- If FNAC is positive, bilateral inguinal and pelvic LAD and contralateral superficial or modified inguinal LAD.
- If contralateral frozen section is negative, surveillance.

**DIFFERENTIAL DIAGNOSIS**
- Reactive LN: Syphilis, herpes, chancroid, lymphogranuloma venereum, genital herpes disease
- Malignant diseases: Metastatic melanoma, lymphoma
- Systemic diseases: HIV, leprosy, human immunodeficiency virus, cytomegalovirus

**TREATMENT**

**GENERAL MEASURES**

**MALIGNANT DISEASES**
- HPV infection
- Phimosis
- Circumcision
- HPV vaccination may reduce risk (unproven)

**REACTIVE CONDITIONS**
- Autoimmune diseases: Sarcoidosis, lupus
- Systemic diseases: Mononucleosis, rubella, human immunodeficiency virus, cytomegalovirus

**ASSOCIATED CONDITIONS**
- Prepubertal circumcision is protective against penile cancer.
MEDICATION

First Line

- Antibiotics
  - Use of antibiotics has become controversial for enlarged LNs.
  - Historically, a 4-6 wk course of antibiotics such as a cephalosporin or augmentin was recommended to rule out infection in Tis and Ta tumors with palpable LNs.
  - Delay in LAD, a potentially curative treatment, has brought the use of antibiotics into question
  - FNAC can help determine if LNs are due to metastasis or infection

Second Line

N/A

SURGERY/OTHER PROCEDURES

- Radical LAD (2,3)
  - Superior margin: Superior margin of the external ring to the anterior superior iliac spine (ASIS)
  - Inferior margin: 20 cm inferior from the ASIS to 15 cm inferior from the pubic tubercle
- Modified LAD (after Carstons)
  - Includes area lateral to the femoral artery and caudal to the fossa ovalis
  - Preservation of the saphenous vein
  - No transection of the sartorius muscles
- Conversion to radical LAD if there are positive LNs
- Endoscopic LAD (4)
- Radical LAD (2,3)
- Complete radical LAD can be performed through 3 endoscopic ports
- Nerve plexus is equivalent to open surgery
- Decreased complications
- The viability of the skin flaps developed during an inguinal LN dissection is based on the anastomotic vessels within the superficial fat layer of Campers fascia which course lateral to medial along the skin lines. This is a key anatomic dissection plane as the lymphatic drainage of the penis lies beneath Campers fascia allowing this superficial fatty layer to remain attached to the skin flaps during a groin dissection
- When performing an inguinal LN dissection for a clinically negative groin, a modified technique should be used to decrease morbidity. The key components of this technique include the following:
  - Shorter incision (~10 cm), preservation of the saphenous vein, minimizing dissection lateral to the femoral artery, and avoiding transection of the Sartorius muscle

ADDITIONAL TREATMENT

Radiation Therapy

- Adjuvant radiation therapy may improve 3-year LND survival in patients with extensive metastases and/or extranodal disease
  - Side effects include edema and pain
- Radiotherapy in clinical N0 patients is not recommended

Additional Therapies

- Adjunct chemotherapy
  - 3 courses of cisplatin and 5-fluorouracil for pN2–3
  - No adjuvant chemotherapy for pN0

COMPETITIVE COMPLEMENTARY & ALTERNATIVE THERAPIES

None are effective

ONGOING CARE

PROGNOSIS

- 5-yr cancer-specific survivals:
  - 70–80% in pN0 disease
  - 70–40% in pN1 disease
  - <30% in patients with positive pelvic LNs
- Predictors of cancer-specific survival: Pathologic stage of LNs, vascular and/or lymphatic involvement, primary tumor thickness

COMPLICATIONS

- LAD complications:
  - Wound infection
  - Skin necrosis
  - Wound dehiscence
  - Thigh numbness
  - Lymphedema
  - Lymphorrhea
  - Sartorial swelling
  - Suprapubic swelling
  - Pulmonary embolism

FOLLOW-UP

Patient Monitoring

- Recurrences occur most often within 2 yr after inguinal LAD
- Nomograms available
- Evaluation should include an exam and ultrasound-guided FNAC
- Maximum follow-up length of 5 yr
- Surveillance (patient did not have LAD)
- FNAC can help determine if LNs are due to metastasis or infection
- 30% in pN2–pN3 disease
- 90–100% in pN0 disease
- 30–70% in pN1 disease

Follow-up

- Every 6 mo for yr 1 and 2
- Every 6 mo for yr 3, 4, and 5
- Every 3 mo for yr 3, 4, and 5
- Every 6 mo for yr 4, 5, and 6

CLINICAL/SURGICAL PEARLS

- Penile cancer metastasizes to regional LNs before distant disease
- Treatment is dependent on the clinical presence of LNs, tumor stage, and tumor grade.
- Inguinal LAD is potentially curative and can improve long-term outcomes in penile cancer with nodal involvement.
- Careful tissue management, antibiotics, suction drains, and compression stockings can minimize the morbidity associated with LAD.


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Groin/Surgical Mass, Male and Female
- Lymphadenopathy, Inguinal
- Penile, Cancer, General Considerations
- Penile, Lymphadenopathy Image
- Penile Cutaneous Lesion
- Penis, Squamous Cell Carcinoma
- Reference Tables: TNM: Penis Cancer

ICD9

- 187.4 Malignant neoplasm of penis, part unspecified
- 196.5 Secondary and unspecified malignant neoplasm of lymph nodes of inguinal region and lower limb
- 196.6 Enlargement of lymph nodes

ICD10

- C60.9 Malignant neoplasm of penis, unspecified
- C77.4 Sec and unspecified malignant neoplasm of inguinal and lower limb nodes
- R59.0 Localized enlarged lymph nodes

CLINICAL/SURGICAL PEARLS

Penile cancer metastasizes to regional LNs before disseminating systemically.
- Treatment is dependent on the clinical presence of LNs, tumor stage, and tumor grade.
- Inguinal LAD is potentially curative and can improve long-term outcomes in penile cancer with nodal involvement.
- Careful tissue management, antibiotics, suction drains, and compression stockings can minimize the morbidity associated with LAD.

REFERENCEs

PATHOPHYSIOLOGY

In general, 5% of men have evidence of PD.

Prevalence

Incidence

EPIDEMIOLOGY

DESCRIPTION

In the setting of erectile trauma, an altered cell-mediated immunity and anti-elastin antibodies support an immunologic component.

Autoimmune components have been demonstrated in 38–75% of men with PD.

The result is hypertrophic microvascular hemorrhage and inflammation in the tunica albuginea, which may calcify, preventing uniform expansion of the corpora cavernosa during erection.

– Congenital chordee may present as penile curvature. If severe, it can cause dyspareunia.

– Can be a result of complications of penile prosthesis implantation.

– Congenital chordee may present as penile curvature in infants due to a deficiency in formation of the urethra or the Buck fascia ventrally.

– Leporionic chordee secondary to circumcision or other penile skin procedures.

BASICS

In general, 5% of men have evidence of PD.

RISK FACTORS

– Buckling erectile trauma

– Fracture of the tunica albuginea during sexual activity

– Intra cavernous injection of vasoactive agents

– Pharmacologic injection to assess cavernous arterial function, presence of venoocclusive dysfunction, and degree of erectile curvature, lateral indentation or circumferential wasting.

– Nipple self-photography of erect penis using instant (Polaroid) or digital film imaging is useful to classify the extent of the curvature.

– Urethroscopy for urethral pathology

Pathologic Findings

– PD is characterized by a fibrous noncompliant plaque within the tunica albuginea, which may calcify, preventing uniform expansion of the corpora cavernosa during erection.

– Microscopy: A fibrous noncompliant plaque demonstrates nonparallel arrangement of collagen fibers and disordered arrangement of elastin fibers in PD.

DIFERENTIAL DIAGNOSIS

– Balanitis, balanoposthitis, paraphimosis

– Cellulitis

– Chordee

– Congenital penile curvature

– Epididymitis

– Erectile dysfunction

– Fourier gangrene

– Hypospadias

– Idiopathic urethralgia

– Insect bite

– Leukemic infiltration of the penile shaft

– Nipple pain syndrome

– Penile prosthesis problem: 5-shaped or sigmoid curvature with buckling of prosthetic cylinders that are too long; pain also suggests infected prosthesis components

– Priapism

– Psychiatric causes of pain

– Pubic neuralgia

– Referred pain, GI (rectum, hemorrhoids, fistula, fissures)

– Referred pain, GU (prostatitis, urethritis, proctitis, retention, urethral, urethral calculus)

– Reflected syndrome

– STD (herpes, chancre)

– Torn frenulum

– Trauma (ESW, penile fracture)

– Urethral foreign bodies

– Urethral stricture following urethroplasty

– Urethral stricture

DIAGNOSIS

HISTORY

– It is critical to differentiate penile pain from urethral pain. History of voiding symptoms and/or recurrent UTIs.

– Establish duration, degree, and location of curvature and pain

– Dyspareunia

– Painful erection (suggests PD)

– Dysuria

– Establish duration, degree, and location of curvature and pain

– History of penile prosthesis

– History of priapism

– History of penile tumor

– History of penile prosthesis

– History of penile trauma

– History of penile prosthesis

– History of penile trauma

– History of penile surgery as a child

– History of penile trauma

– History of penile prosthesis

– Palpable nodule

– Painful ejaculation

– Dyspareunia

– Usually not useful unless for workup of infections

– Usually useful

– Urinary symptoms and/or recurrent UTIs

– Urethroscopy for urethral pathology

– Urethral stricture

– Urethral foreign bodies

– Urethral stricture following urethroplasty

– Urethral stricture

ASSOCIATED CONDITIONS

– Chronic Intracavernous Injection Therapy

– Dupuytren contracture

– ED (venoocclusive dysfunction)

– Leporionic disease (Plantar fascitis)

– Paget disease

– Leporionic disease (Plantar fascitis)

– Psoriatic arthritis

– Urethral stricture

– Hypoplasia

– Genital trauma

– Liposarcoma

– Penile pain syndrome

– Penile fracture, trauma, or contusion

– Penile surgery

– Penile pain syndrome

– Penile prosthesis problem: 5-shaped or sigmoid curvature with buckling of prosthetic cylinders that are too long; pain also suggests infected prosthesis components

– Priapism

– Psychiatric causes of pain

– Pubic neuralgia

– Referred pain, GI (rectum, hemorrhoids, fistula, fissures)

– Referred pain, GU (prostatitis, urethritis, proctitis, retention, urethral, urethral calculus)

– Reflected syndrome

– STD (herpes, chancre)

– Torn frenulum

– Trauma (ESW, penile fracture)

– Urethral foreign bodies

– Urethral stricture following urethroplasty

– Urethral stricture

IMAGING

– Radiograph of penile shaft if calcification is suspected.

– Duplex Doppler US with intracavernous pharmacologic injection to assess cavernous arterial function, presence of venoocclusive dysfunction, and degree of erectile curvature, lateral indentation or circumferential wasting.

– Nipple self-photography of erect penis using instant (Polaroid) or digital film imaging is useful to classify the extent of the curvature.

– Urethroscopy for urethral pathology

– Penile prosthesis problem: 5-shaped or sigmoid curvature with buckling of prosthetic cylinders that are too long; pain also suggests infected prosthesis components

– Priapism

– Psychiatric causes of pain

– Pubic neuralgia

– Referred pain, GI (rectum, hemorrhoids, fistula, fissures)

– Referred pain, GU (prostatitis, urethritis, proctitis, retention, urethral, urethral calculus)

– Reflected syndrome

– STD (herpes, chancre)

– Torn frenulum

– Trauma (ESW, penile fracture)

– Urethral foreign bodies

– Urethral stricture following urethroplasty

– Urethral stricture

DIAGNOSTIC TESTS & INTERPRETATION

Lab

– Usually not useful unless for workup of infections

– Usually useful

– Urinary symptoms and/or recurrent UTIs

– Urethroscopy for urethral pathology

– Urethral foreign bodies

– Urethral stricture following urethroplasty

– Urethral stricture
TREATMENT

GENERAL MEASURES

Identify the specific cause of the penile pain and/or curvature and treat accordingly.

MEDICATION

First Line

- PD
  - All oral agents yield insignificant therapeutic benefit:
    - Vitamin E (antioxidant), palbociclib (antifibrotic), colchicine (antifibrotic), tamoxifen (antifibrotic), L-carnitine (antioxidant), pentoxifylline
  - Paraphimosis
    - Urgent manual reduction with firm pressure ± local anesthetic (see section on paraphimosis for details)
  - Priapism
    - Irrigation and aspiration
    - Intravesical phenylephrine injection (100-500 mcg/mL)
  - Referred pain to penis or urethra should be aimed at treating primary problem

Second Line

- PD intralesional therapy
  - Plaque incision with graft interposition
  - Steroid therapy
  - Other intralesional agents (off-label) Verapamil, Collagenase clostridium histolyticum (CCH), antimicrobials
  - All oral agents yield insignificant therapeutic benefit:
    - Vitamin E (antioxidant), palbociclib (antifibrotic), colchicine (antifibrotic), tamoxifen (antifibrotic), L-carnitine (antioxidant), pentoxifylline
  - Paraphimosis
    - Urgent manual reduction with firm pressure ± local anesthetic (see section on paraphimosis for details)
  - Priapism
    - Irrigation and aspiration
    - Intravesical phenylephrine injection (100-500 mcg/mL)
  - Referred pain to penis or urethra should be aimed at treating primary problem

Additional Therapies

- Paraphimosis
  - See specific topic for surgical correction
  - Penile fracture
    - See specific topic for surgical correction
  - Priapism
    - Local anesthetic ± regional anesthetic

ADDITIONAL TREATMENT

Radiation Therapy

Indications

- PD or surgical repair

COMPLICATIONS

- Referred pain to penis or urethra

ONGOING CARE

PROGNOSIS

- Prognosis dependent on primary etiology of penile curvature and/or pain.
- Surgical straightening of erection is predictably successful (>95%).
- Shortened penile length and sensory loss may be noted postoperatively.

COMPICATIONS

- Residual pain and curvature
- Dyspareunia
- Erectile dysfunction and loss of penile length due to PD or surgical repair

FOLLOW-UP

Patient Monitoring

Periodic monitoring of erectile function, penile length, and sensory function.

Patient Resources

- The Peyronie Disease Society (www.peyroniesociety.org)
- Urology Care Foundation (http://www.urologyhealth.org/urology/index.cfm?article=115)

REFERENCES

288

PENIS, CUTANEOUS LESION
Kiranpeet K. Khurana, MD
Edmund S. Sabanegh, Jr., MD

BASICS
DESCRIPTION
– Cremasteric, benign, premalignant, malignant
– May be male genitalia-specific (primary) or associated with other cutaneous lesions or systemic disease (secondary)
– May occur at any age

EPIDEMIOLOGY
Prevalence
Varies widely by etiology
Incidence

RISK FACTORS
Systemic disease, irritant or allergic, sexual contact, trauma, uncircumcised penis, family history, inflammation, infections, medications, local skin trauma, obesity, age, smoking

GENETICS
– Reiter syndrome: Associated with HLA-B27 haplotype
– Hailey–Hailey disease: Autosomal dominant
– Perilecan: Associated with altered expression of P53, FAS, c-erb, myc, Rb genes

PATHOPHYSIOLOGY
– Idiopathic, allergic, infectious, autoimmune, inflammatory, sensory, sexual transmission, genetic
– Lesions appear similar; biopsy often needed for diagnosis

ASSOCIATED CONDITIONS
– Leiden–rheumatoid syndrome: increase in size and number of subcutaneous keloidal lesions sometimes signifying internal malignancy
– Stevens–johnson syndrome and toxic epidermal necrolysis: Protracted upper respiratory illness followed by life-threatening desquamating lesions due to medications, infections, or cancers
– Poriodic: Lesions under preputial skin, genitals, or prepuce
– Reiter syndrome (reactive arthritis): Urethritis, arthritus, conjunctivitis, Cervicofacial balanitis
– Behcet disease: Painful ulcers found in 37–89% of patients, mostly on mouth (80%), but glans and shaft also affected
– Inflammatory bowel disease: Arterial thrombosis of penis, periurethral, and perineal granulomas on biopsy, also pyoderma gangrenosum
– Hailey–Hailey disease: Vesiculobullous rash
– Diabetes: Pierce
– HIV: Kaposi sarcoma, serebic dermatitis

GENERAL PREVENTION
– Cremasteric in some cases
– Proper hygiene
– Safe sex practices
– Avoid contact with allergens or irritants

DIAGNOSIS
HISTORY
– Age
– Symptoms: Pain, pruritus, burning, discharge
– Location: Scrotum, glans, shaft, preputial skin, urethral/bladder lining, other sites
– Duration
– Rate of onset: Acute or chronic
– Exposures: New bath/laundry soap, lotions, oils, travel (exotic plants, animals, insects, people), shared towels/linens, new medications, industrial, chemical
– Sexual history: Sexual partner with lesions
– Trauma
– History of systemic diseases or cancers
– Allergies
– Family history
– Previous treatment

PHYSICAL EXAM
– Examine and describe lesion(s): – Elevated, nonelevated
– Color of lesion
– Morphology of lesion
– Configuration of lesion (linear vs. serpiginous)
– Degree of margination
– Degree of firmness
– Examine genitalia: Circumcised, uncircumcised, local skin
– Degree of firmness
– Morphology of lesion
– Color of lesion
– Previous treatment
– Family history
– Previous treatment

DIAGNOSIS
HISTORY
– Age
– Symptoms: Pain, pruritus, burning, discharge
– Location: Scrotum, glans, shaft, preputial skin, urethral/bladder lining, other sites
– Duration
– Rate of onset: Acute or chronic
– Exposures: New bath/laundry soap, lotions, oils, travel (exotic plants, animals, insects, people), shared towels/linens, new medications, industrial, chemical
– Sexual history: Sexual partner with lesions
– Trauma
– History of systemic diseases or cancers
– Allergies
– Family history
– Previous treatment

PHYSICAL EXAM
– Examine and describe lesion(s): – Elevated, nonelevated
– Color of lesion
– Morphology of lesion
– Configuration of lesion (linear vs. serpiginous)
– Degree of margination
– Degree of firmness
– Examine genitalia: Circumcised, uncircumcised, proper placement of foreskin
– Describe primary lesion(s) (1/4A):
  – Pearly penile papule: Small, white/flesh colored, 0.5 cm, solid, dome-shaped
  – Plaque: >0.5 cm, solid, elevated, well-circumscribed
  – Vesicle: <0.5 cm, fluid-filled, well-circumscribed

DIFFERENTIAL DIAGNOSIS
Common benign lesions (1/4A)
– Viral: Human papilloma virus infection with verruca vulgaris
– Acrochordon: “Skin tag”
– Angiokeratoma of Fordyce: Red papules on penis, scrotum, eschara of dermal blood vessels
– Inflammatory: Vasculitis: Arterial, venous, lymphatic
– Infected: Due to sexually transmitted disease or other infection
– Neoplastic: Benign, premalignant, malignant

IMAGING
– If locally advanced lesion or internal lesions/tumors/malignancies suspected
– Workup for associated abnormalities

PROCEDURE/SURGERY
– Cryosurgery: Lesions are treated by freezing
– Excision: Lesion is surgically removed

PATHOLOGIC FINDINGS
– Depth of lesion
– Exam of epidermis, dermis, and subcutaneous tissue and any changes noted
– Infiltration with other cells or infectious agents

DIAGNOSTIC TESTS & INTERPRETATION
Lab
– Urinalysis, Gram stain, culture
– Complete blood count
– Sexen chemistry profile
– STD screening if suspected
Common benign lesions (1)[A]:

- Lipomas
- Papillomas
- Sebaceous cysts
- Hemangiomas

Infections and infestations (1)[A]

- Noninfectious ulcers, lesions extending to dermis
- Vesicobullous disorders, autoimmune blisters
- Fixed drug eruption

TREATMENT

If left untreated, lesions may progress locally or systemically.

General Measures

- Local care
- Analgesics
- Topical care
- Systemic care

For more information, visit: [source](http://www.aad.org/skin-conditions/differential-diagnosis)

MEDICATION

First Line

- Topical antibiotics
- Antiviral agents

Second Line

- Systemic antibiotics

SURGERY/OTHER PROCEDURES

- Surgical excision
- Laser ablation
- Electrocautery

Additional Therapy

- Brachytherapy
- Immunotherapy

COMPLEMENTARY & ALTERNATIVE THERAPIES

- Massage therapy
- Acupuncture

ONGOING CARE

- Follow-up visits
- Education

FOR MORE INFORMATION

- [American Academy of Dermatology](http://www.aad.org)
- [American Urological Association](http://www.auanet.org)

ADDITIONAL READING


PHENOMENA

- Lipomas: Topical corticosteroids, diathermy, or systemic treatment
- Lipomas: Biopsy to exclude SCC
- Long-term follow-up required
- Cytotoxic agents
- Oral corticosteroids, immunosuppressive therapy
- Oral corticosteroids, immunosuppressive therapy
- Topical corticosteroids
-systemic treatment

PHENOMENA

- Topical corticosteroids, diathermy, or systemic treatment
- Long-term follow-up required
- Cytotoxic agents
- Oral corticosteroids, immunosuppressive therapy
- Oral corticosteroids, immunosuppressive therapy
- Topical corticosteroids

PHENOMENA
**PATHOPHYSIOLOGY**

- Risk factors: 
  - Human papilloma virus (HPV) types 16, 18, 31, and 33 (associated with 45–80%)
  - Presence of foreskin and/or phimosis
  - Presence of smegma accumulation
  - Poor hygiene
  - Presence of foreskin and/or phimosis
  - Human papilloma virus (HPV) types 16, 18, 31, and 33
  - Accounts for up to 10% of cancers in men in South America.

**EPIDEMIOLOGY**

- Incidence: 
  - Rare in developed countries. Approximately 1,640 new cases annually in US with approximately 320 deaths in 2014.
  - Hispanics are more commonly affected than whites.
  - Rare in developed countries. Approximately 1,640 new cases annually in US with approximately 320 deaths in 2014.

- Prevalence: 
  - Accounts for 0.4–0.6% of cancers in men

**RISK FACTORS**

- Human papilloma virus (HPV) types 16, 18, 31, and 33 (associated with 45–80%)
- Presence of foreskin and/or phimosis
- Poor hygiene
- Sexually transmitted disease (STD)
- HIV infection
- Chronic inflammation
- Lichen sclerosus
- Smoking

**GENETICS**

- HPV-associated DNA and chromosomal changes
- Smear that forms from desquamated epithelial cells is thought to be a primary instigating factor in penile cancer; good hygiene and circumcision limit smegma accumulation
- Penile SCC spreads by a reliable pattern: Superficial invaginal lymph nodes to deep inguinal lymph nodes

**DESCRIPTION**

- The majority of penile carcinomas are squamous cell carcinoma (SCC) histology
- Can be SCC in situ (erythroplasia of Queyrat, Bowen disease of the penis, boweroid papillosis), low-grade noninvasive (eg, verruous carcinoma), or invasive carcinoma
- Other rare types of penile cancer histologies include adenoid- and adenosquamous carcinoma, basal cell carcinoma, melanoma, sarcomas, Kaposi sarcoma, neuroendocrine (small cell) undifferentiated carcinoma, sebaceous gland carcinoma, and rarely, metastases from other sites (prostate, bladder, colon, kidney)
- Inguinal and pelvic lymph nodes are common sites of metastases

**DIAGNOSIS**

**HISTORY**

- Induration, erythema, nodularity of prepuce and/or shaft
- Bleeding ulcer on glans and/or penis shaft
- Inguinal adenopathy
- Patients often deny or ignore symptoms resulting in presentation at advanced stage

**PHYSICAL EXAM**

- Induration, erythema, nodularity of prepuce and/or shaft
- Bleeding ulcer on glans and/or penis shaft
- Inguinal adenopathy
- Patients often deny or ignore symptoms resulting in presentation at advanced stage

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- Serum CBC, electrolytes (including calcium), and liver function studies
- Urinalysis, urine culture

**Imaging**

- US or MRI of penis for local tumor (T) staging
- CT/ MRI of penis and regional lymph nodes to evaluate for lymphadenopathy and metastatic disease

**Pathologic Findings**

- Most malignancies involve the epithelial surface of the penis.
- Subtypes of SCC:
  - Well differentiated (50–90%)
  - Moderately differentiated (>50% anaplastic cells)
  - Poorly differentiated (<10% anaplastic cells)

**DIFFERENTIAL DIAGNOSIS**

- BKO
- Brown disease (red, flat papules on keratinized skin of the penis typically penile shaft)
- Erythroplasia of Queyrat; shiny red patches on mucosal surfaces (glans and prepuce if uncircumcised)
- Buschke–Löwenstein tumor, and giant condyloma are terms used to describe infrequently seen rare tumors that may invade locally but do not metastasize. Mostly considered to be benign, but malignant degeneration has been reported

**ASSOCIATED CONDITIONS**

- Erythroplasia of Queyrat, Bowen disease of the penis, boweroid papillosis
- Human papilloma virus (HPV) types 16, 18, 31, and 33
- Accounts for up to 10% of cancers in men in South America.
- Hispanic population is more commonly affected than whites.
- Rare in developed countries. Approximately 1,640 new cases annually in US with approximately 320 deaths in 2014.
**TREATMENT**

**GENERAL MEASURES**
- Treatment typically based on grade and stage of primary tumor (1)
- Radiotherapy
  - Fine-needle aspiration (FNA)
  - 4-wk course of oral antibiotics followed by repeat physical exam

**MEDICATION**

**First Line**
- Topical: Imiquimod 5% cream applied for 5 d/wk for 4–6 wk or 5–10% cream every other day for 4–6 wk

**Second Line**
-以外

**SURGERY/OTHER PROCEDURES**
- Primary lesions
  - T1b lesions
  - Lyphadenectomy
  - Wide local excision, Mohs surgery, glansectomy, glansectomy
  - T1 grade 1–2
  - Mohs, wide local excision
  - External beam radiation therapy
  - Radiotherapy with interstitial placement
  - Laser ablation
  - T1 grade 3–4 or T1c
  - Partial penectomy
  - Pelvic lymph node dissection if ≥ 4 cm

- Secondary lesions
- Tis/Ta lesions
- Lasix 5% cream applied for 5 d/wk
- 6-wk course of oral antibiotics followed by repeat physical exam
- Fine-needle aspiration (FNA)

- When applicable, UNL associated with improved disease-specific survival

**COMPLICATIONS**
- Infections
- Vascular injury
- Lymphedema
- Wound breakdown (16%)
- Seroma (24%)
- Infection (43%)
- Urethral stenosis
- Vesical injury
- Erosion of lymphadenopathy into femoral vessels

**FOLLOW-UP**

- Close inspection for local recurrence usually every 3 mo for 5 yr (frequency depends on grade and stage)
- Consider imaging for ambiguous findings on physical exam

**Patient Resources**

**ICD9**
- 170.0 Kaposi’s sarcoma, skin
- 174.9 Malignant neoplasm of penis, unspecified
- 233.5 Carcinoma in situ of penis

**ICD10**
- C46.0 Carcinoma of penis
- C46.9 Malignant neoplasm of penis, unspecified
- D07.4 Carcinoma in situ of penis

**REFERENCES**

**ADDITIONAL READING**

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- External radiation to primary lesion or inguinal lymph nodes
- Typical doses are 50–60 Gy over 4–6 wk
- Intermal brachytherapy for clinically indicated lesions

**Additional Therapies**
- Neoadjuvant chemotherapy
  - TIP: Brachytherapy, paclitaxel, cisplatin
  - Adjunct for high-risk disease
- Pelvic lymph node involvement
- Neoadjuvant chemotherapy

- Metastatic disease
  - TIP
  - Clinical trial
  - Supportive/palliative care

**ONGOING CARE**

**PROGNOSIS**
- Depends on stage and nodal status
- Overall survival for men with node-negative disease is 85–90%
- 20–30% of men with inguinal lymph node metastasis will have pelvic lymph node metastasis
- Pelvic nodal metastasis have a 10%–5 yr survival
- When applicable, UNL associated with improved disease-specific survival

**CODES**

**CLINICAL/SURGICAL PEARLS**
- Grade and stage associated with prognosis
- PNA of palpable nodes is preferred over 6-wk course of oral antibiotics
- Modified ELD is associated with improved nodal clearance
- Bulky inguinital lymph node metastases should be managed by multidisciplinary therapy consisting of neoadjuvant systemic chemotherapy followed by surgical resection (± radiation)
PATHOPHYSIOLOGY
Incidence
- Penile wounds and penetrating injuries make up 40–60% of battlefield wound injuries during times of war. Likely due to lack of protection to external genitalia.
- In the battlefield, use of fragmentation devices (mines, IED) and high-velocity missiles cause a significantly greater percentage of genitourinary injuries to involve the penis and genitalia.
- Pelvic fracture infrequently seen in US, with incidence of 1 in 175,000 hospital admissions.
- Penile fractures are common in Iran where it is a state-sponsored sport.
- Retrograde ejaculation is common in patients prescribed penile constriction devices for the management of erectile dysfunction.

DIAGNOSIS
DESCRIPTION
Acute traumatic injury to the penis may be due to: blunt trauma (penile fracture to the erect penis), penetrating injury (stab wound, firearm, improvised explosive device [IED], or amputation), degloving (blunt force trauma to the erect penis), burns, human and animal bites, or constriction with reduced blood flow.

EPIDEMIOLOGY
Incidence
- Penile wound
- Penile strangulation
- Penile fractures
- Penile amputation
- Rupture of superficial dorsal vein
- Fournier gangrene
- Burn
- Penile “fracture”
- Penetrating injury
- Penile fracture:
  - Type of Injury
  - Magnitude of force transmitted
  - Type of object in penetrating injury
  - Pattern of erections, ecchymosis
  - Associated abdominal pain, nausea, emesis
  - Typical results from impact with partner’s pubic symphysis or perineum
  - Mantle of deep fascia (Buck’s fascia) and superficial skin vascularized all protect from ischemic loss of the penis
  - Penile strangulation:
  - Constricts blood flow, leading to edema, ischemia, constriction
  - Poor perfusion of the corpora cavernosa
  - Adult patients: Penile constricting devices designed for sexual enhancement
  - Pediatric patients: Hair or string causes constriction
  - Associated injuries are common due to the proximity to other pelvic organs
  - Degloving injuries: Loss of superficial penile tissue (skin and dartos fascia)

ASSOCIATED CONDITIONS
- Injury to scrotum, testicles, urethra, or rectum may accompany penile trauma
- Pelvic fracture

GENERAL DIAGNOSIS
- History
  - Type of injury
  - Magnitude of force transmitted
  - Type of object in penetrating injury
  - Pattern of erections, ecchymosis
  - Associated abdominal pain, nausea, emesis
  - Typical results from impact with partner’s pubic symphysis or perineum
  - Mantle of deep fascia (Buck’s fascia) and superficial skin vascularized all protect from ischemic loss of the penis
  - Penile strangulation:
  - Constricts blood flow, leading to edema, ischemia, constriction
  - Poor perfusion of the corpora cavernosa
  - Adult patients: Penile constricting devices designed for sexual enhancement
  - Pediatric patients: Hair or string causes constriction
  - Associated injuries are common due to the proximity to other pelvic organs
  - Degloving injuries: Loss of superficial penile tissue (skin and dartos fascia)

BASICS
- Transferring energy to the penis is most devastating due to penetrating mechanisms
- Adult patients: Penile constricting devices
- Pediatric patients: Hair or string causes constriction

RISK FACTORS
- Occupational (mining, farming, heavy machinery)
- Bicycling is leading sport associated with injury to the external genitalia

GENETICS
- N/A

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urethral culture if infection suspected
- CBC
- For delayed presentation with abscess formation, culture abscesses

Imaging
- Suspect of urethral injury warrants evaluation with retrograde urethrography to evaluate for the presence of injury and injury location
- Penile fracture:
  - MRI or US if useful if rupture of superficial dorsal vein suspected
  - Cavernosography historically described
  - Rectal ultrasound or CT scan may be useful if suspicious for associated injuries

DIFFERENTIAL DIAGNOSIS
- Burn
  - Constriction injury (band or other device placed around base of penis) can include medically approved devices
  - Firefighter's burn
  - Human or animal bite
  - Laceration
  - Penetrating injury
  - Penile “fracture”
  - Rupture of superficial dorsal vein
  - Penile amputation

PHYSICAL EXAM
- Pattern of erythema, ecchymosis
- Assess for injuries of adjacent organs
- Blood at meatus concerning for urethral injury
- Size of laceration, if present
- Transilluminate any palpable scrotal mass
- Symmetry of the penis
- Presence of injury and injury location.

TREATMENT
GENERAL MEASURES
- Establish the overall stability of the patient (1)
- Recognize and appropriately manage injuries to the external genitalia
- Maintain high index of suspicion for urethral injury and assess with retrograde urethrography or cystoscopy
- Association for the Surgery of Trauma (AST) organ injury scale classification (2):
  - I: Cavernosal laceration/contusion
  - II: Buck’s fascia (cavernosal) laceration without tissue loss
  - III: Cavernosal avulsion, laceration through glansmeatus, cavernosal/urethral defect < 2 cm
  - IV: Partial penectomy, cavernosal or urethral defect > 2 cm
  - V: Total penectomy

- For burns see section on “Burns, External Genitalia, and Perineum”
Penile strangulation:
- Penile fracture:
  - Penile amputation
  - Primary skin closure is appropriate unless significant defects due to fracture, gunshot, or stab wound.
  - Surgical exploration is required in almost all cases of penile injury (3–5).

Penile injuries have high likelihood of associated injuries to the external and internal pelvic organs.

With penile fracture there is 10–22% associated urethral injury; surgical repair is associated with lower rates of erectile dysfunction or curvature.

Penile injuries have high likelihood of associated injuries to the external and internal pelvic organs. Urethral injury must be excluded.

Tetanus prophylaxis for all penetrating injuries.

Human bites:
- Should not be closed; antibiotic therapy includes oral dicloxacillin or cephalaxin.

**Additional Reading**
- See Also (Topic, Algorithm, Media):
  - Bites to Penis (Animal and Human)
  - Burns, External Genitalia and Perineum
  - Penis, Transection
  - Penis, Trauma Algorithm
  - Penis, Trauma Images
  - Scrotum and Testicle, Trauma
  - Taghaandan

**Prognosis**
- Most penile injuries can be successfully repaired with low rate of erectile dysfunction when immediate revascularization is performed.
- Delayed repair or nonoperative approach to penile injuries may lead to penile curvature and erectile dysfunction.
- Even after penile amputation, with successful replantation patients can have sensation with erectile function.

**Complications**
- Decreased sensation
- Impotence
- Penile curvature
- Skin loss (particularly with nonmicrovascular penile replantation)
- Urethral stricture
- Urethral stricture or fistula
- Wound infections

**Follow-Up**
- Patient monitoring is required for detection for complications.
- Traumatic injury may result in erectile dysfunction requiring additional therapy.

**Patient Monitoring**
- Euvolemic status should be maintained.
- Adequate fluid resuscitation is critical.
- Urinary drainage should be maintained.
- Temperature control should be maintained.

**Pharmacology**
- Analgesics (local/regional/spinal/local anesthetic):
  - Narcotics (morphine, fentanyl, hydromorphone, meperidine)
  - Benzodiazepines (diazepam, lorazepam)
  - Nonsteroidal anti-inflammatory drugs (ibuprofen, ketorolac)

**Surgical Considerations**
- Penile fracture:
  - Circumferential incision via subcoronal approach with excision of hematoma
  - Close cavernous injuries with absorbable suture (5-0 PDS)
  - Explore for urethral injuries and, if present, repair (5-0 PDS)

**Penile lacerations**:
- Incision of offending agent if possible (cat hair, string, band, soft rings with scissors).
- Solid constraining devices: Attempt removal with lubrication; detailed penile compression with manual pressure may decrease tissue edema long enough to remove foreign body.
- Some devices may require ring cutters, operative drills, industrial drills, various saws; protect phallic with tongue depressor, markable retractor.

**Penile amputation**
- Avulsion (leaving a stump): Neovascularization is a possibility.
- Preservation of the corpus cavernosum at the base of the penis is important.

**Penile amputation**
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Euvolemic status should be maintained.
- Adequate fluid resuscitation is critical.
- Urinary drainage should be maintained.
- Temperature control should be maintained.

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Preservation of the corpus cavernosum at the base of the penis is important.

**Penile amputation**
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Penile amputation:
  - Euvolemic status should be maintained.
  - Adequate fluid resuscitation is critical.
  - Urinary drainage should be maintained.
  - Temperature control should be maintained.

**Penile amputation**
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
- Incision of offending agent if possible (cut hair, string, band, soft rings with scissors).
PEYRONIE DISEASE
Irvin H. Hirsch, MD

ASSOCIATED CONDITIONS
- ED: Occurs in 20% men with PD (1,3)
- Diabetes, Hypertension, Dyslipidemia, Smoking, Coronary disease
- PD is found in 10% men with ED
- Urethral stenosis may occur

GENERAL PREVENTION
Avoidance of penile trauma during intercourse

DIAGNOSIS

HISTORY
- Duration and onset of symptoms, history of erectile trauma. Slight pain or snapping during intercourse
- Pain: With or without erection, during intercourse
- Sensory Loss, partner’s perception

PHYSICAL EXAM
- Erections: Quantify rigidity; sufficient for intercourse
- Pain: With or without erection, during intercourse
- Distress and depression resulting from Peyronie disease

DIAGNOSTIC TESTS & INTERPRETATION
- Lab: Imaging
- No imaging necessary for diagnosis/medical therapy

Prognostic indicators:
- Acute phase:
  - Occurs in 1st 6–18 mo
  - Inflammation of fibroblasts, myofibroblasts, and collagen deposition
  - Pain with erection, slight penile curvature, and nodular formation
- Chronic phase:
  - Medical therapy most effective in acute phase
  - Remodeling of connective tissue into a dense fibrotic plaque
- Stable plaque size, penile curvature possibly causing ED, erections less painful

Natural history: Minority of patients (10%) will have spontaneous regression, yet most patients will not develop disease significant enough to require surgery.

DIAGNOSIS
- Excess collagen deposition and inflammatory infiltrate is found in the tunica albuginea
- Pale plaque: Significant fibrosis
- Deep plaque: Muscle and perineal connective tissue

DIFFERENTIAL DIAGNOSIS
- Cancer: Primary or metastatic to corpora
- Chordee: Usually associated with hypospadias
- Keloid syndrome: Fibrosis of the corpus spongiosum that limits expansion of the ventral corpus cavernosum
- Penile fracture (hematoma)

TREATMENT

GENERAL MEASURES
- A small percent of men will undergo spontaneous remission.
- ED is not a common 1st-line option but ultimately offers definitive resolution of curvature and deformity
- The lack of randomized, placebo-controlled trials makes evaluation of efficacy and comparison between any medical therapies for PD difficult.
- Patients most likely to respond to medical therapy: Young patients in acute phase (1,3)
- Introduction of sexual activity incites healing, trauma. Severe pain or snap or popping during intercourse

PHYSICAL EXAM
- Erections: Quantify rigidity; sufficient for intercourse
- Pain: With or without erection, during intercourse
- Sensory Loss, partner’s perception

DIAGNOSTIC TESTS & INTERPRETATION
- Lab: Imaging
- No imaging necessary for diagnosis/medical therapy

MEDICATION

GENERAL MEASURES
- Oral therapy (2):
  - Acetyl-L-carnitine, 400 mg PO BID
  - Growth factor blocker and anti-inflammatory

DIFERENTIAL DIAGNOSIS
- Cancer: Primary or metastatic to corpora
- Chordee: Usually associated with hypospadias
- Keloid syndrome: Fibrosis of the corpus spongiosum that limits expansion of the ventral corpus cavernosum
- Penile fracture (hematoma)

TREATMENT

GENERAL MEASURES
- A small percent of men will undergo spontaneous remission.
- Surgery is not a common 1st-line option but ultimately offers definitive resolution of curvature and deformity
- The lack of randomized, placebo-controlled trials makes evaluation of efficacy and comparison between any medical therapies for PD difficult.
- Patients most likely to respond to medical therapy: Young patients in acute phase (1,3)
- All medical therapies provide varying decrease in pain, curvature, or plaque size; complete resolution of curvature is uncommon.

MEDICATION

First Line
- Oral therapy (2)
  - No therapy has proven more or less effective than another

TREATMENT

GENERAL MEASURES
- A small percent of men will undergo spontaneous remission.
- Surgery is not a common 1st-line option but ultimately offers definitive resolution of curvature and deformity
- The lack of randomized, placebo-controlled trials makes evaluation of efficacy and comparison between any medical therapies for PD difficult.
- Patients most likely to respond to medical therapy: Young patients in acute phase (1,3)
- All medical therapies provide varying decrease in pain, curvature, or plaque size; complete resolution of curvature is uncommon.

MEDICATION

First Line
- Oral therapy (2)
  - No therapy has proven more or less effective than another

TREATMENT

GENERAL MEASURES
- A small percent of men will undergo spontaneous remission.
- Surgery is not a common 1st-line option but ultimately offers definitive resolution of curvature and deformity
- The lack of randomized, placebo-controlled trials makes evaluation of efficacy and comparison between any medical therapies for PD difficult.
- Patients most likely to respond to medical therapy: Young patients in acute phase (1,3)
- All medical therapies provide varying decrease in pain, curvature, or plaque size; complete resolution of curvature is uncommon.
SURGERY/OTHER PROCEDURES

- Indications: Curvature or erectile dysfunction that preclude intercourse (CHC)
- Patient must be in chronic phase with stable painless plaques
- Progressive US with intracavernous vasoactive challenge is useful to evaluate vasculature and avoid shortening
- Candidates: Shorter penis, proximal plaque, severe erosion/granuloma, penile shortening
- Relative to corporal plaque, plication of opposite side is not recommended
- Intralesional corticosteroids no longer recommended due to local side effects

Second Line

Radiation Therapy

- Mixed results reported; not recommended
- Extracorporeal shockwave therapy: No good studies to support efficacy; not recommended
- Additional Therapies
  - Mixed results reported; not recommended
  - Carnitine supplementation: Mixed results

ONGOING CARE

Erectile Dysfunction/Impotence (ED)

- Patient Monitoring
  - Patients should be re-examined frequently to assess disease status and response to therapy.
  - Depression can be associated

FOLLOW-UP

- Patients with mild curvature and no evidence of erectile dysfunction should be observed.
- Recent studies suggest up to 48% of men with PD should be considered for mental health screening.

PEARLS

- Diagnosis of Peyronie disease is exclusively based on history and physical exam.
- Patients with mild curvature and no evidence of erectile dysfunction should be observed.
- New data suggests that CCH can significantly reduce the symptoms of Peyronie disease.
- The ideal candidate for CCH is having Peyronie disease for at least 12 mo, has stable disease, and a curvature of 30 degrees or greater.

REFERENCES

PHENOCROMOCYTOMA
Shaun G.S. Grewal, MD
Gerald L. Andriole, MD, FACS

PATHOPHYSIOLOGY
- Tumors arise from chromaffin cells of neural crest origin in the sympathetic nervous system
- Rule of 10 (10% bilateral, 10% extra-adrenal, 10% familial, 10% malignant) no longer accurate:
  - 10% of sporadic tumors bilateral
  - Extra-adrenal up to 20%
  - Hereditary 20–30%
  - Malignant up to 5% in adrenal pheochromocytoma
- Histologic determination of malignancy is not possible; diagnosed based on metastases
- Tumors contain enzymes necessary to convert tyrosine to catecholamines
- Clinical manifestations secondary to the release of these catecholamines, NE, and EPI
- Sustained hypertension with superimposed paroxysms: 50% incidence
- Paroxysmal HTNL: dramatic attacks, 3–4 times a week
- Sustained hypertension with superimposed paroxysms: 10% incidence
- Fine tremors, pallor, perspiration
- Papilledema, accelerated hypertensive retinopathy

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Plasma or urinary fractionated metabolites are the best screening tests:
  - Chromaffin cells metabolize NE to NMN and EPI to MN
- Fractionated metabolites refer to MN and NMN
- Both plasma metabolites and urine metabolites are acceptable options; current recommendations do not recommend either test over the other
- Plasma metabolites have a high sensitivity (96–100%) but poor specificity, particularly in older patients (77–89%) (2)
- Urine test: 24 hr urine for NE, EPI, MN, NMN, and VMA
- VMA highly specific (95%) but not sensitive (64%)
- If urinary values are 3 times normal, then proceed to localize the tumor
- If urinary values are 3 times normal and suspicious, then repeat the test and proceed to pharmacoergic testing
- Plasma metanephrine testing
  - No caffeine prior
  - No acetaminophen for 5 days prior
  - No aspirin for 24 hr prior to draw
  - MN > 96 pg/mL, NMN > 130 pg/mL, or total metanephrines > 200 abnormal (2)
- Pharmacologic testing:
  - Stimulation and suppression tests are generally not utilized
  - Provocative tests dangerous, with several reported deaths
  - Clonidine suppression test:
    - Centrally acting α2 agonist that suppresses sympathetic outflow
    - Normally results in decreased BP and lower levels of plasma catecholamines
    - Draw blood for NE/EPI before and 3 hr after administering clonidine (0.3 mg/kg)
    - Plasma metanephrines have a high sensitivity (96–100%) but poor specificity, particularly in older patients (77–89%) (2)
- Histologic determination of malignancy is not possible; diagnosed based on metastases

BASICS
DESCRIPTION
- Phaeochromocytoma is a rare catecholamine-producing tumor arising from chromaffin cells in the adrenal medulla
- Paragangliomas refer to lesions found in extra-adrenal sites arising from the sympathetic nervous system

EPIDEMIOLOGY
- Syndromes are all autosomal dominant
- Germ-line mutations specific to each syndrome
- Von Hippel–Lindau disease (retinal cerebellar hemangioblastomatosis): 10% with brain and spinal cord tumors
- Neurofibromatosis Type 1 (von Recklinghausen disease): 40% with pheochromocytoma
- MEN IIB (MEN III): Pheochromocytoma (50%), medullary carcinoma of the thyroid (50%), and parathyroid adenoma (25%)
- MEN II (MEN III): Phaeochromocytoma (50%), medullary carcinoma of the thyroid (50%), and parathyroid adenoma (25%)
- MEN IIA
- NF1
- NF2

RISK FACTORS
- Familial tumors associated with MEN multiple endocrine neoplasia (MEN) syndromes:
  - MEN IIA (Sipple syndrome):
  - Phaeochromocytoma (50%), medullary carcinoma of the thyroid (50%), and parathyroid adenoma (25%)
  - MEN II (MEN III):
    - Phaeochromocytoma (50%), medullary carcinoma of the thyroid (50%), ganglioneuromatosis, multiple mucosal neuromas (of eyelids, lips, tongue)
    - Neurofibromatosis Type 1 (von Recklinghausen syndrome): 1% has phaeochromocytoma; 5% of patients with neurofibromatosis have neurofibromatosis
    - Von Hippel–Lindau disease (retinal cerebellar hemangioblastomatosis): 10% with pheochromocytoma

GENETICS
- Germ-line mutations specific to each syndrome
- Syndromes are all autosomal dominant
- MEN IIA: Mutation in intracellular domain of RET protein
- Von Hippel–Lindau: VHL tumor suppressor gene on chromosome 3p35
- Von Recklinghausen syndrome: Neurofibromatosis type 1 gene
- Familial neuro-endocrine paraganglioma: Sustinate dehydrogenase gene (1)

HISTORY
- Most patients symptomatic
- Paroxysmal HTNL with severe headache, drenching perspiration, palpitation, and palpitations
- Additional symptoms include nervousness, tremor, palpitations in the chest and abdomen, nausea, fever, and flushing

PHYSICAL EXAM
- Hypertension: Most common sign
- Palpable tumor (rare)
- Fine tremors, pallor, perspiration
- Papilledema, accelerated hypertensive retinopathy
- Sustained hypertension with superimposed paroxysms: 10% incidence
- Paroxysmal HTNL: dramatic attacks, 3–4 times a week
- Sustained hypertension with superimposed paroxysms: 10% incidence
- Fine tremors, palpitation
- Palpable tumor (rare)
- Accelerated hypertensive retinopathy: Papilledema, exudate, A-V nicking
- Raynaud phenomenon
- Hypertrophia cardiaca

IMAGING
- Localization studies should be started only if clinical evidence for the tumor’s existence is strong
- Renal, ureteric, and suprarenal with very high IVU/MRI
- CT or MRI for initial localization
- Neither CT nor MRI is recommended above the diaphragm
- Phaeochromocytoma characteristically hypointense on T2-weighted images
- Scan abdomen and pelvis 1st
- If no tumor found, scan chest and neck
- Metastases in long bones may be missed
- Cannot reliably differentiate between types of adrenal tumors
**PHEOCHROMOCYTOMA**

- Iodine-123-labeled MIBG scintigraphy is more specific for localization of pheo: – Provides both anatomic and functional characterization of the tumor – Concentrated in sympathomedullary tissue through the catecholamine pump – Useful to evaluate for residual or multiple tumors, and MEN syndromes

**Diagnostic Procedures/Surgery**

**Alert**

- Biopsy of adrenal mass should not be performed until pheochromocytoma has been ruled out.

**Pathologic Findings**

- Sporadic tumors are solitary, well-circumscribed, and encapsulated.
- Malignant phae (cannot be differentiated from benign phae) by exam of primary tumor. Malignant phae is defined by metastasis.

**Differential Diagnosis**

- Essential HTN
- Renovascular disease
- Anxiety, tension states, psychoneurosis (rarely)
- Paroxysmal tachycardia
- Hyperthyroidism
- Renovascular disease
- Anemia (rarely)
- Acute hypertension (rarely)
- Nephrologic diseases
- Malignant phae

**TREATMENT**

**General Measures**

- Surgical removal of the tumor is the only definitive method of treatment.

**Medication**

**First Line**

- Alpha-adrenergic blocking agents essential before surgery:
  - Phenoxybenzamine (0-40 mg bid or tid)
  - Prazosin (1-10 mg bid)

- Beta-blocking agents contraindicated in absence of established ad blockades
  - Use only with concurrent cardiac arrhythmias or persistent tachycardia
  - Blockade of peripheral vasodilator beta-adrenergic receptors results in unopposed alpha-adrenergic stimulation with resultant hypertension

- Can precipitate cardiomyopathy and pulmonary edema due to chronic catecholamine excess

**Second Line**

See “Additional Therapies”

**SURGERY/OTHER PROCEDURES**

- Preoperative adrenal blockade is mandatory
- Volume expansion with high sodium diet
- Initial surgery aimed at early ligation and division of the adrenal vein before manipulation of the tumor
- Preoperative adrenergic blockade is mandatory
- Iodine-123-MIBG radiation is the most effective radiation therapy
- Combination chemotherapy with cytokines and interferon may be considered

**Additional Therapies**

- Malignant pheochromocytoma
  - Iodine-123-MIBG scintigraphy is more specific for localization of pheo
  - Initial dissection aimed at early ligation and division of the adrenal vein before manipulation of the tumor
  - Malignant pheochromocytoma is slow growing
  - Re-SECTION should be attempted
  - Large masses can be debulked for palliative surgery

**Follow-up**

- Ongoing care
- 10-yr survival for nonmalignant tumors: >80%
- 5-yr survival for malignant pheo: 34-46%
- Currenty no cure for malignant pheo

**Complications**

- Renal insufficiency
- Hypertensive crisis
- Cerebral vascular accident
- Hemorrhagic necrosis
- Neurogenic pulmonary edema
- Neurogenic pulmonary edema

**Pearls**


**References**


**Additional Reading**


**See Also** (Topic, Algorithm, Media)

- Adrenal Mass
- Adrenal Mass, Algorithm
- Multiple Endocrine Neoplasia (MEN I and II)
- Phaeochromocytoma Image

**Codes**

- ICD9: 237.0 Benign neoplasm of adrenal gland
- ICD10: D35.00 Benign neoplasm of unspecified adrenal gland
- ICD10: D35.01 Benign neoplasm of right adrenal gland
- ICD10: D35.02 Benign neoplasm of left adrenal gland
- ICD10: D55.2 Benign neoplasm of left adrenal gland

**Clinical/Surgical Pearls**

- Hydration and adequate alpha-adrenergic blockade prior to surgery
- Laparoscopic adrenalectomy treatment of choice with early control and ligation of adrenal vein

**Patient Monitoring**

- Because of uncertainties about which tumors are malignant, measure urinary or plasma catecholamines 1-2 wk postoperatively and annually for 5 yr.
- BP should be monitored every month for the 1st 6 mo, then every 6 mo thereafter.
- 25% of patients have persistent HTN after surgery.

**Patient Resources**

www.pheochromocytoma.org
PHIMOSIS AND PARAPHIMOSIS

Michael A. Poch, MD
Philippe E. Spiess, MD

BASICS

DESCRIPTION
- Phimosis (preputial stenosis) is the inability to retract the foreskin.
- Can be seen in children and adults
  - Physiologic (congenital) phimosis: Foreskin (prepuce) is usually not retractile in a newborn.
    - The majority can be retracted by 3–5 yr of age
  - Pathologic (acquired) phimosis: The prepuce cannot be retracted when previously possible or it has never been retractile and is associated with symptoms and/or complications
- Paraphimosis: The prepuce is retracted, left in position causing vascular engorgement of the glans preventing reduction

EPIDEMIOLOGY

Incidence
- Phimosis:
  - 10% nonretractile at 3–5
  - ≤1% nonretractile at puberty
- Paraphimosis:
  - 0.7% of uncircumcised boys

Prevalence
- N/A

RISK FACTORS
- Physiologic phimosis:
  - Local irritation and redness
  - Penile pain
  - Postvoid dribbling
  - Ballooning of the foreskin with voiding
  - Cracking or bleeding from the foreskin
- Penile discharge
  - Dysuria and/or other voiding symptoms
  - BXO

Paraphimosis:
- Hair or thread wraps around a child’s penis and causes penile edema or strangulation
- Diabetes mellitus
- Balanitis xerotica obliterans (BXO)
- Balanoposthitis
- Penile cancer

ASSOCIATED CONDITIONS
- Penis cancer
- Balanitis (inflammation of the glans)
- Posthitis (inflammation of the prepuce)
- Balanoposthitis
- Balanitis xerotica obliterans (BXO)
- Diabetic meatalitis

GENERAL PREVENTION
- Good hygiene
- Don’t prematurely manipulate the foreskin

DIAGNOSIS

HISTORY
- Was foreskin previously retractile?
- Recent urethral manipulation (Foley catheter placement, cystoscopy)
- Circumcision status
- Recent urethral manipulation (Foley catheter placement, cystoscopy)
- Was foreskin previously retractile?

GENERAL MEASURES
- Observation and reassurance
- Manual reduction technique:
  - 1st attempt manual compression for 5 min to reduce edema and reposition foreskin
- Manual reduction should be attempted 1st prior to medication or surgical procedure
- Hair/thread tourniquet:
  - Penile edema
  - Baloconic or circumcised
- Hair or thread wraps around a child’s penis and causes penile edema or strangulation

DIFFERENTIAL DIAGNOSIS
- Phimosis
  - Physiologic vs. pathologic
  - Trapped penis occurs when a dense cicatricial scar traps the penis under the preputial or coronal skin after neonatal circumcision.
  - BXO
- Paraphimosis
  - Penile edema
  - Postcircumcision cicatrix
  - Hair or thread tourniquet
- Urinary tract infection (UTI) or sexually transmitted infection (STI)
- BXO

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Usually not necessary unless symptoms of urinary tract infection (UTI) or sexually transmitted infection (STI) are present
- Imaging
  - Not usually performed

TREATMENT

GENERAL MEASURES
- In the elderly male undergoing bladder catheterization, failure to replace the foreskin to its normal reduced position may result in paraphimosis (1,2)

DIFFERENTIAL DIAGNOSIS
- Phimosis
  - Physiologic vs. pathologic
  - Trapped penis occurs when a dense cicatricial scar traps the penis under the preputial or coronal skin after neonatal circumcision.
  - BXO
- Paraphimosis
  - Penile edema
  - Postcircumcision cicatrix
  - Hair or thread tourniquet
  - Urinary tract infection (UTI) or sexually transmitted infection (STI)
  - BXO

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Usually not necessary unless symptoms of urinary tract infection (UTI) or sexually transmitted infection (STI) are present
- Imaging
  - Not usually performed

DIFFERENTIAL DIAGNOSIS
- Phimosis
  - Physiologic vs. pathologic
  - Trapped penis occurs when a dense cicatricial scar traps the penis under the preputial or coronal skin after neonatal circumcision.
  - BXO
- Paraphimosis
  - Penile edema
  - Postcircumcision cicatrix
  - Hair or thread tourniquet
  - Urinary tract infection (UTI) or sexually transmitted infection (STI)
  - BXO

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Usually not necessary unless symptoms of urinary tract infection (UTI) or sexually transmitted infection (STI) are present
- Imaging
  - Not usually performed

DIFFERENTIAL DIAGNOSIS
- Phimosis
  - Physiologic vs. pathologic
  - Trapped penis occurs when a dense cicatricial scar traps the penis under the preputial or coronal skin after neonatal circumcision.
  - BXO
- Paraphimosis
  - Penile edema
  - Postcircumcision cicatrix
  - Hair or thread tourniquet
  - Urinary tract infection (UTI) or sexually transmitted infection (STI)
  - BXO

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Usually not necessary unless symptoms of urinary tract infection (UTI) or sexually transmitted infection (STI) are present
- Imaging
  - Not usually performed

DIFFERENTIAL DIAGNOSIS
- Phimosis
  - Physiologic vs. pathologic
  - Trapped penis occurs when a dense cicatricial scar traps the penis under the preputial or coronal skin after neonatal circumcision.
  - BXO
- Paraphimosis
  - Penile edema
  - Postcircumcision cicatrix
  - Hair or thread tourniquet
  - Urinary tract infection (UTI) or sexually transmitted infection (STI)
  - BXO
PHIMOSIS AND PARAPHIMOSIS

PHIMOSIS

First Line

- Physiologic phimosis:
  - Topical steroids (0.05% betamethasone) may allow atraumatic retraction (3)
  - Parents should be taught to never force back the foreskin but gradually retract it over time.

- Pathologic phimosis:
  - Topical steroid
  - Aggressive retraction can cause worsening of preputial scarring

Paraphimosis:

- Immediate manual reduction should be attempted
- Pain medication (eg, morphine, Demerol) or local anesthesia (lidocaine without epinephrine, infiltration, or penile block) may be necessary

Second Line

- Paraphimosis:
  - Hyaluronidase injection
  - If manual reduction fails, a dorsal slit or incision of constricting band is indicated
- Recurrent paraphimosis may need definitive circumcision to prevent recurrence.

SURGERY/OTHER PROCEDURES

- Phimosis:
  - Preputioplasty (dorsal slit with transverse closure) for patients wanting to maintain foreskin
  - Circumcision is curative; should be generally avoided in children unless for indications such as recurrent UTI, vesicoureteral reflux, or superficial infections
  - Circumcision is contraindicated in newborns with penile deformities (hypospadias, chordee, webbed penis, etc.) as foreskin may be needed for possible reconstructive surgery

- Paraphimosis:
  - Dorsal or ventral slit urgently treats narrowing and preserves the foreskin
  - Immediate circumcision is occasionally necessary

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

- Compression wraps
- Topical nystatin

REFERENCES


ADDITIONAL READING


CLINICAL/SURGICAL PEARLS

- In most cases physiologic phimosis will resolve. Aggressive retraction of phimosis can cause preputial scarring.
- Manual reduction of paraphimosis should be attempted first prior to surgical intervention.
PNEUMATURIA (GAS IN URINE)
Michael Perrotti, MD

**BASICS**

**DESCRIPTION**
Passage of gas in the urine

**EPIDEMIOLOGY**

**Incidence**
This is a rare disorder.

**RISK FACTORS**
- Diverticular disease
- Other disease of the colon
- Crohn disease
- Advanced age
- Diabetes

**PATHOPHYSIOLOGY**
- Most commonly there is an abnormal connection between the enteric and urinary system secondary to inflammation
- Much less common in gas-producing bacterial urinary tract infection (UTI) (Escherichia coli, Klebsiella pneumoniae) seen most frequently in elderly diabetic females

**ASSOCIATED CONDITIONS**
- Diverticulitis of sigmoid colon
- Colon cancer
- Crohn disease
- Diabetes
- Iatrogenic (radical prostatectomy, radiation)

**GENERAL PREVENTION**
- Colon health
- Prompt treatment of UTI

**DIAGNOSIS**

**HISTORY**
- Pneumaturia
- Dysuria
- Irritative urinary symptoms
- Fecaluria

**PHYSICAL EXAM**
- Depends upon etiology
- May have no significant findings if acute diverticular abscess has resolved
- In emphysematous cystitis there is frequently fever and abdominal tenderness

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urine analysis
- Urine culture
- Complete blood count
- Comprehensive metabolic profile

**Imaging**
- Computed tomography scan identifies air or orally administered contrast in the bladder, colonic, and bladder wall thickening, abscess [1,A]
- Barium enema (definitive: 25%; suggestive: 100%)

**Diagnostic Procedures/Surgery**
- Colonoscopy may directly visualize the fistula, and is essential to inspect the remainder of the colon
- Cystoscopy may visualize the actual fistula, or identify suggestive localized inflammation and edema

**Pathologic Findings**
- Diverticular disease with abscess
- Colon malignancy
- Crohn disease
- Bladder malignancy
- Radiation or surgical induced fistula

**DIFFERENTIAL DIAGNOSIS**
- Emphysematous cystitis
- Emphysematous pyelonephritis
- Unilateral vesical fistula
- Vesical enteric fistula

**TREATMENT**

**GENERAL MEASURES**
- Antibiotic therapy for acute diverticulitis
  - Ciprofloxacin 500 mg PO BID with metronidazole 500 mg PO TID [A]
  - Ampicillin-sulbactam 3 g IV q6h
  - Piperacillin-tazobactam 3.375 g IV q6h
  - Ticarcillin clavulanate 3 g IV q6h
  - Ceftriaxone 1 g IV q24h with metronidazole 500 mg IV q8h

**SURGERY/OTHER PROCEDURES**
- **Emphysematous UTI**
  - Percutaneous management of purulent material and gas
  - Percutaneous nephrostomy placement for emphysematous pyelonephritis
  - Emergent nephrectomy is associated with very high mortality
  - Emergent vesical fistula
  - Enterovesical fistula typically do not close spontaneously
  - The portion of bowel responsible for the fistula is excised in a 1-stage procedure with resection and primary anastomosis
  - Urgent stent placement may be performed preoperatively to allow identification of the ureter intraoperatively
  - Resection of the bladder is rarely necessary
  - A small defect in the bladder can be managed with suture repair, indwelling Foley catheter, and closed suction drain in the pelvis

---
PNEUMATURIA (GAS IN URINE)

ONGOING CARE

PROGNOSIS

- Gas-producing UTI (2)[A]
  - Parenteral antibiotic therapy is successful in the majority of patients with gas limited to bladder
  - Patients with gas in the upper urinary tract are at increased risk of mortality and require percutaneous drainage with parenteral antibiotics
  - Gas in the perinephric space and paranephral tissues are at increased risk of mortality
- Diverticular abscess and enteric vesical fistula
  - Patients have an excellent prognosis after elective resection of the diseased bowel segment
  - In many cases this can be performed laparoscopically (3)[B]

COMPLICATIONS

- Patients with inflammatory disorders such as Crohn may have complex and recurrent fistula
- Patients with fistula following radiation therapy may have impaired healing and experience recurrence

FOLLOW-UP

Patient Monitoring

- Management of associated illness
- Prompt treatment of disease flare

Patient Resources

NA

REFERENCES


ADDITIONAL READING

- See Also (Topic, Algorithm, Media)
  - Cystitis, Emphysematous
  - Fistula, Enterovesical
  - Inflammatory Bowel Disease (Ref: Enteric Colitis and Crohn disease), Urologic Considerations
  - Pneumaturia (Gas in Urine) Image
  - Urinary Tract Infection (UTI), Adult Female
  - Urinary Tract Infection (UTI), Adult Male

CODES

ICD9

- 596.1 Intestinovesical fistula
- 599.0 Urinary tract infection, site not specified
- 599.84 Other specified disorders of urethra

ICD10

- N32.1 Vesicointestinal fistula
- N29.0 Urinary tract infection, site not specified
- R39.89 Other symptoms and signs involving the genitourinary system

CLINICAL/SURGICAL PEARLS

- Pneumaturia is the distinct sensation by the patient of passage of air from the urinary tract.
- Pneumaturia should be considered secondary to an enteric vesical fistula unless proven otherwise.
- The CT scan finding of air in the bladder is abnormal and of high diagnostic value in the evaluation of the patient with suspected pneumaturia and is likely to reveal associated pathology.
- The most common cause of pneumaturia is diverticular disease.
POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL DOMINANT

Megan T. Bing, MD
James A. Brown, MD, FACS

ASSOCIATED CONDITIONS
- Abdominal wall hernia
- Cardiac valvular abnormalities
- Colon diverticula
- Hepatic cysts from 29–71%
- Splenic and pancreatic in a small percentage
- Intracranial aneurysms
- Only screen if patient has previous rupture
- Saccular “berry” aneurysm of cerebral arteries in 3–13%
- Pancreatic cysts
- Polycystic liver disease

DIAGNOSIS

ASSOCIATED CONDITIONS
- Abdominal wall hernia
- Cardiac valvular abnormalities
- Colon diverticula
- Hepatic cysts from 29–71%
- Splenic and pancreatic in a small percentage
- Intracranial aneurysms
- Only screen if patient has previous rupture
- Saccular “berry” aneurysm of cerebral arteries in 3–13%
- Pancreatic cysts
- Polycystic liver disease

DIAGNOSIS

ASSOCIATED CONDITIONS
- Abdominal wall hernia
- Cardiac valvular abnormalities
- Colon diverticula
- Hepatic cysts from 29–71%
- Splenic and pancreatic in a small percentage
- Intracranial aneurysms
- Only screen if patient has previous rupture
- Saccular “berry” aneurysm of cerebral arteries in 3–13%
- Pancreatic cysts
- Polycystic liver disease

DIAGNOSIS

ASSOCIATED CONDITIONS
- Abdominal wall hernia
- Cardiac valvular abnormalities
- Colon diverticula
- Hepatic cysts from 29–71%
- Splenic and pancreatic in a small percentage
- Intracranial aneurysms
- Only screen if patient has previous rupture
- Saccular “berry” aneurysm of cerebral arteries in 3–13%
- Pancreatic cysts
- Polycystic liver disease

DIAGNOSIS

ASSOCIATED CONDITIONS
- Abdominal wall hernia
- Cardiac valvular abnormalities
- Colon diverticula
- Hepatic cysts from 29–71%
- Splenic and pancreatic in a small percentage
- Intracranial aneurysms
- Only screen if patient has previous rupture
- Saccular “berry” aneurysm of cerebral arteries in 3–13%
- Pancreatic cysts
- Polycystic liver disease

DIAGNOSIS
Therapies

Complementary & Alternative Additional Therapies

Radiation Therapy

ADDITIONAL TREATMENT Radiation Therapy

SURGERY/OTHER PROCEDURES

First Line

• Hypertension

– Angiotensin-converting enzyme (ACE) inhibitors
– Angiotensin II receptor blockers (ARBs) such as telmisartan, losartan, irbesartan, and candesartan
– Hydralazine: Sustained

Second Line

• Somatostatin (2)

• Inhibitors of mTOR

• Nephrectomy

• Cyst decortication—typically for pain with large renal cystic disease

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin

• Inhibitors of mTOR

• Somatostatin (2)

• Hyperlipidemia: Statin
POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL RECESSIVE
Kymora Scotland, MD, PhD
T. Ernesto Figueroa, MD, FAAP, FACS

DESCRIPTION
A group of inherited disorders involving cystic dilatation of the renal collecting ducts and varying degrees of biliary dysgenesis and portal fibrosis
Formerly known as infantile polycystic kidney disease
An overlap in the spectrum of renal and liver involvement precludes use of the Blyth and Ormond classification (perinatal, neonatal, infantile, and juvenile subtypes)
Best grouped as polycystic disease of newborn and young infant, polycystic disease of childhood, and congenital hepatic fibrosis

EPIDEMIOLOGY
Incidence
Most common inherited cystic renal disease in infancy and childhood
Incidence: 1–2 in 10,000 live births

Prevalence
Commonly diagnosed in perinatal period; can present early in childhood or adolescence
Survival: For patients living to 1 mo: 86% alive at 1 yr, 67% alive at 15 yr

RISK FACTORS
Definite risk factor: Heterozygous parents
Liver function tests (usually normal)
Coagulation profile
CBC (exclude anemia, hypersplenism)
Electrolytes, blood chemistry, urine analysis, urine culture

PHYSICAL EXAM
– Potter phenotype, pallor
– Polydipsia, polyuria, fatigue, unexplained fever, HTN, respiratory rate, temperature
– For older patient, may suggest evolution of disease

DIAGNOSTIC TESTS & INTERPRETATION
– Normal parents with a normal renal US suggests recessive disease

ASSOCIATED CONDITIONS
– Potter syndrome
– Ectopia cordis
– Potter–Ferguson syndrome

DIAGNOSIS
History
– Age of the patient:
  – Other cystic renal disorders rarely present in the pediatric population:
    – Younger, more exploratory and renal issues
  – Older, more hepatobiliary issues
  – 1/3 are diagnosed before age 1; 1/3 between age 1 and 20 yr; and 1/3 beyond 20 yr
– Present care
  – Characteristic changes on prenatal US after week 30, abnormal ureter growth measurements, maternal w fetoprotein levels, amniocentesis results, history of stillbirth
– Birth history:
  – Delivery: difficult delivery suggests possible flank or abdominal mass
  – Family history:
    – Normal patients with a normal renal US suggests recessive disease
    – Medical history:
      – For other patient, may suggest evolution of disease

Diagnosis
– Potter phenotype
– Polydipsia, polyuria, fatigue, unexplained fever
– Hepatosplenomegaly
– Difficulty breathing and feeding
– Infant with hypotonia
– Abnormal US

DIAGNOSIS TESTS & INTERPRETATION
– Echocardiography
– Abdominal ultrasonography
– MRI, CT scan

MAJOR COMPLICATIONS
– Progressive renal insufficiency
– Renal failure

DIAGNOSTIC PROCEDURES/SURGERY
– Nephrectomy
– Liver biopsy

DIAGNOSTIC TESTING
– Imaging
  – Ultrasound: Enlarged kidneys, oligohydramnios, normal liver, no bladder filling
  – CT scan: Enlarged liver, normal renal US
– CT may be used in confusing cases: More sensitive to inhomogeneity of cysts
– MRI may be used in confusing cases: More sensitive to inhomogeneity of cysts

IMAGING
– Ultrasound
– MRI
– CT
– Angiography
– Renal biopsy
– Liver biopsy

DIFFERENTIAL DIAGNOSIS
– Autosomal dominant polycystic kidney disease (ADPKD)
– Medullary cystic disease
– Meckel–Gruber syndrome
– Autosomal recessive polycystic kidney disease (ARPKD)

IMAGING
– Ultrasound
– MRI
– CT
– Angiography
– Renal biopsy
– Liver biopsy

DIFFERENTIAL DIAGNOSIS
– Autosomal dominant polycystic kidney disease (ADPKD)
– Medullary cystic disease
– Meckel–Gruber syndrome
– Autosomal recessive polycystic kidney disease (ARPKD)
TREATMENT

GENERAL MEASURES
- No specific therapy for ARPKD. Treatments are supportive.
- Pulmonary issues 1st priority initially; survival better with advances in perinatology.
- Goals: Delay progression to renal failure, liver failure, and portal HTN.
- Avoid nephrotoxic medications.
- Social support and intensive care.

MEDICATION

First Line
- Thiazides to help urine-concentrating defect.
- Treatment of renal osteodystrophy with vitamin D and phosphate binders.
- Recombinant human erythropoietin.
- Growth hormone treatment.

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Prophylactic bilateral nephrectomy and peritoneal dialysis catheter (significant pulmonary distress).
- Unilateral nephrectomy (improve feedings; help with breathing).
- Gastrostomy tube placement (improve feedings).
- Splanchnicectomy; or pericaval short procedures (portal HTN).
- Renal transplantation (EJSD).
- Liver transplantation (hepatic failure).
- Progressive liver fibrosis with portal hypertension.

ADDITIONAL TREATMENT

Radiation Therapy
- N/A

Additional Therapies
- Adequate hydration.
- Correct acid-base and electrolyte abnormalities.
- Aggressive HTN control.
- Peritoneal dialysis.
- Enteral feedings.
- Advanced pulmonary support as required.

Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS
- Mortal.
- Abnormal prenatal US (polysplenia, enlarged rib margins, absent egg in bladder, severe IUGR, gestational age <33 wks).
- Neonates: If present at birth, the usual clinical course is death. Patients have feeding intolerance, respiratory distress.
- Infants: Palpable flank masses, abdominal mass, Potter phenotype, GI bleed, hepatosplenomegaly, polyuria, polydipsia, polyuria, HTN, nonspecific GI complaints, edema, growth retardation, fatigue, infection. Will eventually develop renal failure and HTN.
- All patients with ARPKD have liver involvement.
- Those with severe ARPKD have mild congenital hepatic fibrosis and those with severe congenital hepatic fibrosis have mild ARPKD.

COMPLICATIONS
- Renal: Renal failure (concentrating defect with polydipsia and polyuria), HTN, anemia, occasional metabolic acidosis, hyperuricemia, osteodystrophy, growth failure, UTI.
- Hepatobiliary: Hepatoplenomegaly, bleeding esophageal varices, portal thrombosis, cholangitis.
- Pulmonary: Respiratory failure, portal HTN.
- Complications: GI feeding intolerance, failure to thrive.

FOLLOW-UP

Patient Monitoring
- Progressive renal failure in most patients requiring ongoing renal assessments.
- Blood pressure.
- Liver functions and ultrasound at least annually.
- Overall assessment of growth and nutritional status.
- Parental counseling is critical as there is a 1 in 4 chance of another child having the disease.

Patient Resources

REFERENCES

ADDITIONAL READING
- See also (Topic, Algorithm, Media)
- PFDNET (autosomal recessive polycystic kidney disease).
- Meckel–Gruber Syndrome (Medial Syndrome).
- Multicystic Dysplastic Kidney.
- Nephronophthisis (juvenile, infantile, and adolescent).
- Polycystic Kidney Disease, Autosomal Dominant Polycystic Kidney Disease, Autosomal Recessive.
- Image of: Renal Cysts (intrarenal, periampullar, and perirenal).
- Renal Dysplasia, Hypertrophy, and Hypoplasia.
- Renal Mass.

CODES
- ICD9 751.69 Other anomalies of gallbladder, bile ducts, and liver.
- ICD9 751.14 Polycystic kidney, autosomal recessive.
- Nephronophthisis (juvenile, infantile, and adolescent).

Clinical/Surgical Pearls
- Renal and liver involvement is typical.
- Often fatal if present at birth.
- Treatments are supportive; no specific therapy.
**Polyhydramnios/Oligohydramnios**

Bruce J. Schlomer, MD
Laurence S. Baskin, MD, FACS, FAAP

**BASICS**

**DESCRIPTION**
- Oligohydramnios is defined as an abnormally low amniotic fluid (AF) volume.
- Associated with increased fetal morbidity and mortality
- Polyhydramnios is defined as an abnormally high AF volume:
  - Up to 25% of neonates will have a congenital anomaly
  - Associated with increase in aneuploidy, congenital malformations, prematurity, and perinatal death
- These conditions are diagnosed using prenatal US with strict criterion described below

**EPIDEMIOLOGY**

**Incidence**
- Oligohydramnios in 3–5% of pregnancies (1)
- Polyhydramnios in 1–3% of pregnancies (1)
- Usually discovered in 2nd trimester with 40% normal by term

**Prevalence**
- N/A

**RISK FACTORS**
- **Oligohydramnios**
  - Prerenal: Placental insufficiency, umbilical cord
  - Spontaneous/idiopathic
  - Iatrogenic: Amniocentesis
- **Polyhydramnios**
  - Maternal diabetes
  - Nonimmune hydrops fetalis
  - GI obstruction (esophageal atresia, duodenal atresia)
  - Neural tube defects
  - Anencephaly
  - Potter syndrome:
    - Pulmonary hypoplasia, limb abnormalities
    - Multicystic dysplastic kidney or prune-belly syndrome
    - Oligohydramnios: Decreased maternal fundal height
    - Polyhydramnios: Increased maternal fundal height

**ASSOCIATED CONDITIONS**
- **Polyhydramnios:**
  - Pulmonary hypoplasia: Correlated with fetal outcome and main cause of fetal death
  - Intrauterine growth restriction
  - Potter facies with severe oligohydramnios
  - Better outcome if presents in 3rd trimester vs. 2nd trimester (3)
  - Better outcome if cause is PROM vs. congenital anomaly (3)
- **Causes of polyhydramnios**
  - Obligatory: >60%
  - Better outcomes:
    - Maternal causes: ∼15%
    - Maternal diabetes
    - Infections: Syphilis, rubella, TORCH, toxoplasmosis, parvovirus, RH immunization
    - Drug abuse: Polyhydramnios in ∼25–30% of drug-addicted women. Leads to decreased neurologic function of fetus and decreased swallowing
  - Fetal causes:
    - Reduced fetal swallowing: Maternal drug use, fetal neurologic anomalies, aneuploidy
    - GI anomalies: T-E fistula, choanal atresia, facial cleft, esophageal atresia, imperforate anus
    - Cardiac failure with diuresis

**DIAGNOSTIC TESTS & INTERPRETATION**

**PHYSICAL EXAM**
- **Polyhydramnios:**
  - Increased maternal fundal height
  - Pulmonary hypoplasia: Correlated with fetal outcome and main cause of fetal death

**LABORATORY EXAM**
- **Polyhydramnios:**
  - Increased maternal weight
  - Maternal infectious exposure
- **Oligohydramnios:**
  - Poor weight gain
  - Medication history

**GENERAL PREVENTION**
- **Polyhydramnios:**
  - Avoid known medications (NSAIDs, etc.)
  - Avoid maternal dehydration
- **Oligohydramnios:**
  - Prevention of infections transmissible from mother to fetus
  - Avoid drug abuse

**DIAGNOSIS**

**HISTORY**
- **Polyhydramnios:**
  - Increased maternal weight
  - Maternal drug use
  - Maternal infectious exposure
- **Oligohydramnios:**
  - Poor weight gain
  - Medication history

**PHYSICAL EXAM**
- **Polyhydramnios:**
  - Increased maternal fundal height
  - Pulmonary hypoplasia: Correlated with fetal outcome and main cause of fetal death

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- **Polyhydramnios:**
  - Maternal testing for glucose, autoantibodies, TORCH screen, parvovirus, fetal karotype
- **Oligohydramnios:**
  - General: Fetal karotype, pulmonary maturity, maternal autoantibodies (lupus, antiphospholipid, anticonvulsant)
  - Renal: Maternal urinary electrolytes
  - Better outcome associated with β2-microglobulin, α2-microglobulin, and retinal-binding protein

**Imaging**
- US measurements of AF volumes are very operator-dependent and very variable (4)
- No perfect means to determine actual volume, but several surrogate markers are used:
  - Maximum vertical pocket: Polyhydramnios >7 cm, oligohydramnios <1 cm
  - AFI: Sum of largest volumes from each of 4 placental quadrants:
    - Oligohydramnios <5 cm, polyhydramnios >25 cm
  - Fetal MRI increasingly used for better anatomic detail
Differential Diagnosis

- Polyhydramnios
  - Premature rupture of membranes (PROM)
  - Maternal: Rh isoimmunization, neural tube defects, maternal diabetes, maternal HTN, autoimmune disorders, drugs (NSAIDs, ACE inhibitors)
  - Internal: Renal dysplasia, renal agenesis
  - Obstetric: Polyhydramnios, pruritis, blunt trauma, ureteral obstruction, bilateral hydronephrosis
  - Prolonged gestation can lead to polyhydramnios late in pregnancy

- Oligohydramnios
  - Idiopathic — 60%
  - Better outcomes
    - Maternal causes: ~15%
    - Maternal diabetes
    - Infections: Syphilis, rubella, MRSA
    - Drug abuse: Polyhydramnios in ~25–30% of drug-addicted women. Leads to decreased neurologic function of fetus and decreased swallowing
    - Placental chorangioma or arteriovenous fistula
    - Fetal causes:
      - Reduced fetal swallowing: Maternal drug use, anemia, renal tube defects, muscular dystrophy syndromes, aneuploidy
      - GI anomalies: Tetralogy of Fallot, intestinal atresia, facial defects, esophageal atresia, imperforate anus, gastroschisis, duodenal atresia/stenosis, cleft, esophageal atresia, imperforate anus, congenital anomalies (3)
      - Heart failure: Congestive heart failure, severe anemia
      - Karyotype anomalies: Trisomy 21, etc.
      - Multiple malformations: Rh disease, severe anemia, infections in mother (e.g., pneumonia, CMV), twin–twin transfusion syndrome, maternal hypertension, disorders of glycosylation
      - Other: Sclerocystic teratoma, skeletal dysplasia, thrombocytopenia

Prognosis

- Polyhydramnios: If idiopathic, the prognosis is usually good
- Oligohydramnios:
  - With normal agenesis, mortality rate is 100%
  - Fetal outcomes correlated to degree of pulmonary hypoplasia
  - Mild forms of obstructive uropathy may cause renal insufficiency
  - Better prognosis with presentation in 3rd vs. 2nd trimester (c)
  - Better prognosis with PROM as cause vs. congenital anomalies (d)

Complications

- Polyhydramnios can cause increased prematurity labor
- Oligohydramnios can cause fetal distress before or during labor and severe respiratory distress and pneumonia due to pulmonary hypoplasia

Treatment

General Measures

- Polyhydramnios:
  - US every 3–4 wk
  - Follow pregnancy to 38 wk
  - Monitor for UTI
  - Amnioinfusion
- Oligohydramnios:
  - US every 3–4 wk for fetal viability and IUP

Follow-Up

- Close monitoring by prenatal sonography

Prevention

- Early delivery with steroids for severe oligohydramnios and pulmonary hypoplasia
- Consider early delivery with steroids for oligohydramnios due to bladder outlet obstruction

ADDITIONAL READING


ICD9

- 657.00 Oligohydramnios, unspecified as to episode of care or not applicable
- 658.00 Polyhydramnios, unspecified as to episode of care or not applicable
- 761.2 Oligohydramnios affecting fetus or newborn

ICD10

- O41.00X0 Oligohydramnios, unspecified trimester
- O40.9XX0 Polyhydramnios, unspecified trimester
- A21.9000 Oligohydramnios, unspecified trimester, not applicable or unspecified
- A01.00X0 Polyhydramnios, unspecified trimester, not applicable or unspecified
- P01.2 Newborn (suspected to be) affected by oligohydramnios

Clinical/Surgical Pearls

- If amniotic fluid (AF) levels are normal, the fetus is very likely to have adequate urine production even with bilateral hydramnios.
- In cases of intervention with vesicoamniotic shunt, it is controversial.
- Idiopathic polyhydramnios has good outcomes.
POLYOMA VIRUS (BK, JC), UROLOGIC CONSIDERATIONS

Nathan Roberts, MD
Patrick J. Shenot, MD, FACS

DESCRIPTION

- JC and BK viruses are 2 of 10 different human polyoma viruses
- Small DNA viruses in the papovavidae family
- JC and BK viruses named after 1st patients the viruses were isolated from in 1971
- These viruses typically manifest clinical sequelae only in immunocompromised hosts
- BK virus has a tropism for genitourinary epithelium
  - Clinical manifestations: Hemorrhagic cystitis (HC), ureteral stenosis, nephropathy, and rare GU-associated malignancies

EPIDEMIOLOGY

Incidence

- Prevalence
  - BK virus has an 82–99% seroprevalence in adults of the United States, Italy, and Australia
  - 50% at 2 yr of age, 90% at 10 yr of age
  - JC virus has a 38–81% seroprevalence in same regions
  - Clinically manifest only in immunocompromised subjects
- Universal serostatus due to BK virus infection among allograft recipients is approximately 4%
- BK-induced nephropathy: 1–10% of transplants

Hemorrhagic cystitis

- Reported to cause hemorrhagic cystitis in 5.7–7.7% of bone marrow transplant recipients

ASSOCIATED CONDITIONS

- Immunocompromised host
  - Degree of immunosuppression
  - Transplant recipients
    - Solid organ (especially kidney), stem cell transplants
    - HIV/AIDS
  - Prophylaxis toward hemorrhagic cystitis
  - Autoimmune disorders requiring immunosuppression
  - Multiple sclerosis

Genetics

- Small nonenveloped (icosahedral particles of 40–45-nm diameter with a nonenveloped, circular double-stranded DNA genome
- Polyoma viruses encode 6 proteins
  - 3 structural capsid proteins
  - 3 noncapid regulatory proteins
  - Large and small T antigen (cell immortalization and latency), and agnoprotein (assembly of viral particles)
  - Proteins interact with cellular target proteins and impair pathways involved with cell cycle and DNA repair

PATHOPHYSIOLOGY

- Route of transmission is unknown but seems to occur early in life most likely seak spharyngeal exposure (1,2)
- Hyperplasia of subclinical infection leads to viremia that seeds the kidneys
- Pathology is postulated to occur from reactivation of latent infection and not reactivation
- Immunocompromise/inflammation syndrome
  - Dominant inflammatory response to BK virus antigen followed by brisk recovery of the cellular immune response
    - Seen in BKV-associated hemorrhagic cystitis
      - After allogeneic stem cell transplantation
  - Cytopathic inflammatory polyomavirus pathology
    - High-level virus replication and a significant inflammatory response due to lytic viral T-lymphocytic necrosis, with infiltration of granulocytes and lymphocytes
    - Dominant inflammatory response to abundant polyoma virus antigen followed by brisk recovery of the cellular immune response
    - Seen in BKV-associated nephropathy in kidney allografts
- Oncogenic polyomavirus pathology
  - Early viral gene expression activating host cells but without sufficient late gene expression to cause rapid host cell lysis
  - Seen in rare BKV-associated urethral and renal tubular cancers
  - There is conflicting evidence of BK virus involvement in these tumors
- Hemorrhagic cystitis
  - Another theory suggests 3 phases
    - Conditioning regimen for stem cell transplant damages the bladder mucosa providing environment for virus replication
    - Viral replication unchecked in the absence of functional immunity
    - Further damage to the bladder mucosa with immune reconstitution and return of anti-BK immunity
- Immuno-reconstitution inflammatory syndrome
  - Due to denervation of transplanted kidney, patient may not present with pain

ASSOCIATED CONDITIONS

- BK virus has a tropism for genitourinary epithelium
  - Kidney transplant recipients
    - Tubulointerstitial nephritis
    - Ureteral stenosis
  - Stem cell transplant recipients
    - Hemorrhagic cystis
    - JC virus has a tropism for neural tissue
    - Causes progressive multifocal leukoencephalopathy
    - Not as common, but JC can also be related to genitourinary manifestations like BK virus and vice versa

ASSOCIATED CONDITIONS

- Route of transmission is unknown so difficult to prevent
- Competent immune system will prevent clinical sequelae

DIAGNOSIS

HISTORY

- Hemorrhagic cystitis
  - From pink colored urine to clot retention
  - Pt can also have bladder pain
  - Pt may have UTI
  - BK virus nephropathy
    - Typically occurs 10–13 mo after transplant
    - Often asymptomatic
    - May have hematuria
    - May have decreased urine output
    - Transplanted ureteral stricture (3)
      - Typically occurs 2–4 mo after transplant
    - Often asymptomatic
    - May have decreased urine output

PHYSICAL EXAM

- Hemorrhagic cystitis
  - May present with palpable bladder if in clot retention
  - BK virus nephropathy
    - No significant findings on exam
  - Universal stenosis of kidney transplant
    - May have no significant findings
    - Pelvic mass bulge from transplant hydronephrosis
    - Due to denervation of transplanted kidney, patient may not present with pain

DIAGNOSTIC TESTS & INTERPRETATION

LAB

- Urine culture mostly used in research setting
- Takes weeks to months to grow
- Unreliable findings
- Detects virus shedding
- Characteristic finding is an enlarged nucleus with a single large basophilic intranuclear inclusion (“decoy cells”)
- Does not distinguish between various types of polyoma virus
- BK virus quantitative PCR
  - Correlates with BK virus associated nephropathy
  - Can be positive in normal controls, elderly patients and HIV-infected patients without clinical manifestations
  - Difficult to assess clinical significance
- Plasma quantitative PCR
- Hemorrhagic cystitis
  - Urine positive for blood/WBCs
  - BK virus nephropathy
  - Elevated creatinine
  - Urinalysis
    - Pyuria, hematuria, and/or cellular casts of renal tubular cells and inflammatory cells
    - May have decreased urine output
  - Transplant ureteral stricture
    - Can have elevated creatinine

IMAGING

- Hemorrhagic cystitis
  - Ultrason or CT scan show bladder thickening
  - Can show clot retention
  - Transplanted ureteral stricture
  - Hydronephrosis seen on renal ultrasound, CT or MRI
  - Pelvic mass bulge from transplant hydronephrosis
  - May present with pain
POLYOMA VIRUS (BK, JC), UROLOGIC CONSIDERATIONS

Diagnostic Procedures/Surgery
- Hemorrhagic cystitis
  - Cystoscopy can show evidence of obstructive bleeding
- BK virus nephropathy
  - Renal biopsy
  - Most often percutaneous approach
  - Histopathology results listed below
  - Can also use Immunohistologic or in situ hybridization evidence of virally infected cells to make diagnosis
  - Strongly positive using an SV40 immunohistochemical stain

Pathologic Findings
- BK Virus nephropathy
  - Usually infects tubule epithelial cells
  - Adenoviruses, Herpesviridae, and Chromatin clumping of infected cells
  - Interstitial mononuclear or polymorphonuclear cell infiltrates in the areas of tubular damage
  - Tubular injury with tubular cell apoptosis
  - Intravascular bafilomycin viral inclusions with a surrounding halo
- Not pathognomonic for BK virus
- CMV has cytopathic inclusion
- HSV has both intranuclear and cytoplasmic inclusions

Differential Diagnosis
- Hemorrhagic cystitis
  - Medication related (high-dose cyclophosphamide)
    - Often occurs within 7–14 days
  - Adenovirus related
  - Radiation induced
  - Infectious source
  - Trauma
    - Possibly from urethral catheter placement
- BK virus nephropathy
  - Cellular rejection
  - Transplant ureteral stenosis
  - Surgical technique, ischemia of distal ureter
    - Typically occurs in 7–10 days

TREATMENT
GENERAL MEASURES
- Reduction of immunosuppression if possible (4)
  - Often most effective strategy

MEDICATION
First Line
- Quinolones antibiotic (ciprofloxacin, etc.)
  - Suggested for prophylactic role
- Intravenous Immunoglobulin
  - Can be used in hypogammaglobulinemic patients
- Leflunomide: Antiviral activity

Second Line
- Intravenous or intravenous clindamycin
  - Nucleotide analog of cytosine
  - Active against DNA viruses
- Anecdotical evidence for use against polyoma viruses
- Highly nephrotoxic

OTHER PROCEDURES
- Hemorrhagic cystitis
  - Cystoscopic fulguration (electro cautery or laser)
  - Conjugated estrogens: Act by stabilization of microvasculature
  - Intravesical instillation of formalin
    - 60%–1% instilled for 10–20 min
    - May lead to renal failure due to precipitation and obstruction of upper tracts
    - E-aminocaproic acid
      - Inhibits fibrinolysis preventing activation of plasminogen to plasmin
      - Given orally, peripherally, or intravesically
      - Patients can form hard clots that are difficult to flush from the bladder
- Intravesical instillation of prostaglandin
  - PGF2a. May encourage platelet aggregation and induce vasoconstriction
  - PGF2a 0.75 mg in 200 mL of normal saline and left indwelling
  - May cause bladder spasms
    - Painful and needs to be done with general anesthesia
- Intravesical instillation of formalin
  - 40% formoldehyde
    - Hydrolizes proteins and coagulates tissue on superficial level
- Intravesical instillation of silver nitrate
  - Inhibits fibrinolysis preventing activation of plasminogen to plasmin
    - Can result in small contracted bladder
- Intravesical instillation of cadaverine

SPECIAL WEBSITES
- Hemorrhagic cystitis
  - Cystoscopic instillation (electro cautery or laser)
  - Conjugated estrogens: Act by stabilization of microvasculature
  - Intravesical instillation of formalin
    - 40% formoldehyde
    - Hydrolizes proteins and coagulates tissue on superficial level
  - Intravesical instillation of prostaglandin
    - PGF2a. May encourage platelet aggregation and induce vasoconstriction
    - PGF2a 0.75 mg in 200 mL of normal saline and left indwelling
    - May cause bladder spasms
    - Painful and needs to be done with general anesthesia
- Intravesical instillation of formalin
  - 40% formoldehyde
    - Hydrolizes proteins and coagulates tissue on superficial level
- Intravesical instillation of silver nitrate
  - Inhibits fibrinolysis preventing activation of plasminogen to plasmin
    - Can result in small contracted bladder

SURGERY/OTHER PROCEDURES
- Hemorrhagic cystitis
  - Cystoscopic instillation (electro cautery or laser)
  - Selective embolization
  - Vescical or internal iliac artery
- BK virus Nephropathy
  - Kidney re-transplant
  - Limited information for outcomes
  - Recommended patients have absence of BK replication prior to re-transplantation
  - Transplant ureteral stenosis
  - Decompression of the transplanted kidney
  - Periureteral nephroptosis tube
  - Urinary stent placement
  - Surgical excision of stenotic segment

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
- Hemorrhagic cystitis
  - Hyperbaric oxygen: Promotes healing of hypoxic tissues and aid in angiogenesis

COMPLEMENTARY & ALTERNATIVE THERAPIES
N/A

ONGOING CARE
PROGNOSIS
- Hemorrhagic cystitis: Dramatic in presentation but usually resolves spontaneously within 2 wk with supportive care
- BK virus nephropathy: Graft failure in 15–50%

FOLLOW-UP
Patient Monitoring
BK virus nephropathy: After transplant same recommended periodic monitoring for viremia

Patient Resources
N/A

REFERENCES

ADDITIONAL READING
See also (Topic, Algorithm, Media)
- Cryotherapy
- Ureteral stenosis
- BC: 0.75% instilled for 10–20 min

CODES
- 599.3 ST: Cystectomy and structure of bladder or ureter
- 012.7: Cystitis, unspecified

CLINICAL/SURGICAL PEARLS
Polyoma virus will only have clinical sequelae in immunocompromised patients.
POSTERIOR URETHRAL VALVES

Steve J. Hodges, MD
Anthony Atala, MD

**DESCRIPTION**

- Congenital obstruction of the posterior urethra that can cause variable degrees of dysfunction of all segments of the urinary tract, including the bladder, ureters, and kidneys.
- Urinary tract dysfunction can include:
  - Functional bladder disorders including increased bladder wall thickness, fibrosis, and hypercontractility that may progress to incontinence and poor function
  - The bladder changes may affect the upper tracts by transmitting high pressures to the renal parenchyma, causing deterioration of renal function
  - Patients may have congenital renal dysplasia

**Epidemiology**

- Incidence/Prevalence
  - The prevalence is 1:2,400–1:8,000
  - 1 in 4,000–7,500 live male births
  - Congenital disorder
  - Urinary tract dysfunction can include:
    - Type III: Transverse membrane in the posterior urethra
    - Type II: Folds extending from the verumontanum
    - Type I: Folds that extend distally from the posterior urethra

- Risk Factors
  - Only affects males
  - No racial predilection

- Diagnosis
  - High risk of end-stage renal disease in urethral valve patients

**Associated Conditions**

- Renal dysplasia
- Bladder diverticula
- Acholuria
- Urine extravasation
- Vesicoureteral reflux
- Anal stenosis
- Hydroureteronephrosis
- VURD

**Genetics**

- This disorder is usually sporadic
- Cases have been seen in twins and siblings suggesting a poorly understood genetic component

**Pathophysiology**

- Congenital muscular membrane (folds/lisae) in the posterior urethra
- Hugh H. Young Classification (1919)
  - Type I: Folds that extend distally from the verumontanum to divide into 2 membranes that attach to the anterolateral wall, most common variant (95%)
  - Type II: Folds extending from the verumontanum to the bladder neck superiorly, not clinically obstructing, only of historical significance
  - Type III: Transverse membrane in the posterior urethra, has a central aperture, located distal to verumontanum, rare (0.4%)

**Associated Conditions**

- Renal dysplasia
- Bladder diverticula
- Acholuria
- Urine extravasation
- Vesicoureteral reflux
- Anal stenosis
- Hydroureteronephrosis
- VURD

**General Prevention**

- No known methods of prevention

**Differential Diagnosis**

- Anterior urethral valves
- Bilateral urethral obstruction
- Congenital urethral palse
- Congenital urethral stenosis (Cobb collar)
- Megacystis-megaureter
- Megacystis-megaureter
- Multicystic dysplastic kidney
- Neurogenic bladder
- Neurogenic neurogenic bladder (Herman syndrome)
- Phallic caliciform
- Normal anatomic finding
- Represents this folds of mucosa that extend from the verumontanum in the prostatic urethra to the membranous urethra
- Prune belly syndrome
- Urethral atresia

**Diagnostic Tests & Interpretation**

- Lab
  - Urinalysis and urine culture
  - Serum electrolytes, BUN, and Cr
  - Cr has early prognostic value
  - Elevated Cr in 1st few days of life (after the 1st 5 days) indicates renal dysfunction and poor prognosis
  - Cr > 1 at the end of the 1st yr of life predicts of eventual ESRD

- Imaging
  - Renal/bladder US
  - Assesses for hydroureteronephrosis, corticomedullary differentiation, echogenicity, signs of renal dysplasia, thickness of renal parenchyma and bladder wall
  - VCUG
  - Diagnoses urethral valves, detects vesicoureteral reflux and bladder trabeculation diverticula
  - Shows dilated posterior urethra, trabeculated bladder, vesicoureteral reflux, perhaps azotemia
  - Hydroureteronephrosis
  - DMSA Renogram
  - After 6 wk of life may be used to evaluate renal function, dysplasia

- Diagnostic Procedures/Surgery

- Antenatal US: Bilateral hydroureteronephrosis (± oligohydramnios, the earlier the diagnosis the worse the prognosis)
- Postnatal
  - Urinalysis and urine culture
  - Serum electrolytes, BUN, and Cr
  - Cr has early prognostic value
  - Elevated Cr in 1st few days of life (after the 1st 5 days) indicates renal dysfunction and poor prognosis
  - Cr > 1 at the end of the 1st yr of life predictive of eventual ESRD

- Pathologic Findings

- Isolated

- Associated with:
  - Antenatal US: Bilateral hydroureteronephrosis (± oligohydramnios, the earlier the diagnosis the worse the prognosis)

- Postnatal
  - Urinalysis and urine culture
  - Serum electrolytes, BUN, and Cr
  - Cr has early prognostic value
  - Elevated Cr in 1st few days of life (after the 1st 5 days) indicates renal dysfunction and poor prognosis
  - Cr > 1 at the end of the 1st yr of life predictive of eventual ESRD

- Pathologic Findings

- Isolated

- Associated with:
  - Hydroureteronephrosis
  - Vesicoureteral reflux
  - Anal stenosis
  - Neurogenic bladder
  - Neurogenic neurogenic bladder (Herman syndrome)
  - Phallic caliciform
  - Normal anatomic finding
  - Represents this folds of mucosa that extend from the verumontanum in the prostatic urethra to the membranous urethra
  - Prune belly syndrome
  - Urethral atresia

- Pathologic Findings

- Isolated

- Associated with:
  - Hydroureteronephrosis
  - Vesicoureteral reflux
  - Anal stenosis
  - Neurogenic bladder
  - Neurogenic neurogenic bladder (Herman syndrome)
  - Phallic caliciform
  - Normal anatomic finding
  - Represents this folds of mucosa that extend from the verumontanum in the prostatic urethra to the membranous urethra
  - Prune belly syndrome
  - Urethral atresia
POSTERIOR URETHRAL VALVES

TREATMENT

GENERAL MEASURES
- Place urethral catheter immediately after birth to drain the bladder (1)
- Measure daily weights, I/O's (fluid balance), routine vital signs
- Fluid and electrolytes as needed

MEDICATION
First Line
- Prophylactic antibiotics
  - <2 mo age: Amoxicillin 20 mg/kg/d
  - ≥2 mo of age: Trimethoprim-sulfamethoxazole 2 mg/kg/d (concentrates in urine), intravenous is an alternative
- Anticholinergics for bladder dysfunction

SURGERY/OTHER PROCEDURES
- Transurethral ablation of valves is possible in 80% of neonates
- Cutaneous vesicostomy in children too small for endoscopy (usually <2,000 g)
- Bilateral cutaneous pyelostomies of mostly historical significance, but may be used in extreme cases

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Adjuvant Therapies
- Prenatal surgical intervention remains investigational
  - Associated with risk of fetal and maternal morbidity, long-term renal benefit proven
- In children with persistent worsening renal function and hydronephrosis following valve ablation may require upper tract diversion if possible to salvage renal function
- Persistent vesicoureteral reflux following valve ablation may require ureteral reimplantation
- Low compliance fibrotic bladder or myogenic failure (valve bladder) may require enterocystoplasty and/or clean intermittent catheterization (CIC)

Complications
- Follow-up for observation of progress of renal function, as high risk of ESRD
  - Usual late or difficult toilet training, treat voiding dysfunction, incontinence
  - Patients need serial electrolyte and Cr measurements, US evaluations, VCUG following ablation to monitor success of surgery, resolution of reflux
  - UDS for bladder function
  - Prophylactic antibiotics as needed

Patient Resources
http://www.chop.edu/healthinfo/posterior-urethral-valves-puv.html

ONGOING CARE

PROGNOSIS
- Depends on the amount of congenital renal dysplasia, vesicoureteral reflux, bladder function
- Incontinence and later ESRD correlated
- Cr >1 mg/dL at the end of the 1st yr of life correlated with ESRD
- Sexual function and fertility seems to be normal in most patients

FOLLOW-UP
Patient Monitoring
- Follow-up for observation of progress of renal function, as high risk of ESRD
  - Usual late or difficult toilet training, treat voiding dysfunction, incontinence
  - Patients need serial electrolyte and Cr measurements, US evaluations, VCUG following ablation to monitor success of surgery, resolution of reflux
  - UDS for bladder function
  - Prophylactic antibiotics as needed

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Anterior Urethral Valves
- Bladder Outlet Obstruction
- Hydrophrenic/hydronephrotic nephropathy, D bilateral
- Ureteral reflux polyhydramnios, Pediatric
- Hydrophrenic/hydronephrotic nephropathy, D bilateral
- Ureteral reflux polyhydramnios, Pediatric
- Posterior Urethral Valves Image ID
- Urethra, Obstruction
- VURD Syndrome

CODES
ICD9
- 599.69 Urinary obstruction, not elsewhere classified
- 753.8 Other specified anomalies of bladder and urethra
- 753.15 Renal dysplasia

ICD10
- N13.8 Other obstructive and reflux uropathy
- O61.4 Renal dysplasia
- O64.79 Other congenital malformations of bladder and urethra

CLINICAL/SURGICAL PEARLS
- No benefit to early delivery as children with pulmonary hypoplasia also have severe renal dysplasia
- Select centers offer prenatal interventions with dubious efficacy
- Poor kidney function at presentation is associated with worse renal prognosis.
POSTOBSTRUCTIVE DIURESIS
John J. Pahira, MD

PATHOPHYSIOLOGY
- Retained urea, sodium, and water; impaired sodium reabsorption and concentrating ability of the renal tubule; and circulating hormones all contribute:
  - Increased sodium, potassium, and magnesium losses result in increased water excretion
  - Accumulated urea acts as an osmotic agent, bringing fluid with it as it is cleared, thereby increasing diuresis
  - Impaired concentrating ability of the renal tubule leads to continuing fluid losses and hypovolemia
- ANP, which causes vasodilation, natriuresis, and diuresis, has been found to be elevated in patients with ureteral obstruction (1)[B]

ASSOCIATED CONDITIONS
- BPH
- Malignancies (bladder or prostate cancer)
- Urolithiasis
- Any cause of chronic obstruction with hydronephrosis

GENERAL PREVENTION
Treat and repair the cause of obstruction to prevent recurrence

DIAGNOSIS
HISTORY
- Obstruction:
  - Asymptomatic but often associated with flank pain radiating to groin and/or ipsilateral thigh, nausea, vomiting, fevers, chills
  - Resulting uremia may cause mental status changes, tremors, and GI bleeding (2)[A]
- Diuresis:
  - Increase in urine output out of proportion to fluid intake, usually >200 mL/hr
- Chronic obstruction:
  - Weight gain, malaise, fatigue, shortness of breath
  - Abdominal mass, suprapubic tenderness, flank tenderness

PHYSICAL EXAM
- Chronic obstruction:
  - Pulmonary congestion, pitting edema of lower extremities, HTN
- Acute obstruction:
  - Abdominal mass, suprapubic tenderness, flank tenderness

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- CBC, urine culture and sensitivity:
  - Infection in the setting of obstruction requires emergent evaluation and treatment
- SMA-7
  - BUN and creatinine are typically elevated and are monitored after relief of obstruction
  - POD may cause profound hypokalemia
- Magnesium and calcium may need preplacement
- Urine osmolality:
  - Evaluate the kidney’s ability to concentrate urine; typically impaired concentrating ability

Imaging
- US is the screening test of choice to evaluate obstruction
  - Without hydronephrosis, diagnosis of POD should be questioned

Diagnostic Procedures/Surgery
Monitor urine output
Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS
- Causes of polyuria:
  - Medications:
    - Lithium carbonate, methoxyflurane, demethylchlortetracycline, amphotericin B, mannitol, glycerol, diuretics, ethanol, opiate antagonist, phenytoin
  - Diabetes insipidus
  - Diabetes mellitus
  - Renal disease: Diuretic phase of ATN
  - Physiologic diuresis from fluid excess
POSTOBSTRUCTIVE DIURESIS

TREATMENT

GENERAL MEASURES
• After the obstruction is relieved, admit the patient to the hospital to closely monitor hemodynamic status and electrolytes, I&O and daily weights
• Monitor urine output q2h and replace with oral fluids if oral intake is not keeping up then with IV fluids (0.5–1.0 mL of ½ NS/mL of urine output) in addition to PO fluids:
  – If urine output decreases to <250 mL/hr replace fluids volume <50 mL of the urine output per hour. Adjust accordingly as the diuresis resolves
• If patient at risk of congestive heart failure or has pulmonary edema, replace at a slower rate
• Check serum sodium and potassium q6–12h and replace as needed
• Follow BUN and creatinine values until normal:
  – Replace sodium, potassium, magnesium, and bicarbonate as needed

ONGOING CARE

PROGNOSIS
• The rate of recovery is largely determined by the duration and severity of obstructive disease.
• Extent of recovery can be estimated by the improvement in renal function within 7–14 days after the obstruction has been relieved:
  – Some patients may require short-term treatment with dialysis, until their renal function recovers.

COMPLICATIONS
• Uremic death
• Hypovolemic circulatory collapse
• Bladder mucosal bleeding secondary to vein rupture resulting from rapid bladder decompression
• Arrhythmia secondary to electrolyte abnormalities

FOLLOW-UP

Patient Monitoring
Serial (weekly to monthly) renal function testing (creatinine, BUN), renal US imaging if lab values do not return to normal range

Patient Resources
N/A

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
Management of any renal insufficiency

Complementary & Alternative Therapies
N/A

COMPLICATIONS

Uremic death
Hypovolemic circulatory collapse
Bladder mucosal bleeding secondary to vein rupture resulting from rapid bladder decompression
Arrhythmia secondary to electrolyte abnormalities

FOLLOW-UP

Patient Monitoring
Serial (weekly to monthly) renal function testing (creatinine, BUN), renal US imaging if lab values do not return to normal range

Patient Resources
N/A

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
Management of any renal insufficiency

Complementary & Alternative Therapies
N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)
Hydronephrosis/Hydrourachy, (Dilated Ureters/Renal Pelvis), Adult
Polyuria
Urinary Retention, General

CODES

ICD9
592.0 Calculus of kidney
599.60 Urinary obstruction, unspecified
788.42 Polyuria

ICD10
N13.9 Obstructive and reflux uropathy, unspecified
N20.0 Calculus of kidney
R95.8 Other polyuria

CLINICAL/SURGICAL PEARLS

Maintain a high degree of suspicion for the potential for postobstructive diuresis when relieving chronic obstruction of the urinary tract.
• Diuresis is usually self-limiting and typically lasts <48 hr.

ALERT
• If there is persistent hydronephrosis, consider persistent obstruction of ureter(s) above the level of the bladder or a nonfunctioning stent/pseudoaneurysm tube (36A).

MEDICATION

First Line
None needed beyond replacement of fluid and electrolyte losses as noted above

Second Line
N/A

SURGERY/OTHER PROCEDURES
N/A

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
Management of any renal insufficiency

Complementary & Alternative Therapies
N/A
PREGNANCY, UROLITHIASIS

Demetrius H. Bagley, MD, FACS
Kelly A. Healy, MD

### BASICS

- **DESCRIPTION**
  - The presence of calculi in the urinary tract during pregnancy can lead to severe risks and problems in management.
  - Urolithiasis is the most common cause of nondystrophic abdominal pain that requires hospitalization among pregnant patients.
  - Symptoms in urolithiasis can result in premature labor and fetal loss.
  - Stones with obstruction may lead to urosepsis requiring appropriate treatment.
  - Calcium phosphate most common followed by calcium oxalate.

- **EPIDEMIOLOGY**
  - **Incidence**
    - Cystinuria in pregnant women occurs at a rate of 1/1,500 pregnant patients, a rate similar to that of nonpregnant females (0.03–0.5%).
    - Universal stones occur twice as often as kidney stones in pregnant patients.
    - Usually present in the 2nd or 3rd trimester.
    - Incidence—right vs. left side is similar.
    - Hispanics and whites more likely than blacks to develop stones during pregnancy.
    - Multiparous women are more commonly affected than are primiparous women.
  - **Prevalence**
    - N/A

- **RISK FACTORS**
  - **Dietary factors**
    - Relative immobility
    - Voluntary dietary modification (increased calcium)
  - **Genetics**
    - Increased stone formation is likely with a positive family history.
    - Factors related to stone formation tend to group in families.
    - Women with known cystinuria should obtain genetic counseling and management of the stone disease before becoming pregnant.

- **PATHOPHYSIOLOGY**
  - Several factors occur in pregnancy may enhance formation of stones:
    - Pregnancy-induced urinary tract
    - Hypercalcemia and hypercalciuria
    - Decreased renal perfusion
    - Physiologic hyperparathyroidism
    - Pregnancy-induced hypertension
      - Starts 6–20 wk, in 90% by 3rd trimester
    - Right side > left; may persist postdelivery
    - Infection
    - Associated higher incidence of maternal UTI (10–20%)
  - Stone passage can precipitate premature labor and/or interfere with normal labor.
  - Associated with higher incidence of maternal UTI (10–20%).
  - Store passage can precipitate premature labor and/or interfere with normal labor.

- **DIAGNOSTIC TESTS & INTERPRETATION**
  - **Lab**
    - **Urinalysis**
      - Hematuria/pyuria
    - **Serum collection**
      - UTIs are more common in pregnancy associated with stone disease (15–20%).
      - A UTI can induce premature labor.
    - **Serum creatinine**
      - May be lower if the increased GFR (25–50%) in pregnancy.
  - **Imaging**
    - **Renal ultrasound**
      - Standard initial imaging study in evaluation of pregnant patients (1).
      - Hydrocephalus
      - Renal stones/proximal ureteral stones
      - Dilation and decreased peristalsis allowed relative urinary stasis
      - Hydroureteronephrosis is the most significant renal anomaly reported on the fetus.
      - Resistive index (RI) > 0.70 in intrarenal arteries supportive of acute obstruction.
      - No radiation exposure to fetus.
  - **Transvaginal ultrasound**
    - Can demonstrate distal ureteral stones.
    - Can demonstrate pelvic jets, confirming urinary flow.
    - May be able to distinguish acute obstruction from the dilation of pregnancy.
    - Document the diameters of distal ureter.
    - Noncontrast helical CT
      - Although utilized increasingly in nonpregnant patients, delivers a relatively high radiation exposure.
      - Recent techniques have been decreased the radiation exposure.
    - **Other Imaging including standard excretory urogram and computed tomographic scan**
      - Abdominal radiographic and one excretory urogram has been widely used in pregnancy.
      - There has been no adverse effect of contrast material reported on the fetus.
      - **Radiation exposure is the major concern.**
        - Typical program gives 5–15 rads of exposure.
        - 5–15 rads to the maternal pelvis in the 1st trimester increases the risk of congenital anomalies by 1–3%.
        - As little as 0.4–1.0 rads of fetal exposure can increase the risk of childhood malignancy 2.4 times.
        - MRI urography
          - Effect on fetal development poorly defined.
          - May be able to distinguish acute obstruction from the dilation of pregnancy.
  - **Diagnostic Procedures/Surgery**
    - The presence of vesical calculus with obstruction is generally defined before interventional procedures.
    - Occasionally, the diagnosis is not certain and the presence of an obstructing calculus is defined only at the time of ureteroscopy.
Pathologic Findings

DIFFERENTIAL DIAGNOSIS
• Acute pyelonephritis
• Appendicitis
• Cholelithiasis
• Gastroenteritis
• Hypertension of pregnancy
• Neurologic/musculoskeletal pathology
• Obstetric pathology of pain
• Other intra-abdominal conditions
• Renal vein thrombosis

TREATMENT

GENERAL MEASURES
• Often misdiagnosed initially
• Appendicitis/diverticulitis/bacterial abruption
• Conservative measures are taken initially to manage pain and infection so that the stone may pass
• Hydration and analgesia, antianemics and antibiotics are used
• Approximately 60–80% of renal calculi pass spontaneously. Among pregnant patients with dilated ureter, the passage rate is not defined
• Urinary calculi associated with obstruction and upper tract infection demand immediate treatment with drainage and antibiotics

MEDICATION

First Line
• Narcotics including morphine, hydromorphone, butorphanol, meperidine, and acetaminophen can provide short-term pain relief without fetal harm
• Avoid codeine during pregnancy because of its association with fetal defects
• Nonsteroidal anti-inflammatory drugs are contraindicated because of the increased risk of miscarriage in the 1st trimester and other risks, including fetal renal anomalies, fetal pulmonary hypertension, and premature closure of the ductus arteriosus when used near term
• Medical management for the prevention of calcium stones should be delayed until after delivery

Second Line
• N/A

SURGERY/OTHER PROCEDURES
• Intervention may be required in 20–30% of cases (3)
• Drainage may be necessary
• Cystoscopy/stent placement can be done with or without ultrasound guidance (4)
• Stents must be changed every 6 to 8 wk because of rapid encrustation in the pregnant women’s urine
• Percutaneous nephrostomy placement can be done under ultrasound:
• To minimize radiation exposure
• The stone or obstruction can be addressed postpartum
• The tube should be changed every 6–8 wk
• Clearly tube drainage alone must consider the duration of pregnancy
• Ureteroscopy with laser lithotripsy or impact lithotripsy has been very successful in treating stones in the upper urinary tract in the pregnant patient
• Shock wave lithotripsy has generally not been employed because of concerns of safety and the readily available alternatives

ADDITIONAL TREATMENT

Radiation Therapy
• N/A

Additional Therapies
• N/A

Complementary & Alternative Therapies
• Dietary changes including:
  • Limiting high oxalate foods and purines
  • Increase in fluid intake
  • Limiting salt and sodium intake
  • May be best preserved until metabolic evaluation postpartum

ONGOING CARE

PROGNOSIS
• Pregnancy outcome is not appreciably worsened because of symptomatic urolithiasis with appropriate management (3)

COMPLICATIONS
• Premature labor, fetal loss
• Urosepsis, renal insufficiency

FOLLOW-UP

Patient Monitoring

• During gestation:
  • Conservative management with hydration
  • Indications for intervention:
    • Worsening renal function associated with persistent obstruction
    • Irretrievable pain
    • Obstruction of a solitary kidney
    • Persistent infection associated with an obstruction
    • Renal colic, precipitation premature labor that is refractory to treatment
• Preventive medications for stone disease have association with fetal defects
  • Penicillamine: Teratogenic in rats; fetal defects
  • Xanthine oxidase inhibitors: No adverse effects
  • Thiazides: Can cause fetal thrombocytopenia, hypoglycemia, and hyponatremia
  • Allopurinol: No adverse effects on fetal animals but effects on human fetus known
  • Propylene: Teratogenic in rats; fetal defects have been found in infants of mothers who took this during gestation

Postpartum:
• Metabolic screening should be undertaken postpartum and should be delayed until completion of lactation period

Patient Resources
• N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
• Pregnancy, Bacteremia, Pyeluria, and UTI
• Pregnancy, Hematuria
• Pregnancy, Radiologic Considerations
• Pregnancy, Urinary Tract Obstruction
• Pregnancy, Urologic Considerations
• Pregnancy, Urologic Medications
• Urolithiasis, Adult General
• Urolithiasis, General Calculi Algorithm

CODES

ICD9
• 596.1 Calculus of ureter
• 596.9 Urinary calculus, unspecified
• 646.80 Other specified complications of pregnancy, unspecified as to episode of care or not applicable

ICD10
• N91.1 Calculus of ureter
• N92.9 Urinary calculus, unspecified
• O98.9/O98.0 Other specified diseases and conditions comp pregnancy

CLINICAL/SURGICAL PEARLS
• Most urinary stone pain
• Intactable pain or infection with obstruction may necessitate drainage
• Catheter, ureteral stent, or percutaneous nephrostomy (must be changed frequently at 4 to 6 wk because of the risks of encrustation)
• Ureteroscopic treatment with endoscopic lithotripsy appears to be the most efficacious and possibly safest treatment.
PRIAPISM
Hunter Wessells, MD, FACS
Brad Figler, MD

DESCRIPTION
- Prolonged, usually painful erection, occurring in the absence of sexual stimulation
- Named for Priapus, the Greek god of fertility who had an oversized, eternally erect penis
- Ischemic priapism (low-flow, veno-occlusive) is most common: Compartment syndrome of the erectile bodies causing ischemia, and ultimate necrosis of the cavernosal smooth muscle
- Nonischemic priapism (high-flow, arterial) is less common: Uncontrolled arterial inflow into the cavernosal sinusoids without ischemia or necrosis of cavernosal smooth muscle

Incidence
- FDA data (2007): 93 cases due to PDE5 inhibitors

PATHOPHYSIOLOGY
- Ischemic priapism comprises the great majority of cases of prolonged erection
  - Ischemic priapism is caused by a veno-occlusive phenomenon in which a variety of environmental factors lead to hypoxia, acidosis, and downregulation of cavernosal smooth muscle relaxation leading to persistent veno-occlusion, a compartment syndrome, with absent further arterial inflow
  - A feature of ischemic priapism is the ischemia reperfusion injury and oxidative stress that occurs after release of the ischemic insult
  - Hematologic abnormalities generally cause a low-flow state with little arterial ulceration and veno-occlusion (sickle cell disease, thrombophilia, leukemic infiltration, sepsis, encephalitis, hemorrhage with heparin, total parenteral nutrition)

Diagnosis
- Color Doppler US imaging of the cavernous arteries
- Hemoglobin electrophoresis
- Urethral catheterization

ASSOCIATED CONDITIONS
- Alcohol abuse, psychiatric disorders
- Attention deficit hyperactivity disorder (ADHD): Methylphenidate use
- Blood dyscrasias
  - Cocaine abuse
  - Epidural anesthesia and analgesia
- Hemoglobinopathies
- Hypercoagulable states
- Intracavernous or intravaginal ED therapy
- Oral PDE5 inhibitors ( sildenafil, etc.)

DIAGNOSTIC TESTS & INTERPRETATION
- CBC with differential and platelet count
- Retinoblastoma (may be increased in sickle cell disease)
- Sickle cell prep for “S” hemoglobin
- Hemoglobin electrophoresis
- Urine toxicology for prohibited drugs

DIAGNOSTIC PROCEDURES/SURGERY
- Administration of cavernosal blood with a “coralike needle” and blood gas sampling for “penile blood gas” allows differentiation between ischemic priapism (low pH, low PO2, high PCO2, blood is very dark) vs. nonischemic priapism (normal penile blood gases, blood is bright red). Typical values:
  - Ischemic priapism (pH < 7.1, PO2 < 40 mm Hg, PCO2 > 60 mm Hg, pH < 7.15)
  - Nonischemic priapism (pH > 7.4, PO2 > 60 mm Hg, PCO2 < 40 mm Hg, pH > 7.4)

Pathologic Findings
- Initially liquefactive necrosis of the corporal tissue; later corporal smooth muscle fibrosis

DIFFERENTIAL DIAGNOSIS
- Ischemic vs. nonischemic priapism
- “Pseudo-priapism” in men with pelvic prosthetics, vacuum constriction device with band, intravaginal foreign body causing penile rigidity
TREATMENT

GENERAL MEASURES
- Appropriate differentiation between ischemic and nonischemic priapism is critical (1).
- Ischemic priapism of longer than 4 hr duration is a urologic emergency that requires prompt penile decompression. This is usually a bedside corporal aspiration with or without irrigation.
- Appropriate candidate for “penile blood gas” - Duplex color ultrasound has been suggested in lieu of penile blood gas to differentiate ischemic and nonischemic priapism.
- All patients should undergo monitoring of blood pressure and pulse, peripheral IV placement, appropriate use of pain medication and sedation.

MEDICATION
First Line (1)
- **Ichoric priapism**
  - Use local anesthesic (lidocaine without epinephrine) and choose technique (local injection site, dorsal nerve block, etc.).
  - Corporal body aspiration – irrigation with dilute adrenergic agent
  - Phenylephrine (10-50 mg/ml) 1-4 ml directly into the corpora every 3-5 min until a response. Can be repeated to a max of 1.5 mg phenylephrine has been administered or a total of 1 hr (if no response after 1 hr should be considered initial treatment failure)
  - Use lower volumes in children or with significant cardiovascular disease
  - Corporal compression helps facilitate the process
  - This technique has best results for priapism <24 hr in duration.
  - Aspirate with a large needle (16-18G) connected to a 90-ml syringe and a 3-way stopcock. Insert the needle perpendicular into the skin into the lateral aspect of the corpora and aspirate 20-30 ml at a time (the glans is a less desirable site). Continue until the dark ischemic blood turns bright red.
  - If not successful, aspirate and irrigate the corpora with dilute solution of phenylephrine (10 mg in 500 ml saline) using 10-20 ml each time. When aspirations and irrigations are completed, apply pressure for 5-10 min to limit hematoma and swelling of corpora.
- Ischemic priapism is sickle cell disease:
  - Opioid, analgesic, aggressive hydration, and supplemental oxygen - 4-4 hr treatment
  - Standard treatment if > 4 hr, as for ischemic priapism above
  - Terbutaline or other oral agents not recommended per AUA guidelines.
- Nonischemic priapism
  - No role for pharmacologic therapy
  - Stuttering priapism
  - Treat as for ischemic priapism
  - Urinary antispasmodics may be considered (but not for children/adolescents)
  - Intracavernous self-injection who fail or reject systemic treatment

Second Line
- Injection of isosorbine (1 mg in 1,000 ml saline) has been used in place of phenylephrine; however, phenylephrine is more of a pure α-agonist with a lower systemic side effect profile

SURGERY/OTHER PROCEDURES
- Surgical intervention is considered 2nd line after corporal aspiration and attempts fail
- **Ichoric priapism**
  - If aspiration/irrigation fails, cavernosal glanular shunting is recommended; creating a fistula between the corpora cavernosa and the glans. Unilateral usually sufficient; if not successful perform bilateral procedure
  - Distal cavernosal glanular shunt is 1st line
  - Winter shunt: 16G core biopsy needle passed through the glans and tunica to the meatus on both sides, and rotated (blade-edge 90 degrees laterally). Consider proximal shunting if distal shunting fails
  - Cavernosal–spongiosal shunt

- **Nonischemic priapism**
  - No role for shunting in nonischemic priapism
  - Conservative measures are appropriate in the short term as nonischemic cases of priapism do not lead to underlying cavernosal tissue damage
  - Duplex Doppler ultrasonography with color flow to localize potential abnormal vascular accumulation (arteriovenous fistula, see image)
  - Internal pudendal arteriography with selective embolization (cath or gel foam)
  - Surgical exploration of the cavernosal body and ligating in cases refractory to embolization

ADDITIONAL TREATMENT
- **Radiation Therapy**
  - Immediate placement of penile prosthesis if priapism is of significantly prolonged duration and ED is highly unlikely is advocated by some
- Complementary & Alternative Therapies

ON GOING CARE
- **PROGNOSIS**
  - Based on duration/ severity of ischemia. Priapism associated with sickle cell disease may resolve in 35% of patients treated systemically.
  - Risk of permanent erectile dysfunction increases substantially after 24 hr of ischemic priapism (92% potency preserved with < 1 day of priapism vs. 69% or less if more prolonged) (2).
  - Monitoring of ischemic priapism may be clinical (complete flaccidity of the penis) or radiologic (color duplex Doppler ultrasonography showing persistent flow in cavernosal artery)

COMPLICATIONS
- Erectile dysfunction, particularly with cases of prolonged ischemic priapism
- Cavernosal urethral fistula (after cavernosal spongiosal shunt)
- Cavernositis and corporal fibrosis
- Penile deformity

FOLLOW-UP
- **Patient Monitoring**
  - Cavernosal Priapism should be monitored for development of erectile dysfunction
  - Patient should undergo appropriate testing to complete workup for any hematologic abnormalities or other potential underlying causes

Patient Resources
- AUA Foundation. www.auanet.org/education/guidelines/priapism

REFERENCES

ADDITIONAL READING
- N/A
- See Also (Topic, Algorithm, Media)
- Priapism Algorithm
- Sickle Cell Disease, Ediologic Considerations

CODES
- ICD10: N48.33 Priapism
- ICD9: N/A

CLINICAL/SURGICAL PEARLS

- The hallmark of a priapism: Corpora are involved but the glans is flaccid and soft.
- Penile blood gas allows appropriate diagnosis.
- Ischemic priapism is an emergency and intervention should start within 4-6 hr, including decompression of the corpora cavernosa by aspiration and intra cavernous injection of sympathomimetic drugs (eg, phenylephrine).
- Nonischemic priapism can be managed in a semielective manner once diagnosis confirmed.
RISK FACTORS

- For the diagnosis of prostate cancer:
  - Older age
  - Family history of prostate cancer

- For infectious complications the following have been suggested as risk factors:
  - Number of previous prostate biopsies was suggested as risk factors:
  - Family history of breast cancer
  - African American race
  - Older age
  - 1st-degree relatives with prostate cancer

ASSOCIATED CONDITIONS

Benign prostate hyperplasia

GENERAL PREVENTION

Consult urine culture before prostate biopsy if there is any concern over subclinical UTI

PROCEDURE ENEMA does not appear to have any impact on complication rates

Continuing or resuming of antibiotics or anti-inflammatory medications prior to biopsy is based upon risk/benefit for each patient. Consider discussion with the patient’s cardiologist or primary care physician as needed

DIAGNOSIS

PHYSICAL EXAM

Digital rectal exam may reveal nodularity, induration, or an asymmetry (gland)

Additional biopsy of palpable nodule or hypoechoic areas may be performed at the discretion of provider

DIFFERENTIAL DIAGNOSIS

- ASCAP
- Benign prostatic hyperplasia
- No evidence of malignancy

TREATMENT

GENERAL MEASURES

Although many clinicians have patients perform a self-administered enema, this is not needed. There is little evidence to support their use.

MEDICATION

First Line

- For our institution (Cleveland Clinic), patients receive an oral single dose of fluoroquinolone as well as a single-dose of intramuscular antistaphylococcal beta-lactam (80 mg gentamicin)
- AKI guidelines (see “Complications” below)

Second Line

None

SURGERY/OTHER PROCEDURES

- For patients with anterior rectal maneuvers or previous colorectal operations preventing TRUS, a transperineal biopsy can be performed.
- The increasing incidence of antibiotic resistance with increasing concerns of the risk of sepsis is favoring renewed interest in transperineal biopsy as a relatively sterile alternative to standard TRUS-guided biopsy.

PATHOPHYSIOLOGY

- Normal adult prostate is approximately 10 g
- The majority of prostate cancer is adenocarcinoma and located in the peripheral zone of the prostate
- In the absence of antibiotic prophylaxis, bacteremia and bacteriuria occur in 16% and 44% respectively of transrectal ultrasound-guided prostate biopsy

ASSOCIATED CONDITIONS

Benign prostate hyperplasia

GENERAL PREVENTION

- Consult urine culture before prostate biopsy if there is any concern over subclinical UTI
- Procedure enema does not appear to have any impact on complication rates
- Rectal swab with culture and sensitivity has been suggested as a method to identify potentially resistant pathogens and is not considered standard of care
- Transperineal biopsy may have a lower rate of infection than the transrectal approach
- Transperineal biopsy strategy using local anesthesia may result in a potential for decreased discomfort and pain
- Additional biopsy of palpable nodule or hypoechoic areas may be performed at the discretion of provider

Pathologic Findings

- Prostate adenocarcinoma
- Prostatic intraepithelial neoplasia (PIN)
- Atypical small acinar proliferation (ASAP)
- Benign prostate tissue

DIFFERENTIAL DIAGNOSIS

- ASCAP
- Benign prostatic hyperplasia
- No evidence of malignancy

TREATMENT

GENERAL MEASURES

Although many clinicians have patients perform a self-administered enema, this is not needed. There is little evidence to support their use.

MEDICATION

First Line

- For our institution (Cleveland Clinic), patients receive an oral single dose of fluoroquinolone as well as a single-dose of intramuscular antistaphylococcal beta-lactam (80 mg gentamicin)
- AKI guidelines (see “Complications” below)

Second Line

None

SURGERY/OTHER PROCEDURES

- For patients with anterior rectal maneuvers or previous colorectal operations preventing TRUS, a transperineal biopsy can be performed.
- The increasing incidence of antibiotic resistance with increasing concerns of the risk of sepsis is favoring renewed interest in transperineal biopsy as a relatively sterile alternative to standard TRUS-guided biopsy.
PROSTATE BIOPSY, INFECTIONS AND COMPLICATIONS

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

- A retrospective analysis from Israel suggests that a single injection of 240 mg gentamicin along with a quinolone for 3 days significantly reduces infectious complications.
- Another case series demonstrated that 500 mg intravenous amikacin 30 min before the biopsy along with several days of ciprofloxacin reduced the incidence of urosepsis/septicemia following prostate biopsy.

Complementary & Alternative Therapies

Topical lidocaine with povidone-iodine reduced in a 62% reduction in infectious complications in a prospective clinical trial but was not statistically significant.

ONGOING CARE

PROGNOSIS

Although prostate biopsy is usually generally safe and well tolerated, it is an invasive procedure that is not without risk and required a clear understanding through informed consent of the patient.

COMPLICATIONS

- Bleeding is the most common complication and includes hematuria, hematospermia, and rectal bleeding.
- Bleeding is usually self-limiting, and resolves with conservative measures. More significant bleeding has been reported and may require transfusion or colostomy intervention.
- The 2nd most common complication is infection.
  - The incidence of infectious complications, including sepsis, is increasing.
  - Compared to controls, men undergoing biopsy have a significant risk for serious infection requiring hospitalization (approximately 2.2% risk increase and 2.5% risk increase, respectively).
  - Updated AUA Best Practice Policy Panel (BPP) 4.

Antibiotic prophylaxis should be given for all prostate biopsy procedures. Duration of therapy is 24 h. Recommended 1st/2nd/3rd generation cephalosporin.

- Fluoroquinolones or
- Trimethoprim-
- Sulphamethaxazole (TMP-SMX) or

- Aminoglycosides (Aztreonam can be substituted for aminoglycosides in patients with renal insufficiency).
- Familiarity with local resistance patterns including fluoroquinolone-resistant bacteria is important.

FOLLOW-UP

Patient Monitoring

- Prompt medical evaluation for patient with signs and symptoms of infection or significant bleeding.
- Counseling regarding transient hematuria and the potential for hematospermia that may last for several weeks.
- Follow-up of prostate biopsy results

Patient Resources

http://www.webmd.com/prostate-biopsy

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostate Cancer, General
- PSA Elevation
- Urgency

CODES

ICD9

- B52.9 Unspecified disorder of prostate
- 998.19 Other postoperative infection
- 998.9 (unspecified complication of procedure, not elsewhere classified)

ICD10

- N42.9 Disorder of prostate, unspecified
- I91.400A Infection following a procedure, initial encounter
- T81.9XXA Unspecified complication of procedure, not elsewhere classified

CLINICAL/SURGICAL PEARLS

- A minimum of 12 cores is considered standard of care in the United States.
- Additional biopsy of nodules and hypoechoic areas may be needed.
- Be familiar with local resistance patterns when selecting antibiotic prophylaxis.
- In men with prostate cancer on active surveillance the number of previous prostate biopsies may be associated with a significant risk of infectious complications and every previous biopsy increases the risk of infectious complication.
PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING CRYOTHERAPY

Michael C. Large, MD

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- PSA spikes initially from necrosis of the prostate tissue
- Following cryotherapy PSA rechecked every 3 mo × 1 yr, then every 6 mo thereafter
- PSA may not decrease to undetectable
- PSA-based definition for biochemical recurrence is not standardized. Various parameters used:
  - PSA > 0.4 ng/mL, > 0.5 ng/mL, > 1.0 ng/mL
  - 3 consecutive increases (“ASTRO” definition)
  - Nadir + 2 ng/mL (“Phoenix” definition)

Imaging
- Complete metastatic workup may include:
  - CT
  - MRI of bones

Diagnostic Procedures/Surgery
- Transrectal biopsy
  - Commonly performed post-cryotherapy
  - Recommend waiting 6 mo for inflammation to resolve
- Negative biopsy reported in 75–95% (1B), (2C)

DIFFERENTIAL DIAGNOSIS
- Necrosis, especially if within 3 mo of procedure
- Treatment failure
- Recurrent disease (local or metastatic)

TREATMENT

GENERAL MEASURES
- Confirmation of recurrence via transrectal biopsy

MEDICATION

First Line
- No first-line medication therapy
  - Consider androgen-deprivation therapy or clinical trial if metastatic disease
  - No significant data on the use of androgen-deprivation after local cryotherapy failure

Second Line
- PSA

SURGERY/OTHER PROCEDURES
- Salvage prostatectomy feasible but large series are lacking
  - Reported techniques include:
    - Open retropubic or perineal
    - Laparoscopic or robotically assisted
  - Salvage cystoprostatectomy with urinary diversion
  - Option for extensive local recurrence with severe, treatment-refractory lower urinary tract symptoms

ADDITIONAL TREATMENT

Radiation Therapy
- Conformal or intensity-modulated radiotherapy
  - Largest series 49 patients, received conformal RT
  - Mean preadmission PSA 2.4 ng/mL
  - Mean RT dose 62.9 Gy
  - At median follow-up 32 mo, biochemical-free survival rate 61%

Additional Therapies
- Repeat cryotherapy
  - Largest series 32 patients (4C)
  - Median follow-up 63 mo
- 22, 23, and 29 were biochemical disease free by definitions of 0.5 ng/mL, 1.0 ng/mL, and ASTRO definition

Complementary & Alternative Therapies
- None widely studied
PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING CRYOTHERAPY

ONGOING CARE

PROGNOSIS
- Biochemical recurrence-free survival after primary cryotherapy (Phoenix definition)
  - 5-yr estimates based on D’Amico risk category:
    - Low risk: 85–90%
    - Intermediate risk: 80%
    - High risk: 60–70%
  - 10-yr estimates based on D’Amico risk category:
    - Low risk: 80%
    - Intermediate risk: 75%
    - High risk: 45%

COMPICATIONS
- No large series following postcryotherapy salvage treatment
- Surgery:
  - Intraoperative rectal injury
    - Small injury: 2-layer primary repair and omental interposition
    - Large injury, gross spillage, poor tissue viability:
      - Primary repair and diverting colostomy
  - Urinary incontinence, impotency
- Radiation
  - Rectourethral fistula, urethral stricture, urinary incontinence, impotency, and bladder and rectal toxicities
- Repeat cryotherapy
  - Rectourethral fistula, urethrocutaneous fistula, urethral stricture, urinary incontinence, impotency, and bladder and rectal toxicities

FOLLOW-UP

Patient Monitoring
- No standards exist for postcryotherapy recurrence follow-up
- If biochemical disease untreated, may treat patient according to algorithms for (1) localized or (2) advanced prostate cancer outlined in prior chapters
- If patient has undergone salvage treatment after cryotherapy, no standards exist
  - PSA often performed every 3 mo after salvage therapy
  - Re-biopsy may be offered 6 mo after treatment, or if clinically indicated

Patient Resources

REFERENCES

ADDITIONAL READING
AUA best practice policy statement on cryosurgery for the treatment of localized prostate cancer: [http://www.auanet.org/content/media/cryosurgery08.pdf](http://www.auanet.org/content/media/cryosurgery08.pdf) (Accessed July 22, 2014)

See Also (Topic, Algorithm, Media)
- Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radiation Therapy
- Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy
- Prostate Cancer, General
- PSA Elevation, General Considerations
- Reference Tables: TNM: Prostate Cancer

CODES
ICD9
- 185 Malignant neoplasm of prostate
- 790.93 Elevated prostate specific antigen (PSA)

ICD10
- C61 Malignant neoplasm of prostate
- R97.2 Elevated prostate specific antigen (PSA)
- Z85.46 Personal history of malignant neoplasm of prostate

CLINICAL/SURGICAL PEARLS
- An early rise in PSA after cryotherapy is normal, and further testing should be deferred until at least 3 mo following treatment
- Various definitions of PSA failure after cryotherapy exist: >0.4 ng/mL, >0.5 ng/mL, >1.0 ng/mL, 3 consecutive rises, and nadir + 2 ng/mL
- Prostate biopsy is useful in the workup of postcryotherapy biochemical recurrence
- Postcryotherapy treatment of recurrent disease should be reserved for highly experienced surgeons and radiation oncologists
PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING RADIATION THERAPY

Robert B. Den, MD
Mark Hurwitz, MD

ASSOCIATED CONDITIONS
Symptoms of urinary outlet obstruction can occur but are uncommon during the initial period of biochemical recurrence.

GENERAL PREVENTION
- Optimized radiation therapy including dose escalation with daily image guidance to ensure proper targeting with external beam irradiation and use of proper brachytherapy techniques
- Use of androgen deprivation in combination with radiation for high risk and selected intermediate risk patients

DIAGNOSIS

HISTORY
- Prior radiation treatment information should be obtained including type of radiation, technique, and dose prescribed. For prostate brachytherapy postimplant dosimetry analysis should be reviewed to determine if there were underdosed regions.
- Thorough assessment of general health with emphasis on urinary and bowel function is important in guiding the advisability of potential salvage therapies.

PHYSICAL EXAM
General physical exam including rectal exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- PSA. – In addition to total PSA, PSA kinetics may be helpful in identifying patients at greater risk of development of distant vs. local recurrence.
- Patients with short time to PSA nadir after treatment and short doubling times (PSADT) are at greater risk of subsequent diagnosis of metastatic disease (PSADT < 3–6 mo).
- Testosterone establishes baseline for future hormonal intervention
  - Basic metabolic panel
  - CBC

Imaging
- Bone scan
- CT of abdomen and pelvis
- Pelvic/rectal MR. Magnetic resonance spectroscopic imaging may improve results over MR alone.
- New techniques for PET/CT including use of [18F]Fluorodeoxyglucose may be useful in select cases
- Other imaging as clinically indicated

Diagnostic Procedures/Surgery
- Prostate biopsy should be considered if more than 2 yr have elapsed since completion of radiation therapy and additional local therapy is being contemplated.
  - As the full effects of radiation are not manifested for 24–30 mo, biopsy before this time is not indicated.
  - Approximately 20% of patients who have prostate irradiation biopsies will have no clinical evidence of disease with additional long-term follow-up.
  - Conversely, given the limitations of sampling, local recurrence may be present despite negative biopsy.
  - Biopsy to assess findings concerning for distant metastases as clinically indicated.

Pathologic Findings
- Occurrence of prostate cancer in ipsilateral nodal metastases as clinically indicated.

DIFFERENTIAL DIAGNOSIS
- PSA bounce phenomenon
  - 35% incidence after brachytherapy
  - Less common with external beam radiation
  - Testosterone rebound after completion of androgen deprivation with associated rise in PSA

TREATMENT

GENERAL MEASURES
- Efforts should be made to discern if biochemical recurrence is due to presence of local vs. distant disease or a combination of both.
- In the presence of metastatic disease androgen ablation is the standard choice.
- In cases of only localized disease there are many more options including observation, androgen ablation or salvage therapies including radical prostatectomy or cryotherapy.
  - In general candidates for local salvage therapy should have original clinical stage tumor T1, T2 N0M0, life expectancy of ≥ 10 yr, and a PSA < 10 ng/mL (1)
  - Patient who are not ideal candidates for salvage therapy should be treated by androgen deprivation or observation
MEDICATION

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies

- Thermal ablative therapies including cryosurgical and high-intensity focused ultrasound remain investigational.
- Cryotherapy in particular has shown promise in selected series.
- 5–10 yr freedom from biochemical recurrence with cryotherapy ranges between 34–59%.
- Rates of ≥3 GU and GI complications average approximately 10% and 3% across reported series.
- Focal ablative therapies that attempt to identify the site of recurrence and ablate the site are investigational (5).

Complementary & Alternative Therapies

Low-fat diets and diets high in polyphenols as found in broccoli, turmeric, pomegranate, and green tea may be beneficial.

PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING RADIATION THERAPY

PEARLS

ON GOING CARE

Ongoing Care

- Participation in clinical trials should be encouraged in areas such as this where no consensus exists.

ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Cryoablation
- Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy
- Prostate Cancer, Metastatic (CNS and Pathologic N+ M+)
- PSA Evaluation, General Considerations
- PSA, Bounce
- PSA, General Considerations
- Reference Tables: TNM: Prostate Cancer
PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING RADICAL PROSTATECTOMY
Gurdarshan S. Sandhu, MD
Gerald L. Andriole, MD, FACS

ASSOCIATED CONDITIONS
- Biochemical recurrence of PSA after surgery when the PSA after surgery was initially undetectable
- Generally predicts metastatic progression and prostate cancer specific mortality by a median of 8 and 13 yr, respectively (4)
- Importantly, not all men with biochemical recurrence will develop metastases or die of prostate cancer (1)
- PSA doubling rate after recurrence is an important factor in assessing the risk of subsequent metastases and prostate cancer mortality

GENERAL PREVENTION
- Although proper surgical technique can limit the risk of PSA recurrence it cannot be guaranteed to do so due to varying tumor biology

DIAGNOSIS

HISTORY
- Preoperative PSA
- Time since surgery
- Pathologic information from the radical prostatectomy
- Postoperative continence and erectile function

PHYSICAL EXAM
- Digital rectal exam to palpate for local recurrence in the prostate bed

DIAGNOSTIC TESTS & INTERPRETATION
- PSA level can vary depending on the lab assay
- PSADT assessment (can be calculated using widely available online calculators)
- Imaging evaluation is necessary to determine if distant metastases are present under some circumstances (eg, short PSA doubling time (PSADT) after recurrence

TREATMENT

GENERAL MEASURES
- Close monitoring of the serum PSA postoperatively
- NCCN Guidelines recommend PSA every 3 mo. A high risk or 6–12 yr up to 5 yr, then annually thereafter, annual DRE
- Follow up treatment decision primarily based on pathology, imaging, and PSA dynamics
- Can include observation, androgen ablation, or pelvic radiation
- Can continue to be considered with slow PSADT, in older patients with other comorbidities

MEDICATION

First Line
- Androgen-deprivation therapy (ADT)

ADT drug classes include Gonadotropin-Releasing Hormone (GnRH) agonists (eg, goserelin, leuprolide, and testosterone (DepoTesta)
- Depot injections of the GnRH agonists allow dosing to extend from 28 days to 1 yr
- GnRH antagonist dosing is every 28 days
- Use “Prostate Cancer metastatic” for more information on drug classes
Therapies

Clinical trials should be available and offered.

ADDITIONAL TREATMENT

SURGERY/OTHER PROCEDURES

- Scrotal orchietomy
  - Can be used instead of ADT
  - Is more cost effective than ADT
  - Does not allow for intermittent androgen deprivation
- Subcapsular scrotal orchietomy can also be offered in lieu of ADT
  - Does not allow for intermittent androgen suppression, the role of ADT as monotherapy may be somewhat limited

Second Line

See “Prostate Cancer, metastatic” and “Prostate Cancer, rising PSA following androgen ablation” for more information on additional drug classes.

PROSTATE CANCER, BIOCHEMICAL RECURRENCE (ELEVATED PSA) FOLLOWING RADICAL PROSTATECTOMY

ONGOING CARE

PROGNOSIS

- Prognosis is dictated by several variables including:
  - Preoperative PSA
  - Pathologic Gleason score
  - Pathologic tumor stage
  - Time to biochemical recurrence
  - PSA=0.3–6 ng/mL associated with the development of metastatic disease
  - For those patients that progress after biochemical recurrence, in general, metastatic progression and prostate cancer specific mortality occur at a median of 8 and 13 yr after biochemical recurrence

COMPLICATIONS

- Patient anxiety
- Complications are dictated by adjuvant and salvage therapy offered
  - Either radiation or ADT

FOLLOW-UP

Patient Monitoring

- Monitoring of serum PSA is necessary to diagnose biochemical recurrence and the response to treatment when/if it is offered
- For patients on ADT, baseline and periodic assessment of bone density is recommended
- If PSA begins to rise on ADT, serum testosterone should be assessed to ensure a castrate level

Patient Resources

- NCCN. http://www.nccn.org/patients/patient_gUidelines/prostatecancer/index.html

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostate Cancer, General
- Prostate Cancer, Locally Advanced (Pathologic T3, T4)
- Prostate Cancer, Metastatic (Clinical and Pathologic N+, M+)
- PSA evaluation, General Considerations
- PSA, General Considerations
- Reference Tables: TMM: Prostate Cancer

CODES

ICD9

- 181 Maligant neoplasm of prostate
- 185 Malignant neoplasm of prostate
- 790.93 Elevated prostate specific antigen (PSA)

ICD10

- C61 Malignant neoplasm of prostate
- D94.77 Acquired absence of organ, genital organs

CRITICAL/SURGICAL PEARLS

- Distinguishing local from systemic disease recurrence dictates adjuvant/salvage therapy options.
- Adjuvant/salvage surgery is supported by randomized trials for patients with adverse pathology at the time of prostatectomy and is endorsed by AUA/ASTRO Guidelines.

Additional Therapies

Clinical trials should be available and offered.

Complementary & Alternative Therapies

No data are available on the optimal PSA value at which to initiate treatment.

- ADT is potentially detrimental to cognitive function, quality of life, sexual health, cardiovascular risk, and bone integrity
- Timing of initiation of ADT should be based on a patient’s risk of metastatic progression and risk of death from disease as opposed to absolute PSA levels
- When ADT is initiated, in the absence of metastases, intermittent ADT is preferred to continuous ADT given the side effects of this treatment and the non inferior overall survival of intermittent ADT (3)
- With the benefits that have been observed with adjuvant/salvage radiation, the role of ADT as monotherapy may be somewhat limited
**DESCRIPTION**
Prostate cancer (CaP) usually refers to adenocarcinoma in other types are rare.

**EPIDEMIOLOGY**
Incidence/Prevalence
- Most common solid tumor in US males.
- 2014: 233,000 new cases; 29,480 deaths.
- Advent of PSA blood test led to a sharp increase of CaP incidence from 1989 to 1993.
- Highest worldwide incidence is in African Americans, with a relative incidence of ~2 compared to US whites.
- Lowest worldwide incidence is in Asian men (1.9/100,000 yr in China), however, Asians who immigrate to US increase risk to that of US men.
- Mortality rate decreased sharply since 1991, now lower than before PSA era.
- 5-yr relative survival rates ~100%.
- Lifetime CaP risk is 16-15%.

**RISK FACTORS**
- Genetic and environmental factors are important in CaP development.
- Family history. Risk is increased by number of affected family members, degree of relation, and age at diagnosis.
- Infection/Inflammation: Prostatitis and STDs.
- Diet: Several genetic determinants of CaP code for proteins that repair oxidant stress.
- Western diet (high levels of meat, dairy, and saturated fat); folate supplements.
- Antidepressants: Essential for development and maturation of prostate gland.
- Lack of androgen associated with decreased risk of CaP. Although this down-stream relationship has been established.
- Shrinked CAG repeat length in the AR gene associated with increased risk.
- Exogenous: Metabolic effects on CaP.
- IGF-1.
- Vitamin D may protect against CaP.

**PATHOPHYSIOLOGY**
- Normal adult prostate 20-25 g; secretes fluid comprising about 30% of ejaculate.
- Most CaP arise in peripheral zone of gland.
- High-grade prostatic intraepithelial neoplasia (HGPIN) may be a premalignant lesion.
- Risk of CaP on subsequent biopsy 16-44%, repeat biopsy within a year not necessary unless other signs of cancer.
- Atypical small acinar proliferation (ASAP) considered premalignant; 43-49% risk of cancer, biopsy should be repeated.

**ASSOCIATED CONDITIONS**
- EOD and urinary incontinence are associated with all local CaP therapies.

**GENERAL PREVENTION**
- Randomized trials have been conducted.
- Prostate Cancer Prevention Trial (PCPT) (finasteride vs. placebo) while there was 23-25% reduction in CaP risk, concern over slight increase in diagnosis of high-grade cancer prevented those from being FDA-approved agents.
- SELECT: Examined antioxidant Vit E and selenium terminated in 2008 due to lack of benefit.
- Increased risk of CaP and diabetes.

**DIAGNOSIS**
- History: Rarely presents with symptoms; most cases are detected by PSA screening and/or DRE.
- Physical exam: Induration, nodularity, or asymmetry in the gland (uncommon in most men).
- Staging:
  - Intermediate: T2b–T2c/Gleason 7/PSA <10 ng/mL.
  - High: T3a or greater or Gleason score 8–10 or PSA >10 ng/mL.

**DIAGNOSTIC TESTS & INTERPRETATION**
- PSA is typically elevated in serum of patients with CaP (See Section I: PSA Elevation, General).
- Pulsed wave Doppler ultrasound and color Doppler imaging of the prostate.
- TRUS-guided needle biopsy extended template now standard (10–12 cores).
- Bone scan: Usually ordered in intermediate- and high-risk patients, blastic bone lesions w/mets.
- CT abdomen/pelvis: Used to assess for visceral or lymph node metastases, indicated for intermediate- and high-risk.
- Prostate-specific antigen assay (PSMA) monoclonal antibody, FDA-approved post-prostatectomy, limited use.

**TREATMENT**
- Localized disease, best treatment controversal and must be individualized; includes active surveillance, radical prostatectomy, radiation therapy, cryosurgery.
- Consider age, overall health, life expectancy, patient and physician preferences.
- Metastatic CaP: Long-term, hormone therapy, chemotherapy.

**DIFFERENTIAL DIAGNOSIS**
- Localized: BPH, prostatitis (granulomatous, acute, chronic), recent instrumentation, nonadenocarcinoma prostate malignancy (cancer, uterine carcinoma).
- Metastatic: Papillary disease, other causes of bladder or prostatic lymphomatoid hyperplasia (lymphoma, TB, etc.).
**Radiation Therapy**

**ADDITIONAL TREATMENT**

**Second Line**

**First Line**

**MEDICATION**

**External beam RT:**
- Cryotherapy uses multiple probes to ablate prostate
- Bilateral orchiectomy provides permanent androgen deprivation

**Radical prostatectomy:**
- For low-risk (T1 and T2a) cancer, 5-yr biochemical disease-free rate is >90%

**Hypofractionation approaches in clinical trials**

**Active surveillance:**
- Selection of patients with low-risk disease
- Initial PSA ≤10 ng/mL; biopsy negative

**Additional Therapies**

**PROSTATE CANCER, GENERAL**

**Gleason score (≥7), high PSA (≥10 ng/mL), and ≥12 biopsies positive (≥50% cancer in any site)**

**Radical prostatectomy:**
- Resection of prostate and seminal vesicles and hypogastric nerves of bladder to urethra

**Neoadjuvant or concurrent androgen deprivation for 6 mo–1 yr with XRT increases survival vs. XRT alone or hormonal therapy alone (select intermediate and high-risk patients)**

**For nodal metastases**
- Androgen deprivation may be considered in men at high risk

**SURGERY/OTHER PROCEDURES**

**Prostatectomy:**
- Open (retropubic, perineal), laparoscopic, or robot-assisted laparoscopic
- Nerve-sparing technique if possible

**PSA every 6–12 mo after radiation for 5 yr; yearly after:**
- 5 yr; yearly after:
- 5 yr
- Bladder outlet obstruction, bone pain, pathologic fracture, seminal vesicle invasion, capsular penetration, lymph node involvement
- New genomic markers available for prognosis (See Section III: “Prostate Cancer, Genomic markers.”)

**Therapy related:**
- Local therapy (surgery, radiation): impotence, incontinence, rectal injury
- Androgen deprivation: hot flashes, loss of libido, impotence, fatigue, osteoporosis

**Follow-up Patient Monitoring:**
- PSA every 6–12 mo; if ≥5 ng/mL, yearly after prostatectomy
- Should drop to <0.5 ng/mL after radiation for best prognosis
- BMI every other year
- CT of abdomen/pelvis and/or bone scan if patient has new bone pain, rapid PSA rise, short doubling time


**REFERENCE**


**ADDITIONAL READING**


**Patient Resources**


**ICD9**

- 61.9 Malignant neoplasm of prostate
- 61.9 Inflammatory disease of prostate, unspecified
- 280.42 Family history of malignant neoplasm of prostate

**ICD10**

- C61 Malignant neoplasm of prostate
- N41.9 Inflammatory disease of prostate, unspecified
- Z08.42 Family history of malignant neoplasm of prostate

**Prostate cancer requires informed decision making and a risk-based approach; consider surveillance if low risk and <10 yr life expectancy.**
PROSTATE CANCER, LOCALIZED (T1, T2)
Nicholas J. Kuntz, MD
Judd W. Moul, MD, FACS

DIAGNOSIS

HISTORY
- LCP is rarely symptomatic
- Unintentional weight loss or new onset skeletal pain suggests nonlocalization disease
- LUTS
  - More commonly attributed to BPH

PHYSICAL EXAM
- Digital rectal exam (DRE)
  - No palpable nodule (cT1)
    - Radiodense confined to prostate gland (T2)
  - Abnormal texture or palpable seminal vesicles suggests more advanced disease than T2

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Prostate specific antigen (PSA)
  - Produced by prostatic epithelium
  - Half-life of 2–3 days; Not specific to CaP
  - A continuous parameter
  - The higher the value, the more likely the existence of CaP (1][A]
- Routine PSA screening is controversial
  - 2013 AUA Guidelines (2):
    - Under age 40 y: Do not screen (C)
    - 40–54 y: average risk: Do not screen (C)
    - >55 y: risk of CaP = 1.3% · year
  - 55–69 yr: Shared decision-making if 10–15 yr life expectancy: Do not screen (C)
  - Under age 40 yr: Do not screen (C)
  - 55 yr at higher risk: Individualized decision (C)
  - 55–69 yr: Shared decision-making if 10–15 yr life expectancy: Do not screen (C)
  - >70 yr and <10–15 y: life expectancy: Do not screen (C)
- Other PSA parameters
  - PSA velocity/doubling time
  - PSA density
  - PSA velocity/PSA density

DIAGNOSTIC IMAGING
- No imaging if low risk
- Bone scan: PSA >10 nmol/L or Gleason ≥8
- Pelvic CT and MRI
- Lymph node involvement risk = 10%

Imaging
- 2016 NCCN Guidelines for LCP
  - No imaging if low risk
  - Bone scan: PSA = 10 nmol/L or Gleason ≥8
  - Pelvic CT and MRI
- Imaging: Not indicated for LCP
  - No imaging modality can accurately estimate the extent of tumor and location within or surrounding the prostate

GENERAL MEASURES
- Access life expectancy, overall health status, and tumor characteristics prior to treatment decisions (4)[A]
- Review risk and benefits of all treatments and engage patient in informed decision making process.
- Treatment recommendations based on cancer biology, patient overall health, life expectancy, and preferences.
- Gleason score and tumor stage are predictive of cancer outcomes
- Risk strata are used to develop treatment recommendations (4)[A]
  - Low risk: PSA 10 and a Gleason score of 6 or less and clinical stage T1c or T2a
  - Intermediate risk: PSA 10–20 or a Gleason score of 7 or clinical stage T1b
  - High risk: PSA >20 or a Gleason score of 8 to 10 or clinical stage T2

MEDICATION

First Line
- Primary androgen deprivation therapy (ADT)
  - Rarely indicated for LCP (4)[C]
  - Radiation of symptomatic patients
  - Extensive or poorly differentiated tumors
  - Short life expectancy
- Not recommended by 2014 NCCN Guidelines

Second Line
- Neoadjuvant ADT for surgical treatment
- Not recommended (1)[A]

Difficulties with the treatment of prostate cancer include:
- Highly prevalent disease
- Large population at risk
- Low prevalence of CaP in any one individual
- The long natural history of the disease
- Many competing health issues
- Many treatment options with varying outcomes and side effects
Radiation Therapy

ADDITIONAL TREATMENT

SURGERY/OTHER PROCEDURES

Radical prostatectomy

Radical prostatectomy (RP)

• Removal of prostate gland, seminal vesicles, and anterolateral wall of the urethra

• Sphincter mechanism for continence

• Pelvic lymph node dissection for elevated risk of positive nodes

• Cancer “cure” in truly localized disease

• Option for low, intermediate-risk with 10-yr life expectancy and selected high-risk patients (T1b)

• Similar survival between RP and watchful waiting in low-risk CAP, 65 yr (4B)
**PROSTATE CANCER, LOCALLY ADVANCED (CLINICAL T3, T4)**

Erin M. Burns, MD
James S. Rosof, MD

---

**DESCRIPTION**
- Clinical stage T3 prostate cancer (CaP) refers to disease that is thought to extend outside the prostate and may be palpable or seen on imaging.
- Pathologic stage T3 CaP refers to extracapsular extension (T3a), or tumor invading seminal vesicles (T3b) based on final surgical pathology.
- Clinical stage T4 CaP refers to palpable tumor that is fixed and/or invading adjacent structures.

**RISK FACTORS**

- Incidence of metastases: 10–15%.

**DIAGNOSIS**

**HISTORY**
- Family history of CaP.
- Voids per day: Obstructive/irritative, hematuria.

**VISCERAL EXAM**

- Digital rectal exam (DRE): Note palpable abnormalities, unilateral or bilateral, whether prostate is fixed, any extension of mass into adjacent structures.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- PSA:
  - Value is decreased by 5-ARIs, elevated with instrumentation, infection, larger prostate volume.
- Lab variability: 20–25% (7)[A].

**PSA density:** Serum PSA/prostate volume.
- Sensitivity 48%, specificity 79%, not currently used for routine screening.

**Free PSA (fPSA)**
- Collected via post-DRE urine sample.
- RNA overexpressed in CaP, higher values indicate higher risk of CaP.
- Should be calculated over 18 mo with 3 PSA measurements.

**Bone scan**
- Sensitivity 48%, specificity 79%, not currently used for routine screening.
- May correlate with Gleason score (8).

**PSA velocity**
- Rate of rise of PSA is a specific marker for CaP.
- Should be calculated over 18 mo with 3 PSA measurements.

**PSA level**
- ≥10% is associated with CaP.
- Higher PSA and PSA velocity are associated with higher risk of CaP.

**Diagnostic Procedures/Surgery**

- TRUS biopsy can confirm T3 disease with biopsy of the capsule or SVs.

**TREATMENT**

**First Line**
- Androgen-deprivation therapy (ADT). Option for patients unable or unwilling to undergo surgery or radiation therapy (RT).
- Orchiectomy, luteinizing hormone-releasing hormone (LHRH) agonist or antagonist.
- Can be administered continuously or intermittently; optimal timing of administration is debated.
- More effective when combined in neoadjuvant or adjuvant fashion with RT.

**Second Line**
- Antihormone monotherapy is less effective and not usually recommended; however, side effects are more tolerable overall.

**SURGERY/OTHER PROCEDURES**

- Radical prostatectomy (RP) with pelvic lymph node dissection (PLND).
- Can be performed in a variety of surgical approaches.
- Provides local control and is the preferred treatment for T3 disease.
- Options include open RP, laparoscopic RP, and robotic-assisted RP.

**ADJACENT RT 55–70 Gy improves local control and reduces the risk of biochemical recurrence for T3 disease.**

**DISCUSSION**

- Neoadjuvant ADT does not confer cancer specific or overall survival (OS) benefit.
- Adjunct RT 55–70 Gy improves local control and reduces the risk of biochemical recurrence for T3 disease.
- Neoadjuvant ADT does not confer cancer specific or overall survival (OS) benefit.
PROSTATE CANCER, LOCALLY ADVANCED (CLINICAL T3, T4)

ADDITIONAL TREATMENT

Radiation Therapy

- 70-80 Gy to prostate, 5% and pelvic lymph nodes, or 40-50 Gy and brachytherapy for cT4d disease

- NCCN guidelines recommend 2-3 g necroa/voiding side effects

- Advanced in 3D-conformal, intensity-modulated, and image-guided RT and are designed to deliver higher doses directly to prostate, avoiding adjacent organs and thus limiting side effects

Additional Therapies

- Cryosurgery of the prostate
  - Higher rates of biochemical failure than RT (87% vs. 53%) for T2c-T3 CaP (13A)
  - High-intensity focused ultrasound (HIFU)
  - Currently investigational, may prove to be an option in combination with ADT for intermediate- and high-risk CaP

Complementary & Alternative Therapies

- Consider additional treatment options such as ADT, RT with ADT, or 1-2 yr of ADT

- RT with ADT: OS 72–87% at 5 yr

- Cancer-specific survival (CSS): 85–92% at 5 yr, 79–82% at 10 yr

- RP should include PLND for locally advanced CaP

- Risk of biochemical recurrence increased in:
  - Patients with pathologic T3 disease
  - Patients with positive surgical margins

- Higher rates of biochemical failure than RT (87% vs. 76–82% after radical prostatectomy)

- Higher disease free and OS in men with T3 and T4 disease (12A)

- RT should be administered in conjunction with ADT

- RT should be performed within 4 wk of RP

- RT with ADT: OS 72–87% at 5 yr

Ongoing Care

Prognosis

- Significant risk of progression and death

- Optimum selection criteria for local CaP

- OS without intervention ranges from 10 to 92% at 5 yr and 14–78% at 10 yr for high-grade stage CaP

- RP for T3 CaP: OS 64–96% at 5 yr, 13–72% at 10 yr

- Cancer-specific survival (CSS): 85–92% at 5 yr, 79–82% at 10 yr

- RT monotherapy: OS 60–70% at 5 yr and 50% at 10 yr

- RT with ADT: OS 72–87% at 5 yr

Complications

- Treatment complications are similar to those for localized CaP

- Untreated T3–T4 CaP may lead to hematuria, obstruction at the level of the prostate requiring indwelling catheter or transurethral resection of the prostate, or vesicourethral junction obstruction requiring ureteral stents or percutaneous nephrostomy

Follow-Up

Patient Monitoring

- Periodic PSA measurements, initially at 3-mo intervals posttherapy and then gradually increasing to annually

- Failure of PSA to nadir or consecutive rises in PSA should prompt further evaluation with bone scan and/or CT

- Risk of biochemical recurrence increased in:
  - Gleason score 8–10, PSA doubling time < 10 mo
  - Prostatectomy may be helpful in identifying local recurrence if bone scan and CT scan are negative

- Consider additional treatment options such as ADT, adjunct RT, and/or chemotheraphy and participation in clinical trials

Patient Resources

- American Cancer Society: http://www.cancer.org

References

See Also (Topic, Algorithm, Media)

- Prostate Cancer, General
- Prostate Cancer, Locally Advanced (Clinical T3, T4)
- Prostate Cancer, Locally Advanced (Pathologic T3, T4)
- Prostate Cancer, Positive Margin Following Radical Prostatectomy
- PSA Evaluation, General Considerations
- Reference Table: TIMF Prostate Cancer

Codas

- ICD9
  - 185 Malignant neoplasm of prostate
  - 198.1 Secondary malignant neoplasm of other urinary organs
  - 198.2 Secondary malignant neoplasm of genital organs

- ICD10
  - C61 Malignant neoplasm of prostate
  - C79.11 Secondary malignant neoplasm of bladder
  - C79.82 Secondary malignant neoplasm of genital organs

Clinical/Surgical Pearls

- Risk assessment requires incorporating serum PSA, clinical stage, Gleason score, tumor volume, and patient age and comorbidities to best provide counseling and treatment recommendations
- RP should include PLND for locally advanced CaP and adjunct RT should be offered for T3–T4 disease, particularly if surgical pathology demonstrates positive margins
- RT should be administered in conjunction with ADT for locally advanced CaP to maximize survival benefit with support from randomized clinical trials.
PROSTATE CANCER, LOCALLY ADVANCED (CLINICAL T3, T4)

PATHOPHYSIOLOGY
- Peripheral zone tumors tend to invade the capsule more often than transition zone tumors
- Tumor spread:
  - T1a (intracapsular invasion) occurs posteriorly and posteriorly by vascular invasion and increases risk of recurrence after RP
  - Tumor volume:
    - Intracapsular invasion is more common in tumors >0.5 cm³ and seminal vesicle invasion is more common in tumors >4 cm³
    - Tumor volume does not independently predict postoperative progression once grade, pathologic stage, and margins are accounted for

ASSOCIATED CONDITIONS
Locally invasive prostate cancer can present with resulting symptoms such as hematuria, obstructive voiding symptoms, and changes in bowel habits

GENERAL PREVENTION
- D’Amico has also suggested a risk stratification into low, intermediate, and high risk groups based on extracapsular extension, seminal vesicle invasion, and surgical margin status predict biochemical recurrence free survival and cancer-specific survival

DIAGNOSIS
HISTORY
- Family history of CaP, race
- Voiding symptoms: Obstructive/irritative, hematuria
- Any bone/back/hip pain or hematuria?

PHYSICAL EXAM
- Digital rectal exam (DRE): Note palpable abnormalities, rectal, levator muscles, or pelvic wall
- Any bone/back/hip pain or hematuria?

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- PSA:
  - Positive predictive value (PPV): 12–32% for PSA >0.75 ng/mL, Gleason score 8 or greater, or a T3/T4 tumor
  - RNA overexpressed in CaP, higher values indicate higher risk of CaP
  - PCA3:
    - Higher PSA density and PCA3 do not correlate with Gleason score or CaP stage
  - PCA3:
    - RNA overexpressed in CaP; higher values indicate higher risk of CaP
    - Collected via post DRE urine sample
    - Sensitivity 48%, Specificity 79%, not currently used for routine screening
    - Recommended to grade with Gleason score

Imaging
- Preoperative imaging for locally advanced cancer:
  - Pelvic CT or MRI is indicated for locally advanced disease (PSA >20 ng/mL, Gleason score 8 or greater, or a T3/T4 tumor) to evaluate for pelvic lymph node involvement
  - Distal metastasis may be ruled out using Technetium 99 bone scan, axial MRI, PET, and immunoscintigraphy

- Multiparametric prostate MRI using a 3T magnet and/or an endorectal coil is being touted to improve accuracy
- Repeat or 1st time staging with bone scan and/or CT may be needed in selected patients who are significantly upstaged and/or upgraded after RP

Diagnostic Procedures/Surgery
Prostate biopsy rarely indicates the presence of pathologic T3 disease; seminal vesical biopsy may confirm T3

Pathologic Findings
- Clinically localized disease is upstaged if pathologic tissue from a prostatectomy indicates T3 or T4 disease
- The risk of cancer recurrence after prostatectomy is based on extracapsular extension, seminal vesicle involvement, lymph node involvement, and correspond most strongly with a positive surgical margin
- A gross PSM carries worse 5y progression survival vs. microscopic margins 65% vs. 40%
- PSA at the bladder neck, vas deferens, and posterolateral surface of the prostate has been shown to have a particularly poor progression-free outcomes in comparison to PSA at the apex, perineum, anterior, or lateral prostate
- With respect to the nerve sparing techniques, when patients are selected appropriately, no statistical difference has been shown in PSA in comparison to the nonnerve sparing technique
NEWER GENERATION ORAL HORMONAL THERAPIES

SECOND LINE

With a median follow-up of 12 yr, (Southwest Cancer Study Group 2009;181:956–962.) Chemo hormonal downstaging trials are ongoing (43% vs. 54%) and overall survival (41% vs. 52%) to early radiation therapy in this pT3 setting (4) for high-risk prostate cancer after RP. The benefit of therapy was observed with or without positive margins (5).

Additional Therapies Protocols to extend external radiation therapy is offered at selected major US centers. However, there is no level I evidence that it is superior to photon-based radiotherapy using an intensity modulated method.

COMPLIANCE & ALTERNATIVE THERAPIES

No level I evidence of benefit

PROGNOSIS

GROWTH WITH A THERAPIES

In the setting of clinical T3/T4 disease, extended lymph node dissection is gaining support in these patients (obturator, external iliac, internal iliac, and presacral nodes) (Accessed May 21, 2014). The American Society of Therapeutic Radiation Oncology (ASTRO) and the American Urologic Association (AUA) have a joint guideline on the use of adjuvant and salvage radiotherapy after prostatectomy (2013;190(2):144–149.).

CODES

ICD10

C79.11 Secondary malignant neoplasm of bladder

C79.82 Secondary malignant neoplasm of genital organs without positive margins (5).

C79.82 Secondary malignant neoplasm of genital organs

C79.99 Secondary malignant neoplasm of unknown primary

PROSTATE CANCER, LOCALLY ADVANCED (CLINICAL T3, T4)

Additional Treatment

Radiation Therapy

If randomized trials have been completed demonstrating a benefit to early adjuvant radiation therapy (346–368.). Treatment is optimally offered after continence is restored, to allow healing to take place after surgery (from biopsy cores) predict more advanced disease at 4 yr after salvage EBRT – Patients with no adverse risk features achieved a 4-progression-free survival probability of 77%. A nomogram based on established risk factors no more accurately identify patient-specific risks to assist in clinical decision-making is available (6).

COMPLICATIONS

– Morbidity from pelvic RT include radiation proctitis, cystitis, incontinence, ED, lymphedema, and stricture disease

– Morbidity from hormone therapy include hot flushes, breast tenderness, osteoporosis, diabetes mellitus, depression, and cardiac disease

FOLLOW-UP

Patient Monitoring

For pT3/T4 after RP, patients are generally followed every 3 mo for the 1st yr, every 6 mo for the next 2–5 yr and yearly thereafter depending on risk.

Patient Resources

• AUA Prostate Cancer: http://www.auanet.org/content/media/AUA_ProstateCancerAtA glance.pdf


REFERENCES


ADDITIONAL READING


CLINICAL/SURGICAL PEARLS

Pathologic T3/T4 prostate cancer includes extracapsular cancer than extends beyond the gland, without distant metastasis.

– Prostate cancer, General

– Prostate cancer, Locally Advanced (Clinical T3, T4)

– Prostate Cancer, Locally Advanced (Pathologic T3, T4)

– Prostate cancer, Advanced

– PSA, General Considerations

– PSA, General Considerations

– PSA, General Considerations

– PSA, General Considerations

– PSA, General Considerations

– PSA, General Considerations

CLINICAL/SURGICAL PEARLS

• Pathologic T3/T4 prostate cancer includes extracapsular cancer than extends beyond the gland, without distant metastasis.

• High clinical stage, PSA levels, and Gleason score (from biopsy core) predict more advanced

• Pathologic staged in 3 RCTs support adjuvant EBRT for high-risk pT3/T4 prostate cancer after RP.

• For patients who do not receive adjuvant EBRT, close follow-up with early salvage EBRT is very commonly practiced.

• There is no level I evidence for adding ADT to EBRT as part of adjuvant or salvage EBRT, but selected high-risk patients may benefit.
PROSTATE CANCER, METASTATIC (CLINICAL AND PATHOLOGIC N+, M+)

Divya Ajay, MD
Debasish Sundi, MD
Mioop Han, MD

BASICS

DESCRIPTION
- Metastatic prostate cancer (CaP) can be nodal disease discovered at prostatectomy or on imaging (N+), or can be distant spread (M+). Most commonly, it affects distant lymph nodes and bone.
- The initial presentation or development of previous local therapy for CaP, such as radiation therapy or RP.

EPIEDEMOLOGY
Incidence
With PSA screening, the number of men with metastatic disease at 1st presentation has declined over the last 20 yr (~4%, 2003–2009, SEER data).
Prevalence
Nearly 20,800 men annually (US) from metastatic disease.
RISK FACTORS
- African American ancestry
- High-fat diet
- Family history
Genetics
None

PATHOPHYSIOLOGY
- CaP arises in prostate glandular epithelium and can spread through the lymphatics or hematogenously.
- Bone pain is paravertebral veins that extend up to the vertebral column.
- Testosterone and DHT are the primary regulators of prostate growth.
- 2 sources of androgens in men: testes (95% of total androgens) and adrenal glands (remaining 5%).

ASSOCIATED CONDITIONS
- Osteoporosis secondary to hormonal therapy

GENERAL PREVENTION
- Early androgen blockade for high-risk patients with localized cancer may delay the development of metastatic disease.

DIAGNOSIS

HISTORY
- Urinary symptoms can be indistinguishable from those of BPH and include increased urinary frequency, nocturia, difficulty initiating and maintaining a steady stream of urine, dysuria, and hematuria, and sexual dysfunction.
- The most common symptom of metastatic disease is bone pain, often in vertebral, pelvic, or rib.

PHYSICAL EXAM
- DRE may reveal a nodular or enlarged prostate, but the exam may be unreliable.
- After RP the fossa may be empty or contain palpable recurrent cancer.
- Adrenalectomy may be detected in the supraventricular and inguinal lymph nodes.
- Painful lesions apparent on vertebral bodies or ribs may be indicative of spinal or epidural metastases.

LAB
- Serum PSA should be obtained in all patients prior to the start of therapy and is a useful marker of response to therapy.
- Prostate and phosphatase is elevated in up to 67% of men with metastatic disease.
- Monitor serum testosterone to verify that androgen ablation has testosterone <50 ng/mL.
- CT of the abdomen and pelvis and bone scan should be performed after initial diagnosis. Bone metastases are typically osteoblastic.
- Evaluate for hydronephrosis secondary to ureteral obstruction.

DIFFERENTIAL DIAGNOSIS
- Pelvic disease; bone metastases from other malignancies
- Adrenopathy due to lymphoma or other advanced malignancy

TREATMENT

GENERAL MEASURES
- Androgen blockade for metastatic disease, which is usually considered nontoxic.
- Androgen deprivation therapy (ADT) can be administered continuously as well as intermittently (intermittent hormonal therapy or IHT), studies suggest similar survival when combined androgen blockade (CAB) is compared to intermittent CAB, especially with lower disease burdens.
- ADT using high-dose bicalutamide (150 mg/d), LHRH agonist, and an antiandrogen is associated with >50% of patients with measurable disease on bone or CT scan of the abdomen and pelvis, the disease is classified as metastatic castration-resistant prostate cancer (mCRPC).
- The ECOS2107 clinical trial demonstrated a 12 month survival advantage when docetaxel was initially combined with androgen deprivation therapy.

Second Line
- Most patients initially benefit from ADT, but the disease usually progresses after 1–4 yr.
- Castration-resistant CaP (CRPC): Progression on primary hormonal with a testosterone level of <50 ng/mL, and a rising PSA.
- With metastatic disease on bone or CT scan of the abdomen and pelvis, the disease is classified as metastatic castration-resistant prostate cancer (mCRPC).
- Castration-resistant disease usually progresses after 1–4 yr.
- Castration-resistant CaP is a systemic disease and often progresses despite ADT.
- Secondary hormonal therapy is essentially used in CRPC patients without metastases.
- If after ADT, the androgen should be discontinued, this will result in a PSA decline 1–20% of patients.
- Addition of an antiandrogen will result in PSA decline of 50% in 15–54% of patients, with median duration of response 4–6 mo.
- Antiandrogen blockade as initial therapy is associated with >50% of patients.
- Hormone therapy is a systemic approach to CaP.
- Several systemic therapies have demonstrated improved overall survival for metastatic castrate-resistant disease and are discussed in detail in the section on Prostate cancer, rising PSA, following androgen ablation (Castration-Resistant Prostate Cancer (CRPC), and mCRPC). Section II.

Androgen deprivation therapy (ADT)
- ADT to achieve castrate levels of testosterone, generally considered <50 ng/mL, with some advocating <20 ng/mL, similar to orchiectomy levels.
- Testicular androgen secretion is regulated by the hypothalamus, and the pulsatile secretion of luteinizing hormone releasing hormone (LHRH) – LHRH agonists (leuprolide, goserelin, triptoreline) interfere with this pulsatile secretion, and after initial flare (testosterone increase) at 7–10 days, achieve medical castration at about 30 days.
- LHRH antagonists (degarelix) rapidly decrease testosterone levels with 44% testosterone castration (<50 ng/mL) at day 1, 96% by day 3. No flare, so useful in situations such as spinal cord compression.
- Antihormonal (bicalutamide, flutamide, nilutamide) block the LHRH flare reaction initially caused by LHRH agonists and should be used for an immediate chemohormonal therapy (cabazitaxel + LHRH agonists past the flare period, or CAB) is commenced.
- ADT using high-dose bicalutamide (150 mg/d), called antihormone monotherapy, is associated with less side effects but may also be less effective form of ADT and should not be routinely used (not FDA approved in US).
- Initial chemohormonal therapy has recently been reported to extend survival in men presenting with newly diagnosed metastatic prostate cancer (mCRPC).
- ECOS3489 clinical trial demonstrated a 12 month survival advantage when docetaxel was initially combined with androgen deprivation therapy.

Second Line
- Most patients initially benefit from ADT, but the disease usually progresses after 1–4 yr.
- Castration-resistant CaP (CRPC): Progression on primary hormonal with a testosterone level of <50 ng/mL, and a rising PSA.
- With metastatic disease on bone or CT scan of the abdomen and pelvis, the disease is classified as metastatic castration-resistant prostate cancer (mCRPC).
- The ECOS2107 clinical trial demonstrated a 12 month survival advantage when docetaxel was initially combined with androgen deprivation therapy.

Second Line
- Most patients initially benefit from ADT, but the disease usually progresses after 1–4 yr.
- Castration-resistant CaP (CRPC): Progression on primary hormonal with a testosterone level of <50 ng/mL, and a rising PSA.
- With metastatic disease on bone or CT scan of the abdomen and pelvis, the disease is classified as metastatic castration-resistant prostate cancer (mCRPC).
- The ECOS2107 clinical trial demonstrated a 12 month survival advantage when docetaxel was initially combined with androgen deprivation therapy.

Second Line
- Most patients initially benefit from ADT, but the disease usually progresses after 1–4 yr.
- Castration-resistant CaP (CRPC): Progression on primary hormonal with a testosterone level of <50 ng/mL, and a rising PSA.
- With metastatic disease on bone or CT scan of the abdomen and pelvis, the disease is classified as metastatic castration-resistant prostate cancer (mCRPC).
- The ECOS2107 clinical trial demonstrated a 12 month survival advantage when docetaxel was initially combined with androgen deprivation therapy.
**PROSTATE CANCER, METASTATIC (CLINICAL AND PATHOLOGIC N+, M+)**

**SURGERY/OTHER PROCEDURES**
- Resection of solitary bone metastases is not generally performed with curative intent.
- Decompression of epidural metastases can result in stabilization of the spinal cord and neurologic symptoms. Best results are obtained if the procedure is performed within 24 h of the onset of symptoms.
- Stabilization of weight-bearing bones (femur and hip) by internal fixation or replacement of the joint prophylactically may prevent fracture.
- In one randomized trial, immediate ADT was associated with improved overall and disease-specific survival among men who had pathologically positive lymph nodes after RP [23]. However, this study was limited by sample size and lack of central pathologic review. In a randomized EORTC study with clinically node-positive disease, early ADT did not have any survival benefit. Because of the gradual natural history of CaP (median survival after development of metastasis after RP 5 yr [82] and because the oncologic benefit of early ADT is uncertain, many consider it reasonable to delay ADT until symptoms or measurable disease on imaging are present, to minimize systemic adverse effects of ADT.

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- Radiation can be used to palliate solitary painful bony metastases.
- Strontium$^{89}$ and samarium$^{153}$ ($\alpha$-emitter) can also be used in the setting of symptomatic bone metastasis.

**Additional Therapies**
- **Bone health**
  - Patients should receive calcium (1,200 mg/d) and vitamin D (800–1,000 IU/d) supplements.
  - With ADT, consider zoledronate 4 mg IV yearly, or denosumab—RANK ligand inhibitors; once every 6 mo SQ for men on ADT or Xgeva with bone mets 120 mg SQ q4wk).
- **Antiandrogen withdrawal syndrome** (Flutamide Withdrawal Syndrome)
  - Osteoporosis, obesity, insulin resistance, lipid alteration, and the concern of increased risk of diabetes and cardiovascular disease.
- **Radiation therapy** for CaP is palliative.
- **Bone-marrow ablation** is performed with curative intent.
- **Bone marrow**
  - Ablation (Castration-resistant Prostate Cancer, CRPC) by internal fixation or replacement of the joint is performed within 24 hr of the onset of symptoms.
  - Best results are obtained if the procedure is performed within 24 h of the onset of symptoms.

**COMPLICATIONS**
- ADT: Hot flashes, loss of sexual function and libido, loss of muscle mass, decreased in bone mineral density, weight gain, diabetes, lipid profile changes, and neurocognitive dysfunction.
- In a metaanalysis of 8 randomized controlled trials, long-term ADT was not associated with an increased risk of death from cardiovascular causes, however.
- Antiandrogens: Increased liver function test.
- Skeletal-related events: Defined by pathologic fracture, spinal compression/vertebral body collapse, osteonecrosis of the jaw, radiation or surgery to bone, or change in antihypertensive therapy. Androgen blockade can cause osteoporosis/osteopenia, bisphosphonate/RANK ligand therapy can limit reductions in bone mineral density.
- Zoledronic acid: Renal insufficiency, adjust based on creatinine.
- Osteonecrosis of the jaw can result from bisphosphonates and RANK ligand inhibitors; avoid major dental work (extractions) on therapy; perform oral exam before starting.

**FOLLOW-UP**

**Patient Monitoring**
- Monitoring patients is controversial. With start of ADT or Xgeva with bone mets 120 mg SQ q4wk).
- **Timing of PSA testing** during chemotherapy is controversial; usually every 3 wk.
- **Surveillance** for skeletal-related events: Defined by pathologic fracture, spinal compression/vertebral body collapse, osteonecrosis of the jaw, radiation or surgery to bone, or change in antihypertensive therapy. Androgen blockade can cause osteoporosis/osteopenia, bisphosphonate/RANK ligand therapy can limit reductions in bone mineral density.
- **Monitoring for osteoporosis, obesity, insulin resistance, lipid alteration, and the concern of increased risk of diabetes and cardiovascular diseases** while on ADT should be considered.

**Patient Resources**

**REFERENCES**

**ADDITIONAL READING**

**CODES**
- ICD9
  - 165 Malignant neoplasm of prostate
  - 185.5 Secondary and unspecified malignant neoplasm of lymph nodes of regional and lower limb
  - 198.5 Secondary malignant neoplasm of bone and secondary bone marrow

- ICD10
  - C61 Malignant neoplasm of prostate
  - C77.4 Malignant neoplasm of lymph nodes of regional and lower limb
  - C79.51 Secondary malignant neoplasm of bone

**CLINICAL/SURGICAL PEARLS**
- ADT is the 1st-line treatment for metastatic CaP.
- There are several antiandrogen and chemo-immunotherapeutic options for men with ADT-refractory metastatic CaP.
- Bone-related issues should be considered in this population.
PROSTATE CANCER, POSITIVE MARGIN FOLLOWING RADICAL PROSTATECTOMY

Kiranpreet K. Khurana, MD
Eric A. Klein, MD, FACS

BASICS

DESCRIPTION
- Prostate cancer that extends to the margin of resection upon pathologic analysis of radical prostatectomy specimen
- May be reported as: Focal or extensive, solitary or multiple

EPIDEMIOLOGY

Incidence
- 5–27% for organ-confined prostate cancer (1)
- 17–65% for nonorgan-confined prostate cancer (1)

Prevalence
N/A

RISK FACTORS
- Higher preoperative prostate-specific antigen (PSA)
- Higher clinical stage
- Higher Gleason score
- Higher pathologic stage
- Surgeon experience

Genetics
None directly correlate with positive surgical margin (PSM)

PATHOPHYSIOLOGY

- 3 causes of PSM:
  - Tumor extends beyond prostate to margin of resection
  - Disruption of prostate capsule exposed cancerous glands
  - Artifact from intraoperative manipulation of prostate or pathologic processing

ASSOCIATED CONDITIONS
- Nonorgan-confined prostate cancer: Higher likelihood of PSM compared to organ confined

GENERAL PREVENTION
- Do not dissect too closely at prostatic apex or posterolaterally since PSM frequently seen there
- For radical prostatectomy, choose surgical approach with most familiarity to surgeon

DIAGNOSIS

HISTORY
- History of risk factors (higher PSA, clinical stage, and Gleason grade) may increase chance of PSM

PHYSICAL EXAM
- Digital rectal exam has been shown to be unnecessary if PSA is undetectable

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Monitor PSA at follow-up visits
- In patients with PSM, there is 25–40% chance of subsequent biochemical recurrence (1)

Imaging
- No additional imaging needed after radical prostatectomy for PSM unless there is suspicion of locoregional recurrence or metastatic disease
- Bone scan, pelvic MRI, and/or computer tomography scan may be considered if above suspected (2)
- Indium In 111 ProstaScint is also indicated as a diagnostic imaging agent in postprostatectomy patients with a rising PSA and a negative or equivocal standard metastatic evaluation in whom there is a high clinical suspicion of occult metastatic disease. Limited utility for use in this setting

Diagnostic Procedures/Surgery
- None indicated

Pathologic Findings
- PSM is a pathologic diagnosis
- Most common site is prostatic apex
- Posterior/proximal margin and bladder neck also commonly involved
- Note that capsule is missing at the apex, so PSM at the apex may be artifactual
- Often classified as: Focal or extensive, solitary or multiple
- Extensive and/or multiple PSM increase chance of biochemical recurrence, but these subclassesifications of PSM do not have greater predictive usefulness than comparing positive vs. negative surgical margin alone (1)

DIFFERENTIAL DIAGNOSIS
- Nonorgan-confined disease with extraprostatic extension or locally advanced disease
- Iatrogenic capsular tissue

TREATMENT

GENERAL MEASURES
- Surgical approach (open, laparoscopic, robotic) does not appear to influence rate of PSM (3)
  - Use good surgical principles to avoid PSM
  - PSM vary by different pathologic sectioning
  - Surgical experience decreases size of PSM

MEDICATION
- First Line
  - N/A
- Second Line
  - N/A

SURGERY/OTHER PROCEDURES
- N/A

ADDITIONAL TREATMENT

Radiation Therapy
- External beam, delivered as 3D-conformal or intensity modulated
  - 64–65 Gy usual dose
- Adjuvant radiotherapy shown to decrease biochemical and local recurrence, and clinical progression (2)
- Effect on subsequent metastasis and overall survival not as clear
- Treatment with adjuvant radiotherapy results in lower use of salvage treatment
- Since majority of patients with PSM do not develop clinical recurrence, immediate adjuvant radiotherapy may lead to overtreatment
- However, salvage radiotherapy may not be as effective for high-risk disease
- Controversy over use of immediate vs. salvage adjuvant therapy
PROSTATE CANCER, POSITIVE MARGIN FOLLOWING RADICAL PROSTATECTOMY

Additional Therapies
- Radiation Therapy Oncology Group trial 9601 is investigating radiotherapy with or without long-term androgen deprivation in postprostatectomy men with pT3N0 disease or pT2N0 disease with a positive margin with PSA ≥0.2–4 ng/mL.
  - Preliminary results show that 24 mo of androgen therapy (bicalutamide) and radiotherapy improve biochemical-free survival and incidence of metastatic disease.
  - Full results awaited.
- Radiotherapy and androgen deprivation in combination after local surgery (RADICALS) trial is evaluating immediate adjuvant radiotherapy vs salvage radiotherapy.
  - Also addresses role of androgen deprivation.
  - Results awaited.

Complementary & Alternative Therapies
See “Additional Therapies” above.

ONGOING CARE

PROGNOSIS
- Not all PSM result in biochemical recurrence, nor higher risk of metastatic disease and death, but those with PSM are at higher risk of both than those with negative margins; these risks are associated with other pathologic features as well.
- Prediction tools such as http://nomograms.mskcc.org/ prostatecancer are used at some centers for decision making concerning postradical prostatectomy management.
- Preliminary results with new genomic classifiers may indicate which patients might benefit from adjuvant radiation therapy.

COMPLICATIONS
- Complications related to radiotherapy (2):
  - Grade 1 or 2 acute toxicities: Common, up to 45%.
  - Grade 3 or 4 acute toxicities: Up to 20%.
  - Up to 28% may develop late toxicities.
- Urinary incontinence, stricture more common than gastrointestinal toxicities (rectal).

FOLLOW-UP

Patient Monitoring
- PSA every 3–6 mo for 1st 3–5 yr, then annually thereafter.
- Value ≥0.2 ng/mL after surgery with confirmatory value of ≥0.2 ng/mL defines biochemical recurrence.

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Prostate Cancer: Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy
- Prostate Cancer: Locally Advanced (Pathologic T3, T4)
- Prostate Cancer: Positive Margin Following Radical Prostatectomy Image 2
- PSA Evaluation, General
- Reference Tables: TNM: Prostate Cancer

CODES
ICD9
185 Malignant neoplasm of prostate
V45.77 Acquired absence of organ, genital organs

ICD10
C61 Malignant neoplasm of prostate
Z90.79 Acquired absence of other genital organ(s)

CLINICAL/SURGICAL PEARLS
- PSM most commonly found at prostatic apex, posterosuperiorly, and bladder neck.
- Avoid overzealous dissection at these locations during radical prostatectomy in patients suspected of being high-risk for PSM.
- PSM are diagnosed pathologically and may be real or artificial.
- Subset of men with PSM develop biochemical recurrence.
- Adjuvant radiotherapy decreases chance of biochemical and local recurrence but effect on metastatic disease and overall survival not clear.

PROSTATE CANCER, POSITIVE MARGIN FOLLOWING RADICAL PROSTATECTOMY

Additional Therapies
- Radiation Therapy Oncology Group trial 9601 is investigating radiotherapy with or without long-term androgen deprivation in postprostatectomy men with pT3N0 disease or pT2N0 disease with a positive margin with PSA ≥0.2–4 ng/mL.
  - Preliminary results show that 24 mo of androgen therapy (bicalutamide) and radiotherapy improve biochemical-free survival and incidence of metastatic disease.
  - Full results awaited.
- Radiotherapy and androgen deprivation in combination after local surgery (RADICALS) trial is evaluating immediate adjuvant radiotherapy vs salvage radiotherapy.
  - Also addresses role of androgen deprivation.
  - Results awaited.

Complementary & Alternative Therapies
See “Additional Therapies” above.

ONGOING CARE

PROGNOSIS
- Not all PSM result in biochemical recurrence, nor higher risk of metastatic disease and death, but those with PSM are at higher risk of both than those with negative margins; these risks are associated with other pathologic features as well.
- Prediction tools such as http://nomograms.mskcc.org/ prostatecancer are used at some centers for decision making concerning postradical prostatectomy management.
- Preliminary results with new genomic classifiers may indicate which patients might benefit from adjuvant radiation therapy.

COMPLICATIONS
- Complications related to radiotherapy (2):
  - Grade 1 or 2 acute toxicities: Common, up to 45%.
  - Grade 3 or 4 acute toxicities: Up to 20%.
  - Up to 28% may develop late toxicities.
- Urinary incontinence, stricture more common than gastrointestinal toxicities (rectal).

FOLLOW-UP

Patient Monitoring
- PSA every 3–6 mo for 1st 3–5 yr, then annually thereafter.
- Value ≥0.2 ng/mL after surgery with confirmatory value of ≥0.2 ng/mL defines biochemical recurrence.

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Prostate Cancer: Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy
- Prostate Cancer: Locally Advanced (Pathologic T3, T4)
- Prostate Cancer: Positive Margin Following Radical Prostatectomy Image 2
- PSA Evaluation, General
- Reference Tables: TNM: Prostate Cancer

CODES
ICD9
185 Malignant neoplasm of prostate
V45.77 Acquired absence of organ, genital organs

ICD10
C61 Malignant neoplasm of prostate
Z90.79 Acquired absence of other genital organ(s)

CLINICAL/SURGICAL PEARLS
- PSM most commonly found at prostatic apex, posterosuperiorly, and bladder neck.
- Avoid overzealous dissection at these locations during radical prostatectomy in patients suspected of being high-risk for PSM.
- PSM are diagnosed pathologically and may be real or artificial.
- Subset of men with PSM develop biochemical recurrence.
- Adjuvant radiotherapy decreases chance of biochemical and local recurrence but effect on metastatic disease and overall survival not clear.
PROSTATE CANCER, RISING PSA FOLLOWING ANDROGEN ABLATION
(CASTRATION-RESISTANT PROSTATE CANCER, CRPC AND mCRPC)
Jianqing Lin, MD
Wm. Kevin Kelly, DO

BASICS

DESCRIPTION
• Castration-resistant prostate cancer (CRPC) is defined as prostate cancer with disease progression despite effective androgen deprivation (serum total testosterone <50 ng/dL).
• CRPC patients are classified as having metastatic disease (Bone or soft tissue visible on imaging) (mCRPC) or nonmetastatic disease (CRPC Rising PSA without any radiographic evidence of metastasis)
• CRPC survival is improved significantly with more effective treatment options.
• Synonymous. The preferred term is castrate-resistant prostate cancer but sometimes called castrate refractory prostate cancer. Older terms such as hormone refractory or androgen-independent prostate cancer are not considered accurate.
• Latest data shows that in CRPC prostate cells are still sensitive to low levels of androgens.

EPIDEMIOLOGY
Incidence
• 233,000 cases of prostate cancer will be diagnosed in the United States in 2014.
• There will be 29,480 deaths due to prostate cancer in 2014.
• The vast majority of patients who die with prostate cancer will die from progressive metastatic CRPC.
• Historically, the median survival with mCRPC is ~2 yr; newer agents, most introduced since 2010, have improved overall survival by several months.

Prevalence
• N/A

RISK FACTORS
• No definitive tool is available to determine the risk of developing CRPC.
• Molecular biomarkers and genetic profiles are being explored for prognostic and treatment.
• CRPC risk factors for poor survival:
  – Low hemoglobin
  – Elevated lactate dehydrogenase
  – Elevated alkaline phosphatase
  – Poor performance status
  – Urinary metastasis particularly liver metastasis
  – Narcotic use for pain
  – Hormone-based on these clinical features can predict overall prognosis for CRPC (1)

Genetics
• Common chromosomal translocations found in CRPC include the TMPRSS2-ERG fusions. Epigenetic abnormalities are common in CRPC

PATHOPHYSIOLOGY
• Androgen receptor (AR) activity is a major driver of therapeutic failure and CRPC development.
• This may occur through intrinsic (intrinsic) androgen synthesis, AR dereguation; AR mutation and alternative splicing, and posttranslational modifications and collective alterations.

ASSOCIATED CONDITIONS
• Fatigue, muscle wasting, incontinent syndrome
• Bone pain/flare
• Hematuria, urinary retention
• Edema
• Spinal cord compression
• Anemia
• Renal failure, usually due to nephrotoxicity
• Cognitive dysfunction

GENERAL PREVENTION
• N/A

DIAGNOSIS

HISTORY
• Prostate cancer history including Gleason score, disease stage at diagnosis, initial treatment for localized prostate cancer.
• Time of 1st diagnosis of metastatic disease
• Past hormonal treatments including time when treatments were started
• PSA history
• Extent of disease at the time of diagnosis and also current extent of disease on the bone and CT/MRI scan
• Recent changes in bowel and urinary habits
• Potency
• New neurologic symptoms
• Past medical history including any specific cardiac, renal, or gastrointestinal disease
• Performance status
• Mental status evaluation
• Current medications and allergies
• Caregiver
• Family history of prostate cancer or other cancers
• Smoking, alcohol, and drug history

PHYSICAL EXAM
• Examine for adrenopathy
• Gynecomastia
• GU and rectal exam
• Extremity edema and swelling
• Neuropsychologic exam with focus on lower extremity weakness and sensation

IMAGING
• Determine presence of radiographic metastasis as a guide to treatment
• Bone scan, CT, or MRI of the abdomen and pelvis at baseline and then every 6–12 mo or based on clinical setting
• Bone density as needed

Differential Diagnosis
• Bone pain may also be due to degenerative joint disease, osteoarthritis, Paget disease, or secondary malignancy
• Weight loss due to depression, other malignancies, or failure to thrive
• Anemia related to iron and vitamin deficiency, secondary malignancy (ie, multiple myeloma), or prior therapies

Pathologic Findings

DIFFERENTIAL DIAGNOSIS
• Bone pain may also be due to degenerative joint disease, osteoarthritis, Paget disease, or secondary malignancy
• Weight loss due to depression, other malignancies, or failure to thrive
• Anemia related to iron and vitamin deficiency, secondary malignancy (ie, multiple myeloma), or prior therapies

TREATMENT

GENERAL MEASURES
• Initial strategies for nonmetastatic CRPC are unclear as no randomized clinical trial has shown survival advantage in the setting of no radiotherapeutically measurable metastatic disease
• Continuing medical castration recommended
• Verify castrate levels of testosterone. If not <50 ng/dL, consider alternative luteinizing hormone-releasing hormone agonist/antagonist administration or orchiectomy if noncastrate
• Define the treatment objectives for patients: Palliative vs. prolonging survival
• Disease progression based on a rapidly rising PSA, objective changes on bone scan or CT/MRI scan or symptoms from the metastatic CRPC
• Sequencing of newer agents in the setting of disease progression remains under study
• AUA, ASCO, NCCN, and other groups have issued guidelines for the management of CRPC

MEDICATION

First Line
• There are multiple treatment options based on disease stability and prior treatment history such as before or after docetaxel-based chemotherapy, clinical trials always need to be considered.
• Often secondary or tertiary hormonal manipulation is the initial therapy in asymptomatic mCRPC. These include:
  – Antiandrogen withdrawal (ie, stopping bicalutamide, etc.)
  – Paradoxical decrease in PSA after stopping
  – 2nd line hormonal therapy with nonsteroidal antiandrogen bicalutamide, flutamide, nilutamide
• Rarely results in a durable response

Second Line
• Immunotherapy with sipuleucel-T: Autologous immunotherapy for minimally symptomatic or asymptomatic mCRPC, improved survival (2)
PROSTATE CANCER, RISING PSA FOLLOWING ANDROGEN ABLATION (CASTRATION-RESISTANT PROSTATE CANCER)

**ONGOING CARE**

**PROGNOSIS**

Median survival of patients with CRPC ranges from 18 to 27 mos depending on the extent of disease.

**COMPPLICATIONS**

- Neurological
- Gastrointestinal
- Lung
- Hematopoietic
- Urological

**SECOND LINE**

- Consider abiraterone or enzalutamide with mCRPC progression if not used previously
- Consider chemotherapy: Cabazitaxel (20–25 mg/m² IV every 3 wks with 10 mg prednisone daily)
- Approved posttaxane
- Mibolerone: chemotherapy FQA approved for palliation; limited utility
- Consider clinical trials

**ADDITIONAL TREATMENTS**

**Surgical Procedures**

- Bladder outlet procedures such as TURP for urinary retention
- Urinary diversion (stents or percutaneous nephrostomy) in cases of hydronephrosis and renal insufficiency

**Radiation Therapy**

- Palliative radiotherapy
- Radium 223 (Alphadurad)
- Palliative bony radiation
- Palliative care or pain specialist referral for refractory pain

**Bone Health**

- Bisphosphonate (zoledronic acid) or denosumab for symptomatic bone metastases
- Daily calcium (1,200 mg/or 1,000 IU daily)
- Vitamin D (800–1,000 IU daily)
- Consider clinical trials

**First-line chemotherapy:** Docetaxel 75 mg/m² IV

**Androgen–androgen receptor axis remains the key survival factor and treatment target for CRPC.**

**Pearls**

- Antihormonal therapies are all effective to improve survival.
- Immunotherapy, chemotherapy, and bone-targeted therapy are all effective to improve survival.

**REFERENCES**


**ADDITIONAL READING**


**CODES**

ICD-10: **C61** Malignant neoplasm of prostate

**ICD-9:** **790.93** Elevated prostate specific antigen [PSA]

**ICD-10:** **C61.9** Malignant neoplasm of prostate

**ICD-9:** **790.93** Elevated prostate specific antigen [PSA]

**Clinical/Surgical Pearls**

- Castration-resistant prostate cancer must be classified as with (mCRPC) or without (CRPC) radiographic metastasis.
- Bone metastases will evolve if not initially present.
- Androgen–androgen receptor axis remains the key survival factor and treatment target for CRPC.
- Androgen receptor targeted therapy, immunotherapy, chemotherapy, and bone-targeted therapy are all effective to improve survival.
PROSTATE CANCER, UROTHELIAL

Eric A. Klein, MD, FACS
Samuel Haywood, MD

**BASICS**

**DESCRIPTION**

- UC described in 1952 by Millicoe and Hollowell—originally noted as Blower’s disease of the prostate urethra (1)
- Can occur in 1 of the 3 forms:
  - Primary urothelial carcinoma (UC) of the prostate
  - Direct extension of bladder UC
  - Nonbudd extension of bladder UC
- Multiple prior staging systems:
  - Primary UC of the prostate—TNM staging 2001
  - To pu—carcinoma in situ (CIS) affecting prostatic urethra
  - T1 pu—CIS affecting prostatic ducts
  - T1 tumor invading subepithelial connective tissue
  - T2 tumor invading prostatic stroma, spongiosum body, perivesical muscle
  - T3 tumor invading perivesical tissue or bladder neck (extraprostatic extension)
  - T4 tumor involving bladder or surrounding organs
- Prostatic UC concurrent with bladder UC
  - Prior TNM staging defined prostatic invasion of bladder UC as T4a disease
  - However, given the heterogeneity of this classification, did not accurately predict survival
  - Most recent TNM classification (2010) clarifies staging workup involves abdominal and chest imaging (CT vs. MRI) to identify local, regional, and extravesical spread
  - Stomal invasion from subvesical invasion of prostatic urethra classified as organ confined disease
  - Synonyms: Transitional cell carcinoma (TCC)

**EPIDEMIOLOGY**

**Incidence**

- All patients with bladder UC undergoing cystoprostatectomy, 12–48% will have prostatic involvement (1)
- However, underreporting of prostatic involvement
- Body present in radical cystectomy specimens
- Prostatic involvement of UC is a predictor of direct extension to the prostate
  - Stomal invasion of the prostate is present in 7–17% of cystectomy specimens (2)
- Primary UC of the prostate is rare malignancy—1.4% of all primary prostatic tumors (3)

**Prevalence**

- N/A

**RISK FACTORS**

- Risk factors for prostatic involvement
  - CIS of the bladder
  - Multifocal disease in bladder
  - High-stage bladder UC
  - Previous involvement of prostate
  - Tumors involving trigone or bladder neck
  - Risk factors for stromal invasion—presence of CIS (odds ratio 3.2) and location of tumor at or below trigone (odds ratio 3.3) (2)

**Genetics**

- Genetics:
  - No specific genes associated with prostatic UC

**PATHOPHYSIOLOGY**

- May involve any part of the prostatic urethra, prostatic duct system, or prostate stroma
- Arises from extension of bladder primary tumor
- Implantation of malignant cells, or transformation secondary to carcinogenic field effect
- Metastases commonly to bone, lung, liver, gastrointestinal tract

**ASSOCIATED CONDITIONS**

- Almost all cases (>95%) associated with bladder UC

**GENERAL PREVENTION**

- Prevention strategies similar as to bladder UC

**DIAGNOSIS**

**HISTORY**

- Risk factors similar to bladder UC—tobacco exposure, chemical/occupational exposures
- Hematuria is the most common complaint
- Other symptoms include obstructive voiding dysfunction, pain, fatigue, weight loss

**PHYSICAL EXAM**

- Hematuria or bloody urethral discharge
- Lymphadenopathy
- Abdominal digital rectal exam

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- PSA: Elevations rare in UC
- Urine studies: Urinalysis, urine cytology

**Imaging**

- Staging workup involves abdominal and chest imaging (CT vs. MRI) to identify local, regional, and distant spread
- Bone scan: UC lesions osteolytic vs. adenocarcinoma (ADC) lesions osteoblastic

**DIAGNOSTIC PROCEDURES/SURGERY**

- Cystoscopy—sensitivity 63.3%, specificity 95.1% (2E)
- Focus on macroscopic disease and concurrent bladder lesions
- Unlikely to find microscopic disease or CIS
- Transurethral biopsy (TUR)
- No clear consensus on timing or methods
- Spectrum of sampling recommended in literature from few resectoscope swipes to complete TURP
- Pathologic analysis shows involvement most frequently observed around verumontanum
- Biopsies recommended if positive cytology and/or macroscopic lesions
- Methods of biopsy have varying accuracy (1E)
- Transurethral resection (TUR) biopsy is most accurate: 90% accuracy
- Fine needle aspiration (FNA) biopsy: 40% accuracy
- Transrectal needle biopsy: 20% accuracy
- Biopsies poor at accurately detecting stromal invasion—sensitivity 53%, specificity 77%, positive predictive value (PPV) 45%
- Diagnosis of primary UC of prostate requires both transurethral biopsy and random biopsies of bladder to exclude concurrent UC in the bladder (2E)

**Pathologic Findings**

- Urothelial tumor in situ (CIS) of the prostate:
  - Can involve the prostatic urethra, the prostatic ducts, and the prostatic acini
- Most prostatic urothelial UC arises along with bladder urothelial neoplasia or from pagetoid spread from the bladder into the prostate
- Partial or complete replacement of urethra or duct by atypical urothelial cells with pleomorphic nuclei, coarse chromatin, and frequent mitoses
- Fibrosis and chronic inflammation may be seen

- Invasive UC into prostatic stroma consists of irregular nests, clusters, or single atypical cells that infiltrate prostatic tissue
- There are 2 distinct pathways that invade the prostate:
  - Invasive carcinoma arising from the prostatic urethra and duct, which is often associated with CIS within the prostatic duct or acini
  - Prostatic stromal invasion, in which bladder cancer penetrates from posterior periprostatic soft tissue or the bladder neck

**IMMUNOHISTOCHEMISTRY**

- Bladder urothelial neoplasia or from pagetoid spread from the bladder into the prostate
- Spectrum of sampling recommended in literature from few resectoscope swipes to complete TURP
- Pathologic analysis shows involvement most frequently observed around verumontanum
- Biopsies recommended if positive cytology and/or macroscopic lesions
- Methods of biopsy have varying accuracy (1E)
- Transurethral resection (TUR) biopsy is most accurate: 90% accuracy
- Fine needle aspiration (FNA) biopsy: 40% accuracy
- Transrectal needle biopsy: 20% accuracy
- Biopsies poor at accurately detecting stromal invasion—sensitivity 53%, specificity 77%, positive predictive value (PPV) 45%
- Diagnosis of primary UC of prostate requires both transurethral biopsy and random biopsies of bladder to exclude concurrent UC in the bladder (2E)

**DIFFERENTIAL DIAGNOSIS**

- High-grade prostatic intraepithelial neoplasia (HGPIN)
- Prostatic adenocarcinoma
- Other uncommon prostatic tumors

**DIAGNOSTIC PROVENCE**

- Prevention strategies similar as to bladder UC
- All patients with bladder UC undergoing cystoprostatectomy, 12–48% will have prostatic involvement (1)
- However, underreporting of prostatic involvement
- Body present in radical cystectomy specimens
- Prostatic involvement of UC is a predictor of direct extension to the prostate
- Stomal invasion of the prostate is present in 7–17% of cystectomy specimens (2)
- Primary UC of the prostate is rare malignancy—1.4% of all primary prostatic tumors (3)
Therapies
Complementary & Alternative

**Recommendations (1)**

**Radiation Therapy**

- Surgery/Other Procedures

  - Options include TUR alone, TUR with BCG (as in "first line" above), and radical cystoprostatectomy
  - Radical cystoprostatectomy is the treatment of choice for stromal-invasive prostatic UC. It should also be recommended for patients with progression or recurrence after nonsurgical therapies. (1,2,5)[C]
  - Evidence regarding depth of penetration of BCG into prostatic stroma is unclear—CIS of prostatic urethra has response rates to BCG of ∼70–100%. Response rate when combined with bladder primary decreases to 47–72% (1)[C].
  - Response rates of bladder CIS of prostatic urethra to BCG immunotherapy is ∼70–100%.
  - Some propose TUR prior to BCG therapy to increase exposure—improved prevention of recurrence compared to TUR alone (1)[C].
  - Absolute contraindications to BCG: Active urinary infection, gross hematuria, traumatic catheterization.

**Second Line**

- Adverse reactions to BCG therapy
  - Adverse reactions include fevers and/or sepsis, and are managed with hospitalization and antibiotics (eg, isoniazid, rifampin, ethambutol, and fluoroquinolones)
  - Local reactions include hematuria, fever, dysuria
  - BCG infectious complications include fever, urinary tract infection, and/or sepsis, and are managed with hospitalization and antibiotics (eg, isoniazid, rifampin, ethambutol, and fluoroquinolones)

**Prognosis**

- Degree of prostatic invasion has prognostic implications with respect to 5-yr survival rates (1)
  - Involvement of the urethral mucosa: 100% survival
  - Ductal/acinar involvement: 50%
  - Involvement of the urethral mucosa: 100% survival
  - Stromal invasion: 40%
  - Ductal/acinar involvement: 50%
  - Involvement of the urethral mucosa: 100% survival

**Additional Reading**

PROSTATE CANCER, VERY LOW RISK AND ACTIVE SURVEILLANCE

Michael A. Gorin, MD
Trinity J. Bivalacqua, MD, PhD

PATHOPHYSIOLOGY
- A combination of genetic, hormonal, and environmental factors underlies the development of PCA.
- >95% of all tumors are adenocarcinoma.
- Other histologic types include transitional cell, small cell, and sarcoma.
- NCCN risk categories and AS only pertain to adenocarcinoma.
- Early-stage adenocarcinoma is androgen dependent. As PCA becomes more advanced, tumors de-differentiate and lose this dependency.
- ~70% of PCs arise from the peripheral zone of the prostate.
- Tumors are often multifocal.

ASSOCIATED CONDITIONS
- Many men with PCs also have benign prostatic hyperplasia (BPH)/lower urinary tract symptoms.
- BPH is not a precursor to PCA.

PATHOLOGIC FINDINGS
- BPH, prostatitis (granulomatous, acute, or chronic), recent instrumentation, nonadenocarcinoma prostate malignancy (sarcoma, urothelial carcinoma)

DIFFERENTIAL DIAGNOSIS
- Localized PCA:
  - BPH, prostatitis (granulomatous, acute, or chronic), recent instrumentation, nonadenocarcinoma prostate malignancy (sarcoma, urothelial carcinoma)

TREATMENT
GENERAL MEASURES
- Adequate patient evaluation and review of all treatment options is essential
- Identification of patients who may be an appropriate candidate for AS

MEDICATION
First Line
- No role for chemotherapy or androgen deprivation for men who are candidates for AS
- S-Adrs do not appear to prevent disease progression of men on AS

Second Line
- NKI
SURGERY/OTHER PROCEDURES

- Radical prostatectomy may be offered to men who desire treatment.
- A pelvic lymph node dissection may be omitted given the low risk of lymph node metastases in this population.
- When open or robotic or laparoscopic surgery is performed, treatment with either intensity-modulated or 3-dimensional conformal radiation therapy should be utilized to limit toxicity to surrounding organs.
- Major side effects of surgery include urinary incontinence and erectile dysfunction.

ADDITIONAL TREATMENT

Radiation Therapy
- External beam radiation therapy or brachytherapy are acceptable alternatives to AS and surgery.
- Adjacent hormonal therapy is not indicated with either approach in this group of men.
- When external beam radiation therapy is performed, treatment with either intensity-modulated or 3-dimensional conformal radiation therapy should be utilized to limit toxicity to surrounding organs.
- Brachytherapy should be avoided in men with symptoms of bladder outlet obstruction (high International Prostate Symptom Score) due to the risk of worsening lower urinary tract symptoms.

- Major side effects of radiation include urinary incontinence, irritative voiding symptoms, erectile dysfunction, radiation induced proctitis, hemorrhagic cystitis and secondary malignancies most commonly of the bladder and rectum.

Additional Therapies
- Technologies for focal and hemi-ablation are currently in the early phases of investigation.
- Modalities include therapy, high intensity focused ultrasound, interstitial laser and cryosurgery.

Complementary & Alternative Therapies
- Low low appropriate recommendation

FOLLOW-UP

Patient Monitoring
- The optimal protocol for monitoring men on AS is unknown.
- Most advocate for biannual PSA measurements with DRE and annual 12–14 core prostate biopsy.
- PSA kinetics do not appear to be helpful in predicting disease progression.
- Monitoring for disease progression is not indicated after age 75 of when life expectancy is <10 yr.

Patient Resources
- The NCCN Guidelines for Patients: Prostate Cancer (http://www.nccn.org/patients/guidelines/prostate/).
- What You Need to Know About Prostate Cancer from the National Cancer Institute (http://www.cancer.gov/cancertopics/wynewsletter/prostate).

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostate Cancer, General Considerations
- Prostate Cancer, Genomic Markers
- Prostate Cancer, Localised (T1, T2)
- PSA Elevation, General Considerations

PATHOLOGY/BIOLICAL

- PSA kinetics do not appear to be helpful in predicting disease progression.
- Most advocate for biannual PSA measurements with DRE and annual 12–14 core prostate biopsy.

CLINICAL/SURGICAL

- A large percentage of older men with screen-detected PCa will have insignificant tumors and, therefore, not benefit from intervention.
- To avoid the potential morbidity associated with treatment, AS should be offered to men with low–risk PSA and a life expectancy of <20 yr.
- The optimal follow-up protocol is not well defined but typically includes biannual PSA measurements with DRE and annual 12–14 core prostate biopsy.
- PSA kinetics are less useful than biopsy findings for accurately reclassifying men while on AS.
- It is unknown if men reclassified on AS would have been better served with immediate treatment; however, long-term data from a number of centers suggest good oncologic outcomes with this management strategy.
PROSTATE, ABSCESS
Garjae D. Lavien, MD
Michael J. Naslund, MD

BASICS

DESCRIPTION
Prostate abscess is an infection of the prostate with focal accumulation of pus within the prostate gland. It is usually a result of ineffective antibiotic therapy for acute prostatitis, and may occur in nonhospitalized patients.

Epidemiology

Incidence
Decreasing with widespread use of antibiotics.

Prevalence
Diagnosed in 0.2% of patients with urologic symptoms, 0.5–2.5% of patients hospitalized for prostatic symptoms.

RISK FACTORS

Bladder outlet obstruction, history of bacterial prostatitis, chronic hemodialysis, diabetes, etc.

Indwelling catheters
Lower urinary tract instrumentation
Sexually transmitted infections
Lower urinary tract instrumentation
Sexually transmitted infections
Compromised immune system (eg, HIV/AIDS, cancer, diabetes, etc.)
Chronic renal failure, hemodialysis
Cirrhosis
Diabetes
HIV/AIDS

GENERAL PREVENTION

Avoided preventing and treating sexually transmitted infections.

DIFFERENTIAL DIAGNOSIS

Pathologic Findings

Gram stain and culture of material will give causative agent, most commonly bacterial.

MRI

May guide drainage and aspiration

TRUS

Will reveal hypoechoic zones with irregular internal echoes, septations, and indistinct borders

CT

Nonenhancing fluid-density collections that can be multiseptated or non-enhancing lesions.

LAB

Prostate-specific antigen should not be obtained in this setting as it will usually be elevated due to the inflammatory process.

IMAGING

Transrectal ultrasound (TRUS)

Can determine penetration of the abscess into the periprostatic tissues and identify gas within the prostate.

CT findings include nonenhancing fluid-density collections that can be multiseptated or non-enhancing lesions.

MRI

May not be feasible in patients who are critically ill and require acute management.

DIAGNOSTIC PROCEDURES/SURGERY

Transurethral ultrasound (TRUS) with aspiration

Transurethral resection of prostate abscess

Pathologic Findings

Pus and infected material will be expressed from prostate during surgical drainage procedure.

Differential Diagnosis

Chronic prostatitis

Acute prostatitis

Pyelonephritis

Cystitis

Chronic renal failure

DIFFERENTIAL DIAGNOSIS

Chronic prostatitis

Acute prostatitis

Pyelonephritis

Cystitis

Chronic renal failure
Surgery/Other Procedures

Transperineal or transrectal needle aspiration with
- Occasionally the transurethral catheter may block drainage of an acutely inflamed prostate or cause bacteriuria.
- In the setting of extreme discomfort or if the catheter is difficult to pass, a suprapubic punch cystostomy is preferred.

Medication

First Line
- Broad-spectrum IV antibiotic therapy followed by directed therapy after causative organism determined by urine culture or Gram stain/culture of abscess fluid.
- 2nd-generation cephalosporins (cefoxitin, cefmenoxime) or 3rd-generation cephalosporins (ceftriaxone, cefixime, cefditoren pivoxil).
- IV fluoroquinolones.
- Clindamycin for additional anaerobic coverage is recommended.

Second Line
- Vancomycin for coverage of MRSA is suspected.
- 2nd-generation cephalosporins (cefoxitin, cefmenoxime) or 3rd-generation cephalosporins (ceftriaxone, cefixime, cefditoren pivoxil).
- IV fluoroquinolones.
- Clindamycin for additional anaerobic coverage is recommended initially.

- Dose based on renal function.
- After acute phase, continue oral antibiotic regimen based on cultures for up to 4 wk.

Surgey/Other Procedures

- Transperineal or transrectal needle aspiration with US guidance followed by urethral catheter drainage.
- Can be performed using local anesthesia or sedation.
- Higher risk of recurrence of abscess.

- Open incision and drainage through a perineal approach.
- Lithotripsy in patients with penetration of the abscess through the capsule of the prostate or through the levator ani.
- Allows placement of a drain.
- Increased morbidity compared to open perineal or transrectal approaches.
- Suprapubic cystostomy can be used as an adjunct for urinary diversion in patients with urinary retention.

Additional Treatment

Radiation Therapy

- Optional once definitive therapy to confirm that no residual abscess remains.

Complementary & Alternative Therapies

COMPLICATIONS

- May progress to spontaneous fistulization into the urinary bladder, prostatic urethra, rectum, or perineum.
- Urosepsis, and possibly death if diagnosis not made in timely manner.

Follow-Up

- Patient Monitoring: Supportive once definitive therapy performed.
- Once acute events resolve, monitoring focuses on optimizing medical comorbidities and improving voiding symptoms.
- Author recommendation: CT or TRUS 4–6 wk after definitive therapy to confirm that no residual abscess remains.
- Follow-up urine culture recommended.

Patient Resources

Treatments

General Measures

- Initial treatment should focus on broad-spectrum antibiotics, IV hydration, and pain control.
- In the setting of acute urinary retention, a Foley catheter placement can be attempted.
- Occasionally the transurethral catheter may block drainage of an acutely inflamed prostate or cause bacteriuria.
- In the setting of extreme discomfort or if the catheter is difficult to pass, a suprapubic punch cystostomy is preferred.

- Open incision and drainage through a perineal approach.
- Lithotripsy in patients with penetration of the abscess through the capsule of the prostate or through the levator ani.
- Allows placement of a drain.
- Increased morbidity compared to open perineal or transrectal approaches.
- Suprapubic cystostomy can be used as an adjunct for urinary diversion in patients with urinary retention.

Additional Treatment

Radiation Therapy

- Optional once definitive therapy to confirm that no residual abscess remains.

Complementary & Alternative Therapies

Reference


Additional Reading

- See Also (Topic, Algorithm, Media)
  - Prostatitis, Acute, Bacterial (NIH I)
  - Urinary Tract Infection (UTI), Adult Males
  - Urosepsis

ICD Codes

- 509.0 Bladder neck obstruction
- 509.1 Acute prostatitis
- 601.2 Abscess of prostate

Clinical/Surgical Pearls

- Prostate abscess is uncommon and thus often overlooked in the differential diagnosis.
- Prostate abscesses in patients presenting with fever and persistent lower urinary tract symptoms that do not respond to antibiotics.
- A pelvic CT scan is generally the best test to evaluate for the possibility of a prostate abscess.
- A delay of antimicrobial therapy in the management of acute bacterial prostatitis can increase the risk of prostatic abscess.
PROSTATE, BENIGN HYPERPLASIA/HYPERTROPHY (BPH)
Shaun G.S. Grewal, MD
Gerald L. Andriole, MD, FACS

BASICS

DESCRIPTION

Benign prostatic hypertrophy (BPH) refers to histologic changes within the prostate gland.

– May not imply the presence of an enlarged prostate or symptoms.
– LUTS are not manifestation of BPH.
– Synonym(s): Nodular hyperplasia

Definitions from the International Continence Society (ICS):

– Benign prostatic hyperplasia is a term used (and reserved for) the typical histologic pattern which defines the disease.
– Benign prostatic obstruction is a form of bladder outlet obstruction (BOO) and may be diagnosed when the cause of outlet obstruction is known to be benign prostate enlargement, due to histologic benign prostatic hyperplasia.
– Benign prostatic enlargement (BPE) is defined as prostate enlargement due to histologic benign prostatic hyperplasia. The term “prostatic enlargement” should be used in the absence of histologic pathology.

EPIDEMIOLOGY

Incidence

– 10% of men >40 will develop histologic evidence of BPH.
– 50–75% of these men will develop bothersome LUTS (1)

Prevalence

– Histologic prevalence of BPH increases with age:
  – 10% to men in their 30s
  – 20% to men in their 40s
  – 50–60% to men in their 60s
  – 80–90% to men in their 70s and 80s

– Men with significant prostate enlargement (>50 cc) 3.5 times more likely to have moderate-to-severe LUTS (2)

– BPH is a histologic diagnosis that does not always result in clinical LUTS

RISK FACTORS

– Although family history and advancing age are risk factors for BPH, evidence for comorbidity, environmental, dietary, or lifestyle-related risk factors are generally weak.

Massachusetts Male Aging Study: Cigarette smoking and increased physical activity protective against BPH; heart disease correlated with development of BPH. Possible association between obesity and prostate volume/LUTS.

Genetics

Some men with younger age of onset and larger glands have a family history of BPH.

PATHOPHYSIOLOGY


– Detrusor response to increased resistance is to generate higher pressures to overcome the outlet resistance. Leads to a variety of cellular and morphologic changes in the bladder. Causes the common storage symptoms of frequency, urgency, and nocturia.

– May lead to bladder decompensation, in which the bladder is no longer able to generate sufficient pressures to empty.

– Primary androgen-dependent growth process involves perineural and transition zones of the prostate.

ASSOCIATED CONDITIONS

– GDM (diabetic bladder defined as urinary frequency, urgency, nocturia, urge incontinence)
– Sexual dysfunction (erectile and/or ejaculatory dysfunction)

GENERAL PREVENTION

– Randomized clinical trials (MtCnTIP) suggested that the combination of an α-blocker with a 5α-reductase inhibitor (5-ARI) can reduce the lifetime risk of acute urinary retention and may prevent symptomatic disease progression in men with enlarged prostate volume (>25 cc) (3).

– Bladder decompensation may be prevented by treatment of BOO.

DIAGNOSIS

HISTORY

– Focus on identifying the presence of LUTS

– Voiding symptoms (previously called obstructive symptoms): Hesitancy, intermittency, weak stream, abdominal straining to void, postvoid dribbling, incomplete emptying, double voiding

– Storage symptoms (previously called irritative symptoms): Daytime frequency, nocturia, urgency, urge incontinence, dysuria, dribbling

– Identify other contributing factors to LUTS

– Medications (ie, diuretics, cold medications)
– Comorbidities (ie, diabetes, multiple sclerosis, Parkinson)

– Previous interventions/therapies

– Family history

– IPSI is a reproducible, validated index designed to determine disease severity and response to therapy:
  – Scores of 0–7, 8–19, and 20–35 signify mild, moderate, and severe symptoms, respectively.

– Equivalent to AUASI with the addition of a quality of life (QOL) score

PHYSICAL EXAM

– Evaluation of the abdomen, pelvis, perineum
– Examine external genitalia
– DRE to estimate prostate size and detect any nodularity suggestive of prostate cancer.
– Anal sphincter tone and sensation should be noted
– Focused neurologic exam on the anus and lower extremity motor and sensory function. A more extensive neurologic exam is indicated for patients with possible neurogenic lower urinary tract dysfunction

DIAGNOSTIC TESTS & INTERPRETATION

Lab

– PSA:
  – May be a proxy for prostate size
  – PSA of 1.5 ng/ml correlates with prostate volume ~30 mL in most men (4)
  – Information about potential benefits of PSA screening warranted

Imaging

– Not indicated unless there is evidence of upper tract obstruction or a need to further evaluate hematuria
– TRUS may be beneficial in determining accurate size prior to surgical intervention

Diagnostic Procedures/Surgery

– Uroflowmetry is a simple noninvasive urodynamic measurement in which a patient voids into a device that measures the volume/time of urine flow:
  – Combined with a measurement of PVR (post void residual) volume (see next heading below), it is an excellent screening tool for BPH in men with LUTS

– Uroflowmetry measures voided volume, voiding time, average flow rate, and maximum flow rate (Qmax), also called the PFR.

CT Scan:

– Former: The single best measurement obtained by this study to assess voiding dysfunction. While formal definitions vary, in general with a voided volume of 125–150 mL, a Qmax of >15 mL/s is often considered normal, whereas a value of ≤7 mL/s is suggestive of significant obstruction.

– May need urodynamics to differentiate BOO from hypercontractile bladder (pressure flow study).

– Observation confirmed with low flow (Qmax <15 mL/s) and high voiding pressure >40 cm water.

– PI-RADS: Although generally used, PI-RADS does not convincingly correlate with the severity of LUTS, the presence of BOO, or treatment outcomes:

– Voids to evaluate for occult polyuria or polydipsia.

– Cystoscopy not essential unless there is concern for malignancy, obstruction due to foreign body, or stricture. May be useful to evaluate for most appropriate surgical or minimally invasive treatments.

Pathologic Findings

– Varying degrees of glandular and stromal nodular hyperplasia (as such, hypertrophy is a misnomer).

– The glandular component is made up of small and large acini lined by basal and secretory cells. The stromal component is rich in smooth muscles.

– Nodular growth is a major histologic component of BPH.

– Diffuse stromal infiltration of plasma cells and lymphocytes can be seen, but no infectious agent nor clinical diagnosis of prostatitis is typically present.
DIFFERENTIAL DIAGNOSIS
- Obstructive symptoms: Bladder outlet dysfunction, neurogenic bladder, pelvic floor dysfunction, prostate cancer, prostatic abscess, prostatic syndrome, urethral obstruction (stricture, constrictions)
- Irritative symptoms: Bladder cancer, detrusor hyperreflexia/OAB, interstitial cystitis, pelvic congestion, prostatic syndrome.

TREATMENT

GENERAL MEASURES
- Directed at OAB, unless evidence of significant damage to urinary tract from obstruction (hydrothorax, bladder calculus, recurrent infections)
- Guidelines suggest watchful waiting for men with mild symptoms (IPSS <7) or for more severe symptoms if they are not bothersome to the patient. Simple behavior modification (fluid restriction, decreased alcohol/caffeine) may help
- Medical therapy considered 1st-line by most, but usually requires continuous therapy to maintain benefit
- α-Blocker and 5-ARIs often prescribed together

MEDICATION

First Line
- α-Blockers (reduce muscle tone in prostate/bladder neck): Tamsulosin (0.4 mg to max 0.8 mg)
- α-Blockers (reduce muscle tone in prostate/bladder neck): Silodosin (8 mg/d)
- α-Blockers (reduce muscle tone in prostate/bladder neck): Alfuzosin (10 mg/d)
- α-Blockers (reduce muscle tone in prostate/bladder neck): Tamsulosin (start 0.4 mg to max 0.8 mg)
- α-Blockers (reduce muscle tone in prostate/bladder neck): Doxazosin (start 1 mg/d to max 8 mg; XL form: 2.5 mg)

Second Line
- Nonselective α-blockers: Dutasteride (0.5 mg)
- Selective α1-blockers (reduce muscle tone in prostate/bladder neck): Bicalutamide (5 mg)

Additional Therapies
- Phosphodiesterase-5 inhibitors: Tadalafil (2.5–5 mg/d)
- Phosphodiesterase-5 inhibitors: Silodosin (8 mg/d)
- Phosphodiesterase-5 inhibitors: Alfuzosin (10 mg/d)
- Phosphodiesterase-5 inhibitors: Tamsulosin (start 0.4 mg to max 0.8 mg)
- Phosphodiesterase-5 inhibitors: Doxazosin (start 1 mg/d to max 8 mg; XL form: 2.5 mg)

COMPLICATIONS
- Symptoms usually well managed by medications
- Prostate cancer, when risk factors identified, can be well managed
- Progressive disease, when risk factors identified, can be well managed
- Incontinence, erectile dysfunction, ejaculatory dysfunction are most common side effects
- 5-ARIs block intracellular DHT conversion; generally best for large glands, may take 6–12 mo for improvement
- Dutasteride (5 mg)
- Dutasteride (0.5 mg)

PROGNOSIS
- Symptoms usually well managed by medications
- Prostate cancer, when risk factors identified, can be well managed
- N/A

FOLLOW-UP
- Periodic monitoring depends on severity of symptoms
- Monitor response to therapy with history, AUA SS, PVR, flow rate
- Upper tract imaging and measurement of renal function if elevated PVR (>300 cc)

SURGERY/OTHER PROCEDURES
- Open simple prostatectomy usually for glands >100 g
- Transurethral resection of prostate: useful for causing problems such as very large bladder calculi or to repair diverticulum
- Retroperitoneal simple prostatectomy: Excision of adenoma through incision in anterior prostate commissure
- Open simple prostatectomy: Excision of adenoma through incision in anterior prostate commissure
- Many minimally invasive alternative surgical procedures: Microwave and water-induced hyperthermia, transurethral needle ablation, laser vaporization (contact, noncontact, interstitial, diode), laser prostatectomy (hulium, KTP)

ADDITIONAL TREATMENT
- Radiation Therapy

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
- Reference Tables: AUA Symptom Index/International Prostate Symptom Score (IPSS)

REFERENCES

ADDITIONAL_CODES
- ICD-10-CN Hypertrophy (benign) of prostate without urinary obstruction and other lower urinary tract symptoms (LUTS)
- N40.0 Enlarged prostate without lower urinary tract symptoms (LUTS)
- N40.1 Enlarged prostate without lower urinary tract symptoms (LUTS)
- N40.2 Nodular prostate without lower urinary tract symptoms (LUTS)
- N40.3 Nodular prostate without urinary obstruction
- N40.4 Enlarged prostate without urinary obstruction
- N40.5 Nodular prostate without lower urinary tract symptoms (LUTS)
- N40.7 Nodular prostate without lower urinary tract symptoms (LUTS)
- N40.83 Enlarged prostate without lower urinary tract symptoms (LUTS)
- N40.89 Other nodular prostate without lower urinary tract symptoms (LUTS)
- N40.9 Prostatic hypertrophy/hyperplasia (benign prostatic hyperplasia) (NOS)

PROSTATE, BENIGN HYPERPLASIA/HYPERTROPHY (BPH)
**PROSTATE, CALCULI**

Christopher Amling, MD, FACS
Nicholas Cowan, MD

---

### BASICs

**DESCRIPTION**
- Prostatic calculi are extremely common and rarely symptomatic.
- Most stones are discovered incidentally.
- Treatment typically reserved for severely symptomatic men.
- Stones within the prostatic urethra rare and likely due to bladder or upper tract stones that become trapped in the prostatic urethra.
- Reports of calculi in the prostatic urethra following transurethral resection of the prostate.

**EPIDEMIOLOGY**

**Incidence**
- 7% in pathologic specimens.
- 20% in autopsies.
- 30% in radiologic studies, with higher percentages in ultrasound scan exams.

**Prevalence**
- Small areas of microcalcification can be seen in 2nd and 3rd decades of life.
- Almost all men (99%) have some degree of prostatic calcification noted at autopsy.
- Stone burden and size typically increase as a man ages.

**RISK FACTORS (1)**

- **Intraprostatic calculi**
  - Recurrent urinary tract infections (UTIs).
  - Pelvic radiation (for prostate cancer).
  - Studies are mixed on role of inflammation in stone development.
- **Stones within the prostatic urethra**
  - Urolithiasis.
  - Enlarged prostatic utricle.
  - History of transurethral resection of the prostate.

**GENETICS**
- N/A

---

### PATHOPHYSIOLOGY

- Urinary intraprostatic reflux implicated in stone formation.
- Intraprostatic calculi presumed to form by the precipitation of prostatic secretions and calcification of the corpora amylacea under inflammatory conditions.
  - Impaction of prostatic secretions within the prostatic ducts.
  - Concentric layering of calcium phosphate and calcium carbonate on inspissated core result in growth.
  - Stone elements may contain constituents found only in urine and not in prostatic secretions.
  - Stones may harbor bacteria and serve as source for relapsing UTI.
  - For prostatic utricle stones, prostatic utricle distends during voiding and then passively drains.
  - Impaired emptying results in urinary stasis stone formation. Patients present clinically with chronic UTI, hematuria, urethral discharge, epididymitis, and voiding dysfunction.

**ASSOCIATED CONDITIONS**

- Chronic pelvic pain syndrome.
- Prostatitis.
- No association between prostate calculi and risk of prostate cancer.
- Hypospadias (enlargement of the prostatic utricle, a Mullerian duct remnant).

---

### DIAGNOSIS

**HISTORY**

- Typically stones are asymptomatic.
- Evaluate for history of lower urinary tract symptoms (LUTS) (2).
- Presence of large calcui associated with moderate LUTS.
- 25–47% of men with chronic pelvic pain have significant prostatic calcifications.
- Correlation seen with stone size, not number.
- Prostatitis history.
- With prostatic utricle stones patients typically present with chronic UTI, hematuria, urethral discharge, epididymitis, and voiding dysfunction.

**PHYSICAL EXAM**

- Genitourinary exam including DRE.
  - DRE unlikely to localize stones.
- Presence of hypospadias.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**

- **Urine culture**
  - Escherichia Coli, enterococci, and Klebsiella spp. more common.
- **Expressed prostatic secretions**
  - May see increased leukocytes.
- **PSA optional**
  - PSA levels not influenced by presence or volume of prostatic calculi, but infection related to chronic nids may falsely elevate PSA (3).

**Imaging**

- Stones often identified incidentally.
- Transrectal ultrasound (TRUS).
  - Highly sensitive for large calculi.
- Sometimes seen on plain film.
Diagnostic Procedures/Surgery
- Postvoid residual (PVR)
- Uroflow if significant obstructive voiding symptoms present
- If intraurethral stones are suspected, cystoscopy is diagnostic

Pathologic Findings
- Majority of calculi are found in the posterior and posterolateral zones of the prostate
- Rare to find large stones obstructing the urethra

DIFFERENTIAL DIAGNOSIS
- Benign prostatic enlargement (BPE)
- Calcified prostatic utricle cyst or utricle stone
- False prostatic calculi: Calculi trapped in dilated prostatic urethra or in dilated prostatic utricle
- Prostate cancer
- Prostatitis
- Seminal vesical calculi
- UTI

TREATMENT

GENERAL MEASURES
Evaluate and treat coexisting conditions such as UTI, prostatitis, and BPO

MEDICATION
First Line
Culture-directed antibiotic therapy if urine culture positive

Second Line
TBA

SURGERY/OTHER PROCEDURES
- Surgery rarely indicated and is typically for severely symptomatic patients
- Transurethral resection of the prostate
- Stone burned usually visible on TRUS
- Open prostatolithotomy for large stones
- Cystoscopy with lithotripsy for stones within the prostatic urethra or prostatic utricle

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
Excellent, as majority of stones are asymptomatic

COMPICATIONS
- Rarely results in urinary obstruction
- May predispose to chronic UTI

FOLLOW-UP
Patient Monitoring
- No follow-up necessary for asymptomatic incidentally identified stones
- Consider postoperative PVR or uroflow if surgical intervention undertaken

Patient Resources
N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Corpora Amylacea
- Prostate, Benign Hyperplasia/Hypertrophy
- Prostate, Nodule
- Prostatic Utricle Anomalies
- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostate, General
- Urinary Tract Infection, Adult Male

CODES
ICD9
- 599.0 Urinary tract infection, site not specified
- 599.70 Hematuria, unspecified
- 602.0 Calculus of prostate

ICD10
- N39.0 Urinary tract infection, site not specified
- N42.0 Calculus of prostate

ICD11
- N28.0 Urinary tract infection, site not specified
- N83.9 Hematuria, unspecified

CLINICAL/SURGICAL PEARLS
Prostate calculi are very common and rarely require treatment.
PROSTATE, NODULE
Gurdarshan S. Sandhu, MD
Gerald L. Andriole, MD, FACS

BASES

DESCRIPTION
A prostate nodule is usually described as a palpable lesion detected on digital rectal exam (DRE) raise concern for prostate cancer (CaP).
- Nodules can be described as soft, rubbery, firm, hard, or rock hard.
- Nodules can be well circumscribed or irregular and diffuse.
- A normal prostate is about the size of a chestnut and has a consistency similar to that of the contracted thresem. It expanse of the thumb.
- This can be simulated by opposing the thumb to the little finger and palpating the contracted muscle.
- Consistency of nodule can denote underlying pathology.
- Rapidity of appearance and changes in size and consistency can infer malignant potential.
- Nodule detection by DRE is recommended as part of prostate cancer detection programs.
- Current recommendations from the American Cancer Society are, if men decide to be tested for prostate cancer, they should have the PSA blood test with or without a rectal exam.

EPIDEMIOLOGY
Incidence
- Prostate nodule as an isolated finding with normal PSA is found in ~10% of cases of prostate cancer in the US.
- Increasingly men are being diagnosed with prostate cancer based on an elevated serum prostate-specific antigen (PSA) and not an abnormal DRE (50% of diagnoses in 2002) (1).
- 80% of men diagnosed with prostate cancer in 2004–2005 have localized disease (CT1 or CT2) (2).
- 5–10% of men in screening programs have abnormal/suspicious DRE.

RISK FACTORS
- Prostate cancer:
  - Nodule that changes in consistency and size over time
  - Elevated serum PSA (>2.5–4 ng/mL)
  - Positive family history
  - Benign nodules
  - No significant change over time
  - Nodule may be softer
  - Prior episodes of prostatitis, biopsy, or prostate surgery (transurethral resection)
- Prior therapy with intravesical Bacillus Calmette–Guérin (BCG)
- Granulomatous nodules can be due to infectious causes (eg, tuberculosis [TB]) or systemic granulomatous diseases

GENETICS
See “Prostate Cancer, General Considerations”

PATHOPHYSIOLOGY
- Normal prostate has a soft, uniform consistency.
- Prostate enlarges with age.
- Microscopically, nodular prostastic hyperplasia consists of nodules of glands and intervening stroma. May occasionally form benign palpable nodules.
- Nodule can be subjectively graded by degree of firmness/hardness (grades 1–3).
- CaP has to have a volume of 0.7 ml or larger to be detected by DRE.

ASSOCIATED CONDITIONS
- Prostate adenocarcinoma
- Benign prostatic hyperplasia (BPH)
- History of intravesical BCG for bladder cancer

GENERAL PREVENTION
None

DIAGNOSIS
HISTORY
- History of lower urinary tract symptoms
  - Irritative voiding symptoms
  - Obstructive voiding symptoms
- Fever
- Obstructive voiding symptoms
- Irritative voiding symptoms
- History of intravesical BCG for bladder cancer
- History of intravesical BCG for bladder cancer
- History of intravesical BCG for bladder cancer
- History of intravesical BCG for bladder cancer
- History of intravesical BCG for bladder cancer

PHYSICAL EXAM
- DRE:
  - Carcinoma (prostatic or urothelial cell carcinoma)
  - Firm, indurated nodules within the prostate gland
  - Prostate cancer most often arises in the posterior peripheral zone of the prostate
  - Advanced prostate cancer can make the entire gland firm and cause obliteration of the median and lateral line
- Advanced cancer can also extend into the seminal vesicles or toward the side wall laterally

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - PSA—Serum levels vary with age, race, and prostate volume
  - Improvement in the positive predictive value of DRE for cancer
  - No cut-off value below which the absence of prostate cancer can be guaranteed
  - Risk of prostate cancer is continuous as PSA increases (3).
  - See “PSA Elevation, General Considerations” for further specifics on PSA.
- Urinalysis:
  - Variable findings in men with abnormal DRE; sterile pyuria in granulomatous prostatitis
  - Urethral cytology can be positive in urothelial cancer
- Imaging:
  - Transrectal ultrasound (TRUS):
    - Classic appearance of prostate adenocarcinoma is a round or oval hypoechoic lesion located in the peripheral zone
    - Not very sensitive as 39% of tumors can be missed
    - Also nonspecific as granulomatous lesions can be hypoechoic
    - BPH can have variable appearance
  - Distinguishable from prostate cancer only by biopsy
- Abdominal computed tomography (CT) or magnetic resonance imaging (MRI)
- Bone scan to detect bone metastases in patients with high-risk prostate cancer
- Bone scan to detect bone metastases in patients with high-risk prostate cancer
- Bone scan to detect bone metastases in patients with high-risk prostate cancer
- Bone scan to detect bone metastases in patients with high-risk prostate cancer

PREVALENCE
5–10% of cases of prostate cancer in the US.

BASICS
**DIAGNOSTIC PROCEDURES/SURGERY**

TRUS-guided biopsy (4)
- Used to widely sample the prostate during biopsy in men with an elevated PSA and/or abnormal DRE
- Modern biopsy schemes have modified the standard sextant biopsy scheme to focus on lateralized cores
- Generally 12 cores

Cytoscopy
- Used to evaluate bladder outlet obstruction and hematuria when present

Pathologic Findings

See “Prostate Cancer, General Considerations”

**DIFFERENTIAL DIAGNOSIS**

- Neoplasms, malignant
  - Prostate adenocarcinoma
  - Other prostate malignancies
  - Sarcoma
  - Small cell carcinoma
- Other rare tumors and metastasis
  - Urothelial carcinoma
  - BCG related or other cause
- Urinary retention
  - BPH
- Calculus
- Benign prostatic hyperplasia
- Granulomatous prostatitis
- Urinary tract infection or sepsis
- Granulomatous prostatitis
- Urinary tract infection or sepsis
- Urinary retention

**TREATMENT**

**GENERAL MEASURES**

- Abnormal DRE is an indication for TRUS-guided biopsy of the prostate
- Workup includes assessment of PSA
- Staging investigations including bone scan, CT, and/or MRI are reserved for high-risk cases as dictated by PSA, Gleason score, and DRE

**MEDICATION**

**FIRST LINE**

Antibiotics may be required for infectious causes of prostatitis or TB

**SECOND LINE**

Antibiotics may be required for infectious causes

**SURGERY/OTHER PROCEDURES**

See “Diagnostic Procedures/Surgery” above

**ADDITIONAL TREATMENT**

This is dictated by the results of the TRUS biopsy and presence/extent of prostate cancer

**RADIATION THERAPY**

While not a specific treatment of the nodule, it can be used as primary therapy or as additional adjuvant/salvage therapy after prostatectomy in patients with prostate cancer

**ADDITIONAL THERAPIES**

May be required in cases with metastatic disease or disease that recurs after definitive local therapy

**COMPLEMENTARY & ALTERNATIVE THERAPIES**

N/A

**ONGOING CARE**

Depends on diagnosis after TRUS-guided biopsy

**PROGNOSIS**

- TRUS-guided biopsy
  - Hematuria
  - Hematospermia
  - Urinary tract infection or sepsis
  - Urinary retention

Other complications are dictated by the treatment received for prostate cancer

**FOLLOW-UP**

Patient Monitoring

- Negative biopsy in a patient with an abnormal DRE or elevated PSA requires follow-up with serial PSA and DRE

**PATIENT RESOURCES**


**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- BCG Sepsis/BCG Ossis
- Prostate Biopsy, Infections and Complications
- Prostate Cancer, General Considerations
- Prostate Cancer, Localized (T1, T2)
- Prostate Cancer, Urthelial
- Prostate Nodule, Image @
- Prostatic, Granulomatous
- Tuberculosis, Genitourinary, General Considerations

**CODES**

- ICD9 = 790.93 Elevated prostate specific antigen (PSA)

- ICD10 = C61.3 Male prostate without lower urinary tract symptoms

**CLINICAL/SURGICAL PEARLS**

- A firm prostate nodule generally deserves further workup with a serum PSA and prostate biopsy
- Up to 40% of patients may develop granulomatous prostatitis after intravesical BCG that may present as a prostate nodule.
PROSTATIC INTRAEPITHELIAL NEOPLASIA (PIN)

Joseph C. Klink, MD
Eric A. Klein, MD, FACS

**BASICS**

**DESCRIPTION**
- Prostatic intraepithelial neoplasia (PIN) describes cytologically atypical cells confined within architecturally benign prostatic glands and acini.
- Historically subclassified—Low-grade PIN (LGPIN) and high-grade PIN (HGPIN)
- PIN 1, 2, or 3
- LGPIN no longer reported because not reliably distinguished from benign prostatic by pathology
- LGPIN carries no increased risk of prostate cancer (PCA) on future biopsies
- HGPIN, and atypical small acinar proliferation (ASAP) are both considered by most to be premalignant
- Antiquated names for PIN include intraductal large acinar atypical hyperplasia, marked atypia, ductal-acinar dysplasia
- Remnant of this chapter will focus on HGPIN

**ASSOCIATED CONDITIONS**
- PIN 1, 2, or 3
- With modern 12-core biopsies, a single focus of HGPIN does NOT increase the risk of PCA diagnosis on subsequent biopsy
- Multifocal HGPIN Predicts Increased Risk of PCA on repeat biopsy
- Historically, HGPIN on prostate biopsy often represented failure to sample a nearby PCA (2)
- The number of cases routinely sampled at prostate biopsy increased, the predictive value of HGPIN for PCA decreased
- With modern 12-core biopsies, a single focus of HGPIN does NOT increase the risk of PCA diagnosis on subsequent biopsies
- Decision for repeat prostate biopsy should be made on other clinical factors (elevated PSA, high PSA-velocity, new nodule on DRE) not influenced by the presence of 1 focus of HGPIN
- Multifocal HGPIN indicates higher risk of PCA on repeat biopsy (3)
- Multivariate odds ratio 3.2 for increased cancer detection with multifocal HGPIN
- 16–75% (usually around 30%) PCA rate on repeat biopsy for multifocal HGPIN
- Repeat biopsy usually done 1 yr after initial biopsy

**PREVENTION**
- Dutasteride reduced the incidence of HGPIN from 6–3.7% in the REDUCE trial
- Finasteride daily for 7 yr decreased the incidence of PIN but are not FDA approved for this use
- Dutasteride daily for 7 yr decreased the incidence of HGPIN from 7.1–6% in the Prostate Cancer Prevention Trial
- Dutasteride reduced the incidence of HGPIN from 6–3.7% in the REDUCE trial
- The risk posed by unifocal HGPIN to a patient’s health and life in the absence of PCa is so low that prevention is not indicated

**PATHOPHYSIOLOGY**
- HGPIN may be precursor of PCA (1)
- PCs can develop without HGPIN
- HGPIN extent and frequency greater when PCs present
- Usually in peripheral zone
- Often multifocal

**HISTORY**
- HGPIN produces no symptoms

**DIAGNOSIS**

**PHYSICAL EXAM**
- Digital rectal exam (DRE) is usually normal, but may reveal a prostate nodule or induration
- No other physical exam findings

**DIAGNOSTIC TESTS & INTERPRETATION**
- Transrectal ultrasound-guided biopsy of the prostate taking at least 12 cores
- Indicated to look for PCA. HGPIN is an incidental finding

**Pathologic Findings**
- Characterized by proliferation of secretory cells with significant architectural change within prostate glands and acini
- Secretory cells are enlarged with increased nuclear/cytoplasmic ratio and prominent nucleoli
- Cytoplasm of the HGPIN cells stains positively for α-reductase inhibitors
- Cytokines of the HGPIN cells tend to stain positively for α-reductase inhibitors and nuclear protein p63
- Most of these features are shared by PCs
- In PCs, basal cells are absent. In HGPIN the basal cell layer is retained although is often discontinuous on H&E stain (Figure 2)
- Transrectal ultrasound-guided biopsy of the prostate

**DIAGNOSIS**

**HISTORY**
- HGPIN produces no symptoms

**PHYSICAL EXAM**
- Digital rectal exam (DRE) is usually normal, but may reveal a prostate nodule or induration
- No other physical exam findings

**DIAGNOSTIC TESTS & INTERPRETATION**
- Transrectal ultrasound-guided biopsy of the prostate taking at least 12 cores
- Indicated to look for PCA. HGPIN is an incidental finding

**Pathologic Findings**
- Characterized by proliferation of secretory cells with significant architectural change within prostate glands and acini
- Secretory cells are enlarged with increased nuclear/cytoplasmic ratio and prominent nucleoli
- Cytoplasm of the HGPIN cells stains positively for α-reductase inhibitors and nuclear protein p63
- Most of these features are shared by PCs
- In PCs, basal cells are absent. In HGPIN the basal cell layer is retained although is often discontinuous on H&E stain (Figure 2)
- Transrectal ultrasound-guided biopsy of the prostate

**DIAGNOSIS**

**HISTORY**
- HGPIN produces no symptoms

**PHYSICAL EXAM**
- Digital rectal exam (DRE) is usually normal, but may reveal a prostate nodule or induration
- No other physical exam findings

**DIAGNOSTIC TESTS & INTERPRETATION**
- Transrectal ultrasound-guided biopsy of the prostate taking at least 12 cores
- Indicated to look for PCA. HGPIN is an incidental finding

**Pathologic Findings**
- Characterized by proliferation of secretory cells with significant architectural change within prostate glands and acini
- Secretory cells are enlarged with increased nuclear/cytoplasmic ratio and prominent nucleoli
- Cytoplasm of the HGPIN cells tends to stain positively for α-reductase inhibitors and nuclear protein p63
- Most of these features are shared by PCs
- In PCs, basal cells are absent. In HGPIN the basal cell layer is retained although is often discontinuous on H&E stain (Figure 2)
- Transrectal ultrasound-guided biopsy of the prostate taking at least 12 cores
- Indicated to look for PCA. HGPIN is an incidental finding

**Pathologic Findings**
- Characterized by proliferation of secretory cells with significant architectural change within prostate glands and acini
- Secretory cells are enlarged with increased nuclear/cytoplasmic ratio and prominent nucleoli
- Cytoplasm of the HGPIN cells stains positively for α-reductase inhibitors and nuclear protein p63
- Most of these features are shared by PCs
- In PCs, basal cells are absent. In HGPIN the basal cell layer is retained although is often discontinuous on H&E stain (Figure 2)
- Transrectal ultrasound-guided biopsy of the prostate taking at least 12 cores
- Indicated to look for PCA. HGPIN is an incidental finding
**Differential Diagnosis**
- Prostate Cancer (PCa)
- ASAP
  - Confers an increased risk of subsequent PCa diagnosis
  - Requires repeat prostate biopsy in a few months to rule out PCa
- Normal anatomic structures and embryonic rests
- Atypia induced by inflammation, infection, or radiation
- Lobular atrophy and postprostatic hyperplasia
- Transitional cell metaplasia
- Typical and atypical basal cell metaplasia
- Cribriform hyperplasia
- Cribiform, sclerotic, and intraductal urothelial carcinoma

**Treatment**

**General Measures**
- If HGPIN was found on initial prostate biopsy of <10 cores, the biopsy should be repeated with an extended scheme
- If multifocal HGPIN is found on initial prostate biopsy, the biopsy should be repeated within 1 yr
- Repeat biopsy should sample the entire prostate, not just the HGPIN area

**Medication**

**First Line**
- Not necessary to treat HGPIN
- HGPIN often used to identify patients at “high risk” of developing PCa
- May require repeat biopsy at 1 yr
- LPIN should not be diagnosed on pathology and, therefore, does not require any follow-up

**Second Line**
- No

**Surgery/Other Procedures**
- Radical prostatectomy not indicated for HGPIN in the absence of PCa

**Additional Treatment**

**Radiation Therapy**
- Not indicated for HGPIN in the absence of PCa

**Additional Therapies**
- No

**Complementary & Alternative Therapies**
- Green tea catechins for 1 yr in men with HGPIN reduced the incidence of PCa from 30 to 3%
- Soy, vitamin E, and selenium did not slow the rate of progression of HGPIN to PCa in a randomized double-blind trial (SELECT Trial)
- None of these therapies routinely recommended to men with HGPIN

**Ongoing Care**

**Prognosis**
- Excellent prognosis in the absence of PCa
- Most monitor for the development of PCa as outlined above

**Complications**
- None other than the risks of biopsy

**Follow-Up**

**Patient Monitoring**
- In certain situations as noted, HGPIN may indicate an increased risk of PCa and, therefore, may require repeat biopsy at 1 yr
- HGPIN should not be diagnosed on pathology and, therefore, does not require any follow-up

**Patient Resources**
- http://prostatecancerinfolink.net/diagnosis/pin/

**References**

**See Also** (Topic, Algorithm, Media)
- Atypical Small Acinar Proliferation, Prostate (ASAP)
- Prostate Cancer, General
- Prostate Nodule
- Prostatic Intraepithelial Neoplasia (PIN) Images
- PSA Elevation, General Considerations

**ICD**
- 185.4 Carcinoma in situ of prostate
- 622.3 Dysplasia of prostate

**Clinical/Surgical Pearls**
- If HGPIN was found on initial prostate biopsy of <10 cores, the biopsy should be repeated with an extended scheme
- If multifocal HGPIN is found on initial prostate biopsy, the biopsy should be repeated within 1 yr
- With modern 12-core biopsies, a single focus of HGPIN does NOT increase the risk of PCa diagnosis on subsequent biopsies
- Decision for repeat prostate biopsy should be made on other clinical factors (elevated PSA, high PSA velocity, new nodule on DRE), not influenced by the presence of 1 focus of HGPIN
PROSTATITIS, ACUTE, BACTERIAL (NIH I)
Nicholas J. Kuntz, MD
Judd W. Moul, MD, FACS

DESCRIPTION
Acute bacterial prostatitis is a rare, potentially life-threatening bacterial infection of the prostate. The symptoms are typically severe and sudden and usually cause the patient to seek emergency care. The NIH prostatitis classification system is referred to as NIH I.

EPIEDEMOLOGY
Incidence
- Usually a single bacterial uropathogen
- Hematogenous seeding
- Direct invasion or lymphogenous spread from the bladder:
  - Ascending urethral infection:
    - History of sexually transmitted disease
    - Indwelling urethral catheter
    - Immunocompromise
    - Phimosis
    - Lower urinary tract procedures
- Previous episodes of prostatitis
- Bladder outlet obstruction
- Diabetes
- Human immunodeficiency virus (HIV)
- Prostate biopsy or urethral catheterization
- Stricture disease
- Benign prostatic hyperplasia (BPH)

Prevalence
- Estimated to be ∼5% for all types of prostatitis worldwide (1B)

RISK FACTORS
- Bladder outlet obstruction
- Benign prostatic hyperplasia (BPH)
- Stricture disease
- Previous episodes of prostatitis
- Lower urinary tract procedures
- Prostate biopsy or urethral catheterization
- Phimosis
- Immunocompromise
- Immunodeficiency virus (HIV)
- History of sexually transmitted disease

ASSOCIATED CONDITIONS
- BPH
- Urinary stricture disease
- Diabetes
- HIV
- UTI

GENERAL PREVENTION
Safe sex practices may prevent some cases.

UTI
- HIV
- Diabetes
- Urethral stricture disease
- BPH

DIAGNOSIS
HISTORY
- Systemic symptoms
  - Fever, chills, malaise, arthralgia, myalgia
  - Intermittent or obstructive voiding symptoms
  - Dysuria, urgency, frequency
  - Acute urinary retention (20%)
  - Due to bladder neck spasm
  - Pelvihertral pain, lower back pain

PHYSICAL EXAM
- Avoid vigorous prostatic exam or massage in a patient with suspected acute bacterial prostatitis. This may cause bacteremia and sepsis.

PHYSICAL EXAM
- NIH classification: [IA]
  - I: Acute bacterial prostatitis
  - II: Chronic bacterial prostatitis: Recurrent infection
  - III: Chronic prostatitis/chronic pelvic pain syndrome (CPS): No demonstrable infection:
    - IIIA: Inflammatory CPS: White blood cells (WBCs) present in semen/voided prostatic secretions or voided bladder urine (VBU)
    - IIIB: Noninflammatory CPS: WBCs not present in semen/voided prostatic secretions or voided bladder urine (VBU)
  - IV: Asymptomatic inflammatory prostatitis: Detected by prostate biopsy or presence of WBCs in prostatic secretions during evaluation for other conditions

LAB
- Complete blood count
  - Leukocytosis with left shift
- Blood cultures
- Urine culture
- Stool softeners
- Analgesics/antipyretics

DIFFERENTIAL DIAGNOSIS
- UTI
- Prostatodynia
- Perirectal abscess
- Prostate cancer
- Prostatic abscess
- Prostatitis

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - Complete blood count
  - Leukocytosis with left shift
  - Blood cultures
  - Urine culture
  - Stool softeners
  - Analgesics/antipyretics
  - Prostatodynia
  - Blood cultures
  - Particularly for immunosuppressed patients
  - Prostate-specific antigen (PSA)
  - Little clinical value in the acute setting
  - US will be elevated in the majority of cases
  - Should be repeated 1–2 mo following treatment

Imaging
- Not routinely required
- Indicated if fever persists despite appropriate treatment to evaluate for prostatic abscess
  - CT scan
    - Areas of low attenuation
    - Rim enhancing with IV contrast
  - Ultrasound
  - Hypoechoic lesion
  - MRI
    - High intensity on T2-weighted images
    - Rim enhancing with gadolinium

TREATMENT
- General measures
  - Indications for admission and IV antibiotics:
    - High fever
    - Significant leukocytosis
    - Septis
  - Analgesics/antipyretics
  - Stool softeners
  - Bladder drainage if there is evidence of urinary retention:
    - An anterior catheter should be placed cautiously
    - With any difficulty or if the patient is too uncomfortable, percutaneous suprapubic tube should be placed
If no clinical response in 48 hr despite appropriate treatment consider prostatic abscess.

- Prostate biopsy: prostatitis suspect resistance to antibiotics.

**ADDITIONAL TREATMENT**

- Radiation Therapy

**ADDITIONAL READING**


**CLINICAL/SURGICAL PEARLS**

- E. coli is most common organism in acute bacterial prostatitis.
- Avoid vigorous prostatic exam or massage during an episode of acute bacterial prostatitis.
- It is not advisable to measure serum PSA during an episode of acute bacterial prostatitis as it will most likely be falsely elevated.
- Urinary retention requires bladder drainage.
- May require hospital admission and IV antibiotics.
- Consider prostatic abscess if no clinical response in 48 hr.
PROSTATITIS, CHRONIC NONBACTERIAL, INFLAMMATORY AND NONINFLAMMATORY (NIH CP/CPPS III A AND B)
Amin S. Herati, MD
Robert M. Moldwin, MD, FACS

BASICS
DESCRIPTION
- Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), NIH categories IIA and IIIB are characterized by pelvic, perineal, and/or testicular pain ± LUTS in the absence of other well-defined pathology.
- IIA: Inflammatory CPPS: WBBCs present in prostatic secretions
- IIIB: Noninflammatory CPPS: WBBCs not present in prostatic secretions

RISK FACTORS
- Approximately 2,000,000 US men
- Estimated prevalence of CP/CPPS is 1.8%, equating to

EPIDEMIOLOGY
PREVALENCE
- N/A
- Prevalence
- Estimated prevalence of CP/CPPS is 1.8%, equating to

INCIDENCE
- N/A

INCIDENCE
- Estimated prevalence of CP/CPPS is 1.8%, equating to

DIAGNOSIS
HISTORY
- Determine duration of symptoms (of at least >3 mo durations)
- Pain in the suprapubic region, lower back, penis, testes, and/or scrotum
- Painful ejaculation: One of the most discriminatory

EXAM
- Careful exam of the genitalia, groin, perineum, and testes
- Pelvic floor muscle spasms
- Sexual dysfunction
- Pain in the suprapubic region, lower back, penis, testes, and/or scrotum
- Difficulties encountered with interpretation of

PATHOLOGY
- Nonbacterial colonization
- Atypical bacterial infection
- Invasive bacterial infection
- Voiding dysfunction causing intraprostatic urinary reflux and elevated intraprostatic pressure
- Pelvic floor muscle dysfunction
- Endocrine
- Neuropathic
- Autoimmune
- Stricture of each patient into a 6-point clinical

IMAGING
- Ural reflex or urethral abnormalities
- Bladder neck contracture
- Intravesical cysts
- Primary voiding dysfunction
- Prostate abscess
- Prostate cancer
- Prostate cyst
- Radiation cysts
- Tuberculosis of the prostate
- Urinary tract infection
- Urethritis

ASSOCIATED CONDITIONS
- Allergies
- Sinusitis
- Erectile dysfunction
- Irritable bowel syndrome
- Depression
- Fibromyalgia
- Fatigue
- Neurologic disorders

GENERAL PREVENTION
- N/A

DIFFERENTIAL DIAGNOSIS
- Acute or chronic bacterial prostatitis
- Benign prostatic hyperplasia
- Bladder calculus
- Bladder cancer
- Bladder neck contracture
- Interstitial cystitis
- Primary voiding dysfunction
- Prostate abscess
- Prostate cancer
- Prostate cyst
- Radiation cysts
- Tuberculosis of the prostate
- Urinary tract infection
- Urethritis

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis and urine culture
- Stamey test (Meares-Stamey 4-glass test)

DIAGNOSTIC PROCEDURES/SURGERY
- Cystoscopy
- Primary voiding dysfunction
- Prostate abscess
- Prostate cancer
- Prostate cyst
- Radiation cysts
- Tuberculosis of the prostate
- Urinary tract infection
- Urethritis

IMAGING
- Pelvic imaging with ultrasonography, CT, or MRI is

PATHOLOGIC FINDINGS
- Not formally reported for Category II, therefore N/A

DIFFERENTIAL DIAGNOSIS
- Acute or chronic bacterial prostatitis
- Benign prostatic hyperplasia
- Bladder calculus
- Bladder cancer
- Bladder neck contracture
- Interstitial cystitis
- Primary voiding dysfunction
- Prostate abscess
- Prostate cancer
- Prostate cyst
- Radiation cysts
- Tuberculosis of the prostate
- Urinary tract infection
- Urethritis
GENERAL MEASURES

Antibiotic therapy: Data conflicting on the benefit

The choice of agents in the 1st- or 2nd-line setting is

Focus of therapy should be on symptom relief

Treatment should also be targeted to the etiologic

A meta-analysis comparing – Oral prednisolone – Rofecoxib 25–50 mg daily: Symptom relief at – Dutasteride 0.5 mg daily or

α–Can be considered in antibiotic-naïve patients to 4 wk of initiating therapy – Side effects of αmade of treatment failure or success.

or longer may be needed before assessment can be

practitioner dependent with no specific agent

CP/CPPS III often requires multimodal therapy


treatment. Last resort unless other

Muscle relaxants

Gabapentanoids

Pentonol polystyrene 100 mg TID

Galantamine

Pregabalin 150–600 mg daily

Muscle relaxants

Diazepam

Diltiazem

Surgery/Other Procedures

Not recommended. Last resort unless other indications are discovered during the workup

Transurethral microwave therapy

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

See below

Complementary & Alternative Therapies

Dietary and lifestyle modification

Stress management/cognitive-behavioral therapy

Myofascial physical therapy

Acupuncture

Phytotherapy

Dietary and lifestyle modification

Stress management/cognitive-behavioral therapy

Myofascial physical therapy

Acupuncture

Phytotherapy

Adjuvant therapy: Pain control

Pelvic floor exercises

Transcutaneous electrical nerve stimulation

Topical lidocaine

Antidepressants

Tramadol

Selective serotonin reuptake inhibitors

SNRIs

Antispasmodics

Ongoing Care

Remissions and flare-ups common over the long term

Complications

Necrotizing prostatitis

Follow-up

Patient Monitoring

Long-term supportive care

Patient Resources

Campbell-Walsh Urology: 10th ed.


References


Additional Reading


See Also (Topic, Algorithm, Media)

NIH-CP/CPPS Questionnaires

Prostatitis, Acute Bacterial (NIH I)

Prostatitis, Asymptomatic Inflammatory (NIH II)

Prostatitis, Chronic Bacterial (NIH III)

Prostatitis, Chronic Nonspecific, Inflammatory and Noninflammatory NIH-CP/CPPS III A and B

Images

Prostatitis, General

Stamey Test (3-glass test, 4-glass tests, Meares-Stamey Test)
PROSTATITIS, CHRONIC, BACTERIAL (NIH II)
John J. Pahira, MD

PATHOPHYSIOLOGY

- Increased incidence of prostatic calculi may serve as a nidus for infection.
- Bacteria are present in inflamed ducts in protected areas of the prostate.
- Progresses to chronic intraductal inflammation.
- Obstructive, turbulent, and/or high-pressure voiding contributes to the development of prostatic calculi.
- With progressive benign prostatic enlargement, obstructive voiding becomes more pronounced.
- Unprotected intercourse, new partners, sexual activity, and ejaculation may increase the risk of prostatic calculi formation.

RISK FACTORS

- Type I: Acute bacterial prostatitis
- Type II: Chronic bacterial prostatitis, recurrent infection
- Type III: Chronic abacterial prostatitis (CAP); no demonstrable infection

EPIDEMIOLOGY

- Prostatitis affects 10–14% of men of all ages and accounts for 50 million office visits annually.
- Chronic bacterial prostatitis is the most common cause of recurrent UTI in the adult male population.

DIAGNOSIS

- **Histories:**
  - Fever and chills are not usual and suggest acute bacterial prostatitis.
  - Rectal or perineal pain, rectal, or urethral discharge may increase the risk of developing prostatic calculi.

- **Examination:**
  - Perineal, penile, scrotal, suprapubic, or groin pain; tenderness may be present.
  - Urethral catheterization or other lower genitourinary tract procedures may be performed.

Association of prostatic calculi with other diseases:

- **Prostate:**
  - Prostatic calculi may be palpable.
  - DRE may reveal a minimally tender or boggy prostate.
  - Perineal tenderness may be present.

- **PSA:**
  - PSA may be elevated in the setting of prostatic inflammation.

DIAGNOSTIC TESTS & INTERPRETATION

- **Urine analysis and culture:**
  - Positive: Routine urine culture may be negative. A positive culture may be obtained as part of the Meares-Stamey 4-glass test (see below).
  - Negative: Prostatic calculi can occur in the absence of infection.

- **Meares-Stamey 4-glass test:**
  - Void 10 mL into sterile container (VB1).
  - After voiding 100 mL, collect 10 mL midstream voided bladder urine (VB2).
  - Clean the glans thoroughly with antimicrobial solution. Retract foreskin as necessary.
  - Replace VB1 or VB2, bacterial prostatitis is present.

- **EPS:**
  - EPS result is lower than VB1 or VB2, bacterial prostatitis is present.

- **Prostatic massage:**
  - Perform prostatic massage to collect EPS from the prostate.
  - After voiding 10 mL into sterile container (VB1), collect the next voided 10 mL into another sterile container (VB2).
  - Perform bacterial culture on the urine:
    - VB1 or VB2, bacterial prostatitis is present.
  - **Diagnostic Procedures/Surgery:**
    - Prostatitis involves isolated cultures of different portions of the lower urinary tract.
    - In men, bacterial prostatitis is a treatable cause of the patient's symptoms.

- **Physical examination:**
  - **Examination of the penis:**
    - Examiners may reveal vague widespread pelvic discomfort.
  - **Prostatic infection:**
    - Perineal tenderness may be present.

- **Lab:**
  - PSA may be elevated in the setting of prostatic inflammation.

- **Meares-Stamey 4-glass test:**
  - Positive: Routine urine culture may be negative. A positive culture may be obtained as part of the Meares-Stamey 4-glass test (see below).
  - Negative: Prostatic calculi can occur in the absence of infection.

- **Imaging:**
  - Imaging has low yield and is performed only to exclude the presence of other more definable and treatable causes of the patient's symptoms.

- **Bacterial infection:**
  - Positive: The patient has a full bladder.
  - Negative: The patient has an empty bladder.

- **Diagnostic Procedures/Surgery:**
  - Prostatitis involves isolated cultures of different portions of the lower urinary tract.
  - In men, bacterial prostatitis is a treatable cause of the patient's symptoms.

- **Physical examination:**
  - **Examination of the penis:**
    - Examiners may reveal vague widespread pelvic discomfort.
  - **Prostatic infection:**
    - Perineal tenderness may be present.

- **Lab:**
  - PSA may be elevated in the setting of prostatic inflammation.

- **Imaging:**
  - Imaging has low yield and is performed only to exclude the presence of other more definable and treatable causes of the patient's symptoms.

- **Bacterial infection:**
  - Positive: The patient has a full bladder.
  - Negative: The patient has an empty bladder.

- **Diagnostic Procedures/Surgery:**
  - Prostatitis involves isolated cultures of different portions of the lower urinary tract.
  - In men, bacterial prostatitis is a treatable cause of the patient's symptoms.
PROSTATITIS, CHRONIC, BACTERIAL (NIH II)

A modified Meares–Stamey test (2-glass test) can also be performed that is considered more convenient and practical:

- After cleansing the glans, obtain 10 mL of a midstream urine for culture (prostate massage). Represents bladder flora. Should also be dipped for white cells.
- Perform prostate massage and obtain 10 mL of urine (prostate massagely may fail) for culture and microscopic exam. Represents prostate and bladder flora. If white cells are present, they may represent bacterial prostatitis or NIH type IIIA.
- If postmassage colony counts are 10× higher than postvoid sample, bacterial prostatitis is present. If both cultures have similar counts, cystitis is present.
- Semen culture is of limited use, demonstrating low sensitivity but high specificity compared to Stamey test.
- Uroflowmetry may demonstrate diminished flow with intermittency.
- Elevated PVR may be present.

Pathologic Findings

NI/A

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis/systemic abscess
- Bladder outlet obstruction (BPH)
- Chronic nonbacterial prostatitis (NIH IIIA/B)
- Cystitis
- Interstitial cystitis
- Prostatitis cyst
- Serosal vesiculitis
- STDs
- Tuberculosis/granulomatous prostatitis
- Urethritis or urethral pathology (stricture)

TREATMENT

GENERAL MEASURES

- Antibiotic course normally extends for 6–8 wk and sometimes longer with refractory infections. Goal is to eradicate the risk of infection in the prostate.
- Follow culture results (3–4).
- Avoid alcohol, spicy foods, perineal pressure for extended times (sitting or bicycle riding), acidic beverages.
- Continue to engage in safe protected sexual activity, as this is thought to reduce prostatic congestion.

MEDICATION

First Line

- Current sensitivity patterns are showing increased resistance to quinolones. TMP/SMX, apricillin is choosing antibiotic coverage prior to culture sensitivity reports, know local resistance patterns based on your hospital antibiogram.
- Fluoroquinolones still preferred—no difference in bacterial eradication between levofloxacin and ciprofloxacin, although prostatic fluid concentration of levofloxacin is higher than ciprofloxacin. Levofloxacin has daily dosing and may have better prostatic penetration.
- Ciprofloxacin 500 mg PO 8–12 h or levofloxacin 500 mg for at least 6–8 wk.
- Trimethoprim 80 mg/d sulfamethoxazole 160 mg BID for at least 6–8 wk.
- Tetracycline derivatives (eg, doxycycline) only if Chlamydia or Mycoplasma suspected
- A modified Meares–Stamey test (2-glass test) can also be performed that is considered more convenient and practical:
- Follow culture results (3–4).
- Avoid alcohol, spicy foods, perineal pressure for extended times (sitting or bicycle riding), acidic beverages.
- Continue to engage in safe protected sexual activity, as this is thought to reduce prostatic congestion.

Second Line

- Anti-inflammatory (ibuprofen) for symptoms
- α-blockers (tamsulosin, alfuzosin, doxazosin) may help with LUTS

SURGERY/OTHER PROCEDURES

- Not generally recommended
- TURP
- May be considered in select cases of refractory prostatitis with infected calculi and/or obstruction

ADDITIONAL TREATMENT

Radiation Therapy

NI/A

Additional Therapies

- Frequent ejaculation (in patients with enlarged, symptomatically enlarged glands)
- Dietary modifications of common comestibles found to irritate the lower urinary tract
- Moist heat with sitz baths or heating pad for symptomatic relief

Complementary & Alternative Therapies

- Prostate massage (very controversial):
  - May work by stimulating hibernating bacterial biofilms (making them more susceptible to antimicrobials), draining the obstructed inflammatory ducts (allowing for better antimicrobial penetration), and stimulating blood supply to the area.
- Avoid bicycling or other activities that cause perineal pressure.
- Zinc supplements: Unproven benefit
- Phytotherapy: Plant extracts and herbal medications
  - Saw palmetto: popular but may only be as effective as placebo (5)

ONGOING CARE

PROGNOSIS

- Fluoroquinolones have improved the ability to clear the infection (60–90% cure reported).
- Variable course with flare-ups possible. If culture-positive infection persists, consider longer course of therapy (6–8 mo) with a lower daily dose.
- Treating underlying obstruction or prostatic calculus if necessary may prevent further infections.

COMPLICATIONS

- Recurrent cystitis, epididymitis, unexplained fever
- CPPS
- Infection effect on semen quality debatable
- Primarily affects IQOL
- Unknown if predisposes to prostate cancer

FOLLOW-UP

Patient Monitoring

- Document clearing of positive culture
- Following prostate cancer screening guidelines is recommended. Do not obtain PSA for at least 6 wk after culture clears.

Patient Resources


REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Asymptomatic Inflammatory (NIH IV)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS I)
- Prostatitis, Chronic, Nonbacterial, Noninflammatory (NIH CP/CPPS II)
- Prostatitis, General
- Prostatitis, Granulomatous
- Stamey Test (3-Glass Test, 4-Glass Tests, Meares–Stamey Test)

CODES

COD9

- D41.49 Other and unspecified Escherichia coli [E. coli]
- 131.03 Trichomonal prostatitis
- 601.1 Chronic prostatitis

ICD10

- A59.02 Trichomonal prostatitis
- B96.20 Unsp Escherichia coli as the cause of disease, unspecified
- N01.1 Chronic prostatitis

CLINICAL/SURGICAL PEARLS

Inadequately treated acute bacterial prostatitis may increase risk for developing chronic prostatitis syndrome including chronic bacterial prostatitis.
PROSTATITIS, GENERAL

Ryan S. Levey, MD
Justin D. Ellett, MD, PhD

DESCRIPTION

- Prostatitis is a general term that refers to inflammation of the prostate.
- Traditionally classified as acute bacterial prostatitis, chronic bacterial prostatitis, nonbacterial prostatitis, and prostatodynia today the definitions used are much more precise and based on the NIH system (1).
- Revised 1995 NIH classification of prostatitis is standard nomenclature:
  - NIH Class I: Acute bacterial prostatitis, infection of prostate, sudden onset, often associated with UTI
  - NIH Class II: Chronic prostatitis: insidious onset, relapsing, recurrent UTI
  - NIH Class III: Chronic prostatitis: CP/CPPS

EPIDEMIOLOGY

- Most common urologic diagnosis in men
- NIH Class IIIB: Noninflammatory: Insignificant amounts of pain, prostatic calculi
- NIH Class III: Chronic prostatitis (CP)/Chronic pelvic pain syndrome (CPPS)
- NIH Class I: Acute bacterial prostatitis; infection of prostatic secretion, seminal fluid, postprostatic massage urine

PATHOPHYSIOLOGY

- Acute prostatitis: Infected prostatic tissue, prostatic abscess
- Chronic prostatitis: Infected prostatic tissue

ASSOCIATED CONDITIONS

- Conditions in lower urinary tract (dysuria, urinary frequency)
- Depression
- Chronic prostatitis
- Psychiatric conditions

DIAGNOSIS

HISTORY

- Acute bacterial prostatitis (NIH I):
  - Fever, chills, malaise
  - Perineal, suprapubic pain
  - Urgency, frequency, dysuria
- Chronic bacterial prostatitis (NIH II):
  - Recurrent UTIs
  - Asymptomatic prostate (CP/CPPS) (see below)
- Chronic bacterial prostatitis/CP/CPPS (NIH III)
- Rare sepsis
- Sepsis: Fever, chills, rigors

DIAGNOSTIC TESTS & INTERPRETATION

- PSA may be elevated with prostatic PSA should not be checked in cases of acute bacterial prostatitis
- Suspected acute bacterial prostatitis:
  - Urinalysis, urine culture, CBC, blood culture
- Suspected CP/CPPS (NIH III)
- Urinalysis, urine culture
- PSA, DRE

LAB

- PSA may be elevated with prostatic PSA should not be checked in cases of acute bacterial prostatitis
- Suspected acute bacterial prostatitis:
  - Urinalysis, urine culture, CBC, blood culture
- Suspected CP/CPPS (NIH III)
- Urinalysis, urine culture
- PSA, DRE

- Suspected acute bacterial prostatitis (NIH I):
  - Fever, chills, malaise
  - Perineal, suprapubic pain
  - Urgency, frequency, dysuria
- Chronic bacterial prostatitis (NIH II):
  - Recurrent UTIs
  - Asymptomatic prostate (CP/CPPS) (see below)
- Chronic bacterial prostatitis/CP/CPPS (NIH III):
  - Rare sepsis
  - Sepsis: Fever, chills, rigors

ALERT

Do not perform massage or aggressive rectal exam in the face of acute prostatitis or prostatic abscesses.
**Medical Information**

**Prostatitis**

### General Measures
- **Antibiotics:** For acute bacterial prostatitis (inpatient).
- NIH IV is only a histologic diagnosis and no specific therapy necessary.
- NIH II: Long-term antibiotic therapy.
- NIH IIIA/B: Similar management; empiric antibiotics when symptoms do not resolve with conventional measures; must rule out prostate abscess.
- NIH III: Acute prostatitis:
  - Afebrile 24–48 hr may change to oral antibiotics.
  - Ceftriaxone 1–2 g IV or IM daily.
  - Fluoroquinolones (e.g., levofloxacin 750 mg PO twice daily or ciprofloxacin 500 mg PO BID or tid) are effective in most cases.
- **NSAIDs/analgesics/antipyretics** useful adjuncts in this population.
- **α-adrenergic blockers:** Often used with variable success, focus on symptomatic and supportive therapy.
- **Neuromodulation (CP/CPPS):** Amitriptyline, baclofen, or tizanidine.
- **Dietary modification:** Frequent ejaculation (in patients with enlarged, symptomatic prostate) may be beneficial.
- **Stool softeners** for patients with chronic symptoms.
- **Avoid** prostate massage (not in acute prostatitis).
- **Follow-up:** Men with chronic symptoms do not benefit from further antibiotic therapy.

### Additional Therapies
- Numerous unproven therapies have been suggested with little to no evidence for treatment of CP or CPPS, including: Allopurinol, balloon dilation, TUNA, acupuncture, neuromodulation.
- Frequent ejaculation (in patients with enlarged, symptomatic prostates) is beneficial.
- Dietary modification.
- Sex therapy for symptom relief.

### Complementary & Alternative Therapies
- Prostatitis therapy provides modest benefits in CPPS.
- Neuromodulation and other modalities (e.g., TUNA, acupuncture).

### Ongoing Care
- **Follow-up:** Prostatic enlargement, prostate biopsy, and prostate cancer.
- **Complications:** Acute urinary retention, chronic prostatitis with incomplete resolution of acute bacterial prostatitis.
- **Imaging:** CT, MRI, ultrasound, transrectal US.
- **Staging:** T1, T2, T3, T4.
- **Prostate cancer:** Localized, regional, metastatic.
- **Prostatic abscess:** With conventional measures; must rule out acute prostatitis.

### Prostate Resources

### Prostatitis Code
- ICD-9: 601.0 Acute prostatitis
- ICD-10: N41.0 Acute prostatitis

### Additional Reading
- See Also (Topic, Algorithm, Media): Prostatitis, Acute; Prostatitis, Chronic; Prostatitis, Radiation Therapy; Prostatitis, Surgical; Prostatitis, Symptomatic.

### ICD-9 Code
- 601.0 Acute prostatitis
- 601.1 Chronic prostatitis
- 601.9 Prostatitis, unspecified

### ICD-10 Code
- N41.0 Acute prostatitis
- N41.1 Chronic prostatitis
- N41.9 Prostatitis, unspecified

### Prostatitis Pearls
- Prostatitis is considered the most common urological diagnosis in men men—50%.
- If suspected CPP/CPPS, perform 2-glass test to help establish the diagnosis.
- Most chronic bacterial prostatitis cases improve after 3–4 wk of antibiotics.
PROSTATITIS, GRANULOMATOUS
Christopher Amling, MD, FACS

PATHOPHYSIOLOGY
- Specific subtypes:
  - Caused by identifiable infectious agent (mycobacterium, fungi, syphilis, brucellosis, virus, parasites)
  - It is often associated with systemic TB
  - With HIV, TB may cause prostatic abscess
- Non-specific subtypes:
  - Usually an incidental finding on biopsy
- Iatrogenic:
  - After TURP or TRUS-guided biopsy, necrotizing lesions may resemble lesions associated with neutrophilic diseases.
- Eosinophilic subtypes:
  - May occur, may suggest allergic etiology
  - Associated with systemic condition (asthma, Wegener granulomatosis, Churg–Strauss syndrome)
- Autoimmune based:
  - HLA-DR15–linked T-cell–mediated response against PSA

DIAGNOSIS
HISTORY
- Often asymptomatic
- Previous urinary tract infection (UTI) or STD
- Syphilis, TB, or other infectious etiology
- Often associated with UTI 2–3 m prior to onset of symptoms
- History of lower urinary tract symptoms (LUTS)
- Voiding symptoms including urgency, frequency, dysuria
- Obstructive voiding symptoms, including acute urinary retention
- Systemic granulomatous disease:
  - It is associated with systemic vasculitis or granulomatous disease, may have constitutional symptoms
- History of prostate or bladder cancer:
  - BCG or TURP can cause granulomatous prostatitis
  - Reves, chills, or other constitutional signs
- Suggest infectious, systemic etiology

PHYSICAL EXAM
- DRE may be normal or abnormal
- Abnormal DRE:
  - Indurated gland with/without nodule
  - Tender or non-tender
- TB prostatitis should be suspected if a draining perineal fistula is present

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis may be unremarkable
- Urine cultures:
  - Are often sterile
- Elevated erythrocyte sedimentation rate (ESR), acid phosphatase, serum eosinophils may be present
- PSA may rise transiently
- It evidence of TBMycotic disease, appropriate testing includes:
  - AFB stain of urine and semen
  - TB cultures (may take up to 10 wk)
  - Polymerase chain reaction (PCR): Genomic amplification of Mycobacterium Tuberculosis DNA
  - High sensitivity/specificity
  - Rapid: Takes 48 hr

Imaging
- TRUS
  - Limited utility except to direct biopsy
  - Appears as focal hypoechogenic area
  - Difficult to discern granulomatous prostatitis and prostate cancer
  - MRI:
    - Limited utility
    - Difficult to discern granulomatous prostate from prostate cancer on MRI

Diagnosis Procedure/Surgery
TRUS-guided prostate biopsy is needed for pathologic diagnosis.

Pathologic Findings
- Histologically granulomatous prostatitis appears as noncaseating granulomas, prominent macrophage infiltrates with occasional multinucleated giant cells (Bacillus cells) which are characteristic of granulomas
- Immunohistochemistry for osteopontin (CAM 5.2) may stain glands positive but not the macrophage infiltrate
- Macrophage infiltrate stains for macrophage marker CD68
- Fibrosis replaces parenchyma
- BCG therapy related
  - Causing or noncaseating granulomas located next to benign prostatic glands (not engulfing them)
  - Usually AFB negative
PROSTATITIS, GRANULOMATOUS

Differential Diagnosis
- Nodular DRE (necroinflammatory)
- Carcinosarcoma
- Sarcoma, small cell carcinoma, and other rare tumors and metastases
- Urethral carcinoma
- Granulomatous prostatitis
- Infectious, iatrogenic, etc. (See Risk Factors)
- Nodular DRE (benign)
- Posteric calcification and incontinence
- Erythritic duct cyst
- Scarring/erosion from prior surgery or infection
- TURP prostate biopsy
- Granulomatous prostatitis
- Rectal wall lesions (thrombosed hemorrhoid, carcinoma, etc.)

Treatment

General Measures
- Majority of granulomatous prostatitis symptoms resolve spontaneously including those that are BCG related (3–15)
- DRE changes and PSA elevation may persist
- Use antibiotics as indicated for UTI
- Symptom control
- Sit bath, fluids, anti-inflammatory or block, and other symptomatic medications
- Temporary transurethral urinary catheterization if acute urinary retention or severe symptoms are present
- TRUS biopsy is indicated for:
  - Differentiating granulomatous prostatitis from prostatic carcinoma
  - Consider rebiopsy if PSA remains elevated or DRE remains abnormal several months after treating symptomatic granulomatous prostatitis

Medication

First Line
- Antibiotics as indicated for documented UTI
- Anti-TB medications for TRB prostatitis
  - Use only for documented TB cause
  - Isoniazid, rifampin, pyrazinamide, and other ethambutol or streptomycin for initial regimen, then change based on TB isolate sensitivities
  - Pyridoxine (Vitamin B6) 25–50 mg/d to prevent isoniazid neuropathy

Second Line

Medication

Antibiotics as indicated for documented UTI
- Isoniazid, rifampin, pyrazinamide, and other ethambutol or streptomycin for initial regimen, then change based on TB isolate sensitivities
- Pyridoxine (Vitamin B6) 25–50 mg/d to prevent isoniazid neuropathy

Ongoing Care

Follow-up
- Patient Monitoring
  - Rebiopsy may be indicated if DRE remains abnormal or PSA remains elevated after treatment to avoid missing coincident prostate cancer (reported in 10–14% of cases).
  - Possible infertiltity
- Possible undetected prostate cancer

Pearls

Clinical/Surgical Pearls
- Majority of symptomatic cases of granulomatous prostatitis resolve spontaneously.
- Up to 40% of patients may develop granulomatous prostatitis after intravesical BCG
- DRE changes and PSA elevation may persist for months
- TRUS-guided prostate biopsy is needed for pathologic diagnosis.

Additional Reading
- See Also (Topic, Algorithm, Media)
  - Prostate, Nodule
  - Prostatitis, General
  - Prostatitis, Granulomatous Image 1
  - Prostatitis, Tuberculosis
  - Tuberculosis, Gentamicin, General Considerations

References

ICD-9
151.3 Sarcoidosis
446.4 Wegener’s granulomatosis
601.8 Other specified inflammatory diseases of prostate

ICD-10
M31.30 Wegener’s granulomatosis without renal involvement
N41.4 Granulomatous prostatitis
PROTEINURIA

Anthony J. Tracey, MD, MPH
Raju Thomas, MD, MHA, FACS

**BASICS**

**DESCRIPTION**

- Persistent abnormal amounts or types of protein in the urine
  - May be 1st indication of renal disorders either primary (e.g., proliferative glomerulonephritis) or secondary (e.g., hypertension [HTN], lupus nephritis, diabetes [DM])
  - Marker of overall cardiovascular health

- Healthy adult excretes 80–150 mg of protein per day in urine, consisting of 30% albumin, 30% serum globulins, and 40% tissue proteins.

- Dipstick urinalysis detects proteinuria only when protein excretion > 300 mg/d:
  - Microalbuminuria: 30 and 300 mg/d
  - Most sensitive to detect early renal disease (2)

- Important to distinguish between benign (no significant proteinuria due to increased risk of associated disease) and pathologic causes of proteinuria:
  - Transient proteinuria:
    - Age
    - Associated symptoms that would suggest clinically significant proteinuria:
      - Hematuria, bone pain (myeloma)

- Presence of underlying systemic disease:
  - DM, HTN, autoimmune disorders, cardiac disease, multiple myeloma

- Quantitative test that is reliable and not dependent on concentration

- Glomerular permeability and decreased tubular reabsorption have both been proposed as possible mechanisms (2)

**ASSOCIATED CONDITIONS**

- See “Differential Diagnosis”

**DIAGNOSIS**

- Presence of underlying systemic disease:
  - DM, HTN, autoimmune disorders, cardiac disease, multiple myeloma

- Transient proteinuria triggered by:
  - Exercise, emotional stress, fever, recent illness
  - Medication-induced glomerular injury

- Associated symptoms that would suggest clinically significant proteinuria:
  - Hematuria, bone pain (myeloma)
  - Age <30 and healthy (orthostatic proteinuria) (1,2)

**RISK FACTORS**

- DM
- HTN
- Obesity (BMI > 35 kg/m²), but progression to renal disease not proven

**PATHOPHYSIOLOGY**

- **Glomerular proteinuria:**
  - Results from increased glomerular capillary permeability to albumin
  - Usually >1 g/24 hr
  - When total protein > 3 g/24 hr: Nephrotic syndrome (look for hyperlipidemia, lipoproteinuria, edema, ascites)

- **Tubular proteinuria:**
  - Inability of proximal convoluted tubule to absorb low-molecular-weight proteins such as immunoglobulin light chains, ß₂-microglobulin, amino acids, and retinol-binding protein

- **Proteinuria usually 2–3 g/24 hr**

- **Overflow proteinuria:**
  - No underlying renal disease
  - Absorptive capacity of PCT is overwhelmed by overproduction and accumulation of immunoglobulin and low-molecular-weight proteins.

- **Tissue proteinuria:**
  - Associated with a variety of diseases: myeloma, multiple myeloma.

- **Diagnosis**

- **DIAGNOSTIC TESTS & INTERPRETATION**

- **Urine dipstick:**
  - Detects all types of proteinuria
  - False positive: Alkaline urine; concentrated urine; contamination with blood; recent IV contrast dye; dilute urine; dipstick only detects albumin and will miss other plasma proteins (eg, Bence Jones proteinuria in multiple myeloma)

- **Serum creatinine to rule out renal insufficiency**

- **Blood glucose, DM**

- **Albumin to creatinine ratio or total protein-to-creatinine ratio in a random urine sample:**

- **Quantitative test that is reliable and not dependent on concentration. Less cumbersome than 24-hr collection**

- ** Split urine collection: Daytime (7 AM to 11 PM) and overnight (11 PM to 7 AM) to rule out orthostatic proteinuria**

- **Urine protein electrophoresis:** To assess for light chain immunoglobulins/Bence Jones protein associated with multiple myeloma

- **Other as indicated: Hepatitis and/or HIV testing, autoantibodies (ANA, etc.) (2)**

**PHYSICAL EXAM**

- BP measurement to rule out HTN
- Edema with nephrotic syndrome, heart failure
- Rapid pulse: Uncontrolled HTN
- Jugular venous pressure elevated, heart sounds (heart failure, HTN)
- Abdominal bruits: Renal artery stenosis

**DIAGNOSTIC TESTS & INTERPRETATION**

- **Urine dipstick:**
  - Qualitative test only (1+ to 4+); detects protein concentration > 20–30 mg/dl
  - Cannot detect microalbuminuria; if persistently positive proceed to quantitative test (spot or 24-hr protein)

- **Urine protein electrophoresis:**
  - False positive: Alkaline urine; concentrated urine; contamination with blood; recent IV contrast dye; dilute urine; dipstick only detects albumin and will miss other plasma proteins (eg, Bence Jones proteinuria in multiple myeloma)

- **Urease for associated hematuria, casts (glomerulonephritis)**

- **Serum creatinine to rule out renal insufficiency**

- **Blood glucose, DM**

- **Albumin to creatinine ratio or total protein-to-creatinine ratio in a random urine sample:**

- **Quantitative test that is reliable and not dependent on concentration. Less cumbersome than 24-hr collection**

- **Split urine collection: Daytime (7 AM to 11 PM) and overnight (11 PM to 7 AM) to rule out orthostatic proteinuria**

- **Urine protein electrophoresis:** To assess for light chain immunoglobulins/Bence Jones protein associated with multiple myeloma

- **Other as indicated: Hepatitis and/or HIV testing, autoantibodies (ANA, etc.) (2)**
**Imaging**
- Renal US in cases of persistent proteinuria to rule out anatomic abnormality
- 3-phase CT if renal function sufficient and associated hematuria
- MRI unarguable

**Diagnostic Procedures/Surgery**
- Tissue analysis
  - Renal biopsy strongly considered for:
    - Proteinuria with hematuria
    - Proximal ARF of unknown etiology
    - Nephrotic proteinuria
    - Transplanted kidney (3)
- Cystoscopy if concurrent hematuria
- Cystoscopy with retrograde pyelogram if upper tract imaging indicated (hematuria, nephrocalcinosis) and unable to evaluate upper tracts with excretory phase imaging

**Pathologic Findings**
Depends on underlying etiology

**Differential Diagnosis**
- Glomerular proteinuria:
  - IgA nephropathy
  - Diabetic nephropathy
  - Mediation (eg, NSAIDS, captopril, lithium)
  - Minimal change
  - Primary glomerulonephritis
  - Autoimmunemia (eg, SLE, amyloidosis)
- Tubular proteinuria:
  - Obstructive uropathy
  - Trauma and drugs
  - Fanconi syndrome
- Overflow proteinuria:
  - Multiple myeloma
  - Monoclonal gammopathy of unknown significance
  - Rhabdomyolysis causing myoglobinuria
- Any hemolytic state causing hemoglobinuria
- Transplant proteinuria:
  - Revers
  - Strenuous exercise
  - Emotional stress
  - Pregnancy
  - Cold exposure
- Orthostatic proteinuria

**TREATMENT**

**GENERAL MEASURES**
- Treat specific underlying etiology.
- All patients with persistent proteinuria should be referred to a nephrologist.
- Hematology–oncology evaluation for patients with therapy-resistant proteinuria for treatment of multiple myeloma
- Mild dietary protein restriction may prevent progression of chronic kidney disease.
- Strict glycemic and BP control in diabetics
- Salt/fluid restriction for edema associated with orthostatic proteinuria

**MEDICATION**

**First Line**
- ACE inhibitors reduce proteinuria and can both prevent and slow deterioration of renal function in patients with diabetic or nondiabetic renal disease, independent of their antihypertensive effects (364): Can reduce protein excretion by 20–45%  
  - Lisinopril 2.5 mg PO, increase as tolerated
  - Ramipril 2.5–5 mg PO, 20 mg max
  - Captopril 1.25–25 mg PO BID/TID, 50 mg TID max

**Second Line**
- Angiotensin II receptor antagonists:
  - Use if side effects such as cough and angioedema develop from ACE inhibitors
  - Candesartan, eprosartan, ibesartan, losartan, valsartan
- Calcium channel blockers: May be better for HTN

**SURGERY/OTHER PROCEDURES**
N/A

**ADDITIONAL TREATMENT**

**Radiation Therapy**
N/A

**Additional Therapies**
N/A

**COMPLEMENTARY & ALTERNATIVE THERAPIES**
N/A

**ONGOING CARE**

**PROGNOSIS**
- Isolated proteinuria: degree dependent:
  - Renal transplant proteinuria: high risk of progressive kidney disease (362)
  - Nephrotic proteinuria (>3 g/d) associated with glomerular disease and high risk of progression to chronic kidney disease
  - Japanese study of screened healthy patients; cumulative incidence of ESRD over 17 yr:
    - 1.4% with 1+ proteinuria
    - 7.1% with 2+ proteinuria

**COMPLICATIONS**
- Progression to renal failure
- Proteinuria is a marker for overall cardiovascular health (362)

**FOLLOW-UP**

**Patient Monitoring**
- Transient proteinuria: Active monitoring unnecessary
- Nephrologist for any patient with large quantity of proteinuria and high-risk patients with microalbuminuria
- Monitor urine albumin-to-creatinine ratio
- Monitor serum creatinine

**REFERENCES**

**ADDITIONAL READING**

**CODES**
ICD9 100.1 Proteinuria
ICD10 1. R80.0 Isolated proteinuria
2. R80.2 Orthostatic proteinuria, unspecified
3. R80.9 Proteinuria, unspecified

**CLINICAL/SURGICAL PEARLS**
Proteinuria in excess of 500 mg/d likely represents glomerular disease.
PRUNE BELLY (EAGLE–BARRETT OR TRIAD) SYNDROME
Bruce J. Schlomer, MD
Laurence S. Baskin, MD, FACS, FAAP

DESCRIPTION

Prune belly refers to the classic appearance of abdominal wall wrinkling and bulging flanks caused by varying degrees of abdominal wall deficiency, found almost exclusively in males (T1:1) 

- Prune belly syndrome (PBS) triad:
  - Deficient abdominal musculature
  - Bladder hypoplasia
  - Upper urinary tract anomalies (eg, dilated prostatic urethra, renal dysplasia, hydroureteronephrosis)

- Incomplete variants lack abdominal wall features; females lack genital anomalies

- Woodard classification:
  - Type I: Usually fatal, marked oligohydramnios due to severe renal dysplasia or bladder outlet obstruction with pulmonary hypoplasia and skeletal anomalies (Potter sequence)
  - Type II: Full spectrum of disease with no immediate threat to life; renal dysplasia, hypodysplastic, possible mild pulmonary hypoplasia
  - Type III: All external features of triad or incomplete variant; no evidence of pulmonary hypoplasia, mild unsalutary

- Synonyms: Eagle–Barrett or Triad syndrome

EPIDEMIOLOGY

Incidence

- 3–8/100,000 live births
- 95% males
- Higher incidence in African Americans
- Lower incidence in Hispanic population
- Increased incidence in younger mothers

Prevalence

N/A

RISK FACTORS

- Slightly increased risk in African Americans and younger mothers

Genetics

- Most cases are sporadic, with normal karyotype
- Potential inheritance patterns in rare familial cases (influenced autosomal recessive, X-linked)
- Monozygotic twins reported concordant and discordant for PBR suggests some non-genetic basis

PATHOPHYSIOLOGY

- Exact mechanism unknown:
  - Early intrauterine transient urethral obstruction
  - Mesodermal developmental defect
  - Abdominal defects due to deficient musculature medially and inferiorly
  - May be partial hypoplasia of the abdominal wall to complete absence of musculature

- Tests:
  - Usually intra-abdominal (over iliac vessels)
  - Epididymis poorly attached
  - Descent in part affected by mechanical forces (eg, large bladder, low intra-abdominal pressure)
  - Kidneys:
    - Dysplasia in 50%, to varying degrees
    - Nonobstructive hydronephrosis is common; does not correlate to degree of dysplasia
    - Urinary:
      - Dilated, tortuous, and redundant; dilated proximal
      - Increased ratio of collagen to smooth muscle
      - Poor peristalsis and ureteral coaptation lead to stasis and reflux
      - ≤75% with reflux
    - Bladder:
      - Enlarged with no significant hypotrophy
      - May have urologic pseudodiverticulum
      - Urodynamics commonly show normal compliance, delayed sensation, large capacity, 50% void with normal pressures and flow, and have low postvoid residual
  - Prostatic urethra:
    - Dilated due to prostatic hypoplasia
    - 20% can have distal obstructive lesions (eg, valves, atresia, stenosis)
  - Anterior urethra:
    - Usually normal
  - Most common anomalies:
    - Megalourethra and urethral atresia (latter can be fatal unless patent urachus)
    - Megalourethra can be caused by transient obstruction
    - Urethral defect in corpus cavernosum and spongiosum; entire phallic diates on voiding
  - Scaphoid: Defect in spongiosum; entire phallic dilates on voiding
  - Urodynamic:
    - Normal pressures and flow, and have low postvoid residual

ASSOCIATED CONDITIONS

- Genetic:
  - Turner syndrome; trisomy 13, 18, and 21
  - Beckwith–Wiedemann syndrome
  - Cardiac:
    - Atrial and ventricular septal defects, total anomaly of tricuspid valve, valvar anomalies, patent ductus arteriosus
  - Musculoskeletal:
    - Scoliosis, vertebral anomalies, congenital hip dislocation, club feet

GENERAL PREVENTION

None known

DIAGNOSIS

HISTORY

- Generalized history (eg, oligohydramnios, prenatal hydronephrosis)
- Rarely positive family history

PHYSICAL EXAM

- 75% will have nonurologic manifestations
- General: Observe for Potter facies (eg, wide-set eyes, flattened nasal bridge)
- Heart: Auscultate for murmurs due to atrial or ventricular septal defects, patent ductus arteriosus
- Lung/chest: Auscultate for pneumonia/hypertension/evaluated for pectus excavatum/carinatum
- GI: Associated with gastroschisis or omphalocele; hypoplastic anus; intestinal malrotation, atresia, or stenosis
- Urologic: Evaluate micturition, observe urinary stream, attempt to palpate testes
- Abdomen: Winkled, redundant skin over lower abdomen with bulging flanks

- Extremities: Observe for dimpling on lateral aspect of knees, knuckled knuckles, clubfoot, hip dislocation, scoliosis

PHYSICAL EXAM

BASICS

RISK FACTORS

PERINATAL HISTORY

GENETIC HISTORY

PHYSICAL EXAM

HISTORY

ASSOCIATED CONDITIONS

GENERAL PREVENTION

DIAGNOSIS
PRUNE BELLY (EAGLE–BARRETT OR TRIAD) SYNDROME

DIAGNOSTIC TESTS & INTERPRETATION

Laboratory
- Serum electrolytes, urea nitrogen, and creatinine:
  - Nadir creatinine <0.7 mg/dL is predictive of adequate renal function through childhood.
- Urinalysis and urine culture as indicated

Imaging
- Renal US: Bladder hypertrophy, thin-walled, dilated bladders, possible oligohydramnios
- Chest x-ray (pneumothorax)
- Abdominal/pelvic MRI: to evaluate renal parenchyma
- Diagnostic ultrasound: to assess presence/degree of obstruction

Diagnosis Procedures/Surgery
- VCUG:
  - Perform while on antibiotic prophylaxis
  - Reflux in up to 75% of cases
- Reflux in up to 75% of cases
- VCUG:
  - Perform while on antibiotic prophylaxis
  - Ureteral reimplantation with or without tapering
  - DMSA at 4–6wk to assess renal parenchymal function
  - MAG3 scan to assess presence/degree of obstruction

Pathologic Findings
- Renal dysplasia on biopsy
- Ureter and bladder with increased collagen and fibrous tissue

Differential Diagnosis
- Megacystis microcolon
- Postoperative urosepsis
- Respiratory failure (early)
- Renal failure

TREATMENT

General Measures
- Primary goal is to preserve renal function and prevent UTI.
- Early aggressive surgery for dilated urinary tract without evidence of progressive renal dysfunction or UTIs should be avoided
- High complication rates
- Demonstrate proper bladder emptying
- Double voiding
- Tined voiding
- Clean intermittent catheterization (CIC)
- UTI prophylaxis
- Avoid instrumentation early to reduce UTI risk

Medication
First Line
- UTI prophylaxis: Amoxicillin 25 mg/kg/day in neonates
- Trimethoprim-sulfamethoxazole 2 mg/kg once daily or intravenous 1–2 mg/kg once daily beyond 3 mo of age

Second Line
- None

Surgery/other Procedures
- Percutaneous nephrostomy for oligohydramnios in 2nd trimester (controversial)
- Consider circumcision to reduce incidence of UTI
- Urinary tract reconstruction (eg, reimplant) is controversial due to potential for improvement or resolution, stabilization of function, and high complication rates (2)
- Early intervention may be warranted with progressive/ureteral hydroureteronephrosis, progressive renal failure, or recurrent UTIs (2)
- Temporary cutaneous orifice or bilateral cutaneous pyelostomies (avoid prolonged urethrostomies)

Follow-up

Patient Monitoring
- Serial evaluation of renal function, bladder function and emptying, and for UTIs
- Imaging is individualized

Patient Resources
- Prune belly syndrome network: www.prunebelly.org

References

Additional Reading
See Also (Topic, Algorithm, Media)
- Polyhydramnios/Oligohydramnios
- Prune Belly (Eagle–Barrett or Triad) Syndrome
- Image 4: Undescended Testes (Cryptorchidism)

Codes
- ICD9: 756.71 Prune belly syndrome
- ICD10: Q79.4 Prune belly syndrome

Clinical/Surgical Pearls
- Antireflux surgery with high complication rates; avoid if possible
- Prenatally can be difficult to distinguish from posterior urethral valves
- Goal is to avoid renal damage, UTIs

Prognosis
- Degree of renal dysplasia most important determinant of long-term survival
- Up to 1/3 develop renal failure and will require dialysis/transplantation

Complications
- Renal failure
- Respiratory failure (early)
- Recurrent UTIs
- Ureterostomy

ONGOING CARE

Follow-up
- Serial evaluation of renal function, bladder function and emptying, and for UTIs
- Imaging is individualized

Patient Resources
- Prune belly syndrome network: www.prunebelly.org

References

Additional Reading
See Also (Topic, Algorithm, Media)
- Polyhydramnios/Oligohydramnios
- Prune Belly (Eagle–Barrett or Triad) Syndrome
- Image 4: Undescended Testes (Cryptorchidism)

Codes
- ICD9: 756.71 Prune belly syndrome
- ICD10: Q79.4 Prune belly syndrome

Clinical/Surgical Pearls
- Antireflux surgery with high complication rates; avoid if possible
- Prenatally can be difficult to distinguish from posterior urethral valves
- Goal is to avoid renal damage, UTIs
PSA ELEVATION FOLLOWING NEGATIVE PROSTATE BIOPSY

Michael J. Amirian, MD
Leonard G. Gomella, MD, FACS

RISK FACTORS

Prevalence

- In the United States annually, 800,000–1.2 million prostate biopsies are performed.

Incidence

- EPIDEMIOLOGY

- PSA ELEVATION FOLLOWING NEGATIVE PROSTATE BIOPSY

PATHOPHYSIOLOGY

- 12-biopsy cores from a standard 18G needle enables only 0.04% of prostate gland to be evaluated for pathology.
- PSA elevations can be from non-PCa causes.
- Series reporting follow-up biopsy results (1):
  - In 2012 Ca detection rates on follow-up biopsies 1, 2, 3, and 4 were 2%, 10%, 5%, and 4%, respectively, 58%, 60.9%, 86.3%, and 100% of patients who had RP had organ-confined disease on biopsies 1, 2, 3, and 4.
- A 2008 series with extended biopsies found CaP 18%, 7%, and 14% of patients had CaP in 2nd, 3rd, and 4th biopsies, respectively, significant CaP in 85% of cases (3).

ASSOCIATED CONDITIONS

The following can cause elevated PSA; infection, recent instrumentation, benign prostatic hypertrophy (BPH)

GENERAL PREVENTION

- Obtain serial PSA at same lab, avoid sexual activity for 24 hr before
- Preventing a false-negative PB is greatly dependent on technique
  - 12-core template is now standard
  - 6 parasagittal plus 6 lateral cores
  - Szent (6-core) biopsy can miss up to 50% of small tumors
  - No evidence of increased complication rate of 12-core compared to sextant biopsy

DIAGNOSIS

HISTORY

- Prior history of negative prostate biopsies
- Evaluate for nonmalignant causes of elevated PSA
  - Prostatitis
  - Recent instrumentation of prostatic ducts
  - Rarely sexual activity, bicycling can briefly elevate
  - Recent instrumentation of genitourinary tract
  - Endo-anal ultrasound
  - BPH more likely with elevated PSA and negative biopsy
  - Consider exogenous androgen exposure

DIAGNOSTIC TESTS & INTERPRETATION

- Lab
  - Prostate-specific antigen (PSA) (4)
  - Prostate-specific antigen < 3 (PCa)
  - 1st voided urine after attentive digital rectal exam
  - PSA approved for men >50 yr who have had or more previous negative biopsies
  - Cutoff debatable 25–35
  - Compared to PSA
    - Lower sensitivity (67%); Higher specificity (83%)
    - Some studies suggest superior to F/T PSA
    - Patient stratified into lower risk or higher risk of having a positive biopsy

- Imaging
  - MRI may identify anterior tumor not reached by biopsy needle
  - 12-weighted MRI
  - Observe local lesions within gland
  - Need to wait 6–8 wk after negative biopsy as recent biopsies cause distortion
  - Multiparametric (mp) MRI
  - Combination of dynamic contrast-enhanced MRI, MR spectroscopic imaging, and diffusion-weighted imaging; need access to experienced center
  - Contrast enhanced TRUS
  - Neovascularity of tumor enhances with microbubble contrast agent (not FDA approved)
  - Targeted biopsy show increase sensitivity from 38–65% vs. untargeted imaging
  - Color Doppler of limited utility w/o contrast
  - Elastography ultrasound: Tumors allow less displacement with compression than normal tissue; color coded map allows targeted biopsy; not widely available
  - MRI TRUS fusion biopsy may help identify specific lesions for directed biopsy

Diagnostic Procedure/Surgery

- Mapping/saturation biopsy
  - Dilation of 20 or more cores with standard biopsy technique; can be transrectal but more likely to be done transperineally using a brachytherapy-like template guide
  - Studies vary in yield of detection with increased cores; increased morbidity
  - Usually require additional anesthesia
  - Transthoracic zone targeted biopsy
  - 15% increased detection in gland >50 cc
SURGERY OTHER PROCEDURES
• The number of cores on repeat biopsy is debatable. NCCN guidelines suggest performing a 2nd extended biopsy and consider saturation biopsies only in with high risk of cancer after multiple negative biopsies
• Transrectal needle prostate biopsy
• Once advocated for diagnosis of transition zone cancers
• Less than 5% CaP are transitional zone CaP without concomitant peripheral zone tumors
• Improved TRUS technique in sampling transitional zone, no definite value in performing transperineal repeat biopsy

ADDITIONAL TREATMENT
Radiation Therapy

Additional Therapies
• The European Randomized Study of Screening for CaP (ERSPC) model has several calculators to determine outcome after negative biopsy (http://www.prostatecancer-riskcalculator.com/)
• Genomic testing may help determine risk after negative biopsy
• Confirm MDxTM Epigenetic assay to distinguish negative biopsy
• Confirms microscopically occult cancer

Ongoing Care

See Also (Topic, Algorithm, Media)
• PSA (Prostate Specific Antigen, percentage free)
• Prostate Cancer, General
• Prostate Biopsy, Infections and Complications
• PSA, General Considerations
• PSA, Free and Total
• PSA, General Considerations

CODes
ICD9
• 790.93 Elevated prostate specific antigen (PSA)
• 185 Malignant neoplasm of prostate
• 186 Malignant neoplasm of prostate

ICD10
• C61 Malignant neoplasm of prostate
• 185.9 Prostate cancer, unspecified
• 186.9 Prostate cancer, unspecified

Clinical/Surgical Pearls
• Threshold for repeat biopsy should be low if any疑 on initial biopsy.
• PCA3 can elucidate the need for further biopsy in those with prior negative biopsy and persistently elevated PSA.
• Emerging imaging modalities are promising in detecting CaP not found on initial MR.
EPIDEMIOLOGY

- PSA is used for diagnosis and treatment of prostate cancer (CaP).
- CaP is only diagnosed through tissue biopsy and not by PSA alone.
- Normal PSA level is controversial, and can be elevated due to malignant or benign causes:
  - Elevated PSA traditionally ≥ 4.0 ng/mL, based on the Baltimore Longitudinal Study of Aging.
  - Specificity 91%, sensitivity 21% (51% for Gleason ≥ 3, P< 0.0001).
- Elevated PSA ≥ 2.5 ng/mL has support based on genetic specific risk, but controversial.

<table>
<thead>
<tr>
<th>Range (yr)</th>
<th>Asian</th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>0–2.0</td>
<td>0–2.0</td>
<td>0–2.5</td>
</tr>
<tr>
<td>50–59</td>
<td>0–4.0</td>
<td>0–4.0</td>
<td>0–5.5</td>
</tr>
<tr>
<td>60–69</td>
<td>0–4.0</td>
<td>0–4.5</td>
<td>0–4.5</td>
</tr>
<tr>
<td>70–79</td>
<td>0–5.0</td>
<td>0–5.5</td>
<td>0–6.5</td>
</tr>
</tbody>
</table>

- Based on Prostate Cancer Trial Trial (prior): regardless of PSA, can have CaP with "low" PSA. No lower cutoff or normal PSA to indicate absence of cancer: ICFP data.

- PSA is used for diagnosis and treatment of prostate cancer.
- CaP associated with kallikrein genes (family): long arm of chromosome 19 region q13.2–q13.4. (HNLX1).

PATHOPHYSIOLOGY

- PSA: A serine protease produced by the prostatic epithelium and perineural glands that liquefies seminal coagulum.
- Seminal fluid has high PSA concentrations (mg/mL).
- Several forms of serum PSA: Free PSAs (nicked, intact), proPSA (prostate forms: stable complex (no serum enzymatic activity)) (2).
- 60–90% complexed to ALP, free portion is also detected by assay, while that bound to MS is not detected by assay.
- Consider %FPSA (FPSA/TPSA or F/T PSA).

DIAGNOSTIC TESTS & INTERPRETATION

- PSA elevation likely (See "Risk Factors" above).
- Consider PSAD: PSA density (PSAD), PSA velocity (PSAV), newer PSA derivatives may overcome problem, but not yet clear.
- Complexed PSA: Hepatic clearance (1/2-life 2–3 hr).
- FPSA cleared by glomerular filtration (1/2-life 3.5 days).
- Complexed PSA: Hepatic clearance (1/2-life 2–3 days).
- FPSA clearance.
- Consider evaluation for prostatitis by modified DRE.

DIAGNOSIS

- Difficulty with urination, such as hesitancy, straining, weak stream, or intermittency.
- Dysuria, frequency, or urgency.
- Previous PSA levels or prostate biopsies.
- Family history of prostate carcinoma.
- Medications, including herbs.
- Markedly elevated PSA > 20 ng/mL with bone, back, or hip pain suggests metastatic CaP.

PHYSICAL EXAM

- DRE: Nodules, induration, asymmetry, boginess, tenderness. Note: American Cancer Society recommends PSA screening with or without DRE.
- Adenopathy, suprapubic.
- Bony pain, point tenderness with metastasis.
- Neurologic: lower extremity strength/sensation.

PSA ELEVATION, GENERAL CONSIDERATIONS

Leonard G. Gomella, MD, FACS
Adam P. Dicker, MD, PhD
GENERAL MEASURES

DIFFERENTIAL DIAGNOSIS

See Section I: “Prostate Cancer, General.”

Pathologic Findings

Imaging

Some published prostate biopsy indications:

AUA 2013 CaP Early Detection Guideline (4):
- Due to PSA fluctuations, confirm an elevated PSA with a 2nd reading before biopsy. Patient should not ejaculate for 48 hr before test.
- With bacterial prostatitis, treat and repeat PSA 4 wk after: Fluoroquinolone (eg, ciprofloxacin 500 mg BID) or TMP-SMX (180/800 mg BID)

Second Line

SURGERY/OTHER PROCEDURES

If patient has undergone prostatectomy, consider transperineal prostate biopsy for CaP diagnosis

ADDITIONAL TREATMENT

- CaP risk calculators are available on the internet to predict outcome of biopsy:
  - PCA3 urine testing after attentive DRE; FDA approved only after initial negative biopsy
  - PCA3/TMPRSS2-ERG urine test (investigational)

Additional Therapies

- Any PSA rise while on finasteride/dutasteride baseline is now standard for CaP.

PSA ELEVATION, GENERAL CONSIDERATIONS

- Failure to diagnose cancer; patient anxiety over repeat testing; risk of biopsy and drugs.

FOLLOW-UP

- Patient Monitoring:
  - There is no single threshold PSA which should prompt prostate biopsy. Decision making based on PSA, DRE and multiple factors (FT/PSA, age, PSA density, family history, ethnicity, prior biopsy history, comorbidities, patient preferences)
  - F/T PSA: Consider biopsy or obtain FPSA

CLINICAL/SURGICAL PEARLS

- Some published prostate biopsy indications:
  - Prostate nodule, regardless of PSA
  - PSA > 10 ng/mL in the absence of prostatitis
  - PSA > 4.0 ng/mL and PSAV < 0.25 ng/mL/yr
  - PSA > 4.0 ng/mL and PSAV < 0.03–0.05 ng/mL/yr
  - PSA > 2.5 ng/mL and PSAV < 0.4 ng/mL/yr
  - PSA < 1.5 ng/mL and PSAV < 0.1 ng/mL/yr

- Numerous assays under study to help differentiate benign from malignant PT elevation (See Section II: “PSA, General Considerations.”)

REFERENCES


ADDITIONAL READING

- See Also (Topic, Algorithm, Media)
  - Prostate Cancer Screening Guidelines
  - Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Cryotherapy
  - Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radiation Therapy
  - Prostate Cancer, Biochemical Recurrence (Elevated PSA) Following Radical Prostatectomy
  - Prostate Cancer, General
  - PSA Evaluation Following Negative Prostate Biopsy

CODES

- ICD9: 185.1 Malignant neoplasm of prostate
- C61.00 Hypertrophy (benign) of prostate without urinary obstruction and other lower urinary tract symptoms (LUTS)
- 790.93 Elevated prostate specific antigen (PSA)
- C61.10 Malignant neoplasm of prostate

- N90.0 Enlarged prostate without lower urinary tract symptoms

- C61.2 Elevated prostate specific antigen (PSA)
PSEUDOHERMAPHRODITISM, MALE (XY DSD) AND FEMALE (XX DSD)

Luigi Avolio, MD

DESCRIPTION
- Pseudohermaphroditism is an obsolete term that referred to pathologic conditions in which chromosomal sex is inconsistent with phenotypical sex.
- Disorders of sexual development (DSD) is the preferred term which indicates a congenital condition in which development of chromosomal, gonadal or anatomic sex is unusual.
- Female pseudohermaphroditism is now defined as XX DSD.
  - Karyotype 46 XX
  - Gonads: Normal ovaries
  - External genitalia: Incomplete virilization
  - Karyotype 46 XY
  - Gonads: Normal testes
  - External genitalia: Incomplete virilization

EPIDEMIOLOGY
- Incidence
  - 1 in 5,000 live births
- Disorders of androgen synthesis
  - Maternal androgen excess:
    - P450 oxidoreductase (POR) deficiency: Combined 11β-hydroxylase deficiency (11-OHD, CAH) and aromatase deficiency
  - β-Hydroxysteroid dehydrogenase (HSD17B3) deficiency
  - perinatal males with ambiguous genitalia and normal gonadal sex
  - Edwards syndrome (5 or more de novo translocations of chromosome 18)
  - Philadelphia translocation (abnormality of chromosome 22)
  - Fetal exposure to maternal androgens: Absence of maternal estrogen or high levels of maternal androgens

BASICS
- Newborns with salt-wasting 21-OHD CAH are at risk for life-threatening salt-wasting crisis.
- β-Hydroxysteroid dehydrogenase (HSD17B3) deficiency: Deficiency of this enzyme results in adrenal insufficiency due to lack of conversion of 11-deoxycorticosterone (DOC) to 11-deoxycortisol (DC). This is the 2nd most common cause of congenital adrenal hyperplasia (CAH). 1:1,150,000 live births

ASSOCIATED CONDITIONS
- Hypopituitarism
- Cryptorchidism
- Inguinal hernia

GENERAL PREVENTION
See "Disorders of Sex Development" chapter
**DIFFERENTIAL DIAGNOSIS**

- Congenital Adrenal Hyperplasia
- Feminizing genitoplasty (during the 1st 6 mo of life) (3)

**ADDITIONAL READING**


**ADDITIONAL TREATMENT**

- Fertility: LHRH agonist for male adolescents
- Hormone replacement therapy: Glucocorticoid and mineralocorticoid replacement
- Avoidance of exposure to glucocorticoids during pregnancy

**REFERENCES**


**ADDITIONAL READING**


**CODES**

- ICD9: 752.7 Indeterminate sex and pseudohermaphroditism
- ICD10: Q56.3 Pseudohermaphroditism, unspecified

**CLINICAL/SURGICAL PEARLS**

- Infants with a DSD presenting with truly ambiguous genitalia are a rare occurrence.
- DSD should be regarded as a heterogeneous group of conditions with substantially different prognoses and treatment prospects.
- DSDs represent a broad complex field that requires the interaction of multiple disciplines with a diverse knowledge base.
BASICS

DESCRIPTION

- An inflammatory process that involves the renal pelvis and parenchyma.
- Most often ascending infection from the lower urinary tract.
- It is most often a result of bacterial infection, but fungi, parasites, and viruses may be involved.
- Classified as uncomplicated or complicated (ie, associated with obstruction, anatomic anomaly, or stones) making treatment more difficult.

EPIDEMIOLOGY

Incidence

- Estimated at 15–17 cases per 10,000 females and 3–4 cases per 10,000 males.
- Highest among young women, then infants, then the elderly.

RISK FACTORS

- Anatomic or functional abnormalities: Incomplete emptying of the bladder—vulvar is more prone to infection.
- Peptic ulcers, reflux nephropathy, neurogenic bladder, BDD
- Foreign body: Acts as a nidus for bacterial colonization and infection.
- Calculous disease: Mediastinal sponge kidney
- Indwelling catheters
- Medical conditions: Diabetes mellitus, immunosuppression, alcohol abuse
- Social: Poor perineal hygiene (soiling)

Genetics

Related to vesicoureteral reflux

PATHOPHYSIOLOGY

Women are at increased risk because the female urethra is shorter and in close proximity to the anus, allowing enteric organisms to more easily colonize the urinary tract.

- Most common organism are gram-negative rods: Acinetobacter, Aeromonas, Pseudomonas, Proteus, or Enterobacter sakazakii
- Other organisms: Bacteroides fragilis, Clostridium perfringens, enterococcus, and Clostridium difficile
- Enterococcus faecalis is the 2nd most common organism (5–10%)

Bacteria enter urinary tract:
- Ascending infection: Urithra and bladder
- Results from colonization of the vaginal intritus with local flora in females.
- Lymphatic and hemogenous dissemination to the kidneys is uncommon.
- Bacteria adhere to the urothelium, with subsequent invasion and inflammatory response
- Adhesins and fimbrins: Allow bacteria to adhere to urothelium
- Lipo polysaccharides: Have toxic and inflammatory effects
- Hemolysins: Allow for bacterial invasion by damaging cells
- Aerobacter: Enables bacteria to compete for iron, necessary for aerobic metabolism and reproduction

ASSOCIATED CONDITIONS

See “Risk Factors”

GENERAL PREVENTION

- Eliminate anatomic/functional abnormalities
- Patients with recurrent infections may require low-dose prophylactic antibiotics
- Proper indwelling catheter management

DIAGNOSIS

HISTORY

- Fever, chills, malaise, nausea, vomiting (2)
- Pain or abdominal pain
- Dysuria, urgency or frequency, gross hematuria
- Prior episodes of UTI
- History of renal calculus or urinary tract abnormalities
- History of vaginal discharge and irritation makes a urinary source less likely
- History of diabetes, immunosuppression, or alcoholism; recent instrumentation
- Children may present with failure to thrive

PHYSICAL EXAM

- Vital signs for signs of sepsis
- CVA tenderness
- Vital signs for signs of sepsis
- WBC casts indicate renal source of infection

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis with neutrophil predominance (80%)
- Serum chemistry: Renal failure uncommon unless obstruction is present (2)
- Blood culture: 12% of hospitalized pyelonephritis patients may have bacteremia
- Pregnancy test in women
- Urinalysis: Pyuria = 5–10 WBC/mm³
- WBC cast indicates renal source of infection
- Hematuria and bacteria may be present
- Leukocyte esterase often positive, but nitrite may not be positive with staph or enterococci
- Gram stain urine may rapidly identify organism

Pathologic Findings

- Urine culture: Positive with > 100,000 bacteria/mL and identifies causative organism; 10,000 bacteria/mL suggests acute pyelonephritis in patients with catheterized urine samples
- Newer data suggests that urine cultures may be negative especially if patients were started on antibiotics prior to presentation

Imaging

- In uncomplicated acute pyelonephritis, imaging studies are unnecessary; however, the combination of fever and flank pain especially with elevated WBC count requires imaging to rule out urolithiasis, a compromised urinary tract, which, with fever and infection, is a surgical emergency (2)
- Failure to respond to appropriate therapy within 72 hr requires radiographic evaluation to rule out obstruction, abscess, or other abnormalities
- Pediatric patients are at risk of sepsis and should undergo imaging

- Abdominal e-ray (KUB): Evaluate for renal or ureteral calculus
- Intravenous pyelogram: Empyema of pyelonephritis
- Renal shadow may be enlarged and poorly defined secondary to parenchymal edema
- IVP: 75% of patients with uncomplicated acute pyelonephritis will have a normal IVP
- EUS: Mostly used to rule out other abdominal pathology

- CT: Noncontrast CT of the abdomen reveals an enlarged kidney (> 5 cm in length or 1.5 cm greater than the unaffected side with decreased nephrogram and delayed excretion)
- Contrast administration may be seen
- Focal enlargement of the kidney is consistent with focal bacterial nephritis, or acute focal nephronia may be confused with tumor or abscess
- Noninvasive assessment of the renal pelvis and ureter may be present (endoscopy: inferimal ureteral stent)

- US: Renal enlargement with hyperechoic parenchyma and loss of corticomedullary differentiation
- Noninvasive; no ionizing radiation
- CT: Noncontrast CT of the abdomen reveals an enlarged kidney with decreased attenuation of parenchyma, and perinephric fat stranding
- Contrast administration shows delayed excretion with delayed excretion
- Radiocalcium scan: Cortical agents (eg, DMSA) reveal decreased activity in the affected kidney
- Useful to identify areas of scarring

Diagnostic Procedures/Surgery

- Delayed renal function evaluation
- Urinary tract infection identified
- Renal stone removal

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis with neutrophil predominance (80%)
- Serum chemistry: Renal failure uncommon unless obstruction is present (2)
- Blood culture: 12% of hospitalized pyelonephritis patients may have bacteremia
- Pregnancy test in women
- Urinalysis: Pyuria = 5–10 WBC/mm³
- WBC cast indicates renal source of infection
- Hematuria and bacteria may be present
- Leukocyte esterase often positive, but nitrite may not be positive with staph or enterococci
- Gram stain urine may rapidly identify organism
- Urine culture: Positive with > 100,000 bacteria/mL and identifies causative organism; 10,000 bacteria/mL suggests acute pyelonephritis in patients with catheterized urine samples
- Newer data suggests that urine cultures may be negative especially if patients were started on antibiotics prior to presentation

Pathologic Findings

- Gross: Erythematous kidney with multiple foci of infarction
- Microscopic: Focal areas of destruction of renal architecture with lymphocytic infiltrates

DIFFERENTIAL DIAGNOSIS

- Any intra-abdominal inflammatory process
- Appendicitis, cholecystitis, diverticulitis, pancreatitis, peptic ulcer disease
- Gynecologic conditions: Pelvic inflammatory disease, atrophic pregnancy, ruptured ovarian cysts
- Urologic conditions: Renal colic with fever
- Renal and perinephric abscesses
- Lower lobe pneumonia
- Musculoskeletal pain
**TREATMENT**

**GENERAL MEASURES**
- Supportive care consists of hydration, antipyretics, and analgesics.
- Empirical antibiotics that are active against the possible causative organisms and achieve adequate levels in the renal parenchyma and urine are used.

**MEDICATION**

**GENERAL MEASURES**
- Assess for underlying causes before therapy is started.
- Inpatient therapy: If signs of sepsis, bacteremia, or high probability of complications, hospitalization is preferred.
- Outpatient therapy: In uncomplicated acute pyelonephritis, outpatient therapy can be considered.
- Empiric antibiotics that are active against the possible causative organisms and achieve adequate levels in the renal parenchyma and urine are used.

**SURGERY/OTHER PROCEDURES**
- Diversion with indwelling stent or percutaneous nephrostomy may be needed in patients with urinary tract obstruction.
- Neonatal candidemia should be treated with a longer course of antifungal agents.
- Radiographs and renal ultrasonography may be needed to detect calculi or urinary tract obstruction.
- Pregnancy considerations: Pregnant patients have recurrent episodes of pyelonephritis may benefit from prophylactic antibiotics.

**ONGOING CARE**
- With 1st episode of acute pyelonephritis, 1-yr risk of a 2nd episode was 9.2% in females and 5.7% in males.
- With a 4th episode, the risk of a 5th infection was 50% for females and males.

**COMPLICATIONS**
- Short term:
  - Septic shock
  - Abscess formation (corticomedullary, perinephric)
  - Papillary necrosis
  - Long term: Renal failure

**AORTIC INFECTIONS**
- Patients with calculi or urinary tract obstruction who have recurrent episodes of pyelonephritis may develop xanthogranulomatous pyelonephritis: Characterized by large nonfunctioning renal mass and stones present in 80% of cases.

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- Pyelonephritis, Acute, Adult Female
- Pyelonephritis, Chronic
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

**CODES**

ICD9 590.10 Acute pyelonephritis without lesion of renal medullary necrosis
593.73 Other urologic reflex with reflex nephropathy NOS

ICD10 B96.20 Unsp Escherichia coli as the cause of disease elsewhere
N13.729 Vesicoureter-reflux w reflux nephropathy non-inferiority trial

**CLINICAL/SURGICAL PEARLS**
- Some patients may be unresponsive to therapy if started on recent antibiotics.
- If fever lasts for more than 72 hr after antibiotics, obtain an CT scan to rule out obstruction, soft tissue infection, or abscess formation.
PYELONEPHRITIS, ACUTE, PEDIATRIC
Ross M. Decker, MD, FRCS
Paul H. Smith III, MD

ASSOCIATED CONDITIONS
- Tubular nephritis: Pyelonephritis affecting only an isolated focus within the kidney
- Pyonephrosis: Purulent material within the collecting system
- Renal abscess

GENERAL PREVENTION
- Prophylactic antibiotics in patients with recurrent episodes of UTI or with VUR
- Surgical correction of anatomic urinary tract anomalies

DIAGNOSIS

DESCRIPTION
- Inflammatory response initiated by interaction between bacterial endotoxin and toll-like receptor (TLR) 4 (1)

DIAGNOSTIC TESTS & INTERPRETATION
- Elevated CRP, ESR, procalcitonin
- Blood cultures: Leukocytosis with left shift
- Urine culture: Specimen collected by clean catch, catheterization or suprapubic aspiration (SPA)

GENERAL SUPPORTIVE MEASURES
- Volume resuscitation, antipyretics, analgesics

GENERATING REALITY
- E. coli – P fimbriae
- Other common organisms are Klebsiella, Enterobacter, Enterococcus, Pseudomonas, Staphylococcus saprophyticus, Enterobacter

HISTORY
- Non-specific symptoms or failure to thrive in young children
- Fever, nausea, vomiting
- Flank or abdominal pain
- Hematuria, dysuria, foul smelling urine, frequency, urgency
- History of UTIs
- Functional or anatomic urinary tract anomalies

PHYSICAL EXAM
- Fever
- Sepsis
- CVS tenderness
- Exam findings non-specific in young children

DIFFERENTIAL DIAGNOSIS
- Other intra-abdominal process
- Pyonephrosis
- Renal abscess

IMAGING
- Renal and bladder ultrasonography (RBUS)
- Failure to improve clinically within 1st 2 days of antibiotic treatment should prompt evaluation with RBUS to evaluate for complications
- Renal abscess
- Pyonephrosis

LAB
- Urinalysis
- Urine culture
- WBCs: >5 per HPF
- Presence of any bacteria
- Positive leukocyte esterase
- Positive nitrites: ∼50,000 CFU signifies positive culture
- FBC: leukocytosis with left shift
- Blood cultures
- Elevated CRP, ESR, procalcitonin

FIRST LINE MEDICATION
- Empiric coverage
- Tailor to local antimicrobial resistance patterns

TREATMENT
- First Line
- Ampicillin (25–50 mg/kg/d) + gentamicin (2–3.5 mg/kg TID)
- 3rd generation cephalosporin in alternative to ampicillin if low risk for enterococcal UTI
PYELONEPHRITIS, ACUTE, PEDIATRIC

**FOLLOW-UP**

- **Patient Monitoring**
  - Current American Academy of Pediatrics guidelines recommend RUS in children with febrile UTI.
  - Selective VCGUS in patients with abnormal RUS or recurrent episodes (2).
  - Indications for radiographic imaging in children with 1st episode of febrile UTI remain controversial.
  - Delayed DMSA scan to detect renal scarring.

- **Patient Resources**

**REFERENCES**


**ADDITIONAL READING**


**ADDITIONAL TREATMENT**

- **Radiation Therapy**
  - N/A
- **Complementary & Alternative Therapies**
  - Probiotics (experimental)

**ONGOING CARE**

- **PROGNOSIS**
  - Related to degree of renal injury from pyelonephritic scarring.

- **COMPLICATIONS**
  - Pyelonephritic scarring, especially with recurrent episodes and delayed treatment.
  - Pyonephrosis.
  - Renal abscess.
  - Xanthogranulomatous pyelonephritis.
  - Hypertension.

**CODING**

- **ICD9**
  - 041.49 Other and unspecified Escherichia coli [E. coli]
  - 590.10 Acute pyelonephritis without lesion of renal medullary necrosis
  - 593.73 Other vesicoureteral reflux with reflux nephropathy I65

- **ICD10**
  - B96.20 Unsp Escherichia coli as the cause of diseases classified elsewhere
  - N10 Acute tubulo-interstitial nephritis
  - N13.729 Vesicoureter-reflux w reflux nephropathy w/o hydrour, unsp

**CLINICAL/SURGICAL PEARLS**

- Signs and symptoms are often nonspecific in infants and young children with pyelonephritis.
- Culture of appropriately collected urine specimen mandatory in patients with suspected UTI and in infants with fever and no obvious source.
- Acute imaging (RUS) recommended if critically ill or failure to respond to treatment.

See Also (Topic, Algorithm, Media)

- **Pyelonephritis, Acute, Pediatric Image**
- Pyonephrosis
- Urinary Tract Infection (UTI), Complicated, Pediatric
- Urinary Tract Infection (UTI), Pediatric
- Vesicoureteral Reflux, Pediatric

**SECOND LINE**

- Vancomycin if penicillin allergic.
- Aztreonam an alternate to aminoglycoside if renal insufficiency.

**SURGERY/OTHER PROCEDURES**

- Urethral catheter if critically ill or poor bladder emptying.
- Surgery generally not indicated in acute treatment.
- Ureteral stent or nephrostomy tube if obstruction.
- Percutaneous aspiration/drainage if progression to renal abscess.

**ONGOING CARE**

- **PROGNOSIS**
  - Related to degree of renal injury from pyelonephritic scarring.

- **COMPLICATIONS**
  - Pyelonephritic scarring, especially with recurrent episodes and delayed treatment.
  - Pyonephrosis.
  - Renal abscess.
  - Xanthogranulomatous pyelonephritis.
  - Hypertension.
ASSOCIATED CONDITIONS
- VUR
- Spinal cord injury
- Xanthogranulomatous pyelonephritis (XGP) is a form of chronic pyelonephritis.
  – Presents with foamy lipid laden macrophages
  – Often unilateral and associated with longstanding obstructing nephrolithiasis

GENERAL PREVENTION
- Upper urinary tract evaluation in patients with recurrent bacteriuria or recurrent acute pyelonephritis
- Early detection, evaluation, and treatment of childhood VUR
- Prompt detection and management of VUR
- Detection and treatment of obstructive uropathy

Diagnostic Tests & Interpretation
- CT reveals the typical findings of chronic pyelonephritis.
  – Small or atrophic kidney, unilaterally or bilaterally
  – Compensatory hypertrophy with unilaterial atrophy
  – Blurred and dilated calyces
  – Renal cortical scarring and thinning of the cortex
- Renal US to evaluate for hydronephrosis, renal anatomy, or stones. Not a good test to identify active reflux, but dilated ureters suggest obstruction or reflux.
- VCUG for the evaluation of reflux
- CT is more sensitive than US for nephrolithiasis; also to rule out obstruction, hydronephrosis, stone disease, urinary tract abnormality. Pyelonephritis or abscesses are usually identified if present.
- Technetium-99m DMSA is the best study to evaluate for renal scarring

Diagnosis Procedure/Surgery
- VUR or anatomical abnormality
- Reflux nephropathy
- Renal biopsy

Pathologic Findings
- Gross kidney is often diffusely contracted, scarred at periphery with thin cortex
- Microscopically, an interstitial infiltrate of lymphocytes, plasma cells, and occasional neutrophils is present
- Scarring is often polar with underlying calyceal blunting. Histologic changes are patchy.
- Periglomerular fibrosis is often seen
- Leukocytes and hyaline casts can be present in tubules, and the hyaline casts may resemble thyroid collagen, hence the description renal thyroidization

PHYSICAL EXAM
- HTN may be present
- Nonspecific, unless associated with an episode of acute pyelonephritis
- May be mild flank pain or CVA tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis may be normal or indicate proteinuria or pyuria. WBC casts can be seen.
- Urine culture is usually only positive with an active, symptomatic infection. Culture is often negative.
- Microalbuminuria/proteinuria is an adverse prognostic sign.

Imaging
- CT reveals the typical findings of chronic pyelonephritis.
  – Small or atrophic kidney, unilaterally or bilaterally
  – Compensatory hypertrophy with unilaterial atrophy
  – Blurred and dilated calyces
  – Renal cortical scarring and thinning of the cortex
  – Renal US to evaluate for hydronephrosis, renal anatomy, or stones. Not a good test to identify active reflux, but dilated ureters suggest obstruction or reflux.
  – VCUG for the evaluation of reflux
  – CT is more sensitive than US for nephrolithiasis; also to rule out obstruction, hydronephrosis, stone disease, urinary tract abnormality. Pyelonephritis or abscesses are usually identified if present.
  – Technetium-99m DMSA is the best study to evaluate for renal scarring
Differential Diagnosis
- Acute nephritis
- Diabetic nephropathy
- Glomerulonephritis
- Infections
- Nephrotic syndrome
- Renal artery disease
- Renal transplantation
- Renal tuberculosis
- Urolithiasis
- Xanthogranulomatous pyelonephritis (XGP) [2]

Treatment

General Measures
- Chronic pyelonephritis is difficult to manage as it is an irreversible process
- With mild VUR, suppressive antibiotics are used until resolution or puberty in children
- Severe reflux may require reimplantation
- Correct anatomic anomalies or stones if possible

Medication

First Line
- Acute episodes of pyelonephritis should be treated (See Section 1: “Pyelonephritis, Acute”) [3]
- Suppressive antibiotics VUR in children has become controversial:
  - In children <3-6 mo, use low-dose amoxicillin or cephalaxin, cefazolin, or other 1st-generation cephalosporin can be considered
  - In children >6 mo, switch to trimethoprim-sulfamethoxazole, or trimethoprim alone can be considered
- Hyperension is best treated by ACE inhibitors (lisinopril, enalapril, ramipril) that may also protect the kidney from progressive renal failure
  - ACE inhibitors are contraindicated in pregnancy

Second Line
- Based upon urine culture sensitivities, prior treatment attempts and patient presenting symptoms

Surgery/Other Procedures
- Correction of reflux may be necessary in children with high-grade reflux (Grade 4-5). Low-grade reflux (Grade 1-3) often resolves with time
- Nephrectomy for persistent/recurrent infection unresponsive to systemic treatment, markedly decreased function (ie, 10%), pain, or refractory HTN

Additional Treatment
- Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

Additional reading
- See Also (Topic, Algorithm, Media)
  - Pyelonephritis, Acute
  - Pyelonephritis, Chronic
  - Pyelonephritis, Xanthogranulomatous
  - Vesicoureteral Reflux, Pediatric

Codes

ICD9
590.00 Chronic pyelonephritis without lesion of renal medullary necrosis

ICD10
N11.1 Chronic obstructive pyelonephritis
N11.8 Other chronic tubulo-interstitial nephritis
N11.9 Chronic tubulo-interstitial nephritis, unspecified

Clinical/Surgical Pearls

For best determination of renal function the bladder should be empty and kidneys unobstructed (ie, ureteral stone if large stones).

References

PYELONEPHRITIS, EMPHYSEMAOUS

Jennifer E. Heckman, MD, MPH
Stephen Y. Nakada, MD, FACS

BASICS

DESCRIPTION
• Acute necrotizing infection of the renal parenchyma and perirenal tissues caused by gas-forming organisms
  – Onset may be acute or insidious
  – Course is potentially life threatening (mortality: 11–42%)
• 1st report in 1898
  >200 reported cases

EPIDEMIOLOGY
Incidence
• All documented cases in adults
  – Most patients >60 yr old
  – Bilateral cases, unusual but reported (L > R)
Prevalence
N/A

RISK FACTORS
• Diabetes mellitus (DM) (up to 95%)
  – Especially with poor glycemic control
• Urinary tract obstruction
  – Urinary calculi
  – Papillary necrosis
  – Neoplasm
  – Immunosuppression
Genetics
N/A

PATHOPHYSIOLOGY
• Poorly understood
• Impaired host response allows microorganism proliferation
• Hypothesized that elevated tissue glucose levels provide substrate for microorganisms
  – Bacterial fermentation of sugar produces carbon dioxide
  – Low oxygen tension allows urinary tract infection to proceed
• E. coli is primary causative organism (70–90%)
  – Klebsiella, Proteus, Staphylococcus, and coagulase-negative Staphylococcus are less common
  – Candida, Entamoeba histolytica, and Aspergillus famigatus are rare causes

ASSOCIATED CONDITIONS
• Alcohol abuse
• Diabetic ketoacidosis
• Immunocompromised states, including transplant patients
• Impaired renal function
• Malnutrition
• Urinary tract obstruction, including urinary calculi, papillary necrosis, or neoplasm

GENERAL PREVENTION
• Effective glycemic control in diabetes mellitus (DM)
• Adequate treatment of pre-existing pyelonephritis
• Prompt relief of urinary tract obstruction, if present

DIAGNOSIS

HISTORY
• Classic triad:
  – Fever, chills
  – Nausea, vomiting
  – Flank pain and/or abdominal pain
• Urinary frequency/urgency, dysuria
• Malaise
• Altered mental status
• History of DM, urinary calculus, and/or immunocompromise
• Pneumaturia absent unless infection involves collecting system

PHYSICAL EXAM
• Pyrexia
• Abdominal or flank tenderness
• Cough over flank (vague)
• Leukocyte, confluence, altered mental status
• Septic shock (tachycardia, hypotension)

LAB
• Complete blood count (CBC)
• Basic metabolic panel (BMP)
• Urinalysis
• Blood cultures
• Abdominal radiograph may show tissue gas in surrounding kidney
  – Foci of micro- and macroinfarctions
  – Glomerulosclerosis, arteriosclerosis, intrarenal vascular thrombosis, or papillary necrosis

DIAGNOSTIC TESTS & INTERPRETATION

Physeal:
• Ultrasound may show highly echogenic area
• Abdominal radiograph or CT scan (most sensitive and specific)
• Pyuria, bacteriuria, positive urine culture
• Blood cultures
• Bacteremia (isolated organism same as that in urine)

Imaging
• Abdominal radiograph may show tissue gas in parenchyma (nonspecific, low sensitivity)
• Renal ultrasound may show highly echogenic area with skin shadowing
• Computed tomography (CT) is imaging modality of choice (most sensitive and specific)
  – May see:
    – Absence of fluid or presence of streaky or mottled gas
    – Bubbly and localized gas in renal parenchyma, collecting system, and/or perirenal tissue
    – Rim-like or crescent-shaped gas distribution surrounding kidney
    – Gas in renal vein, inferior vena cava, or retroperitoneum
    – Urinary tract obstruction (seen in ~25% of cases)
• Contrast not necessary for diagnosis (and may be contraindicated in renal impairment)

CLASSIFICATION
• Class 1: Gas confined to collecting system
• Class 2: Gas confined to renal parenchyma without extension to extrarenal space
• Class 3A: Perinephric extension of gas or abscess
• Class 3B: Pararenal extension of gas or abscess
• Class 4: Bilateral emphysematous pyelonephritis or emphysematous pyelonephritis in a solitary kidney
  – Therapeutic and prognostic implications:
    – Class 1 and 2: Percutaneous drainage successful, low mortality
    – Class 3 and 4: Percutaneous drainage less successful, increased mortality

DIFFERENTIAL DIAGNOSIS
• Acute pyelonephritis
• Emphysematous cystitis
• Fistulous communication with gastrointestinal or respiratory tracts
• Sarcoïdosis (nodularization of urinary tract)
• Nephrectomy with urinary tract obstruction
• Renal abscess
• Xanthogranulomatous pyelonephritis

GENERAL MEASURES
• Rapid supportive measures:
  – Fluid resuscitation
  – Correction of electrolyte imbalances
  – Vasopressors as needed
  – Usually requires ICU status
• Indwelling urethral catheter to maximize urinary tract drainage and monitor urine output

TREATMENT

Alert
Emphysematous pyelonephritis is urologic emergency that requires prompt diagnosis and intervention to prevent morbidity and mortality.
ADDITIONAL TREATMENT


ADDITIONAL READING


ADDITIONAL READING


ADDITIONAL READING


PYELONEPHRITIS, XANTHOGRANULOMATOUS

Demetrius H. Bagley, MD, FACS
Kelly A. Healy, MD

PHYSICAL EXAM

- Fever
- Flank tenderness
- Palpable flank mass
- Rarely elevated BP
- Weight loss
- Less common hematuria

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Arteria 71%
- Leukocytosis 62%
- Pyuria 81%
- Urine culture: Proteus and E. coli are most common

Imaging
- CT is the 1st-choice imaging study
- MRI shows enlarged kidney with mass, usually diffused
- Ultrasonography: shows Hydronephrosis
- CT is the 1st-choice imaging study
- IV urogram shows nonvisualization in 30–80% of patients

DIAGNOSIS

BASICS

DESCRIPTION
- Xanthogranulomatous pyelonephritis (XGP) is an uncommon chronic destructive granulomatous process of renal parenchyma in association with long-term urinary tract obstruction and infection

RISK FACTORS
- Diabetes
- History of stones
- History of UTIs

GENETICS
- N/A

PATHOPHYSIOLOGY
- Stones
- Obstruction
- Infection

Microscopic findings:
- Fissure formation with extension of inflammatory response beyond kidney

ASSOCIATED CONDITIONS
- Diabetes
- Renal calculus, including staghorn (35%)
- Immunosuppression

GENERAL PREVENTION

Diagnose and follow up of known UTIs

DIAGNOSTIC PROCEDURES/SURGERY

Phenotypic signs:
- Fever, chills, flank pain, fatigue, anorexia
- Persistent bacteremia even after antibiotic therapy

Pathologic Findings:
- Diffuse involvement of the entire kidney occurs in 80–90% of cases
- Segmental involvement is much less common
- XGP commonly extends beyond the kidney and may:
  - Fibrosar, pyelocutaneous and unilobarated have been noted

TREATMENT

GENERAL MEASURES
- Antibiotics, culture specific if possible continued until urine cultures are negative
- Usually managed by nephrectomy
- Renal abscesses
- Renal lymphoma
- TB

MEDICATION

First Line
- Broad-spectrum antibiotics pending urine culture, such as amoxicillin 1 g q 8h and an aminoglycoside 40 mg/kg q12h

Second Line
- N/A
SURGERY/OTHER PROCEDURES
- Nephrectomy is the most common treatment
  - Diffuse inflammatory process
  - Nonfunctioning kidney
  - Concern for malignancy
  - Inflammatory reaction, nephrectomy can be technically difficult
- Partial nephrectomy in rare cases of segmental XGP
- Mechanical and antibiotic bowel prep is performed since XGP may involve any adjacent organs or tissues
- Drains should be placed in renal bed
- Laparoscopic nephrectomy has been shown to be safe without increasing complications but, again, difficult (6)

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
Percutaneous drainage with antibiotics (7)

Complementary & Alternative Therapies
N/A

ONGOING CARE
PROGNOSIS
- Preservation of renal function related to the function of the contralateral kidney
- Chance of recurrent stones is high

COMPLICATIONS
- Renal failure related to complications
- Wound infection
- An injury to adjacent organs can occur during nephrectomy
- Major vascular injury related to the inflammatory process
- Fistulas or abscesses postoperatively require drainage and antibiotic therapy
- Renal insufficiency related to the function of the contralateral kidney
- Recurrent stone formation

FOLLOW-UP
Patient Monitoring
- Urinalysis and urine culture
- Serum creatinine, CBC, liver enzymes repeated to follow for normalization
- Further radiographic studies depending upon the histopathology of the kidney specimen

Patient Resources
N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Pyelonephritis, Acute, Adult
- Pyelonephritis, Acute, Pediatric
- Pyelonephritis, Xanthogranulomatous Image
- Renal Mass
- Urinary Tract Infection (UTI), Complicated, Adult
- Urolithiasis, Renal

CODES
ICD10
- B96.4 Proteus (mirabilis) (morganii) infection in conditions classified elsewhere and of unspecified site
- N90.00 Chronic pyelonephritis without lesion of renal medullary necrosis
- N91.60 Bladder obstruction, unspecified

CLINICAL/SURGICAL PEARLS
- Be suspicious in patients with fever, flank pain, and weight loss.
- Persistent OTI with adequate treatment is a warning.
- CT scan for diagnosis and extent of disease.
- XGP is primarily a surgically managed disease usually by nephrectomy with antibiotics critical to the management of this condition.
- Usually unilateral and frequently confused clinically and radiographically with renal cell carcinoma.
PYONEPHROSIS

Anthony J. Tracey, MD, MPH
Raju Thomas, MD, MHA, FACS

BASICS

DESCRIPTION
- Pyonephrosis is a collection of purulent material in the renal collecting system
- Typically resulting from an underlying obstruction within the upper urinary tract (2)
- With concomitant urinary tract infection
- Considered a surgical emergency with drainage of obstructed collecting system necessary (1)

EPIDEMIOLOGY

Incidence
- True incidence is unknown
- Increased in patients with upper urinary tract obstruction

Prevalence
See above

RISK FACTORS

- Upper urinary tract obstruction
- History of prior urologic instrumentation
- Immunosuppressed patient
- History of prior urologic instrumentation
- History of prior urologic instrumentation
- Renal nuclear scan

ASSOCIATED CONDITIONS

- Pyelonephritis
- Pyelonephritis
- Xanthogranulomatous pyelonephritis
- Urothelial carcinoma (UC) of upper tracts
- Ureteropelvic junction obstruction (UPJO)

GENERAL PREVENTION

- Relief of underlying urologic obstruction
- Proper medical management of immunosuppression
- Identification of any anatomic urologic abnormality

DIAGNOSIS

HISTORY

- Fever
- Flank pain
- Clinical evidence of UTI

PHYSICAL EXAM

- CVI tenderness or without palpable abdominal mass (hydronephrotic kidney)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine culture of obstructed system
- Elevated C-reactive protein

Imaging

- CT scan of IV contrast
- MRU
- MRU
- MRI
- Ultrasonography

Pathologic Findings

- Ascertainment of obstructed system will usually show:
  - MRU
  - CT scan
  - MRU
  - Ultrasonography

DIFFERENTIAL DIAGNOSIS

- Neutrophilia/leukocytosis
- Xanthogranulomatous pyelonephritis
- Ureteropelvic junction obstruction (UPJO)
- Urothelial carcinoma (UC) of upper tracts
- Ureteral stricture
- Ureterocalculus
- Hydronephrosis

ALERT

- Patients may rapidly decline clinically and become septic.

Etiologies of obstruction (1)
- Stones and sloughed calculus
- In as many as 75% of patients
- Infectious adenocarcinoma of the renal pelvis
- Pregnancy
- Prolonged milk
- Metastatic retroperitoneal fibrosis—eg, abdominal tumors
- Renal tumors, testicular cancer, colon cancer
- Obstructing transitional cell carcinoma
- Ureteropelvic junction obstruction (UPJO)
- Obstructing ureteroceles
- Ureterohydronephrosis
- Chronic stasis of urine and hydronephrosis secondary to neurogenic bladder
- Urinary strictures
- Nephrolithiasis
- Nephrotic syndrome
- Tuberculosis
- Debris
- Hydronephrosis

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING

- CT scan with IV contrast
- MRU
- Ultrasonography
- MRU
- MRI

Pathologic Findings

- May be useful for patients with impaired renal function
- Elevated C-reactive protein

IMAGING
**TREATMENT**

**GENERAL MEASURES**
- Drainage of obstructed collecting system is the mainstay of treatment
  - Antegrade nephrostomy tube placement
    - Indicated in the clinically unstable patient
    - Best for maximal decompression
  - Retrograde ureteral stent placement
    - Indicated in the stable patient able to tolerate general anesthesia
    - Best for maximal decompression
  - Treatment of source obstruction:
    - Once collecting system has been decompressed and appropriate antibiotic/antifungal therapy has been given for 2 wk
    - May include endoscopic, percutaneous, transurethral, laparoscopic, robotic, extracorporeal, or open approaches
    - Depends on the nature of obstruction (ie, stone, stricture) (1)
- Clinical feasibility of intervention

**MEDICATION**

**First Line**
- Broad spectrum intravenous antibiotics (ie, piperacillin and tazobactam, gentamicin, and ampicillin) and antifungals if clinically indicated for funguria
- Antibiotics can be focused once cultures result

**Second Line**
N/A

**SURGERY/OTHER PROCEDURES**
- Indication for nephrectomy is controversial
  - May be indicated if source of infection is not found
  - To exclude malignant etiology of obstruction
  - Lack of response to percutaneous drainage and IV antibiotics/antifungals
  - Poorly functioning kidney

**ADDITIONAL TREATMENT**

**Radiation Therapy**
N/A

**Additional Therapies**
N/A

**Complementary & Alternative Therapies**
N/A

**ONGOING CARE**

**PROGNOSIS**
- Good in patients who receive prompt diagnosis and therapy
- Most patients will improve 24–48 hr after drainage of obstructed renal collecting system
- Recovery of renal function is rapid

**COMPLICATIONS**
- Sepsis is the most common complication of delayed treatment
- Other complications of delayed treatment include:
  - Rupture of pyonephrotic kidney resulting in:
    - Generalized peritonitis
    - Renocolic fistula
    - Renoduodenal fistula
  - Sepsis
    - Septic shock
    - Fungal sepsis
  - Loss of renal function
- Complications from nephrostomy tube:
  - Blood transfusions
  - Hematoma
  - Nephrostomy tube replacement/revision
  - Increased risk of infection if nephrostomy is not performed when indicated

**FOLLOW-UP**

**Patient Monitoring**
- Treatment of underlying obstruction (ie, calculus, stricture, malignancy)
- Treatment and control of any predisposition to infection (ie, DM, HIV/AIDS, neurogenic bladder)

**Patient Resources**

**REFERENCES**

**ADDITIONAL READING**

**CODES**
- ICD9: 590.80 Pyelonephritis, unspecified
- N13.6 Pyonephrosis
- N28.89 Other specified disorders of kidney and ureter
- N39.0 Urinary tract infection, site not specified

**ICD10**
- N13.6 Pyonephrosis
- N28.89 Other specified disorders of kidney and ureter
- N39.0 Urinary tract infection, site not specified

**CLINICAL/SURGICAL PEARLS**
- Patients with pyonephrosis may be asymptomatic or present with a picture of an abscess with fever and chills
- Unilateral staghorn calculi, and fungus balls are the most common clinical causes of pyonephrosis.
PYURIA

Christina Carpenter, MD
Mark L. Jordan, MD, FACS

BASICS

DESCRIPTION
• Presence of WBCs in the urine
  • Normal WBCs in a urine specimen
    – Men > 2 WBC/hpf
    – Women ≤ 5 WBC/hpf
  • When seen with bacteriuria, suggests inflammatory response of ureteral (4, infection)
  • When seen without bacteriuria (sterile pyuria), raises suspicion for tuberculosis, partially treated UTI, stones, and/or malignancy

EPIDEMIOLOGY
When seen in a voided urine specimen, has an 80–95% sensitivity for detecting patients with a urinary tract infection (UTI)

RISK FACTORS
• Urinary tract infection (UTI)
• Bacteriuria
• Urinary tract stone
• Cystitis
• Pyelonephritis
• Interstitial nephritis
• Tuberculosis
• Cancer
• Drugs/medications (corticosteroids, nonsteroidal anti-inflammatory agents, diuresis)

PATHOPHYSIOLOGY
• Clean-catch midstream urine may contain contaminants (bacteria, squamous epithelial cells)
• Significant pyuria (at least 10 WBCs/mm³) is uncommonly seen in patients without true infection

ALERT
• 10% of all elderly women have significant pyuria without associated bacteriuria (1,2,4).
• Can be caused by bacteria in the urinary tract producing an inflammatory response
• Bacteria can colonize the genitourinary system in a retrograde fashion
• Certain bacteria are more frequently the cause of UTIs as they are more efficient at adhering to the mucosal cells of the urinary tract (eg, Escherichia coli)

ASSOCIATED CONDITIONS
• Bacteriuria
• UTI
• Pyelonephritis
• Nephrolithiasis

GENERAL PREVENTION
• Proper toileting habits
• Complete bladder emptying
• Adequate fluid intake (stone prevention)

DIAGNOSIS

HISTORY
• Common symptoms: Dysuria, frequency, urgency, malaise
• Fever (more common with upper tract infection)
• Hematuria (gross)
• Occasional
• More common in females
• Rare in children
• Physical presentations
  • Young patients
    – Difficulty with bladder training, urgency, incontinence
  • Abdominal discomfort, failure to thrive, fever, vomiting, jaundice
• Elderly
  • Incontinence, fevers, frequency, urgency
• May be asymptomatic
• History of recurrent childhood fevers—may imply frequent UTIs and potential congenital anomalies
• History of UTIs among female family members

PHYSICAL EXAM
• Suprapubic tenderness
• Costovertebral angle tenderness
• Suprapubic tenderness
• History of recurrent childhood fevers—may imply frequent UTIs and potential congenital anomalies
• History of UTIs among female family members

DIAGNOSTIC TESTS & INTERPRETATION

Lab
• Dipstick
  – Best screening tool
  – Leukocyte esterase (LE)
  – Produced by granulocytes that catalyze the hydrolysis of an indoxylcarbonic acid ester to indoxyl, which reacts with a diazonium salt to produce a purple color on the reagent strip
  – 75–96% sensitive for a culture-positive UTI (GFA)
• Sterile pyuria: Imaging to identify source/evaluate bladder pathology, obstruction, stone disease, and/or malignancy

DIAGNOSTIC PROCEDURES/SURGERY

• Localization of bacteria
  • Segmented urine specimen
  • Urinalysis/cultivation in OR
  • Immunologic/antibody studies
• Isotopic function studies
• Cystoscopy
• CT localization of indwelling abnormality responsible for bacteriuria/pyuria (4, abscess)

• CT: Localization of nidus/abnormality responsible for bacteriuria/pyuria (4, abscess)

DIFFERENTIAL DIAGNOSIS

• Pyelonephritis—acute, chronic pyelonephritis, xanthogranulomatous
• Recurrent urinary tract infection
• Interstitial cystitis
• Immunodeficiency
• Neoplasm
• Kidney stones
• Tuberculosis
• Chronic kidney disease
• Nephrotic syndrome
• Diabetic nephropathy
• Leukocyte esterase
• Indoxyl
• N-acetyl-β-D-glucosaminidase
PYURIA

**TREATMENT**

**GENERAL MEASURES**
- Identify cause of inflammatory response
- Direct treatment at cause of pyuria
- UTI is most commonly the origin

**MEDICATION**

**First Line**
- In infection, should be empiric until targeted therapy can be initiated based on culture results (4)
- See “Urinary tract infection (UTI), adult female,” “Urinary tract infection (UTI), adult male” and “Urinary tract infection (UTI), pediatric”

**Second Line**
- N/A

**SURGERY/OTHER PROCEDURES**
- Correct underlying abnormality
- Treat calculus
- Remove foreign body (eg, ureteral stent)

**ADDITIONAL TREATMENT**
- Bacteriuria with pyuria is treated as a UTI in children and premenopausal women
- Persistent or recurrent bacteriuria may require prolonged antibiotic treatment followed by chronic low-dose prophylactic antibiotics
- High-risk patients (children with congenital abnormalities, immunocompromised adults) may need chronic suppressive antibiotic treatment
- Postmenopausal women
  - May have chronic pyuria with mild bacteriuria
  - Require treatment only if symptomatic or if associated with complicating factors
- Diabetics, patients with obstructive uropathy, and immunocompromised patients may have additional requirements to address ongoing pyuria adequately

**ONGOING CARE**

**PROGNOSIS**
- Dependent upon etiology

**COMPLICATIONS**
- Ascending bacterial infections
- Urosepsis
- Renal failure
- Death

**FOLLOW-UP**

**Patient Monitoring**
- Repeat exam 2-wk post UTI treatment
- Urinalysis, urine culture
- Routinely screen asymptomatic individuals over the age of 65 years
- Routine periodic evaluation to check for recurrence of pyuria

**Patient Resources**
- www.UrologyHealth.org

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)
- Bacteriuria
- Pyelonephritis, Chronic
- Pyelonephritis, Empyema
- Pyelonephritis, Xanthogranulomatous
- Prostatitis, Chronic, Bacterial
- Prostatitis, Chronic, Nonbacterial, Inflammatory
- Prostatitis, General
- Pyuria Algorithm
- Pyuria, Image
- Tuberculosis, Genitourinary
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

**CODES**

ICD9 791.9 Other nonspecific findings on examination of urine

ICD10 N39.0 Urinary tract infection, site not specified

**CLINICAL/SURGICAL PEARLS**

- Absence of pyuria should lead the clinician to question a diagnosis of UTI.
- Sterile pyuria does not suggest a benign process.
- Persistent asymptomatic pyuria requires further workup, ie, cystoscopy, imaging.
- Atypical presentations in children, the elderly, and the immunocompromised require the clinician to maintain a high index of suspicion.
RECTAL INJURY DURING RADICAL PROSTATECTOMY OR RADICAL CYSTECTOMY
Debasish Sundi, MD
Misop Han, MD

BASICS

DESCRIPTION
• Rectal injury is a rare, potential complication of radical prostatectomy or radical cystoprostatectomy, with a reported incidence ranging from 0.1–1.7%.
  – Reported for radical prostatectomy: Retropubic, laparoscopic, and robotically assisted approaches.
  – Reported for radical cystectomy: Open and robotically assisted approaches.
• Intraoperative recognition of the rectal injury is paramount; this will allow primary repair in layers and minimize the chance of subsequent rectovaginal fistulas.
• Occasionally, the injury will not be identified until the postoperative period.

EPIDEMIOLOGY
Incidence
• The rate of rectal injury during urologic pelvic procedures varies by procedure and approach.
  – For radical prostatectomy, rectal injury rates are quite low, ranging from 0.1–0.5% (open retropubic, pure laparoscopic, or robot assisted).[2][C]
  – Rectal injury rates are higher for radical cystoprostatectomy (up to 1.7%)[3][C], and highest for perineal prostatectomy (8–11%)[4][C]
Prevalence
• Extrapolating from the number of procedures performed annually in the United States, the prevalence of rectal injury for radical prostatectomy ranges from 85–400 cases per year, and for radical cystectomy, up to 150 cases per year.

RISK FACTORS
• History of pelvic radiation therapy or prior pelvic surgery
• Genetics
  – N/A

PATHOPHYSIOLOGY
• N/A

ASSOCIATED CONDITIONS
• Prior pelvic radiation or surgical procedures may increase the risk of rectal injury.
• Extensive transurethral resection of bladder floor for urethral carcinoma
• Inflammatory bowel disease
• Locally advanced malignancy

GENERAL PREVENTION
• Adequate intraoperative hemostasis to aid visualization.
• Bowel preparation has not been proven to reduce the risk of intraoperative bowel injury but may limit contamination in the event of an injury.
• Placement of a rectal tube at the start of the procedure may aid in the identification of the rectal wall in difficult cases (ie, salvage prostatectomy following radiation).
• Careful identification of the anterior and posterior layers of Denonvilliers fascia will aid in avoiding rectal injury.

DIAGNOSIS
HISTORY
• After removal of the specimen (open surgery), inspection of the surgical bed using posterior traction to efface folds of tissue will typically reveal a rectal injury by direct visualization.
• Obtaining good hemostasis will aid visualization.
• Copious irrigation of the pelvis with sterile saline may also reveal air bubbles emanating from the rectal vault.[2][C]
• Symptoms may include abdominal or pelvic pain; nausea and vomiting may also be present.

PHYSICAL EXAM
• Postoperative manifestations may include exam findings that may indicate tenderness to palpation, fever, tachycardia, hypotension, ileus.[2][C]

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Acute injury may not manifest any lab abnormalities.
• Lab workup postoperatively may be unrevealing.
• These patients’ GI tracts can be brought back in continuity if a cystogram and/or Gastrografin enema are negative in 2–3 mo. If these patients have persistent fistulas, they should be surgically repaired with a transvesical advancement flap.[2][C]

Imaging
• Pelvis CT ± cystourethrography
  – Free air in pelvic and/or peritoneal spaces
  – Contrast communicating between rectum and bladder

TREATMENT
GUT CONNECTING INJURY
• After removal of the specimen (laparoscopic or robotic surgery) from the prostatic fossa, a suspected rectal injury can be confirmed by flooding the pelvis with saline irrigation and gently insufflating the rectum with air injected via a Foley catheter.
• A rectal enterotomy will be evident by air bubbling through the incision.

Pathologic Findings
• A through-and-through injury will involve both the rectal serosa and mucosa.

DIFFERENTIAL DIAGNOSIS
• Intraoperative differential diagnosis is limited.
• Postoperative differential includes:
  – Small bowel or large perforation (iatrogenic)
  – Colonic perforation secondary to pathologic distension such as in colonic pseudoobstruction, or Ogilvie syndrome
  – Pelvic abscess

MEDICATION
• When a rectal injury is diagnosed postoperatively, management depends on the patient’s clinical picture.
• Patients who are minimally symptomatic and have a small injury radiographically may be initially managed conservatively by indwelling urethral catheter with reassessment by cystoscopy after 2–3 mo.[3][C]
• The 50 patients who are symptomatic, septic, or have a history of prior pelvic radiation should be diverted with an end colostomy.[1][C]
• These patients’ GI tracts can be brought back in continuity if a cystogram and/or Gastrografin enema are negative in 2–3 mo. If these patients have persistent fistulas, they should be surgically repaired with a transvesical advancement flap.[2][C]

First Line
• 7–14 days of antimicrobial therapy.[4][C]
  – Antibiotic regimen should cover both gram negatives and anaerobes (such as Bacteroides and metronidazole)

Second Line
• N/A

EPIDEMIOLOGY
Incidence
• The rate of rectal injury during urologic pelvic procedures varies by procedure and approach.
• For radical prostatectomy, rectal injury rates are quite low, ranging from 0.1–0.5% (open retropubic, pure laparoscopic, or robot assisted).[1][C]
• Rectal injury rates are higher for radical cystoprostatectomy (up to 1.7%)[2][C], and highest for perineal prostatectomy (8–11%)[3][C]

Prevalence
• Extrapolating from the number of procedures performed annually in the United States, the prevalence of rectal injury for radical prostatectomy ranges from 85–400 cases per year, and for radical cystectomy, up to 150 cases per year.

RISK FACTORS
• History of pelvic radiation therapy or prior pelvic surgery
• Genetics
  – N/A

PATHOPHYSIOLOGY
• N/A

ASSOCIATED CONDITIONS
• Prior pelvic radiation or surgical procedures may increase the risk of rectal injury.
• Extensive transurethral resection of bladder floor for urethral carcinoma
• Inflammatory bowel disease
• Locally advanced malignancy

GENERAL PREVENTION
• Adequate intraoperative hemostasis to aid visualization.
• Bowel preparation has not been proven to reduce the risk of intraoperative bowel injury but may limit contamination in the event of an injury.
• Placement of a rectal tube at the start of the procedure may aid in the identification of the rectal wall in difficult cases (ie, salvage prostatectomy following radiation).
• Careful identification of the anterior and posterior layers of Denonvilliers fascia will aid in avoiding rectal injury.

DIAGNOSIS
HISTORY
• After removal of the specimen (open surgery), inspection of the surgical bed using posterior traction to efface folds of tissue will typically reveal a rectal injury by direct visualization.
• Obtaining good hemostasis will aid visualization.
• Copious irrigation of the pelvis with sterile saline may also reveal air bubbles emanating from the rectal vault.[2][C]
• Symptoms may include abdominal or pelvic pain; nausea and vomiting may also be present.

PHYSICAL EXAM
• Postoperative manifestations may include exam findings that may indicate tenderness to palpation, fever, tachycardia, hypotension, ileus.[2][C]

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Acute injury may not manifest any lab abnormalities.
• Lab workup postoperatively may be unrevealing.
• These patients’ GI tracts can be brought back in continuity if a cystogram and/or Gastrografin enema are negative in 2–3 mo. If these patients have persistent fistulas, they should be surgically repaired with a transvesical advancement flap.[2][C]

Imaging
• Pelvis CT ± cystourethrography
  – Free air in pelvic and/or peritoneal spaces
  – Contrast communicating between rectum and bladder

TREATMENT
GUT CONNECTING INJURY
• After removal of the specimen (laparoscopic or robotic surgery) from the prostatic fossa, a suspected rectal injury can be confirmed by flooding the pelvis with saline irrigation and gently insufflating the rectum with air injected via a Foley catheter.
• A rectal enterotomy will be evident by air bubbling through the incision.

Pathologic Findings
• A through-and-through injury will involve both the rectal serosa and mucosa.

DIFFERENTIAL DIAGNOSIS
• Intraoperative differential diagnosis is limited.
• Postoperative differential includes:
  – Small bowel or large perforation (iatrogenic)
  – Colonic perforation secondary to pathologic distension such as in colonic pseudoobstruction, or Ogilvie syndrome
  – Pelvic abscess

MEDICATION
• When a rectal injury is diagnosed postoperatively, management depends on the patient’s clinical picture.
• Patients who are minimally symptomatic and have a small injury radiographically may be initially managed conservatively by indwelling urethral catheter with reassessment by cystoscopy after 2–3 mo.[3][C]
• The 50 patients who are symptomatic, septic, or have a history of prior pelvic radiation should be diverted with an end colostomy.[1][C]
• These patients’ GI tracts can be brought back in continuity if a cystogram and/or Gastrografin enema are negative in 2–3 mo. If these patients have persistent fistulas, they should be surgically repaired with a transvesical advancement flap.[2][C]

First Line
• 7–14 days of antimicrobial therapy.[4][C]
  – Antibiotic regimen should cover both gram negatives and anaerobes (such as Bacteroides and metronidazole)

Second Line
• N/A
RECTAL INJURY DURING RADICAL PROSTATECTOMY OR RADICAL CYSTECTOMY

SURGERY/OFFER PROCEDURES
- When a rectal injury is diagnosed intraoperatively, it should be repaired immediately, closing the rectal mucosa and skin in separate layers.
- Suture choice includes mucosal layer with 3-0 chronic and the serosa with 3-0 silk or other suitable alternatives (1).
- An additional flap of unvascularized tissue (omentum or peritoneum) should be interposed between the rectal repair and the bladder/urethra. Immediate repair minimizes the risk of subsequent rectourethral fistula.
- If a rectourethral fistula does form in spite of immediate repair, management options are conservative treatment via Foley catheterization or surgical repair via diverting colostomy and, if necessary, a transanastomotic advancement flap (2).

ADDITIONAL TREATMENT
Radiation Therapy
N/A
Additional Therapies
N/A
Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Among patients undergoing immediate intraoperative repair, there is a 12.5% incidence of subsequent rectourethral fistula (2).
- Rectal injuries of increasing length are associated with a higher risk of rectourethral fistula, as are those recognized and repaired in delayed fashion.

COMPLICATIONS
- Need for temporary colostomy diversion
- Rectourethral fistula
- Wide excision rectourethral fistula after radical prostatectomy: incontinence (1).
- Sepsis

FOLLOW-UP

Patient Monitoring
- After repair, routine monitoring on a regular surgical floor with daily labs is appropriate.
- Prior to routine Foley catheter removal after radical prostatectomy, perform cystogram to rule out fistula at 14 days after surgery.
- If rectourethral fistula is demonstrated, continue Foley catheter, as resolution of fistula with period of catheterization up to 9 wk has been demonstrated.

Patient Resources
None

REFERENCES

ICD9
- S36.60XA Unspecified injury of rectum, initial encounter
- N36.0 Urethral fistula
- K91.72 Acc pnctr & lac of a dgstv sys org during oth procedure
- 536.60XA Unspecified injury of rectum, initial encounter

CLINICAL/SURGICAL PEARLS
- Rectal injury during radical urologic pelvic surgery is a rare but serious complication.
- This injury can occur during open, laparoscopic and robotically assisted laparoscopic pelvic surgery.
- When recognized preoperatively, immediate primary repair assures the best outcomes.
- When immediate repair is not possible or contraindicated, the patient may be temporized with a diverting colostomy until the rectal injury heals, and the GI tract can be brought back into continuity.
- Rectourethral fistula is a delayed complication of rectal injury repair, the chance of which can be minimized with immediate recognition and repair of rectal injury.

CODES
ICD9
- 536.60XA Unspecified injury of rectum, initial encounter
- 566–570. Mechanical bowel preparation ameliorate damage
- 863.45 Injury to rectum, without mention of open wound into cavity
- 998.2 Accidental puncture or laceration during a procedure, not elsewhere classified

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Fistula, Transurethral
- Fistula, Transanal
RENAL AND PERIRENAL ABSCESS
Mary K. Powers, MD
Raju Thomas, MD, MHA, FACS

DESCRIPTION

- Renal abscess (pyonephrosis): Collection of purulent material confined to the renal parenchyma
- Perirenal abscess: Extension of an acute cortical abscess into the perirenal space, confined by Gerota fascia
- Psoas/perirenal abscess: Results from rupture of a perinephric abscess through Gerota fascia into the psoas space

EPIDEMIOLOGY

Incidence

Perinephric and renal abscesses are uncommon but potentially lethal complications of UTI.

Prevalence

- 2/3 of gram-negative abscesses are associated with renal calculi or kidneys with poor function
- Premature women with uncontrolled bacteriuria are associated with a higher incidence of pyelonephritis and subsequent diagnosis of abscess
- Renal infection is among the most common sites for potentially lethal complications of UTI

RISK FACTORS

Diabetes mellitus, polyplastic kidney disease, hemodialysis, necrotizing bladder, IV drug users, tuberculosis, recurrent urinary tract infection and/or extrapulmonary disease in patients with TB

Genetics

N/A

PATHOPHYSIOLOGY

- Gram-negative organisms have been implicated in the majority of adults with renal abscesses
- Escherichia coli, Proteus mirabilis, and Staphylococcus aureus account for the majority of infections in descending order of occurrence (7)
- Hematogenous renal seeding by gram-negative organisms may occur, but this is not likely to be the primary pathway for gram-negative abscess formation
- Hematogenous renal seeding: Skin infection with gram-positive organisms, IV drug abuse, immunocompromised status
- Ascending infection associated with tubular obstruction from prior infections, urocutaneous reflex, or calculi appears to be the primary pathway for the establishment of gram-negative abscesses

ASSOCIATED CONDITIONS

See “Risk Factors” above

GENERAL PREVENTION

Increased clerical suspicion, prompt recognition, and treatment of infection, especially in the face of obstruction in high-risk patients

DIAGNOSIS

HISTORY

- Significant chronic or acute illnesses including diabetes, neurogenic bladder dysfunction, chronic renal failure, hemodialysis, and polyplastic renal disease
- Renal CaCulii
- IV drug abuse
- Gram-positive source of infection 1–8 wk before the onset of urinary tract symptoms
- Previous infection can occur in any area of the body (eg, skin lesions, dental infections)
- Patients with UTI and abdominal or flank mass
- Persistent fever with suspected genitourinary source after 3–5 days of antimicrobial therapy

PHYSICAL EXAM

- Elevated temperature
- CVI or flank tenderness
- Abdominal and/or flank mass
- Distended or palpable bladder
- Look for skin carbuncles or dermatologic evidence of IV drug abuse
- Heart murmurs

DIAGNOSTIC TESTS & INTERPRETATION

- Urine analysis:
  - Pyuria and bacteria often present, although pyuria/bacteriuria may not be evident unless the abscess communicates with the collecting system
  - Sterile pyuria often seen with TB
- CBC:
  - Patients typically have marked leukocytosis
- Urine culture:
  - When abscesses contain gram-negative organisms, urine culture often demonstrates the same organism isolated from the abscess
  - Since gram-positive organisms are most commonly blood borne, urine culture in these cases typically show no growth or a microorganism different from that isolated from the abscess
  - Catherized urine collection recommended for female patients
- Blood cultures:
  - Gram-negative organisms are most commonly cultured
  - Gram-positive organisms are not routinely similar to those cultured from abscess

LAB

- Serum creatinine:
  - Common findings include an echo-free or hypoechoic renal mass
  - Absence of psoas shadow on affected side
  - Bubbles of extraluminal gas can be seen surrounding the kidney in large perirenal abscesses

DIAGNOSTIC TESTS/SURGERY

CT or ultrasound

- Differentiation between early renal abscess and acute pyelonephritis is difficult due to small size
- Abdominal CT:
  - Diagnostic procedure of choice
  - Can often delineate the route of spread of infection into surrounding tissues
  - Abscesses are characterized by well-defined borders and after contrast agent enhancement
  - Acute findings include renal enlargement and focal, rounded areas of decreased attenuation
- Chronic findings include obliteration of adjacent tissue planes, thickening of Gerota (perirenal) fascia, a round or oval parenchymal mass of low attenuation, and a surrounding inflammatory wall of slightly higher attenuation that forms a ring when the scan is enhanced with contrast material (ring sign)

- See Figure 1, Renal Abscess
- IV urography (IVP performed):
  - Abnormal in up to 80% of patients, although findings often are nonspecific
  - Generalized enlargement of involved renal unit with distortion of renal contour and collecting system
- Abscesses are characteristically well defined both on nonenhanced and contrast-enhanced scans

- See Figure 1, Renal Abscess

- Differentiation of emphysematous pyelonephritis which may require urgent surgical intervention. See Section I, Emphysematous pyelonephritis

DIAGNOSTIC PROCEDURES/SURGERY

CT or US-guided needle aspiration may be necessary to differentiate an abscess from a hypernephroma or tumor. Aspirated material can be collected for culture to guide appropriate antimicrobial therapy.

- Percutaneous drainage may be left in place and clinical course can be evaluated

PATHOLOGIC FINDINGS

Abscess fluid will demonstrate neutrophils and gram stain will reveal bacteria
**Differential Diagnosis**
- Pyelonephritis (S)
- Pyonephrosis
- Xanthogranulomatous pyelonephritis
- Empyema pyelonephritis
- Renal TB
- Local perforation with retroperitoneal spread of infection

**Treatment**

**General Measures (3,4)**
- Hospitalization with initiation of IV antibiotics and fluid resuscitation.
- Suspected pyelonephritis treated with antibiotics for 48–72 hr without significant improvement requires radiographic evaluation to rule out obstruction and/or abscess formation.
- Recent evidence indicates that for very small (<3 cm abscesses), careful observation and IV-tailed antimicrobial agents may obviate surgical procedures.
- Abscesses 3–5 cm in diameter and smaller abscesses in immunocompromised hosts or those that do not respond to antimicrobial therapy should be drained percutaneously.
- Surgical drainage, however, currently remains the procedure of choice for most renal abscesses (>5 cm in diameter or if perirenal extension of abscess occurs.
- Observation, if present, must be reviewed.

**Medication**

**First Line**
- Antibiotic therapy. May prevent surgical intervention unless abscess involves periureteral space.
- Initiate empiric treatment with fluid resuscitation and broad-spectrum IV antibiotics.
  - Third-generation cephalosporins
    - Ceftriaxone—1–2 g IV/Q12h
  - Aminoglycosides
    - Gentamicin—1.7 mg/kg IV/Q8h
    - Amikacin—7.5 mg/kg IV/Q12h
  - Piperacillin/Tazobactam—3.375 g IV/Q6h
  - IV antibiotics until sterile for 48–48 hr, switch to PO for at least 2 wk based on culture.

**Second Line**
- For a suspected hematogenous source, expand coverage to include penicillin-resistant Staphylococcus.
  - Vancomycin—1 g IV/Q12h

**Surgery/Other Procedures**
- Standard treatment for renal abscesses >5 cm or those that fail to respond to percutaneous drainage and if IV antibiotic therapy has been rapid and effective.
- Relief of coexisting obstruction is mandatory.
- Primary treatment remains drainage for all perinephric abscesses.
- Nephrectomy may be required for adequate treatment if medical therapy/Incision and drainage fails.

**Additional Treatment**

**RADIATION THERAPY**
- N/A

**Additional Therapies**
- CT or US-guided placement of percutaneous drains with concurrent IV antibiotic therapy is currently an accepted method of treatment for abscesses 3–5 cm in size and smaller abscesses in immunocompromised patients who fail to respond to medical therapy.

**Complementary & Alternative Therapies**
- N/A

**Ongoing Care**

**Prognosis**
- Perinephric abscess is historically associated with mortality rates approaching 39–50%.
- Recent series with prompt implementation of IV antibiotics and subsequent percutaneous or surgical drainage report mortality rates of 3–12%.

**Complications**
- Delay in diagnosis is associated with higher mortality rate.
- Delay in diagnosis and treatment is associated with loss of renal function and, in rare circumstances, perithoracic fissures to the pleura, colon, skin, etc.

**Follow-Up**

**Patient Monitoring**
- Address the underlying medical conditions to prevent recurrent infections.
- Repeat radiographic studies to confirm complete resolution.
- Extended antibiotic therapy is often required.

**Patient Resources**
- Medline Patient Information:
- Urology Care Foundation Patient Guide:
  - http://www.urologyhealth.org/urology/index.cfm/article=18

**References**

**Additional Reading**

**Clinical/Surgical Pearls**
- Abscesses >3 cm can be managed with medical treatment initially.
- Continued fevers require surgical drainage of abscess.
- Include gram-positive antibiotic coverage if suspect hematogenous spread (IV drug use).
**Ganesh V. Raj, MD, PhD, FACS**

**RENAH ANGIO MYOLIPOMA**

**Casey Allison Steideman, MD**

**Ganesh V. Raj, MD, PhD, FACS**

**DIAGNOSIS**

**HISTORY**
- Most asymptomatic, discovered incidentally
- Occasionally diagnosed by flank pain, hypertension, and spontaneous hemorrhage
- History of LAM, TSC
- GI complaints due to mass effect
- Hematuria, hypertension, anemia

**PHYSICAL EXAM**
- Hypertension, or hypotension (in the setting of hemorrhage)
- TSC: Mental retardation, adenoma sebaceum, ungual/subungual fibromas, lung disease
- Flank pain/tenderness
- Up to 50% of patients who are symptomatic may have a palpable mass

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Anemia
- Gross/micro hematuria
- Renal insufficiency
- Genetic testing if TS is suspected

**Imaging**
- CT: AML is commonly diagnosed on CT scans that reveal solid masses with areas of fat density (Hounsfield units below —20), most reliable imaging modality; IV contrast not necessary
- 10 mg once daily with or without food
- Approved in adults with renal AML and TSC not requiring immediate surgery
- Most TSC-associated disease manifestations, such as skin manifestations, pulmonary LAM, cardiac rhabdomyomas, and epilepsy
- Oral: Everolimus (4)
- Fstedlin (4)
- Approved in adults with renal AML and TSC not requiring immediate surgery
- May benefit other TSC-associated disease manifestations, such as skin manifestations, pulmonary LAM, cardiac rhabdomyomas, and epilepsy
- An inhibitor of mammalian target of rapamycin (mTOR), a serine-threonine kinase, downstream of the PI3K/AKT pathway

- **DIFFERENTIAL DIAGNOSIS (2)**
  - Renal masses:
    - Oncocytoma
    - Renal and retroperitoneal liposarcoma
    - Renal cell carcinoma
    - Renal cyst
    - Renal lipoma
    - Sarcoma (including fibrosarcoma, leiomyosarcoma, and liposarcoma)
  - Neurofibroma
  - Upper-tract urothelial carcinoma
  - Wilms tumor
  - Xanthogranulomatous pyelonephritis
  - Renal/retroperitoneal hemorrhage:
    - Atherosclerotic malformation
    - Coagulopathy
    - Hemorrhage of other renal mass such as renal cell carcinoma
    - Iatrogenic
    - Traumatic injury
    - Vasculitis

**GENERAL MEASURES (3)**
- Benign renal masses, rarely transform to malignant entities
- Observation unless large, or symptomatic

**MEDICATION**

**FIRST LINE**
- Medical management is not currently standard

**SECOND LINE**
- Everolimus (4)
- Approved in adults with renal AML and TSC not requiring immediate surgery
SURGERY/OTHER PROCEDURES
- Indications: Diagnostic uncertainty, hemorrhage causing significant symptoms, pain, hematuria, risk of rupture.
- Asymptomatic AML: <4 cm:
  - Observation with serial imaging at 12-mo intervals
  - Treatment should be considered; observation with serial imaging
  - The risk of spontaneous hemorrhage appears greatest in masses <4 cm
  - Women of childbearing age may consider proactive treatment
- Symptomatic AML: >4 cm:
  - Selective arterial embolization or nephron-sparing surgery
  - Acute hemorrhage:
    - Initially treated with embolization (stabilizes patient and often eliminates need for more intervention)
    - If explored emergently, total nephrectomy usually necessary

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
- Limited reports of treatment using cryoablation and radiofrequency ablation
- In patients with LAM or TS, mTOR inhibitors such as everolimus (mTOR inhibitor) can shrink large masses by 30%.
- Limited reports of treatment using cryoablation and radiofrequency ablation
- Acute hemorrhage:
  - Symptomatic AML/lesion
  - Asymptomatic AML

Indications: Diagnostic uncertainty, hemorrhage due to complications and recurrence risk.
- Women of childbearing age may consider conservative management: Serial imaging (usually >4 cm)
- Observation for small masses, consider embolization
- Diagnosis is usually made by imaging.
- Larger lesions have increased risk of spontaneous hemorrhage.

ADDITIONAL READING

RENSA F/P Y

MORE INFO
• Benign renal tumor characterized by presence of vascular, muscle, and adipose components.
• Larger lesions have increased risk of spontaneous hemorrhage.
• Diagnosis is usually made by imaging.
• Observation for small masses, consider embolization for larger masses.
• Everolimus (mTOR Inhibitor) can shrink large multifocal lesions in patients with tuberous sclerosis (TS) and lymphangiomyomatosis (LAM).

REFERENCES

CODES
ICD9
• 239.0 Benign neoplasm of kidney, except pelvic.

ICD10
• D17.71 Benign epithelioid neoplasm of kidney.
• N28.89 Other specified disorders of kidney and ureter.
• Q85.1 Tuberous sclerosis.

CLINICAL/SURGICAL PEARLS
• Benign renal tumor characterized by presence of vascular, muscle, and adipose components.
• Observation for small masses, consider embolization for larger masses.
• Everolimus (mTOR Inhibitor) can shrink large multifocal lesions in patients with tuberous sclerosis (TS) and lymphangiomyomatosis (LAM).
RENAL ARTERY STENOSIS/RENOVASCULAR HYPERTENSION

Brian M. Benway, MD
Gerald L. Andriole, MD, FACS

**BASICS**

**DESCRIPTION**
- Renal artery stenosis (RAS) refers to anatomic vascular lesion that causes decreased blood flow to the kidney
- May not be associated with hypertension (HTN)
- May be atherosclerotic in nature (atherosclerotic renal artery stenosis or ARAS)
- Rarely caused by fibromuscular dysplasia (FMD)
- Renovascular HTN (RVH) refers to HTN that is caused by renal hypoperfusion and is reversed by correction of the lesion or nephrectomy

**EPIDEMIOLOGY**

- **Incidence**
  - RVH found incidentally
  - 20% of patients with aortic occlusive disease
  - 41% of patients with diabetes
  - 7% of asymptomatic normotensive adults
  - 1% of hypertensive patients

- **Prevalence**
  - RVH diagnosed in hypertensive patients

**RISK FACTORS**
- Atherosclerosis
- Diabetes
- CAD
- Advanced age

**GENETICS**
- N/A

**PATHOPHYSIOLOGY**

- Atherosclerosis
  - Accounts for 70% of all RAS
  - Nerves and arterial endothelium
  - May cause high-grade stenosis

- CAD
  - Common cause of RAS
  - Accounts for 70% of all RAS

- Diabetes
  - 7% of asymptomatic normotensive adults
  - 20% of patients with coronary artery disease (CAD)

- Advanced age
  - 65 yr (1)

**ASSOCIATED CONDITIONS**

- High-grade retinopathy
- Atherosclerosis
- Diabetes
- CAD
- Renal vascular disease

**GENERAL PREVENTION**

- Reduction of risk factors for cardiovascular disease and diabetes

**DIAGNOSIS**

**HISTORY**

- Onset of HTN after age 50
- No family history of HTN
- Difficult-to-control HTN, on multiple antihypertensives
- Increase in serum creatinine with use of ACE inhibitors or angiotensin receptor blockers (ARBs)

**PHYSICAL EXAM**

- Blood pressure measurement
- Abdominal exam with auscultation for bruit
- Retinal exam

**DIAGNOSTIC TESTS & INTERPRETATION**

- **Lab**
  - Plasma renin activity (PRA)
  - By itself, not diagnostic of RAS or RVH
- **Captopril test**
  - Useful for excluding RVH
  - Diuretics and ACE inhibitors stopped 1 wk prior
  - PRA measured before and 1 hr after 25-mg dose of captopril
  - Positive test if postdose PRA > 12 ng/mL/h, absolute increase of PRA > 10 ng/mL/h, 4-fold increase in PRA over baseline
  - Not appropriate in children or in patients with anemia

- **Imaging**
  - Angiography is gold standard
  - Highly sensitive and specific (99%)
  - Provides detailed anatomy, and allows for discrimination between FMD subtypes
  - Allows for simultaneous endovascular treatment
  - Usually bilateral
  - Accounts for 10% of FMD

- **Typically performed in patients with high suspicion for RVH**
- Captopril renography
  - Keep well hydrated on a liberal salt diet
  - Off ACE inhibitors for 3–5 days prior to exam
  - PRA measured before and 1 hr after captopril dose
  - Diagnostic criteria for RVH: Delay in maximal activity > 11 min, asymmetrical peak activity, cortical retention of isofluorolof, significant decrease in glomerular filtration rate
  - recommended as initial diagnostic intervention in patients with low- to moderate suspicion for RVH

- **Arteriography**
  - Positive diagnostic criteria: Peak systolic velocity > 120 cm/s, ratio of diameter of renal artery to aorta > 3.5
  - Invasive, noninvasive, but quality of study is operator dependent

- **Magnetic resonance angiography (MRA)**
  - May be more sensitive than ultrasound or renography, but inferior to conventional angiography
  - Poorly visualizes distal arteries
  - Contraindicated in patients with renal insufficiency (12)

- **Computed tomography angiography (CTA)**
  - Uses potentially nephrotoxic contrast agents
  - More widely available and cost-effective compared to MRA
RENAL ARtery STENOSIS/RENOVASCULAR HYPERTENSION

Diagnostic Procedures/Surgery
- Renal angiography
- Renal vein renin sampling
  - Useful in determining which kidney is primary contributor to RVR in patients with bilateral lesions

Pathologic Findings
- Renal biopsy indicated in patients with creatinine >4 mg/dL.
  - Tubular atrophy, interstitial fibrosis, arteriosclerosis indicate functional recovery may be possible
  - Widespread glomerular hyalization indicates irreversible injury

DIFFERENTIAL DIAGNOSIS
- Acute aneurysm
- Essential HTN
- Functional renal adenoma
- Intrarenal renal disease
- Renal artery aneurysm

TREATMENT

GENERAL MEASURES
- Recognition of underlying cause is critical in guiding management
- Smoking cessation
- Weight loss
- Reduction of risk factors for cardiovascular disease and diabetes

MEDICATION

First Line
- ACE inhibitors/ARBs: Improves HTN in 96% of patients with RVR. May not prevent progression of atherosclerotic lesions.
  - Captopril: 25-50 mg PO BID-TID
  - Lisinopril: 10–40 mg PO QD
  - Losartan: 25–100 mg PO divided QD-BID
  - Valsartan: 20–80 mg PO QD
  - Aspirin 81 mg PO QD
  - Statins

Second Line
- Thiazide diuretics
- Loop diuretics
- Calcium channel blockers
- P-blockers

SURGERY/OTHER PROCEDURES
- Surgical intervention recommended for patients with high-grade stenosis, bilateral disease, solitary kidney, declining renal function, pulmonary edema, congestive heart failure (3)
  - Angioplasty with or without endovascular stenting
  - Percutaneous access through common femoral artery
  - Selective angiography performed
  - ≥70% stenosis treated with angioplasty and deployment of balloon-mounted stent
  - Angioplasty without stenting is associated with increased risk of restenosis
  - One recent clinical trial suggests that the addition of renal artery stenting to comprehensive, multifaceted medical therapy did not confer a significant benefit (4)
  - Anticoagulant (heparin or saphenous vein)
  - Necropsy (especially in patients with a poorly functioning ipsilateral renal unit)

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies
- Treatment of concomitant disease
  - Antiplaque agents
  - Statins
  - Smoking cessation
  - Weight loss

Complementary & Alternative Therapies
- Symptomatic renal denervation using radiofrequency ablation is investigational at the present time, but shows promise (5)

ONGOING CARE

PROGNOSIS
- Untreated disease, except for medial fibroplasia, is often progressive and can result in renal functional loss

COMPlications
- Functional loss, worsening HTN, pulmonary edema, congestive heart failure in untreated patients
- Endovascular interventions: Access site hematomas, renal artery dissection, thrombosis, contrast-induced nephropathy
- Surgical interventions: Hemorrhage, wound infection, hemotoma, anesthetic complications

FOLLOW-UP
- Patient Monitoring
  - High-risk patients and those on medical therapy should be observed with serial metabolic and renal function studies in addition to Doppler ultrasonography

Patient Resources

REFERENCES

CODES

ICD9
- 443.90 Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled
- 405.91 Unspecified renovascular hypertension

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- HTN, Urologic Considerations
- Renal Artery Aneurysm
- Renal Artery FMD
- Renin, Plasma and Renal Vein
- Renal Artery Stenosis Imaging: O

CLINICAL/SURGICAL PEARLS
- RVR HTN is caused by significant stenosis of the renal artery and is reversed by correction of stenosis or nephrectomy.
- Renal angioplasty remains gold standard for diagnosis.
- With the exception of medial fibroplasia, untreated RVR disease often leads to progressive renal functional loss.
RENAL CAPSULAR NEOPLASMS

Mathew C. Raynor, MD
Raj S. Pruthi, MD, FACS

**BASICS**

**DESCRIPTION**
- Predominantly mesenchymal neoplasms arising from the renal capsule encompassing a wide variety of cell progenitors:
  - Tumors can be composed of fibrous, smooth muscle, vascular, adipose, nerve, or other tissue differentiation.
  - Encompasses benign and malignant neoplasms.

**EPIDEMIOLOGY**
- **Incidence**:
  - Very rare tumors.
  - Represent up to ~1.5% of all surgically treated benign renal masses (1).
  - Incidentally found at autopsy in up to ~5% of cases (1).
  - Similar gender preference.

- **Prevalence**:
  - Unknown, due to rarity of tumor.

**RISK FACTORS**
- None known.
- Increased cross-sectional imaging use may identify incidental mass.

**PATHOPHYSIOLOGY**
- **Benign**:
  - Leiomyoma, hemangiopericytoma, hemangioma, lymphangioma, lipoma, fibroma, myxoma.
  - Solitary fibrous tumor.
- **Malignant**:
  - Leiomyosarcoma, malignant fibrous histiocytoma, fibromyxoid sarcoma, hemangiosarcoma, liposarcoma, fibrosarcoma.

**ASSOCIATED CONDITIONS**
- Some renal hemangiomas may be associated with Sturge–Weber or Klippel–Trénaunay syndromes (1).

**GENERAL PREVENTION**
- No preventive strategies identified.

**DIAGNOSIS**

**HISTORY**
- Usually asymptomatic or discovered incidentally.
- May present with hematuria or flank pain.
- Weight loss, anorexia, malaise, or bone pain may signify metastatic disease.

**PHYSICAL EXAM**
- Usually normal.
- Rarely, flank mass may be palpable.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urinalysis:
  - Microscopic hematuria may be identified, but usually normal.
- CBC:
  - Anemia may be present with advanced disease or bleeding mass.
- Serum chemistries usually normal.

**Imaging**
- CT or MRI with and without contrast:
  - May show enhancing mass arising from the kidney.
  - Indistinguishable from renal cell carcinoma in most cases.
  - Presence of fat may signify angiomyolipoma, lipoma, or liposarcoma.
  - May also be useful for evaluating for metastatic disease.

**Diagnostic Procedures/Surgery**
- Core needle biopsy:
  - May be used in cases of suspected renal malignancy or if active surveillance considered.
- Angiography:
  - May be utilized for bleeding lesions.
- Gross appearance usually hypovascular.
- Excise hemangiopericytoma, which is highly vascular.

**Pathologic Findings**
- Leiomyoma:
  - Firm, well-circumscribed, exophytic mass.
  - Microscopically, composed of spindle cells arranged in fascicles typical of smooth muscle.
  - Immunostaining positive for desmin, smooth muscle actin, and usually HMB-45 (1,2).
- Hemangiopericytoma:
  - Solid, encapsulated mass.
  - Microscopically, varied cell shapes and sizes with morphologic variability.
  - Immunostaining positive for vimentin, BCL2, CD99 and negative for S100, c-kit, and SMA (1,2).
- Lymphangioma:
  - Well-encapsulated, multilocular cystic mass.
  - Microscopically, communicating cysts lined with flattened endothelial cells.
  - Immunostaining positive for CD31 (1,2).
- Solitary fibrous tumor:
  - Well-encapsulated firm mass without necrosis, opt, or hemorrhage.
  - Microscopically, usually shows areas of spindle cells intermixed with hypocellular areas of fibrous tissue.
  - Immunostaining strongly positive for CD34 and HMB-45.
  - May also be positive for CD90 and CD117 and can be misclassified as hemangiopericytoma (1,2).
- Leiomyosarcoma:
  - Usually large circumscribed mass with areas of necrosis.
  - Microscopically, spindle cells with haphazard growth pattern, nuclear pleomorphism, mitoses, and necrosis.
  - Immunostaining positive for SMA, desmin, and calponin (1,2).
- Fibrosarcoma:
  - Large encapsulated mass.
  - Microscopically, elongated spindle cells with “Herringbone” pattern.
  - Immunostaining positive for vimentin.
  - Differentiates fibrosarcoma from sarcomatoid RCC and leiomyosarcoma (1,2).
- Malignant fibrous histiocytoma:
  - Solid, well-encapsulated mass.
  - Microscopically, proliferation of fibrohistiocytes.
  - Immunostaining positive for vimentin and CD68.

**REFERENCES**


**ABBREVIATIONS**

RCC: Renal cell carcinoma
CD31: VascularCAM
CD34: VascularCAM
CD90: VascularCAM
CD99: VascularCAM
HMB-45: VascularCAM
SMA: Smooth muscle actin
Desmin: Smooth muscle actin
Calponin: Smooth muscle actin
RENAL CAPSULAR NEOPLASMS

DIFFERENTIAL DIAGNOSIS
- Angiomyolipoma
- Renal cyst
- Cystic nephroma
- Juxtamedullary renal cell carcinoma
- Renal pseudotumour
- Spleen xenograft
- Teratoma
- Wilms tumor
- Xanthogranulomatous pyelonephritis

TREATMENT
GENERAL MEASURES
- Surgical excision is both diagnostic and therapeutic
- Multimodal therapy generally recommended for malignant tumors such as sarcoma

MEDICATION
First Line
- Chemotherapy may be beneficial for certain advanced renal capsular malignancies (sarcoma) and metastatic lesions
- Usually given in the adjuvant setting
- Targeted therapies may be beneficial in certain cases
- Sunitinib, sorafenib, bevacizumab active in angiosarcoma, solitary fibrous tumor, and hemangiopericytoma

SURGERY/OTHER PROCEDURES
- Surgical excision remains gold standard
  - Radical nephrectomy
  - Partial nephrectomy
  - Renal capsule margin should be excised with mass
  - Should be procedure of choice for patients with chronic kidney disease, when feasible
  - Active surveillance
  - Similar surveillance protocol for patients with small renal masses

ADDITIONAL TREATMENT
Radiation Therapy
- May be beneficial in cases of renal capsular sarcoma
  - Usually given in adjuvant setting

Additional Therapies
- Arterial embolization for bleeding masses

Ongoing Care

PROGNOSIS
- Surgical excision usually curative
- Renal capsular sarcoma has poor prognosis
  - Locally advanced disease is common
  - Recurrence and metastases common
  - Overall prognosis is poor, despite adjuvant chemoradiation
  - 5-yr overall survival — 15%-
  - Median survival 28 mo (4)

Complications
- Injury to adjacent organs
- Thromboembolic event
- Delayed bleed
  - ARF
  - Pseudoaneurysm
- Development of metastatic disease

Follow-Up
- Patient Monitoring
  - Periodic surveillance imaging
  - Serum chemistry panel and liver function tests

Patient Resources
- None due to rarity of disease

REFERENCES

ADDITIONAL READING
- Soft Tissue Sarcoma. NCCN Clinical Practice Guidelines in Oncology (www.nccn.org).

See Also (Topic, Algorithm, Media)
- Hemorrhage, Retroperitoneal and Perinephric
- Renal Capsular Neoplasms Image
- Renal Mass
- Renal Masses, Benign WHO Classification
- Renal Sarcoma, Adult and Pediatric

CODES
ICD9
- 189.0 Malignant neoplasm of kidney, except pelvis
- 223.0 Benign neoplasm of kidney, except pelvis
- 239.5 Neoplasm of unspecified nature of other genitourinary organs

ICD10
- C64.9 Malignant neoplasm of unspecified kidney, except pelvis
- D30.00 Benign neoplasm of unspecified kidney
- D49.5 Neoplasm of unspecified behavior of other genitourinary organs

CLINICAL/SURGICAL PEARLS
- Renal capsular neoplasms difficult to distinguish from RCC by imaging alone.
- Surgical excision (partial or radical nephrectomy) can be diagnostic and curative in most cases.
- Renal capsular sarcomas carry generally poor prognosis, despite adjuvant therapy.
Genetics history.

RISK FACTORS

Incidence

There are approximately 62,930 cases of RCC diagnosed each year; about 10% have IVTT.

Prevalence (T)

- RCC with IVTT is seen in 4–15% of cases.
- In 50% of these cases, IVTT only extends to the RV.
- Level II—IVC > 2 cm above RV.
- Level III—Suprahepatic/infrahepatic IVC/right atrium

EPILOGUE

PHYSICAL EXAM

- Flank/abdominal mass (2%)
- Constitutional symptoms including fatigue, weight loss, or paraneoplastic syndrome (9%)
- Flank/abdominal pain (17%)
- Flank/abdominal mass
- Constitutional symptoms including fatigue, weight loss, or paraneoplastic syndrome

DIAGNOSIS

HISTORY

- Presentation of patients with RCC with IVTT is similar to RCC without tumor thrombus, but those with tumor thrombus are more likely to be symptomatic.

- Up to 95% of patients with intracaval extension present with symptoms. It is an incidental finding in 23%.

- Symptoms include:
  - Hematuria (35%)
  - Flank/abdominal pain (17%)
  - Constitutional symptoms including fatigue, weight loss, or paraneoplastic syndrome (9%)
  - Flank/abdominal mass (6%)

- Physical exam findings can include:
  - Bilateral lower-extremity edema
  - Varicocele (right side)
  - Dilated superficial abdominal wall veins
  - Caput medusa

DIAGNOSTIC TESTS & INTERPRETATION

- Basic lab work is necessary for preoperative workup including:
  - Liver function tests
  - Complete blood count
  - Basic metabolic panel
  - Ultrasound

- Chest imaging (preferably CT) and bone scan should be ordered as part of staging workup

- Assessment of IVTT cephalad extension should be performed 7–14 days before surgery because it can affect the surgical approach and the need for bypass procedures

- Ultrasoundography and standard CT can be used to detect the presence of IVTT, but may not be sufficient for surgical planning

- MRI (T1-weighted images) is the gold standard imaging technique used to assess the cephalad extent of the IVTT, the degree of occlusion, and its relationship to liver, diaphragm, and atrium

- Multidetector CT (MDCT) can also be used in patients who are not candidates for MRI

SURGERY/OTHER PROCEDURES

- Surgery is the gold standard for the treatment of RCC with IVTT (2,3,4)
- Most common TKIs used preoperatively are sorafenib and sunitinib; may decrease tumor size

- Tumor felt not to be surgically resectable

- Cytoreductive nephrectomy with tumor thrombus development and propagation below the tumor may be considered for patients with IVTT to prevent bland thrombus growth and propagation below the tumor

- Anticoagulation (preoperatively) should be considered for patients with IVTT to prevent bland thrombus development and propagation below the tumor

- Contraindications to preoperative anticoagulation include smoking, obesity, hyper tension, family history

- General measures

- General measures

- Differential diagnosis

- Other tumors associated with IVTT include urothelial cell carcinoma, adenocarcinoma, and angioleiomyoma

- Diagnosis

- Incidence

- Risk factors for RCC with IVTT are the same for RCC

- General measures

- General measures

- Associated conditions

- Pulmonary embolus

- Bilateral lower-extremity edema

- Lower-extremity DVT

- Varicocele

- Caput medusa

- General prevention

- Modification of above risk factors for RCC

- General measures

- General measures

- Differential diagnosis

- Other tumors associated with IVTT include urothelial cell carcinoma, adenocarcinoma, and angioleiomyoma

- General measures

- General measures

- Treatment

- First line

- Anticoagulation (preoperatively) should be considered for patients with IVTT to prevent bland thrombus development and propagation below the tumor

- Mediastinal, subclavicular (if present), or thoracosabdominal incisions can be used

- Median sternotomy or thoracoabdominal approaches can be used for IVTT above the diaphragm

- Surgical procedures/surgery

- Surgery is the gold standard for the treatment of RCC with IVTT (2,3,4)

- Diagnostic findings

- All subtypes of RCC have been associated with IVTT

- Clear cell is the most common histologic subtype associated with IVTT
Level I Thrombus Specifics
- Milks the thrombus into the RV and take a side bite of the IVC using a vascular clamp making sure not to occlude IVC flow
- Incise the IVC and remove the thrombus and kidney under direct vision
- Overview the caval defect

Level II Thrombus Specifics
- Mobilize the liver and divide minor hepatic veins to expose the infrahepatic IVC
- Place flumetl transection or vascular clamps sequentially on the infrarenal vena cava, concomitant IVC and suprarenal vena cava above the thrombus
- Incise IVC, remove the thrombus and kidney
- Flush-exposed IVC with heparinized saline
- Suture caval, release vascular clamps

Level III-IV Thrombus Specifics
- A wide variety of surgical approaches have been described
- Clamping of the IVC at the level can compromise hemodynamic stability
- Cardiopulmonary bypass: Used for IIT above the diaphragm, maintains continuous arterial/venous blood flow during IVC occlusion
- Deep hypothermic circulatory arrest (DHCA) cools the body and creates a bloodless field
- Venous bypass can be used for level II-IV tumors. Venous bypass allows for continuous venous return to the heart while IVC is clamped
- Pringle maneuver (clamping of the hepatic pedicle) can be used to avoid hepatic congestion and IVC bleeding that may occur when IVC is clamped above the hepatic veins (limit exam hepatic ischemia to 20 min)
- Coghill IVC control can be obtained by exposing the infrarenal IVC via pericardiotomy
- Langenbuch maneuver (medial mobilization of level) to expose retrohepatic IVC
- Transperitoneal/extra pericardiacotomy should be used for real time intraoperative monitoring to identify tumor embol
- A multidisciplinary approach, including the involvement of cardiac, vascular, hepatic surgeons as well as a specialized anesthesia team, is highly encouraged for these complex tumors

ADDITIONAL TREATMENT

Radiation Therapy
No role, except for palliation

Additional Therapies
- IVTT can be used to prevent pulmonary embolus; however its use is controversial
- IVTT may become incorporated into IVC filter causing a surgical challenge
- When IVC is thrombosed completely, simple ligation of IVC below hepatic veins may be performed
- Preoperative renal artery embolization
- Avoid for early venous clamping when renal artery control may be difficult; may cause pain and complications (periphlebitic syndrome)
- Can be used as a palliative procedure

COMPLEMENTARY & ALTERNATIVE Therapies
None

ONGOING CARE

PROGNOSIS
- Prognostic factors include TNM stage, nuclear grade, presence of necrosis, histologic type (except for unclassified RCC and collecting duct carcinoma), anatomic features, invasion into adjacent structures (renal sinus, perinephric fat, hepatic veins, collecting system, CV outlet), ECOS performance status, presence of lymph nodes, and distant metastases
- Prognostic significance of tumor thrombus level remains controversial
- Median survival for metastatic disease: 38–116 mo; 5-yr disease specific survival is 4–30%. Patients that present with metastatic disease 5-yr survival 0–10%

COMPLICATIONS
- Overall complication rate is 12.5%, however, the complication rates vary greatly with level of tumor thrombus
- Perioperative death varies from 0.8–10%. There has been a reported rate of mortality up to 40% for level IV IIT
- Most common complications are hemorrhage, pulmonary embolism, wound infection, acute renal failure, ileus, and need for additional surgery.
- The incidence of intraoperative tumor thrombus embolization is 1.5% and is associated with 75% mortality rate.
- Cardiopulmonary bypass is a risk factor for stroke (8% of cases) during nephrectomy for RCC with IIT

FOLLOW-UP

Patient Monitoring
- Surveillance based on TNM staging
- Surveillance labs include metabolic panel, liver function tests
- Surveillance imaging includes abdominal and thoracic imaging

ADDITIONAL READING

None

See Also (Topic, Algorithm, Media)
- Deep Venous Thrombosis and Pulmonary Embolus, Urologic Considerations
- RCC, General
- Renal Cell Carcinoma, Locally Advanced (T3-14)
- Renal Cell Carcinoma with Tumor Thrombus
- Renal Vein Thrombosis, Adult and Pediatric

REFERENCES


RENAI CELL CARCINOMA WITH TUMOR THROMBUS
RENAL CELL CARCINOMA, GENERAL

Matthew A. Meissner, MD
Ganesh V. Raj, MD, PhD, FACS

PATHOPHYSIOLOGY
- Clear cell and papillary RCC develop from the proximal convoluted tubules.
- Chromophobe and collecting duct RCC develop from the distal convoluted tubule and collecting duct, respectively.
- VEGF and TNF-α are growth factors involved in development and progression of RCC.
- Local invasion is common, 20% of cases have invasion of the capsula or collecting system, and 10% have a tumor thrombus.
- Bilateral tumors occur 2–4% of the time with sporadic RCC, either at diagnosis or metachronously.

ASSOCIATED CONDITIONS
- For ESRD patients there is a 2–5-fold increase in risk of developing RCC, most commonly papillary subtype.
- Acquired renal cystic disease in conjunction with ESRD has a 1–2% risk of developing RCC.
- Viral-related RCC is associated with renal anaplasia, pancreatic cysts, ceruleal and spinal hemangioblastomas, and neuroendocrine tumors.
- BHD-related RCC is associated with facial fibrofolliculomas in addition to lung cysts and spontaneous pneumothoraces.

GENERAL PREVENTION
- Smoking cessation reduces the relative risk of developing RCC by 20–50%.
- Weight reduction: it is estimated that 40% of the cases of RCC in USA may be linked to obesity.

DIAGNOSIS
- Physical exam: pain, palpable flank mass, and hematuria. This is rarely seen except in advanced disease.
- Paraneoplastic syndromes found in 20% of patients. These include hypercalcemia (due to paraneoplastic phenomena or osteolytic bone involvement), HTN, polyserositis, and Ca125.
- Constitutional symptoms such as fever, weight loss, and anemia are thought to be due to paraneoplastic syndromes.

PHYSICAL EXAM
- Physical exam findings are usually absent, except in cases of advanced disease.
- Deep palpation for upper quadrant masses and ascites for a renal artery thrombus should be included in the abdominal exam.
- For a suspicious nodule with a careful testicular exam as venous outflow obstruction can occur due to a renal vein tumor thrombus. An epididymal mass may be seen in VHL-related disease.

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Initial evaluation includes CBC, electrolytes, creatinine, LFTs, and UA.
- Elevated ESR is present in 50% of patients.
- Staufer syndrome found in 14.4% of patients.
- Characterized by abnormal LFTs from a paraneoplastic syndrome and not from liver metastases.
- Also find elevated alkaline phosphatase, PTT, low albumin, elevated bilirubin, or transaminases.
- Hypertension seen in 13% overall, and in 4.9% resulting from paraneoplastic syndromes.
- Anemia may be due to blood loss.

Imaging
- Thin-slice renal CT scan with and without IV contrast is the best test for diagnosing renal masses.
- Any enhancing lesion on CT or MRI is RCC until proven otherwise.
- Enhancement generally defined as >20 HU increase between contrast and noncontrast phases.
- R.E.N.A.L. Nephrometry score may provide a standardized system for radiologic comparison of renal masses (See RENAL Nephrometry in Section II).
- Any renal mass with a negative CT attenuation (<−20 HU) consistent with fat density is an AML.
- Metastatic evaluation may include CT or MRI of the abdomen, chest x-ray for pulmonary lesions, and a bone scan in patients with elevated alkaline phosphatase or bone pain.

Diagnostic Procedures/Surgery
- Biopsy of a renal mass is typically not included in the workup due to high false-negative rate, risk of bleeding, and remote possibility of seeding the biopsy tract.
- Difficult to distinguish between oncocytoma and RCC on biopsy.
- 85–90% of solid renal masses thought to be RCC are confirmed on final pathology.
- Sensitivity and specificity of FNAB biopsy is 80% and 95%, which is not better than imaging alone.
- Biopsy helps differentiate primary renal neoplasms from metastatic or renal lymphoma.
- Biopsy is now considered more frequently in patients being considered candidates for observation vs. surgical extirpation.
- Biopsy is being used for surveillance in small RCC with >90% accuracy with adequate specimens.

Pathologic Findings
- RCCs are adenocarcinomas, arising from renal tubular epithelial cells.
- Clear cell RCC (formerly known as "conventional RCC") 75–80% of RCC.
- Papillary RCC accounts for 10–15%.
- Type 1: Associated with hereditary papillary renal cell carcinoma (HPRCC).
- Type 2: Aggressive, associated with hereditary leiomyomatosis and renal cell carcinoma (HLRCC).
- Chromophobe 3–5% of solid renal masses, associated with a poor prognosis.
- Collecting duct (Bellini) RCC is rare (<1%), but associated with a very poor prognosis. Occurs in younger patients (40-50 years of age).

PREVALENCE
- 65,150 estimated new cases of RCC in USA (39,140 in men and 24,780 in women); 12 new cases per 100,000/yr.
- Male RCC has a 3–4% yearly increase in incidence since the 1970s.
- 12 new cases per 100,000/yr.
- Male, 3:2.
- Estimated 13,860 deaths will occur in 2014 from RCC.
- 65,150 estimated new cases of RCC in USA (39,140 in men and 24,780 in women); 12 new cases per 100,000/yr.
- Male, 3:2.
- Estimated 13,860 deaths will occur in 2014 from RCC.
- 65,150 estimated new cases of RCC in USA (39,140 in men and 24,780 in women); 12 new cases per 100,000/yr.
- Male, 3:2.
- Estimated 13,860 deaths will occur in 2014 from RCC.
- 65,150 estimated new cases of RCC in USA (39,140 in men and 24,780 in women); 12 new cases per 100,000/yr.
SURGERY/OTHER PROCEDURES

**Systemic immunotherapy and targeted molecular therapy**

**GENERAL MEASURES**
- Radiofrequency ablation/cryoablation minimally invasive.
- Radical nephrectomy is the standard of care for solid renal masses.
- Partial nephrectomy is now the standard of care for non-functioning kidneys.
- Surgical extirpation (radical or partial nephrectomy)
  - Wilms tumor (nephroblastoma)
  - Reninoma (JG apparatus tumors)
  - Renal sarcomas
  - Renal lymphoma
  - Renal cell carcinoma
  - Pseudotumors (hypertrophied column of Bertin, or oncocytoma)
  - Metanephric adenoma
  - Inflammatory masses (xanthogranulomatous pyelonephritis)
  - Hemangioma
  - Focal pyelonephritis
  - Cysts (hemorrhagic, infected)
  - Cystic nephromas (multilocular cystic nephroma)
  - Collecting duct tumor (Bellini)
  - Angiomyolipoma (fat poor)
  - Sarcomatoid differentiation: Reported as presence of sarcomatoid features.
  - Renal medullary RCC found in African Americans in later stages.

**TREATMENT**

**GENERAL MEASURES**
- Surgical extirpation (radical or partial nephrectomy)
- Chemotherapy: Limited role.
- Immunotherapy: Limited role.

**MEDICATION**
- Surgical removal is the mainstay of treatment for renal cell carcinoma.
- VHL syndrome is associated with chromosome 3p deletion and RCC, as well as other tumors.

**SPECIAL CONSIDERATIONS**
- Ongoing surveillance is recommended for patients with a history of RCC.
- Surveillance is tailored to tumor stage.

**PROGNOSIS**
- The single most important prognostic factor for RCC is pathologic stage (T):
  - pT1a: 90–100% 5-yr survival
  - pT1b: 70–80% 5-yr survival
  - pT2: 50–60% 5-yr survival
- Node-positive RCC: 0–20% 5-yr survival

**ADDITIONAL TREATMENT**
- Radiation Therapy
  - Radiation is limited to palliation of systemic metastases; no role in the management of clinically localized RCC.
- Additional Therapies
  - Resection of solitary metastatic lesions (≤1 lung) may be useful in selected cases.
- No role for adjuvant systemic therapy in localized RCC.

**ONGOING CARE**
- Surveillance is recommended for patients with a history of RCC.
- Surveillance is tailored to tumor stage.

**REFERENCES**

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
  - Bladder-Bud4 Syndrome
  - Renal Cell Carcinoma, General Image
  - Renal Cell Carcinoma, Localized (T1–T2)
  - Renal Cell Carcinoma, Locally Advanced (T3–T4)
  - Renal Cell Carcinoma, Metastatic (M1–M+)
  - Renal Cell Carcinoma, Pediatric
  - Renal Mass
  - Reference Tables: TMM: Kidney Cancer
  - Von Hippel-Lindau Disease/Syndrome

**ICD-10**
- T82.0 Malignant neoplasm of kidney, except pelvis
- N99.70 Hematuria, unspecified
- T98.0 Abdominal pain, other specified site

**ICD10**
- C61.9 Malignant neoplasm of urine, except pelvis
- B10.9 Unspecified abdominal pain

**CLINICAL/SURGICAL PEARLS**
- Most common solid renal mass is clear cell RCC.
- Most renal masses are detected incidentally.
- Von Hippel-Lindau syndrome is associated with chromosome 3p deletion and RCC, as well as other tumors.
- Surgical removal is the mainstay of treatment for RCC.
- Partial nephrectomy is increasingly utilized for larger, clinically localized tumors.
PATHOPHYSIOLOGY

Renal cell carcinoma (RCC) refers to an abnormally growing cell that arises from the renal proximal tubule. RCCs are rare, but they are the most common malignancy of the kidney. The prognosis for RCC depends on several factors, including the stage of the disease, the grade of the tumor, and the presence of metastatic disease.

RCCs are derived from the proximal convoluted tubule of the kidney. They can arise from the renal cortex or the renal medulla. The majority of RCCs are found in the cortical region, while a small proportion are found in the medullary region. RCCs are often characterized by their rapid growth and ability to metastasize to other organs, particularly the lungs.

The pathophysiology of RCC involves several key processes, including angiogenesis, tumor cell proliferation, and evasion of immune surveillance. RCCs are known to produce angiogenic factors, such as vascular endothelial growth factor (VEGF), which promote the growth of new blood vessels in the tumor. This process is crucial for tumor growth and metastasis.

RCCs are also known to evade immune surveillance by downregulating the expression of MHC class I molecules, which are essential for the recognition of tumor cells by the immune system. This allows RCCs to escape immune surveillance and continue to grow and spread.

The histology of RCCs is variable, and the specific histologic subtype can impact the treatment options and prognosis. RCCs can be classified into several subtypes, including clear cell RCC, papillary RCC, chromophobe RCC, and collecting duct RCC.

DIAGNOSIS

The diagnosis of RCC is typically made through imaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI). These studies can help to identify the location, size, and extent of the tumor. Blood tests, such as laboratory tests, can also be used to assess the tumor burden and to monitor the response to therapy.

TREATMENT

The treatment of RCC depends on the stage and subtype of the tumor. General options include surgery, targeted therapy, immunotherapy, and radiation therapy. The choice of treatment depends on several factors, including the tumor stage, the patient's overall health, and the potential side effects of the treatment.

In the case of localized RCC (T1-T2), the treatment options include surgery, such as nephrectomy or partial nephrectomy, which involves the removal of the affected kidney. Targeted therapy, such as sunitinib or axitinib, can also be used to inhibit the growth of the tumor. Immunotherapy, such as pembrolizumab, can be used to stimulate the patient's immune system to fight the tumor.

In the case of metastatic RCC (T3-T4), the treatment options include systemic therapy, such as targeted therapy or immunotherapy. Targeted therapy, such as everolimus or axitinib, can be used to inhibit the growth of the tumor. Immunotherapy, such as nivolumab or pembrolizumab, can be used to stimulate the patient's immune system to fight the tumor.

In the case of advanced RCC, the treatment options include systemic therapy, such as targeted therapy or immunotherapy. Targeted therapy, such as sunitinib or axitinib, can be used to inhibit the growth of the tumor. Immunotherapy, such as nivolumab or pembrolizumab, can be used to stimulate the patient's immune system to fight the tumor.
Therapies Complementary & Alternative

**Additional Therapies**

**Radiation Therapy**

N/A

**First Line**

**MEDICATION**

- No role in localized RCC outside of clinical trials of focal radiotherapy (Cyberknife) or HIFU
- Used for painful/ bulk metastases and CNS metastasis in advanced RCC

**Additional Therapies**

- Complementary & Alternative Therapies

**Ongoing Care**

**PROGNOSIS**

- Local recurrence after resection is ~2–3% after radical nephrectomy and 4–6% after partial depending on pathology
- 5-y risks of recurrence for local or regional RCC fully excised are approximately:
  - ≤5–9% low-risk disease
  - 20–25% intermediate-risk disease
  - ≥60–80% high-risk disease
- Progression for partial nephrectomy with a positive margin is less clear. Related to pathology and biology. Every attempt should be made intraoperatively to avoid a positive surgical margin; with focal positive margin, close observation is often indicated.

**COMPLICATIONS**

- Acute surgical/medical risks depend on treatments, techniques, comorbidities, and complexity of the mass. Overall perioperative death rate ~0.5%. Risk of major Clavien grade 3–5 complications: 6.4%, 11.1%, 21.9% for low-, intermediate-, and high-complexity lesions (4).
- Risks after partial nephrectomy: Urinary leak/ fistula, AIF, bleeding, transient or permanent decline in renal function (5)
- Increased risk of Hypertensive systemic disorder (Hypertension) with gadolinium (eGFR < 30 mL/min per 1.73 m²) and/or risk of contrast-induced nephropathy following use of iodinated contrast for radiographic surveillance

**Follow-up**

- Patient Monitoring
  - Periodic history, physical (including BP monitoring), and selected lab studies (urine analysis) at least yearly
  - Radiographic staging/treatment-specific surveillance mandatory based on clinical stage and mode of treatment. Surveillance may be adjusted for other risk factors (papillary histology).
- Following ablation, initial radiologic follow-up requires lack of enhancement on postcontrast-based CT or MR (≤3–6 mo after procedure). Biopsy confirmation of successful ablation is recommended. Occasionally after stygomy, an area of rim enhancement can be seen that should resolve within 1 to 3 mo.
- NCCN (National Comprehensive Cancer Network) guidelines (level of evidence; based on scientific evidence, practice recommendations)
  - Every 6 mo for 2 yr, then annually for 5 yr. History, physical, metabolic panel
  - At 2 yr (based on recurrence risk) chest and abdominal pelvic imaging then risk-based

**Patient Resources**

- Kidney Cancer Association: www.kidneycares.org

**REFERENCES**


**ADDITIONAL READING**

- NCCN Guidelines: www.NCCN.org
- See Also (Topik, Algorithm, Media)
  - von Hippel–Lindau Syndrome
  - Renal Cell Carcinoma, General
  - Renal Cell Carcinoma, Locally Advanced (T3–T4)
  - Renal Cell Carcinoma, Metastatic (M1+)
  - Renal Cell Carcinoma, Pediatric
  - Renal Mass
  - Reference Tables: TRM: Kidney Cancer
  - von Hippel–Lindau Disease/Syndrome

**CODES**

- 189.0 Malignant neoplasm of kidney, except pelvis
- ICD10
  - C64.1 Malignant neoplasm of right kidney, except pelvis
  - C66.2 Malignant neoplasm of left kidney, except renal pelvis
  - C64.9 Malignant neoplasm of upper kidney, except renal pelvis

**CLINICAL/SURGICAL PEARLS**

- Always review the images and carefully assess the presence of the contralateral kidney and the adrenal glands.
- Do not overtreat or undertreat renal mass.

**403**
**GENETICS**

- **Tuberous Sclerosis (TSC)**
  - Two tumor-gene loci (TSC1, TSC2) on chromosomes 9q34 and 16p13.
  - Mutations in TSC1 or TSC2 predispose to RCC.
- **Birt–Hogg–Dubé Syndrome (BHD)**
  - Mutations in the TSC2 gene.
- **Familial Renal Cell Carcinoma (FIRCC)**
  - Mutations in the VHL gene.
- **Familial Renal Parenchymal Tumors (FRPT)**
  - Mutations in the CDKN2A gene.
- **Familial Hypophosphatemic Rickets (FHR)**
  - Mutations in the PHEX gene.

**RISK FACTORS**

- **Increased Age**
  - RCC incidence increases with age.
- **Increased Obesity**
  - RCC incidence is higher in individuals with obesity.
- **Increased Alcohol Consumption**
  - RCC incidence is higher in individuals who consume alcohol.
- **Increased Smoking**
  - RCC incidence is higher in individuals who smoke.
- **Increased Parity**
  - RCC incidence is higher in individuals with high parity.
- **Increased Menopausal Status**
  - RCC incidence is higher in individuals who are menopausal.
- **Increased Family History**
  - RCC incidence is higher in individuals with a family history of RCC.
- **Increased History of Varicocele**
  - RCC incidence is higher in individuals with a history of varicocele.
- **Increased History of Pulmonary Embolism**
  - RCC incidence is higher in individuals with a history of pulmonary embolism.

**PATOPHYSIOLOGY**

- **Increased Incidence**
  - RCC incidence increases with age.
- **Increased Obesity**
  - RCC incidence is higher in individuals with obesity.
- **Increased Alcohol Consumption**
  - RCC incidence is higher in individuals who consume alcohol.
- **Increased Smoking**
  - RCC incidence is higher in individuals who smoke.
- **Increased Parity**
  - RCC incidence is higher in individuals with high parity.
- **Increased Menopausal Status**
  - RCC incidence is higher in individuals who are menopausal.
- **Increased Family History**
  - RCC incidence is higher in individuals with a family history of RCC.
- **Increased History of Varicocele**
  - RCC incidence is higher in individuals with a history of varicocele.
- **Increased History of Pulmonary Embolism**
  - RCC incidence is higher in individuals with a history of pulmonary embolism.

**DIAGNOSIS**

- **Imaging**
  - **CT Scan**
    - Evaluated for pulmonary metastasis.
  - **MRI**
    - Noncontrast MRI with and without injection of gadolinium to evaluate for renal lesions.
  - **Transabdominal US**
    - Can be used to detect RCC.
  - **Transesophageal Echocardiography (TEE)**
    - Can be used to detect metastases to the heart.
  - **LFTs**
    - Can be used to detect metastases to the liver.
  - **Chest X-ray**
    - Can be used to detect metastases to the lungs.
  - **Bone Scan**
    - Can be used to detect metastases to the bone.
  - **PET Scan**
    - Can be used to detect metastases to distant organs.

**PHYSICAL EXAM**

- **Palpable Abdominal Mass**
  - RCC can present as a palpable abdominal mass.
- **Bilateral Abdominal Tenderness**
  - RCC can present with bilateral abdominal tenderness.
- **Lower Extremity Edema**
  - RCC can present with lower extremity edema.
- **Isolated Right-Sided Varicocele**
  - RCC can present with an isolated right-sided varicocele.

**DIAGNOSTIC TESTS & INTERPRETATION**

- **CT Scan**
  - Can be used to detect both local and distant metastases.
  - Can be used to detect both local and distant metastases.
  - Can be used to detect both local and distant metastases.
  - Can be used to detect both local and distant metastases.
  - Can be used to detect both local and distant metastases.
  - Can be used to detect both local and distant metastases.

**PROGNOSIS**

- **Stage I**
  - RCC that is confined to the kidney.
  - 5-year survival rate is up to 90%.
- **Stage II**
  - RCC that has invaded the renal vein or the inferior vena cava.
  - 5-year survival rate is up to 65%.
- **Stage III**
  - RCC that has invaded the renal vein or the inferior vena cava.
  - 5-year survival rate is up to 30%.
- **Stage IV**
  - RCC that has spread to distant sites.
  - 5-year survival rate is up to 15%.

**TREATMENT**

- **Surgical Resection**
  - RCC can be treated with surgical resection.
  - RCC can be treated with surgical resection.
  - RCC can be treated with surgical resection.
  - RCC can be treated with surgical resection.
  - RCC can be treated with surgical resection.

**PROGNOSIS**

- **Stage I**
  - RCC that is confined to the kidney.
  - 5-year survival rate is up to 90%.
- **Stage II**
  - RCC that has invaded the renal vein or the inferior vena cava.
  - 5-year survival rate is up to 65%.
- **Stage III**
  - RCC that has invaded the renal vein or the inferior vena cava.
  - 5-year survival rate is up to 30%.
- **Stage IV**
  - RCC that has spread to distant sites.
  - 5-year survival rate is up to 15%.
TREATMENT

GENERAL MEASURES
- Pro re nata arterioles embolization may cause the tumor hemorrhage to regress and reduce the mortality of surgery as a result.
- Avoid IVC filter placement.

MEDICATION
The role of neoadjuvant targeted therapies (eg, sunitinib, sorafenib, others) for downsizing the primary tumor and the IVC thrombus is controversial: 5–10%.

SURGERY/OTHER PROCEDURES
- Radical nephrectomy is standard of care.
- Neoplastic surgery is possible in selected patients with locally advanced RCC, with equivalent oncologic efficacy to radical nephrectomy (2).
- 45–70% of T3b patients can be cured with nephrectomy for clear cell renal cell carcinoma.

ADDITIONAL TREATMENT
Radiation Therapy
- Role is limited; no survival benefit to preoperative treatment
- May slow growth if residual tumor left after surgery; rarely used
- May palliate symptomatic local recurrences in nonsurgical candidates

ADDITIONAL THERAPIES
- Targeted agents to growth factors are being evaluated in both an adjuvant and neoadjuvant setting for patients at high risk for recurrence (4).

COMPLEMENTARY & ALTERNATIVE THERAPIES
None proven

ONGOING CARE

PROGNOSIS
- T3a: 60–80% 5-yr survival
- T3b: 40–60% 5-yr survival
- T4: 0–20% 5-yr survival
- Node-positive RCC has 0–20% 5-yr survival
- For T4 tumors, the median time to recurrence is only 5–9 mo

COMPLICATIONS
- Surgical complications are bleeding, infection, injury to surrounding organs (live, spleen, bowel, pancreas). Urine leak in partial nephrectomy.
- Pulmonary embolism from tumor thrombus
- Advanced tumors can bleed spontaneously without causing flank pain or into the urine resulting in hematuria and/or fistula formation.
- Venous congestion resulting in bilateral lower-extremity edema, varicoceles, or portal HTN from tumor thrombus into the renal, caval, or hepatic venous system.

FOLLOW-UP

Patient Monitoring
- T3: Every 6 mo for 3 yr then annually for 5 yr. H+, P, comprehensive metabolic panel, LDH, chest and abdomen imaging at 2–6 mo then as indicated:
- T4: Every 3 mo history and physical exam, CTR, labs, every 6 mo abdominal CT for 3 yr

Patient Resources
- Kidney Cancer Association (www.kidneycancer.org)
- National Cancer Institute, Kidney Cancer (www.cancer.gov/cancertopics/types/kidney)

REFERENCES

ADDITIONAL TREATMENT
- Reduction in primary site.
- Additional therapies (eg, sunitinib, sorafenib, others) for downsizing the primary tumor and the IVC thrombus is controversial: 5–10%.
- Medullary carcinoma associated with sickle cell trait in young African Americans, is often advanced and metastatic at the time of diagnosis; death occurs within a few months of diagnosis.
- Sarcomatoid variants of all subtypes have been described and are associated with a worse prognosis.

DIFFERENTIAL DIAGNOSIS
- Hemangioma
- Wilms tumor (nephroblastoma)
- Urothelial carcinoma
- Oncocytoma
- Metastasis from other primary tumor
- Leiomoma
- Renal lymphoma
- Urachal carcinoma
- Wilms tumor (nephroblastoma)

PROGNOSIS
- Death usually occurs within a few months of diagnosis.
- Few patients with metastatic disease at presentation survive for more than 1 yr.
- None proven

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
- Birt–Hogg–Dubé Syndrome
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cell Carcinoma, Locally Advanced (T3–T4)
- Renal Cell Carcinoma, Metastatic (T4+)
- Renal Cell Carcinoma, Pediatric
- Renal Mass
- Reference Tables: TNM: Kidney Cancer

CODES
- ICD9: 198.0 Malignant neoplasm of kidney, except pelvis
- C64.1 Malignant neoplasm of right kidney, except pelvis
- C64.9 Malignant neoplasm of unsp kidney, except pelvis
- C19.89 Secondary malignant neoplasm of other specified sites

ICD10
- C64.1 Malignant neoplasm of right kidney, except renal pelvis
- C64.9 Malignant neoplasm of unsp kidney, except renal pelvis
- C19.89 Secondary malignant neoplasm of other specified sites

CLINICAL/SURGICAL PEARLS
- Detailed evaluation of extent of the disease is critical.
- Consult vascular and/or cardiovascular surgeon if needed.
RENTAL CELL CARCINOMA, METASTATIC (N+, M+)

Jiang Ling, MD
Wm. Kevin Kelly, DO

DIAGNOSIS

HISTORY
Usually no symptoms in early stage but incidental diagnosis of kidney mass. Metastasis may or may not cause symptoms.

Gross hematuria
Flank or abdominal pain
Symptoms related to involved organ(s)

Constitutional symptoms:
– Fatigue, weight loss, fever, or lower-extremity edema

PHYSICAL EXAM
With attention to abdominal mass, adenopathy, lower-extremity edema

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM

IMAGING

- MRI or CT of abdomen and pelvis (7th edition):
  • N1: Metastasis in regional lymph node(s)
  • N2: Metastasis via lymphatics
  • M1: Metastasis

LAB

- Complete metabolic panel
- CBC: Anemia of chronic disease in up to 30%
- Urinalysis: Hematuria
- Serum electrolytes
- Creatinine
- Ferritin
- Fibrinogen

DIFFERENTIAL DIAGNOSIS

- Renal masses:
  • Angiomyolipoma (fat-poor)
  • Collecting duct tumors
  • Cystic nephroma
  • Cysts (hemorrhagic, infected)
  • Focal/segmental glomerulosclerosis
  • Hemangioma
  • Inflammatory masses (xanthogranulomatous pylephlebitis, abscess)
  • Lymphoma
  • Metanephric adenoma
  • Metastasis from other primary tumor
  • Osteosarcoma
  • Pancreatic adenocarcinoma
  • RCC
  • Renal lymphoma
  • Renal medullary carcinoma
  • Sarcomas
  • Reninoma (phaeochromocytoma tumors)

- Urothelial carcinoma
- Wilms tumor (neuroblastoma)
- Lymphangiomyomatosis
- Inflammatory related to RCC
- RCC
- Infections/Inflammatory:
  • Granulomatous: TB, sarcoidosis, histoplasmosis, lymphangitis, Castleman disease, etc.
  • Non-Nongranulomatous: Viral, bacterial (if abscess in local area), sinus histiocytosis
  • Primary lymphatic malignancy: Lymphoma (non-Hodgkin and Hodgkin, others)
- Other metastatic malignancies:
  • Gastrinoma (Duodenal)
  • Carcinoid tumor, carcinoid syndrome, neuroendocrine tumors
  • Sarcomas
  • Renal medullary carcinoma
  • RCC
  • Oncocytoma
  • Metanephric adenoma
  • Inflammatory masses (xanthogranulomatous pyelonephritis, abscess, etc.)

GENERAL MEASURES

- Stage IV disease may also benefit from systemic therapy
- Minimal regional adenopathy does not preclude surgery
- Potential candidate for nephrectomy and/or surgical metastasectomy
- Reconstructive primary RCC and a solitary resectable metastasis
- A solitary recurrence after prolonged disease-free interval from nephrectomy
- Tends to be resistant to both traditional chemotherapy and radiation therapy

GENERAL PREVENTION

- Smoking cessation helps prevent primary tumor
Cytoreductive nephrectomy in patients with metastatic renal cancer is the mainstay of treatment; improve survival for M1
- Multifocal renal metastases (T1a) or mTOR inhibitors
- mTOR inhibitors or mTOR inhibitors
- Data for non-clear cell RCC therapy limited
- Combination therapies are being explored.

Cytoreductive surgery should be considered for M1 disease.

Other immunotherapy is under development

**mA**
- Strongly consider metastasectomy for amendable and isolated solitary metastasis (synchronous or metachronous).
- Metastasectomy should be performed in radiographically suspicious cases; however, ultimate role and benefit is yet to be defined.

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- Palliative role for osseous or CNS metastasis or pain control

**Additional Therapies**

- Many other agents under study and reported:
  - Non-gonadorelin agonistic: hemostatic cell transplantation
  - Interferon-γ, vaccines, other interleukins alone and in combination
  - Multiple studies under way addressing sequencing and combination of targeted therapies along with immunotherapy

**Complementary & Alternative Therapies**

- N/A

**ONGOING CARE**

**PROGNOSIS**

- 5 yr survival: Improving (7)
  - Stage I: 85–95%
  - Stage II: 50–70%
  - Improved survival with the following characteristics: Long interval between nephrectomy and the appearance of distant metastases, a single metastatic site, and the absence of intrarenal adenopathy

**COMPLICATIONS**

- Related to treatment:
  - High-dose IL-2: Vascular leak syndrome
  - TKIs: Fatigue, HTN, hand and foot syndrome, GI toxicity, hypothyroidism
  - mTOR inhibitors: fatigue, rash, hyperglycemia, dyslipidemia
  - Others related to disease progression

**FOLLOW-UP**

- Patient Monitoring:
  - Depends on stage of disease and treatment
  - Usually chest and abdominal imaging every 3–6 mo if not being treated
  - Imaging every 3–4 cycles if underactive systemic treatment
  - Serum chemistries and liver function tests as routine
  - Usually chest and abdominal imaging every 3–6 mo if not being treated
  - Imaging every 3–4 cycles if underactive systemic treatment
  - Serum chemistries and liver function tests as routine

**Patient Resources**

- Kidney Cancer Foundation
- National Cancer Institute
- American Society of Clinical Oncology
- American Society for Radiation Oncology

**REFERENCES**


**ADDITIONAL READING**

- NCCN Guidelines. Available at:https://www.nccn.org/prof/clinical.asp (Accessed August 20, 2014)

**CODES**

- ICD-10
  - C61.0 Malignant neoplasm of kidney, except pelvis
  - C61.2 Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes

**ICD-O**

- C104.0 Malignant neoplasm of kidney, except pelvis
- C61.2 Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes

**CLINICAL/SURGICAL PEARLS**

- Cytoreductive surgery should be considered for M1 disease.
- Only high-dose IL-2 provide durable complete response (CR).
- No targeted agents show significant complete response (CR).
- Patients achieving response with targeted agents such as TKI have a response duration of <8–10 mo (medium: ~12 mo) with continuous therapy treatment.
- Combination therapies are being explored.
RENAL CELL CARCINOMA, PEDIATRIC
Sarah M. Lambert, MD
Pasquale Casale, MD, FACS

BASICS
DESCRIPTION
Renal cell carcinoma (RCC) is a very rare tumor in childhood arising from the renal tubular epithelium.

EPIDEMIOLOGY
Incidence
• 2–4% of all pediatric renal tumors
• Only ~4 cases of pediatric RCC per year
• Estimated at <0.3% of all pediatric tumors
• Just over 350 cases reported in the literature
• Mean age of presentation between 8 and 10 yr vs. <3 yr for Wilms tumor
• Equal male:female

RISK FACTORS
• Von Hippel-Lindau syndrome
• Tuberous sclerosis

PATHOPHYSIOLOGY
• Thought to arise from renal tubular epithelium
• Most frequently papillary subtype with Xp11 translocation
• Lung and bone are the most common distant metastases

ASSOCIATED CONDITIONS
• Tubular sclerosis, chronic renal failure, nephrolithiasis, and tumor with chemotherapy
• Rarely associated with adult familial RCC

GENERAL PREVENTION
N/A

DIAGNOSIS

HISTORY
• Gross hematuria (~40%), flank pain, abdominal distension (2)
• Nausea, vomiting, malaise common
• Pain in up to 50%
• 30% found incidentally (2)

PHYSICAL EXAM
• Palpable abdominal mass (~40%) (2)
• Triad of hematuria, flank pain, and palpable mass found in ~6% of children (3)

DIAGNOSTIC TESTS & INTERPRETATION

Lab
• CBC: Polycythemia is rare
• Urinalysis: Hematuria found in ~40% of patients (3)
• Liver and renal function tests: Baseline prior to treatment

Imaging
• Abdominal x-ray may show tumor calcifications (~25%) vs. Wilms tumor (~5%) (3)
• US demonstrates solid or cystic renal mass
• CT or MRI with and without contrast reveal enhancing renal mass.
• Pediatric RCCs typically present as large, heterogeneous masses, commonly hemorhage and contain internal calcifications.
• IVP can demonstrate renal mass by displacement of the collecting system.
• Chest x-ray or chest CT scan for workup of metastatic disease.
• Radionuclide bone scan is indicated based on concern for mets.

Diagnostic Procedures/Surgery
• Biopsy is not indicated

Pathologic Findings
• Predominantly papillary histologic features in children vs. clear cell features in adults
• Pathologic staging based on modified Robson staging system
• Up to 25% pediatric RCC cannot be clearly classified due to atypical features
• Pathologic parameters typically associated with poor outcome in adults (metastasis/high tumor stage, high Fuhrman nuclear grade, angiolymphatic invasion, tumor necrosis), do not appear to have similar implications in pediatric patients

DIFFERENTIAL DIAGNOSIS
• Benign renal masses in children:
  – Choledochal cyst, intestinal duplication cyst
  – Congenital mesoblastic nephroma
  – Hydronephrosis
  – Mesoblastic cyst
  – Multilocular cystic renal tumor
  – Papillary kidney
  – Rhabdoid tumor
• Malignant renal masses in children:
  – Neuroblastoma
  – Lymphoma
  – Neuroblastoma
  – RCC
  – Rhabdomyosarcoma
  – Wilms tumor

TREATMENT

GENERAL MEASURES
Management is primarily surgical excision by either radical nephrectomy or partial nephrectomy.

MEDICATION
First Line
• The use of chemotherapy, immunotherapy, or tyrosine kinase inhibitors is not adequately described in pediatric population.
• The use of tyrosine kinase inhibitors should be considered in the pediatric patient with unresectable, metastatic, or advanced-stage RCC.
• Small series of patients treated with neoadjuvant chemotherapy according to Wilms tumor protocol.

Second Line
Surgery/Other Procedures
• Radical nephrectomy (4)
  – Removal of entire kidney and portion of the ureter
• Common approaches in children include flank and abdominal incisions
  – Wilms tumor
  – RCC
• Laparoscopic and robotic assisted radical or partial nephrectomy for RCC in children are described in select cases (6,7)

SURGICAL PROCEDURES
• Radical nephrectomy (4)
  – Removal of entire kidney and portion of the ureter
  – Common approaches in children include flank and abdominal incisions
• Partial nephrectomy (5)

408
ADDITIONAL TREATMENT

Radiation Therapy
Has been used for both initial treatment and recurrence but not well studied in pediatric populations.

Additional Therapies
- Adjuvant chemotherapy for metastatic disease has been tried in the pediatric population but not well characterized.
- Tensiop inhibitors have been used in children with metastatic disease but data are limited (9).

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Overall survival similar to adult RCC and depends on (Robson) stage:
  - Stage I (100%) and II (80%)
  - Stage III (75%), stage IV (15%) (2)

COMPLICATIONS
- Surgical complications (bleeding, infection, diaphragmatic bowel injury)
- Metastasis to lung and bone, multiple other sites

FOLLOW-UP

Patient Monitoring
- Adult protocols followed as there are no pediatric protocols.
- No long-term follow-up guidelines:
  - Physical exam, chest x-ray, chemistry panel, CBC, and urinalysis every 6 mo for 5 yr.
  - CT on yearly basis for 5 yr.
- Risk of chronic kidney disease likely attributed to reduced renal reserve capacity should be recognized and treated with nephrologic evaluation (8).

Patient Resources
National Cancer Institute http://www.cancer.gov/cancertopics/pdq/treatment/wilms/patient

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Neuroblastoma
- Reference Tables: TRM: Kidney Cancer
- Reference Tables: TRM: Kidney Cancer
- RCC, General
- RCC, Localized (T1, T2)
- RCC, Locally Advanced (T3–T4)
- RCC, Metastatic (N+, M+)
- Renal Mass
- Robson Staging System
- Translocation Renal Cell Carcinoma: Translocation Xp11.2
- Von Hippel–Lindau Disease/Syndrome
- Wilms Tumor

CODES

ICD9
- 189.0 Malignant neoplasm of kidney, except parotid
- 197.0 Secondary malignant neoplasm of lung
- 198.3 Secondary malignant neoplasm of bone and bone marrow

ICD10
- C64.9 Malignant neoplasm of unsp kidney, except renal pelvis
- C78.00 Secondary malignant neoplasm of unspecified lung
- C79.51 Secondary malignant neoplasm of unspecified bone

CLINICAL/SURGICAL PEARLS
The most common subtypes of RCC in children are the translocation-associated tumors, papillary RCC, renal medullary carcinomas, and oncocytic RCC.
RENAL COLIC

Scott G. Hubosky, MD

ASSOCIATED CONDITIONS
- Any process causing obstruction of the upper urinary tract
  - Ureteral stone
  - Ureteral stricture
  - Upper tract urethral neoplasm
  - Extrinsic urinary obstruction
  - Intrarenal urinary injury
- Urinary tract infection
  - Pyelonephritis
  - Renal abscess
- Recent urologic surgery
  - Obstructing blood clots from upper tract
  - Ureteral kink in poor position
  - Presence of poorly draining percutaneous nephrostomy tube
- Residual ureteral stone fragments after lithotripsy
- Miscellaneous
  - Renal artery embolus/infarction
  - Renal vein thrombosis

GENERAL PREVENTION
- Empiric advice for nephrolithiasis prevention
  - Adequate hydration
  - Enough fluid consumption to generate 2.5 L of urine output per day
  - Low-sodium diet
  - Daily sodium intake should be <2,500 mg
  - Diet rich in sodium result in hypercalciuria
  - About 82% of renal stones produced have calcium as a constituent
  - Normal calcium diet
  - Calcium intake should range between 800 and 1,200 mg/day
  - Vitamin D, supplements, and antacids should be considered

PHYSICAL EXAM
- General appearance is that of a restless patient unable to be still
- Usually unilateral flank pain with radiation to ipsilateral lower quadrant

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Serum creatinine/BUN and electrolytes
- Complete blood count
- Urinalysis
- Look for signs of blood or infection
- Urine culture

IMAGING
- CT scan of abdomen and pelvis without any contrast
  - Most sensitive way to detect urinary tract calculi (99% sensitivity to detect ureteral stones)
  - Relatively expensive and subjects patients to radiation exposure
  - Low-dose radiation dose protocol still gives 95% sensitivity for ureteral stone detection with 60% less radiation exposure
- CT urogram
- CT scan of abdomen/pelvis with IV contrast which is useful to expand diagnostic capability when no ureteral stones are found
- Can diagnose causes of colic not caused by stones such as UPJ obstructions or intraluminal filling defects such as neoplasms, fungus balls, or blood clots
- Renal/bladder ultrasound
  - No radiation exposureSafe in pregnancy and in pediatric patients
- Ask for double-void assessment of ureteral jets
- Presence of ureteral jets rules out complete ureteral obstruction (although partial obstruction may exist)
- Presence of ureteral jet may indicate obstruction of the renal pelvis
  - Relies on indirect evidence to diagnosis obstruction
  - May detect calicification along the expected course of the ureter
  - Not very sensitive for detecting small ureteral stones
- IVU or urogram
  - May detect calicification along the expected course of the ureter
- Not very sensitive or specific
- Benefits are low-radiation dose and is inexpensive

Diagnostic Procedure/Surgery
- Relief of obstruction may be necessary
  - Unilateral stent placement
  - Percutaneous nephrostomy
- Culture-specific antibiotics
  - If infection is present

Pathologic Findings
N/A

BASICS

DESCRIPTION
- Renal colic is a constellation of symptoms that usually accompanies upper urinary tract obstruction (UCO).
- Pain involving the flank and/or groin, with radiation to the ipsilateral scrotum or labia majora.
- Pain character is colicky with patients demonstrating a restless nature, unable to stay still.
- Pain is abrupt in onset and not associated with physical activity or positions.
- Nausea/vomiting
  - Simultaneously presents with flank pain but not in all cases
- Irritative or obstructive voiding complaints which are not present at baseline
- Urinary frequency, feeling of incomplete emptying, or hesitancy
- Hematuria
- Gross or microscopic
- Presence of hematuria strongly suggests underlying urologic etiology over gastrointestinal origin

EPIDEMIOLOGY

Incidence
- Renal colic accounts for about 1% of all emergency department visits (2,3,4) representing over 1 million cases per year.

Prevalence
- Renal colic caused by nephrolithiasis has an estimated prevalence of 6.5% in men and 4.1% in women over a study period of 1988–1994 (4,5).
- Presence or absence of ureteral jets
  - Presence of ureteral jets rules out complete ureteral obstruction (although partial obstruction may exist)
- Presence of ureteral jet may indicate obstruction of the renal pelvis
  - Relies on indirect evidence to diagnosis obstruction
  - May detect calicification along the expected course of the ureter
  - Not very sensitive for detecting small ureteral stones
- IVU or urogram
  - May detect calicification along the expected course of the ureter
  - Not very sensitive or specific
  - Benefits are low-radiation dose and is inexpensive

DIAGNOSTIC PROCEDURE/SURGERY
- Relief of obstruction may be necessary
  - Unilateral stent placement
  - Percutaneous nephrostomy
- Culture-specific antibiotics
  - If infection is present

Pathologic Findings
N/A

PHYSICAL EXAM
- General appearance is that of a restless patient unable to be still
- Usually unilateral flank pain with radiation to ipsilateral lower quadrant

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Serum creatinine/BUN and electrolytes
- Complete blood count
- Urinalysis
- Look for signs of blood or infection
- Urine culture

IMAGING
- CT scan of abdomen and pelvis without any contrast
  - Most sensitive way to detect urinary tract calculi (99% sensitivity to detect ureteral stones)
  - Relatively expensive and subjects patients to radiation exposure
  - Low-dose radiation dose protocol still gives 95% sensitivity for ureteral stone detection with 60% less radiation exposure
- CT urogram
- CT scan of abdomen/pelvis with IV contrast which is useful to expand diagnostic capability when no ureteral stones are found
- Can diagnose causes of colic not caused by stones such as UPJ obstructions or intraluminal filling defects such as neoplasms, fungus balls, or blood clots
- Renal/bladder ultrasound
  - No radiation exposureSafe in pregnancy and in pediatric patients
- Ask for double-void assessment of ureteral jets
- Presence of ureteral jets rules out complete ureteral obstruction (although partial obstruction may exist)
- Presence of ureteral jet may indicate obstruction of the renal pelvis
  - Relies on indirect evidence to diagnosis obstruction
  - May detect calicification along the expected course of the ureter
  - Not very sensitive for detecting small ureteral stones
- IVU or urogram
  - May detect calicification along the expected course of the ureter
  - Not very sensitive or specific
- Benefits are low-radiation dose and is inexpensive

Diagnostic Procedure/Surgery
- Relief of obstruction may be necessary
  - Unilateral stent placement
  - Percutaneous nephrostomy
- Culture-specific antibiotics
  - If infection is present

Pathologic Findings
N/A

BASICS

DESCRIPTION
- Renal colic is a constellation of symptoms that usually accompanies upper urinary tract obstruction (UCO).
- Pain:
  - Involves the flank and/or groin, with radiation to the ipsilateral scrotum or labia majora
  - Pain character is colicky with patients demonstrating a restless nature, unable to stay still
- Pain is abrupt in onset and not associated with physical activity or positions.
  - Nausea/vomiting
  - Simultaneously presents with flank pain but not in all cases.
- Irritative or obstructive voiding complaints which are not present at baseline
- Urinary frequency, feeling of incomplete emptying, or hesitancy
- Hematuria
  - Gross or microscopic
  - Presence of hematuria strongly suggests underlying urologic etiology over gastrointestinal origin

EPIDEMIOLOGY

Incidence
- Renal colic accounts for about 1% of all emergency department visits (2,3,4) representing over 1 million cases per year.

Prevalence
- Renal colic caused by nephrolithiasis has an estimated prevalence of 6.5% in men and 4.1% in women over a study period of 1988–1994 (4,5).

Risk Factors
- History of nephrolithiasis
- Recent urologic surgery
- History of ureteral stricture
- Pelvic radiation history

Genetics
N/A

Pathophysiology
- Presence of obstruction anywhere along the course of the ureter results in stretching of involuntary smooth muscle lining the ureter and renal pelvis.
- This stretching of the ureteral smooth muscle is exacerbated by baseline ureteral peristalsis.
- Stretching of hollow viscera, such as the ureter renal pelvis, is a well-known stimulus for pain as triated by the autonomic nervous system (TAN).
- The kidneys, proximal ureters, and stomach are all served by the colic plexus thus explaining why nausea and vomiting frequently accompany renal colic.

Diagnosis

History
- Sudden onset of colicky flank pain
  - May be associated with simultaneous nausea or vomiting
  - May have associated gross or microscopic
  - May have radiation to ipsilateral or scrotum/labia majora
- Pain is colicky and intermittent
- The location and characteristics of renal colic pain relating to urolithiasis (6):
  - Stones obstructing UPJ: Mild to severe deep flank pain relieved by fluid intake or voiding
  - Stones obstructing ureter: Abrupt, severe, colicky pain in the flank and/or ipsilateral lower abdomen
    - Radiation to testicles or labia
    - Intense nausea with or without vomiting
  - Ureteral stone: Radiate to flank or lumbar area
    - Intermittent: Radiate anteriorly and caudally
    - Distal ureteral stones: Radiate into groin or perineum
    - Midureteral calculi: Radiate anteriorly and caudally
  - Stones obstructing UPJ: Mild to severe deep flank pain relieved by fluid intake or voiding
  - Stones obstructing ureter: Abrupt, severe, colicky pain in the flank and/or ipsilateral lower abdomen
  - Radiation to testicles or labia
  - Intense nausea with or without vomiting

Diagnostic Procedures/Surgery

- Relief of obstruction may be necessary
  - Unilateral stent placement
  - Percutaneous nephrostomy
- Culture-specific antibiotics
  - If infection is present

Pathologic Findings
N/A
Differential Diagnosis
- Ureteral calculus
- Unilateral obstruction
- UPI obstruction
- Upper tract urothelial neoplasm
  - Upper tract urothelial carcinoma
  - Transitional cell papilloma
- Iatrogenic ureteral obstruction
  - Urinary leakage after nephrectomy or colon resection
  - Obstructing residual stone fragment after lithotripsy
  - Obstructing blood clots following upper tract urothelial resection procedure
- Upper urinary tract infection
  - Pyelonephritis
  - Pyonephrosis
  - Renal abscess
  - Obstructing fretty ball
- Renal vascular etiology
  - Renal artery embolic/luminal obstruction
  - Renal vein thrombosis

Treatment

General Measures
- Rule out sepsis
- Treat infection
- Control pain
- Alleviate obstruction, if present
- Treat infection, if present
- Rule out sepsis
- Treat infection
- Alleviate obstruction, if present
- Control pain
- Treat infection
- Rule out sepsis

Medication
First Line
- Analgesia based on degree of discomfort
  - Narcotic analgesics for more severe pain
    - Oxycodone/APAP
    - Morphine/PD of IV
  - Nonsteroidal anti-inflammatory drugs
    - Naproxen
    - IV acamprosate
  - Less distress and hypotension than morphine in one study
- Antimetics (metoclopramide, ondansetron)

Second Line
- a blockers: Tamsulosin, alfuzosin, silodosin
  - Given to relieve unilateral smooth muscle spasm
  - Only label use in cases of urethral stricture
  - Alfuzosin (30 mg)
  - Silodosin (8 mg/day)
  - Tamsulosin (start 0.4 mg to max 0.8 mg/day)

Surgery/Other Procedures
- Initial stone placement for significant obstruction
  - Lithotripsy for nephrolithiasis
  - Ureteroscopy with laser lithotripsy
  - ESWL (extracorporeal shock wave lithotripsy)
  - PCNL (Percutaneous nephrolithotomy)
- Ureteral stent placement for significant obstruction
  - Balloon dilation, laser incision
  - Open or laparoscopic resection
- UPJ obstruction
  - Ureteroscopy
  - Endopyelotomy (ureterohydropaly, ureterograft)
  - Ureteral stenting for severe obstruction
- Upper tract neoplasm
  - Nephroureterectomy (open or laparoscopic)

Additional Treatment
Radiation Therapy
- N/A

Additional Therapies
- Obtain adequate drainage if necessary, especially if patient appears septic.
- Internal stenting is usually a good 1st choice
- Chronic stricture patients often have significant ureteral tortuosity making retrograde access challenging
- Percutaneous drainage
  - Can be performed with conscious sedation
  - Optimal in cases of significant extrinsic ureteral compression

Complementary & Alternative Therapies
- N/A

Ongoing Care

Diagnosis
- Depends on underlying etiology but usually good once infection treated, if present

Complications
- Persistent obstruction if left untreated
- Renal cortical loss
- Can lead to nonfunctioning kidney
  - Venous infection

Follow-Up
Patient Monitoring
- Renal/bladder ultrasound after treatment to ensure no obstruction is relieved and infection treated, if present

Patient Resources
- Urology Foundation
- Urology Health Patient Resources

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Flank Pain, General
- Pyelonephritis
- Respiratory, Adult
- Renal Colic Image
- Urolithiasis, Adult
- Urolithiasis, General
**RENAL CYSTS (INTRARENAL, PERIPELVIC, AND PARAPELVIC)**

Jeffrey J. Tomaszewski, MD
Robert G. Uzzo, MD

**BASICS**

**DESCRIPTION**
- Renal cysts are fluid-filled renal structures not continuous with the nephron or collecting system
- **Simple cyst**
  - Arises from the renal parenchyma
  - Size varies, often < 2 cm but may be significantly larger
  - Typically asymptomatic, incidentally detected on CT or US
  - Can be single, multiple, and/or bilateral
  - If large, may impinge on the renal pelvis causing obstruction
  - Diagnostic US findings include a mass that is free of internal echoes (anechoic), through transmission with posterior acoustic enhancement
- **Complex cyst**
  - Features not consistent with simple cyst; raise the possibility of malignancy
  - Increased fluid density, internal thick-walled septations, thickened wall, mural projections into the lumen, calcifications, and contrast enhancement
- **Polycystic cysts are infected cysts**
- **Parapelvic cyst** (aka peripelvic, parapelvic lymphatic, parapelvic-cystic lymphangectasia, and renal sinus cysts) arise from the renal sinus

**ALERT**
Parapelvic cysts may be confused with hydroureteronephrosis-given their central location.
- **Acquired cyst**
  - Associated with chronic hemodialysis
  - Occasionally regress spontaneously
- **Boxniak classification used to classify cysts based on CT complexity and likelihood of malignancy**

**EPIDEMIOLOGY**

**Incidence**
- 0.2–2.2% from birth to 18 yr
- 20% by age 40
- 33% by age 60
- In autopsy series, 50% of patients ≥50 have ≥1 simple renal cysts
- Acquired cystic renal disease is more common among men
- Bilateral simple cysts infrequent <50 yr

**Prevalence**
- Age, a known risk factor for simple renal cysts
- Increasing age (7-fold increase from 4th–8th decade or an increased incidence from 5–38%)

**Risk factors**
- Polyposis kidney disease (autosomal dominant and recessive types)
- Hemodialysis
  - In ESRD, cysts in 8–13% prior to hemodialysis (HD)
  - 10–20% have acquired cystic renal disease after 3 yr of dialysis, 40–60% after 5 yr, and >90% after 10 yr

**Genetics**
- *ARPKD*: PKHD1 gene, chromosome 6, protein product fibrocystin
- *ADPKD*: PKD1 & PKD2 genes, chromosome 16, protein product polycystin-1, -2
- Other genetic cystic diseases: Juvenile nephronophthisis, medullary cystic kidney disease, glomerulocystic kidney disease, Von Hippel–Lindau syndrome (VHL), tuberous sclerosis, Birt–Hogg-Dubé syndrome

**PATHOPHYSIOLOGY**
- **Simple cyst**
  - Development of discrete fibrous sacs of clear fluid lined with cuboidal epithelium
  - Estimated growth rate: 2.18 mm/yr
  - Some will involute and disappear over time although most will not
  - It is controversial if renal cysts are causative agents of HTN
- **Parapelvic cysts**
  - Found on ~2% of kidneys at autopsy
  - Can be confused with hydroureteronephrosis

**ASSOCIATED CONDITIONS**
- **ADPKD** (Autosomal dominant polycystic kidney disease)
- **APKD** (Autosomal recessive polycystic kidney disease)
- **Birt-Hogg-Dubé syndrome**
- **ESRD** (End stage renal disease)
- **Tuberous sclerosis**: 20–25% of have renal angiomyolipomas
  - 20–25% of have renal cysts
  - **VHL disease**
    - Individuals develop cysts in multiple organs (kidney, pancreas, liver, epididymis)
    - Increased risk of clear cell renal cell carcinoma (RCC) in cyst wall

**DIAGNOSIS**

**GENERAL PREVENTION**
- Family members of patients with ADPKD and VHL should be screened

**HISTORY**
- Patients may present with an abdominal mass, pain, hematuria, or HTN but most are radiographically incidental
- Family member with polycystic kidney disease or other inherited cystic disease

**PHYSICAL EXAM**
- Abdominal/flank mass (narcotic)
- Often a benign exam

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urinalysis most often normal unless concurrent medical renal disease present
- Renal function tests—calculate eGFR and stage chronic kidney disease (CKD)

**Imaging**
- Ultrasound
  - Simple cyst
  - No internal echoes, distinct walls with defined margins, spherical shape with no internal echoes

**CT**
- Simple cyst
  - Have sharp walls with smooth margins, spherical shape, homogenous throughout

**MRI**
- Bosniak criteria can be applied to MRI (exception: Califications may not be well seen)
- Low signal T1, high signal T2 consistent with benign simple cyst
- Hyperdense cysts can be high signal on T1 and low on T2 but appearance depends on hemoglobin breakdown
- MRI may have a role in subsets of patients (VHL, multiple renal masses) if concern exists regarding excessive radiation due to multiple long-term imaging studies
- May be superior in characterization of internal cyst contents (blood, mucus)

**Bi- or triphasic CT represents the gold standard for distinguishing renal cysts**
- Discern between cysts and collecting system on excretory phase
- Particularly important in assessing hydronephrotic systems
- US may be misleading/difficult to interpret

**Bosniak classification system of cystic renal masses originally based on CT (image 1)**
- Category I: Benign simple cyst; thin wall without septa, calcifications, or solid components, water density, and no contrast enhancement; no further imaging needed
- Nearly all are benign
- Category II: Benign cysts with a thin thin-wall; the wall or septa may contain fine calcification, sharp margins, nonenhancing
- Category III: Wall thickened and may have thin septa or minimal smooth thickening of the septa or wall, which may contain calcification that may also be thick and nodular; no contrast enhancement, includes totally intrarenal nonenhancing complex lesions >3 cm
- These require follow-up (delayed by the F designation)
- 5–20% of Bosniak IIIIF cysts contain malignancy in wall
- Category IV: Indeterminate cysts with thickened irregular or smooth walls or septa; enhancement present
  - 40–60% of these are malignant (cystic RCC and multifocalized cystic RCC)
- Other class III lesions are benign (infected cysts and multifocalized cystic nephroma)
- Category V: Characteristics of category IV cysts plus they contain enhancing soft tissue components that are adjacent to and independent of the wall or septum
- Risk of malignancy is 85–100%
Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)

Diagnosis Procedures/Surgery
- Cyst aspiration is rarely negative; fluid reaccumulates. Infected cysts may require aspiration and catheter placement.
- Infected cysts often represent calyceal diverticula.
- Cyst biopsy is difficult and frequently results in inadequate tissue for pathologic examination.
- Cytologic evaluation of fluid for malignancy or culture based on indication and characteristics of the cyst.

Pathologic Findings
- Simple renal cyst
  - Single layer of cuboidal epithelium
- Not continuous with the collecting system

Differential Diagnosis (3)
- ADPKD (Autosomal dominant polycystic kidney disease)
- ARPKD (Autosomal recessive polycystic kidney disease)
- Cystic dysplasia (septate or cystic renal dysplasia)
- Hydroureter (hydronephrosis)
- Xanthogranulomatous pyelonephritis

ADPKD (Autosomal dominant polycystic kidney disease)

Polycystic Kidney Disease, Autosomal Recessive

Polycystic Kidney Disease, Autosomal Dominant

Multicystic Dysplastic Kidney

Juvenile Nephronophthisis

Hydronephrosis (parapelvic cysts)

Renal Abscess

Urolithiasis

Pararenal (retroperitoneal or adjacent mesenteric/liver/splenic/adrenal cyst)

Sclerosing Nephronophthisis

Cystic fibrosis

Medullary Sponge Kidney

Birt–Hogg–Dubé Syndrome

VHL Disease

Tuberous Sclerosis

Renal Mass

Renal Cell Carcinoma, General

Renal Mass

Tubulointerstitial disease

Clinical/Surgical Pearls

ADPKD

Cystic kidney disease

Bosniak cyst type malignancy risk:

Benign simple cysts demonstrate little risk of progressing to malignancy.

Boasniak classification and risk of malignancy:

- Boasniak I: No risk
- Boasniak II: 5–20% risk depending on imaging characteristics
- Boasniak III: 50% risk
- Boasniak IV: 75–90% risk

Complications

- Rupture and hemorrhage with simple renal cyst; usually associated with flank pain and hematuria
- Infected renal cyst
- ADPKD

ALERT

- Associated with cerebral berry aneurysms.
- In up to 40% of patients.
- 9% mortality (subarachnoid hemorrhage).

Follow-up

- Periodic imaging of Bosniak type IV cysts
- Multiple dysplastic kidney/VHL
- Periodic sonography to monitor for neoplastic changes

Patient Monitoring

- Cystic kidney disease

Patient Resources

RENAL DYSPLASIA, HYPODYSPLASIA, AND HYPOPLASIA
Kymora Scotland, MD, PhD
T. Ernesto Figueroa, MD, FAAP, FACS

DESCRIPTION
Renal dysplasia, hypoplasia, and hypodysplasia are forms of renal dysgenesis, namely, maldevelopment of kidney size, shape, or structure.

- **Renal dysplasia**: Clinically a histologic diagnosis based on the presence of primitive renal components (ie, ducts) and embryonic-mesenchymal cells (ie, cartilage).
  - **Classification of renal dysplasia**:
    - Total dysplasia: Involves both cortex and medulla; spectrum ranging from aplastic (small and solid) to multicystic (enlarged) kidneys (eg, Multicystic dysplastic kidney [MCDK]).
    - Subtotal dysplasia: Segmental distribution in cortex and medulla.
    - Hereditary: Zellweger and Meckel syndromes.
  - **Renal hypoplasia**: Small kidneys that have normal calyces and nephrons and are not dysplastic (1).
    - **Classification**:
      - With ureteral obstruction
      - Prune-belly syndrome
      - True oligonephronia
      - Oligomeganephronia
      - Normal ureteral orifice
      - Segmental (Ask-Upmark kidney)
  - **Renal hypodysplasia**: Small kidneys that have normal nephron density despite smaller size, shape, or structure.
    - **Classification**:
      - Normal ureteral orifice: With and without obstruction
      - Ectopic ureteral orifice: With or without ureteroceles
      - Medial or caudal
      - With ureteral obstruction
      - Prune-belly syndrome
  - **Retrorenal development** is dependent on the interaction between the ureteric bud and the metanephric mesenchyme.

EPIDEMIOLOGY
Incidence
- **Prevalence**
  - **Renal dysplasia**: Unilateral or bilateral in 2–4 per 1,000 births
    - Male > Female (1.9:1)
  - **Renal hypoplasia**: Unilateral or bilateral in 2–4 per 1,000 births
    - Male > Female (1.3:1)
  - **Renal hypodysplasia**: Underdeveloped medulla
    - Male > Female (1:2)
  - **Ask-Upmark kidney**
    - Male > Female (9:1)
    - Increased with low birth weight, often present by age 2
  - **Prune-belly kidney**
    - Male > Female (1:7)
    - Commonly present >10 yr of age

RISK FACTORS
- **Vesicoureteral reflux (VUR)**
- **Posterior urethral valves**
- **Urinary abnormalities**
  - Primary megaloureter, ureteropelvic junction obstruction (UPJO), ureteroureteral reflux
- **Prune-belly syndrome**

GENETICS
- A majority of dysplastic and hypoplastic kidneys disorders are sporadic and nonheritable.
- Genetic pathways can affect ureteric bud formation, branching morphogenesis within the metanephric blastema, and normal nephrogenesis.
- Familial renal dysplasia: Heterogeneous autosomal dominant inheritance of renal agenesis, renal dysplasia, MCDK, etc., within 1 family.

PATHOPHYSIOLOGY
- **Normal metanephric differentiation requires induction via the ureteric bud (1)**.
- The branching of the collecting system, as well as nephron formation, are determined by the ureteric bud.
- **Epicrural–mesenchymal interactions and peptide growth factors play a central role in nephrogenesis**.
- **Dysplasia**: Histologically manifests as distortion of renal architecture, immature or primitive glomeruli, cartilage, and tubules encircled by fibromuscular cells (primitive ducts).
  - **Ask-Upmark kidney**: Region of nonfunctioning parenchyma.
  - **Inhibition of nephron development**
  - **Increased TGF-β**
  - **5-sided bodies and cysts**
  - **Dedifferentiation of renal cells**
  - **Hypoplasia**: Normal nephron density despite smaller size, bilateral or unilateral can be associated with reflux.
  - **Oligomeganephronia**: Reduction in nephron number and hypertrophy of each nephron.
    - Usually bilateral, but contralateral renal agenesis has been reported
    - No direct obstruction between cortex and medulla; reduced number of renal segments, small renal artery, elongated nephrons
    - **Ask-Upmark kidney**
      - Likely secondary to reflux nephropathy
    - Deep grooves on lateral convexity with underlying tubules resembling thyroid tissue
    - **Underdeveloped medulla**
    - **Anterosclerosis and juxtamedullary hyperplasia**
    - **Hypoplasia**: Most often seen in conjunction with an ectopic ureteral orifice or obstruction; extent of dysplasia correlates with degree of ureteral ectopia.
      - **Normal ureteral orifice**:
        - With obstruction: Primary obstructive megaloureter and UPJO
      - **Without obstruction**: Dwarf kidney, according to bud theory is the result of deficient metanephric blastema

ASSOCIATED CONDITIONS
- **Branchio-oto-renal syndrome**
- **Ectopic ureteral orifice**
- **Fraser syndrome**
- **Jeune syndrome**
- **Kallmann syndrome**
- **Meckel–Gruber syndrome**
- **Oxal–facial–digital syndromes**
- **Posterior urethral valves**
- **Potter syndrome**
- **Primary obstructing megaloureter**
- **Prune-belly syndrome**
- **Pulmonary hypoplasia**
- **Renal cell carcinoma**
- **Simpson–Goldblatt–Beutler syndrome**
- **Treach–Renier syndrome**
- **Ureteropelvic junction obstruction (UPJO)**
- **Venous ureteral reflux (VUR)**
- **Zellweger syndrome**

GENERAL PREVENTION
- **FNA**

DIAGNOSIS
- **History**: Systemic• Failure to thrive, abnormal growth, headaches, fever, chills, shortness of breath, nausea, emesis, anorexia, skin pallor, vision change, mental status change
- **Renal**:• Polyuria, polydipsia, abdominal pain or mass, flank pain, hematuria
- **Bilateral disease**:• Lower urinary tract symptoms (LUTS), dysuria, nocturia, incontinence

PHYSICAL EXAM
- **Abnormal weight or height**
- **Vitiligo***Hyperpigmentative***
- **Mental status**: Encephalopathic
- **RENT**: Renal opacity, papillary edema, dehydration
- **Lungs**: Crackles
- **Abdomen**: Distention, palpable mass, guarding, C/O tenderness, ascites
- **Extremities**: Pallor, peripheral edema
DIFFERENTIAL DIAGNOSIS

Pathologic Findings
- Renal dysplasia and hypoplasia
- Renal vein thrombosis
- Simple cysts
- Sporadic glomerocystic kidney disease
- Tuberous sclerosis
- UPJO
- Von Hippel-Lindau disease
- Urolithiasis
- Wilms tumor

TREATMENT

GENERAL MEASURES
Consultation with nephrology and multimodality management.

MEDICATION
First Line
Antibiotics for UTI or as prophylaxis for VUR

Second Line
N/A

SURGERY/OTHER PROCEDURES
- Indications for nephrectomy: Pain, chronic infection, hypertension, or increasing size
- Pyeloplasty for UPJO
- Ureteral reimplantation: Reflux, primary megaureter
- Renal transplantation for end-stage renal disease
- Indications for nephrectomy: Pain, chronic infection, hypertension, or increasing size

ADDITIONAL TREATMENT
Perinatal or hemodialysis for ESRD

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
Varies with degree of renal insufficiency and degree of correlated conditions.

COMPlications
Renal failure, anemia, UTI, failure to thrive

PATIENT MONITORING
- BP and growth chart annually
- Electrolytes, Cr, BUN annually
- Urinalysis and urine culture as indicated
- Bilateral disease: Renal US annually
- MICT: Renal US every 2 yr to 3 yr for diagnosis

PATIENT RESOURCES

REFERENCES

ADDITIONAL READING

See Also
- Topic, Algorithm, Media
- Ask-Upmark kidney
- Chronic kidney disease, pediatric
- Prune belly (Eagle-Barrett or Triad) syndrome
- Renal agenesis (bilateral and unilateral)
- Renal dysplasia, Hypoplasia and Hypodysplasia
- Image Q
- Renal Malrotation
- VUR, Pediatric

ICD9
753.0 Renal agenesis and dysgenesis
753.15 Renal dysplasia
753.71 Prune belly syndrome

ICD10
- Q61.4 Renal dysplasia
- Q60.5 Renal hypoplasia, unspecified
- Q60.2 Renal agenesis, unspecified

CODES
- Q61.4 Renal dysplasia

CLINICAL/SURGICAL PEARLS

Prognosis varies; however, most patients have renal insufficiency and its sequelae.
RENAL ECTOPIA

Vani S. Menon, MD
Derek Matoka, MD

PATHOPHYSIOLOGY

Failure of ascent
- Anomalous vasculature impeding ascent; possibly and abnormally situated umbilical artery
- Thought to occur at the 4th–8th wk of gestation
- Normal kidney ascent to the level of L2 at the end of the 8th wk of gestation
- Abnormality of the ureteric bud or metanephric blastema

Fusion abnormalities occur early in embryogenesis
- Horseshoe kidney is the most common fusion anomaly
- Two renal moieties joined at lower pole in 90% of cases
- Anatomic considerations:
  - Orthotopically located adrenal gland
  - Ureter inserts into bladder in orthotopic position
  - Renal pelvis of ectopic kidney is usually anterior to the parenchyma secondary to malrotation
  - Failure of development of fascial layers in the flanks on the side not occupied by renal tissue
  - Malrotation of the ectopic kidney almost always occurs

ASSOCIATED CONDITIONS

- Recurrent urinary tract infections (UTIs)
- Nephrolithiasis
- Cloacal anomalies: 14% of these patients will have
- Genital anomalies: Estimated incidence between 20–66% of females will have uterine or vaginal ptosis of orthotopically located kidney
- Malrotated kidney
- Supernumerary kidney:
  - Usually caudad to orthotopic kidney

DIAGNOSIS

HISTORY
- UTIs (30%), vague abdominal pain or renal colic
- Incidentally during pre- or postnatal screening
- Abdominal mass, hypertension, hematuria, incontinence, renal insufficiency

PHYSICAL EXAM
- Usually normal
- May find abdominal mass or flank tenderness
- Genitourinary abnormalities

DIAGNOSTIC TESTS & INTERPRETATION

Imaging
- If kidney absent on ultrasound (US), radionuclide imaging should be performed to evaluate for an ectopic kidney
- Average differential function of ectopic kidney is 25% (1/C)
- Skeletal scintigraphy if moderate-to-severe pelvicalyceal dilation or progressive dilation found to evaluate for obstructive process
- Voiding cystourethrogram for mobile UTI and/or pelviccalyceal dilation
- If kidney is nonfunctional, computed tomography scan or abdominal US for localization
- Recent use of magnetic resonance urogram for small, poorly functioning kidneys can be utilized

Diagnosic Procedures/Surgery

Pathologic Findings

DIFFERENTIAL DIAGNOSIS
- Horseshoe kidney
- Malrotated kidney
- Supernumerary kidney:
  - Usually caudad to orthotopic kidney

RISK FACTORS

Potential relationship with maternal teratogenic exposure

Genetics

N/A

GENERAL PREVENTION

N/A
TREATMENT

GENERAL MEASURES
Specific treatment for renal ectopia itself is not indicated. However, special considerations for associated conditions may be necessary.

MEDICATION
First Line
Antibiotic prophylaxis for reflux based on clinical need

Second Line
N/A

SURGERY/OTHER PROCEDURES
- Nephrolithiasis
  – Shock-wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy (PCNL)
  – UP JO
    – <15% are due to an aberrant crossing vessel
    – Goal of management is to achieve dependent pelvic drainage
    – Dilated open or minimally invasive
      – Ureteropyelostomy
      – Endopyelotomy could be a consideration for failed pyeloplasty but is rarely indicated as the initial surgical intervention
    – Nephroureteral reflux
      – Open vs. endoscopic repair for clinically significant reflux

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Outcomes for treatment of nephrolithiasis and UPJO are comparable to management of these entities in the orthotopic-positioned kidney
- Current literature suggests no adverse effects on blood pressure or kidney function (4)
- No evidence for increased risk of malignancy

COMPLICATIONS
- Ureteral reflux
- Nephrolithiasis
  – Most likely due to urinary stasis
  – UPJO/UVJO
  – UTIs
  – Bowel in the region of the empty renal fossa
    – Traumatic injury to renal unit due to poor protection in ectopic location

FOLLOW-UP
Patient Monitoring
- Nephrolithiasis
  – Imaging by renal US and/or CT scans
  – VCUG and/or DMSA
  – Hydronephrosis
  – Renal US and/or nuclear scans
  – Yearly blood pressure measurements
  – Yearly BUN/Cr measurements

Patient Resources
- Urology Care Foundation: Ectopic Kidneys
  http://www.urologyhealth.org/urology/index.cfm?article=22

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
  - Horseshoe Kidney
  - Malrotated Kidney/Renal Malrotation
  - Renal Dysplasia, Hypodysplasia and Hypoplasia
  - Renal Ectopia Image 3
  - Renal Fusion Anomalies
    - UPJO
    - UTS, Complicated, Pediatric
    - Urolithiasis, Pediatric, General Considerations

CODES
- ICD9 753.3 Other specified anomalies of kidney
- ICD10 Q63.2 Ectopic kidney
  - Q63.1 Lobulated, fused and horseshoe kidney

CLINICAL/SURGICAL PEARLS
- Renal ectopia carries an increased risk of urologic abnormalities such as reflux, hydroureter, and genital abnormalities.
- Over half the cases of reflux occur in the orthotopic kidney.
- >30% of ectopic kidneys will have differential function of approximately 35%.
- An anterior renal pelvis and anomalous vasculature must be a consideration prior to surgical intervention.
- Surgical interventions for nephrolithiasis have similar success rates as for orthotopic kidneys.
RENAL FUSION ANOMALIES
Ross M. Decter, MD, FRCS
Paul H. Smith III, MD

BASICS

DESCRIPTION
- Renal fusion is a congenital condition in which the renal units are joined.
- Horseshoe kidney and crossed-fused ectopia are the most common variants.
- Horseshoe kidney:
  - Most common renal fusion anomaly
  - Poles of the kidney are fused by the isthmus
  - Fusion occurs at the lower poles in 95%
- Crossed-fused ectopia:
  - 2nd most common renal fusion anomaly
  - Kidney is on opposite side of where ureter inserts (uterus crosses midline)
  - The ectopic renal unit is fused to its companion in 90% of cases
  - Crossing from left to right is the most common morphotype

EPIDEMIOLOGY

Incidence
- Male >> female
- Horseshoe kidney occurs in 1 in every 400–500 live births
- Crossed-fused ectopia occurs in 1 in every 1,000–2,000 live births

Prevalence
- Horseshoe kidney: ~1:400–500
- Crossed-fused ectopia: ~1:3,000

RISK FACTORS
- Crossed-fused ectopia is frequently seen with vertebral anomalies such as myelomeningocele and sacral agenesis (1)
- Horseshoe kidney is present in 60% of female patients with Turner syndrome and 20% of patients with trisomy 18

Genetics
- Specific genetic causes unknown, but renal fusion anomalies commonly seen in association with a variety of chromosomal and congenital abnormalities (Turner syndrome, trisomy 18)

PATHOPHYSIOLOGY
- Metanephric blastema is the embryologic precursor to the adult kidney
- Development of the kidney begins in the 4th–5th wk with ingrowth of the ureteric bud, an outpouching of the metanephric duct, into the surrounding mesenchyme

- Proper renal development is coordinated through interactions between the metanephric blastema and ureteric bud
- The developing kidney ascends and rotates medially to reach its usual anatomic position by the 9th wk of gestation
- Several theories have been offered to explain crossed ectopia
  - One theory proposes that an abnormally oriented ureteric bud induces renal development in the contralateral mesonephric blastema
  - An alternate theory suggests that the developing kidney is channeled/displaced to the contralateral side during its ascent by the presence of an aberrant umbilical or common iliac artery or other pelvic structures
- The developing left and right metanephric blastemata are in close proximity to each other within the pelvis and, if abutting, may merge to form a horseshoe kidney or other fusion anomaly (2)

ASSOCIATED CONDITIONS
- Other congenital anomalies are present in up to a third of patients with horseshoe kidney
  - Skeletal, cardiovascular, neural tube, and anorectal anomalies are the most common
- Other GU anomalies associated with horseshoe kidney
  - Cryptorchidism or hypospadias in 4% of males

- Several theories have been offered to explain renal fusion anomalies
- Proper renal development is coordinated through interactions between the metanephric blastema and ureteric bud
- The developing kidney ascends and rotates medially to reach its usual anatomic position by the 9th wk of gestation
- Several theories have been offered to explain crossed ectopia
  - One theory proposes that an abnormally oriented ureteric bud induces renal development in the contralateral mesonephric blastema
  - An alternate theory suggests that the developing kidney is channeled/displaced to the contralateral side during its ascent by the presence of an aberrant umbilical or common iliac artery or other pelvic structures
- The developing left and right metanephric blastemata are in close proximity to each other within the pelvis and, if abutting, may merge to form a horseshoe kidney or other fusion anomaly (2)

ASSOCIATED CONDITIONS
- Other congenital anomalies are present in up to a third of patients with horseshoe kidney
  - Skeletal, cardiovascular, neural tube, and anorectal anomalies are the most common
- Other GU anomalies associated with horseshoe kidney
  - Cryptorchidism or hypospadias in 4% of males

- Several theories have been offered to explain renal fusion anomalies
- Proper renal development is coordinated through interactions between the metanephric blastema and ureteric bud
- The developing kidney ascends and rotates medially to reach its usual anatomic position by the 9th wk of gestation
- Several theories have been offered to explain crossed ectopia
  - One theory proposes that an abnormally oriented ureteric bud induces renal development in the contralateral mesonephric blastema
  - An alternate theory suggests that the developing kidney is channeled/displaced to the contralateral side during its ascent by the presence of an aberrant umbilical or common iliac artery or other pelvic structures
- The developing left and right metanephric blastemata are in close proximity to each other within the pelvis and, if abutting, may merge to form a horseshoe kidney or other fusion anomaly (2)

GENERAL PREVENTION
- Preventative measures aim to minimize risk factors for future renal deterioration
- Prophylactic antibiotics or surgical correction if VUR present
- Decompression of obstructed moieties (pyelostomy)

DIAGNOSIS

HISTORY
- Most are asymptomatic and are incidentally discovered
- May be diagnosed on prenatal ultrasonography
- Symptoms are usually the result of infection, stones, or obstruction of the abnormality positioned collecting system (UPJO)
  - Nonspecific abdominal pain, nausea, vomiting, hematuria

PHYSICAL EXAM
- Nontypical abdominal mass (hydronephrosis)

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Urinalysis (hematuria)
- Serum creatinine (elevated with obstruction)
- Complete blood count
- Serum calcium and phosphorus
- Metabolic evaluation for stone disease
- Renal function tests
- 24-hr urine collection
- Voiding cystourethrogram (VCUG): VUR present
- IVP: High incidence of VUR
- Diuretic renography (MAG3): Renal mass
- Serum electrolytes
- Serum alkaline phosphatase

IMAGING
- Renal US: Hydronephrosis
- VCUG
- Intravenous pyelography (IVP)
- Intravenous urography (IVU)
- Nephrosonography
- Diagnostic Procedures/Surgery
  - VCUG
- Nonspecific abdominal mass (hydronephrosis)
- Renal US

Pathologic Findings
- Wilms tumor in children and TCC in adults are more common in horseshoe kidneys
- Ureteric or renal carcinoma related to embryologic mechanisms, urinary stasis, or infection

DIFFERENTIAL DIAGNOSIS
- Renal mass
- Supernumerary kidney
- An accessory organ with its own blood supply and collecting system
- It may not be reniform, but possesses a distinct capsule surrounding a parenchymal mass
- Malpositioned kidney: Can look like a horseshoe kidney on radiographic imaging
RENAL FUSION ANOMALIES

TREATMENT

GENERAL MEASURES
No treatment if asymptomatic. Specific management dictated by complicating features.

MEDICATION

First Line
• Antibiotics: VUR treated the same as in those without fusion anomalies
• Antibiotic prophylaxis may be used until resolution for low-grade reflux

Second Line
N/A

SURGERY/OTHER PROCEDURES
• General operative considerations:
  – Horseshoe and ectopic kidneys often have abnormal and complex renal vasculature
  – Renal vessels may arise from the aorta, common iliac artery, or both, and typically enter the kidney anteriorly
• Angiography (including CT and MRI angiogram) may be useful to delineate renal vascular anatomy for operative planning
  – The renal pelvis and ureteropelvic junction of the horseshoe kidney often have an abnormal configuration, which can result in urinary stasis or obstruction. This anatomic abnormality contributes to the majority of the symptoms associated with horseshoe kidney, including stone formation, infection, hydronephrosis, and flank UPJO.
  – In the horseshoe kidney, the lower poles are joined by an isthmus, which is typically situated just caudal to the inferior mesenteric artery. The isthmus may be divided if necessary during nephrectomy.
• UPJO, best managed with dismembered pyeloplasty:
  – PCNL:
  – Endoscopic management of UPJO is feasible in the horseshoe kidney, including stone formation, infection, hydronephrosis, and flank UPJO.
  – Horseshoe and ectopic kidneys often have an abnormal configuration, which can result in urinary stasis or obstruction. This anatomic abnormality contributes to the majority of the symptoms associated with horseshoe kidney, including stone formation, infection, hydronephrosis, and flank UPJO.
  – The renal pelvis and ureteropelvic junction of the horseshoe kidney often have an abnormal configuration, which can result in urinary stasis or obstruction. This anatomic abnormality contributes to the majority of the symptoms associated with horseshoe kidney, including stone formation, infection, hydronephrosis, and flank UPJO.
  – In the horseshoe kidney, the lower poles are joined by an isthmus, which is typically situated just caudal to the inferior mesenteric artery. The isthmus may be divided if necessary during nephrectomy.
• Ureteroscopy:
  – ESWL:
  – It may be difficult to target stones for ESWL due to the abnormal location of the kidney. ESWL is most appropriate for stones <1.5 cm associated with undistorted collecting systems. Repeat treatments may be required in order to achieve a stone-free status (AIII).
  – Ureteroscopy:
  – Safe and effective approach for calculi associated with horseshoe or ectopic renal moieties; however, the smaller ureteroscopic instruments generally limit this approach to smaller stone burdens

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
Relatively poor due to complicating features. Outcomes comparable to those for anatomically normally positioned kidneys.

COMPLICATIONS
• Possible increased risk of malignancy
• UTR
• Urothelitis
• VUR

FOLLOW-UP

Patient Monitoring
Due to slight increase in incidence of Wilms tumor in children, some advocate imaging every 6 mo once the diagnosis is made

The abnormalities and conditions for crossed fused ectopia are similar to horseshoe kidneys, and treatment often follows similar lines.

Patient Resources

REFERENCES

ADDITIONAL READING
• See Also (Topic, Algorithm, Media)
  – Horseshoe Kidney
  – Malrotated Kidney/Renal Malrotation
  – Renal Ectopia
  – Renal Fusion Anomalies Image © Vesicoureteral Reflux, Pednatin

CODES

ICD9
Q63.1 Ectopic kidney
Q63.2 Ectopic renal arteries
Q63.3 Ectopic renal veins
Q63.4 Other specified anomalies of kidney

ICD10
R61.9 Other specified anomalies of kidney
R61.01 Lobulated, fused and horseshoe kidney
R61.02 Ectopic kidney
R61.1 Malrotated kidney
R61.2 Ectopic renal arteries
R61.3 Ectopic renal veins
R61.4 Other specified anomalies of kidney

CLINICAL/SURGICAL PEARLS

• Renal fusion anomalies often associated with other congenital anomalies
  – Ureteropelvic junction obstruction (UPJO) in up to 1/3 of patients with horseshoe kidney.
  – Renal vasculature usually abnormal.
  – Increased risk of urothelitis due to medical and anatomic abnormalities.

PEARLS

CLINICAL/SURGICAL PEARLS

• Renal fusion anomalies often associated with other congenital anomalies
  – Ureteropelvic junction obstruction (UPJO) in up to 1/3 of patients with horseshoe kidney.
  – Renal vasculature usually abnormal.
  – Increased risk of urothelitis due to medical and anatomic abnormalities.

CODES

ICD9
Q63.1 Ectopic kidney
Q63.2 Ectopic renal arteries
Q63.3 Ectopic renal veins
Q63.4 Other specified anomalies of kidney

ICD10
R61.9 Other specified anomalies of kidney
R61.01 Lobulated, fused and horseshoe kidney
R61.02 Ectopic kidney
R61.1 Malrotated kidney
R61.2 Ectopic renal arteries
R61.3 Ectopic renal veins
R61.4 Other specified anomalies of kidney

CLINICAL/SURGICAL PEARLS

• Renal fusion anomalies often associated with other congenital anomalies
  – Ureteropelvic junction obstruction (UPJO) in up to 1/3 of patients with horseshoe kidney.
  – Renal vasculature usually abnormal.
  – Increased risk of urothelitis due to medical and anatomic abnormalities.
RENAL INFARCTION
Matthew A. Meissner, MD
Ganesh V. Raj, MD, PhD, FACS

PATHOPHYSIOLOGY
- The main mechanism is embolization of the renal vasculature:
  - Clot emboli are the most common (~60%)
  - Atherosclerotic emboli
  - Vegetative emboli (endocarditis)
  - Fat emboli
- Renal arterial occlusion is more common on the left side, due to the more acute angle of the left renal artery with the aorta (1)
- Acute infarction due to trauma may show a hematoma in the vessel wall (intimal flap); infarction due to clot emboli will reveal a clot, blocking the renal artery or its branches (2)
- Renal vasoconstriction from sepsis, α-adrenergics, cocaine, others

ASSOCIATED CONDITIONS
- Anemias of the aorta or renal artery
- Angina
- Atrial fibrillation
- Claudication
- Collagen vascular disease (Ehlers–Danlos, collagen vascular disorders)
- Diabetes mellitus
- Endocarditis
- Hypertension
- Hypercoagulable states (factor V Leiden, protein C or S deficiency)
- Lupus
- Myocardial infarction
- Polyarteritis nodosa
- Pyelonephritis
- Renal artery aneurysm
- Renal artery or vein thrombosis
- Sickle cell disease
- Stroke
- Trauma
- Vascular disease

DIAGNOSIS

HISTORY
- A high suspicion is mandated in patients with underlying heart disease, hypertension, or diabetes
- Suspect a ventricular thrombus in patients with a recent myocardial infarction
- Acute flank pain: ~75%
- Nausea/vomiting: ~50%
- Gross hematuria may be seen

ALER
- The symptoms associated with acute renal infarction closely mimic those of an acute episode of urosepsis or pyelonephritis resulting in delayed diagnosis. This detrimentally impacts long-term renal function and potential for recovery.

BASICS

DESCRIPTION
- Renal infarction is a rare condition that occurs secondary to any process that interrupts or hinders blood flow to the kidney causing necrosis and cessation of function
- Most commonly caused by thromboembolic phenomenon in conditions such as atrial fibrillation
- Hypertension, valvular heart disease, infective endocarditis, bacterial endocarditis, cardiac mural thrombi

RISK FACTORS
- Acute tubular necrosis
- Antiphospholipid antibody syndrome
- Atherosclerosis
- A-fib
- Chagas disease
- Cocaine abuse
- Diabetes mellitus
- Endocarditis
- Hypertension
- Hypercoagulable states (factor V Leiden)
- Lupus
- Marfan syndrome
- Myocardial infarction
- Polyarteritis nodosa
- Pyelonephritis
- Renal artery aneurysm
- Renal artery thrombosis
- Renal artery stenosis
- Resting myocardial ischemia
- Sickle cell disease (papillary necrosis)
- Stroke
- Trauma
- Vascular disease

GENETICS
- Patients with inherited hypercoagulable disorders such as factor V Leiden mutation, protein C or S deficiency, lupus, antiphospholipid antibody syndrome, nephrotic syndrome, Ehlers–Danlos, and other collagen vascular disorders are at increased risk
- Familial history of coronary artery disease, diabetes, or metabolic syndrome portends an increased risk for these diseases, and consequently, renal infarction

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - Leukocytosis: 70% of patients
  - Elevated or normal hematocrit
  - Microscopic hematuria: 80% of patients
  - Proteinuria: 90% of patients
  - Elevated LDH: 100% of patients, if LDH is elevated with normal transaminases, this is highly suggestive of renal infarction in the presence of appropriate symptoms
  - Elevated AST: 83% of patients
  - Elevated ALT: 66% of patients
- Imaging:
  - The best study is abdominal CT with and without IV contrast
  - Classic CT findings of renal infarction:
    - Lack of IV contrast uptake in affected kidney
    - Areas of low attenuation secondary to local edema
    - Sharply demarcated, wedge-shaped area of decreased activity in affected kidney
    - Cortical rim sign: Perfusion to infarcted aspect of kidney
    - Elevated AST: 83% of patients
    - Elevated ALT: 66% of patients
- Physical exam:
  - Noncontrast CT, often obtained due to suspicion for renal calcit, will fail to show a renal infarct

Diagnostic Procedures/Surgery
- Ultrasonography will diagnose any renal vascular occlusion and allow for intervention
- ECG to diagnose arrhythmias
- Echocardiography for diagnosis of mural thrombosis and valvular vegetations
Pathologic Findings
- Acute histology demonstrates apoptosis of glomerular and renal tubal epithelial cells
- Chronic changes include necrosis and nuclear loss in glomerular and tubules

DIFFERENTIAL DIAGNOSIS
- Acute abdominal processes (acute mesenteric ischemia, appendicitis, bowel obstruction)
- Cystic renal disease
- Renal artery stenosis
- Renal calculus
- Renal tumor
- Renal vein thrombosis

TREATMENT
GENERAL MEASURES
- The optimal therapy for renal infarction is not clear
- Initial therapy includes supportive measures with IV fluids and pain control
- Since thromboembolic disease is the most common cause of renal infarction, primary anticoagulation is considered first line
- Other acute treatment options include thrombolysis, endovascular stenting, and thrombectomy

MEDICATION
First Line
- Antihypertensives to control hypertension
- Anticoagulation therapy
  - Hirudin: Start with a bolus of 80 U/kg followed by a continuous infusion titrated to a therapeutic aPTT
  - New oral anticoagulants
- Continue in patients with known causes of thromboembolic disease

Second Line
- Thromolytic therapy may be used, especially in unstable patients
  - Direct intravenous infusion to limit systemic side effects
  - Many contraindications: Cerebral malignancy or AVM, history of cerebrovascular disease, GI bleed, active hemorrhage, or active dissection

SURGERY/OTHER PROCEDURES
- Surgical intervention is not considered a primary treatment for thromboembolic renal infarction.
- Exceptions include:
  - Young patients diagnosed within 6 h of the infarct
  - Bilateral infarcts or infarcts in a solitary kidney
  - For traumatic injuries leading to renal infarction (avulsion of the renal pedicle), open surgical repair may be attempted during exploration for other injuries

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
Percutaneous angioplasty of the renal artery or thrombectomy

COMPLEMENTARY & ALTERNATIVE THERAPIES
N/A

ONGOING CARE

PROGNOSIS
- The duration of renal ischemia is the critical factor in determining prognosis
- Prognosis also depends on the cause of the infarct and the amount of parenchyma affected
- Patients often die of illness related to the concomitant medical conditions causing the infarct

COMPLICATIONS
- Chronic renal insufficiency
- Renal amyloidosis
- Hypertension

FOLLOW-UP
Patient Monitoring
- Regular blood pressure monitoring to assess for new-onset hypertension following infarct
- Follow-up imaging to monitor the progression or recession of an infarct
- Medical therapy for underlying condition that led to the infarct
- Monitoring of serum creatinine

Patient Resources
N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Flank Pain
- Renal Colic
- Renal Infarction Image
- Renal Trauma, Adult
- Renal Trauma, Pediatric
- Renal Artery Stenosis/Renovascular Hypertension
- Sickle Cell Disease, Urologic Considerations

ICD9
- 441.3 Atherosclerosis of renal artery
- 584.5 Acute kidney failure with lesion of tubular necrosis
- 593.81 Vascular disorders of kidney

ICD10
- N17.0 Acute kidney failure with lesion of tubular necrosis
- N35.3 Acute kidney failure with tubular necrosis
- N28.0 Ischemia and infarction of kidney

CLINICAL/SURGICAL PEARLS
- Renal infarction is most commonly due to thromboembolic disease from underlying medical conditions.
- Prompt diagnosis is paramount for preserving renal parenchyma and function.
- Signs and symptoms may mimic more common GU or intra-abdominal pathology.
- Renal infarction should be in the initial differential diagnosis of nephrolithiasis and pyelonephritis.
- Anticoagulation therapy is the primary form of treatment for renal infarction.
RENAL INFARCTION

BASICS

DESCRIPTION

- Most renal masses are benign or malignant, cystic (simple or complex) or solid, unilateral or bilateral, single or multifocal, primary or metastatic.
- Most common renal mass on imaging: Benign cysts (60–70%)
- Most common renal carcinoma (RCC) are now detected incidentally (up to 70%)
- Most common malignant renal mass in RCC (90%), ureteral (5–15%), and kidney (4–8%)
- Asymptomatic patients (CT screening for colon cancer) may have incidental renal masses (5% of time: 90% determined to be benign, 10% immediately following biopsy).
- Most common renal masses in children: Hemangioblastoma (a “pseudoaneurysm”), multicystic dysplastic kidney (MCKD), and Wilms tumor (WT).
- Anjajymphoma (AA) is most common benign renal tumor in children in addition to onychomatricoma.

EPIDEMIOLOGY

- RISK FACTORS:
  - Genetics:
    - TSC1/TSC2 (50:50), chromosome 16 & TSC same risk for RCC as general population based on other factors.
    - Folliculin (papillary type 2)—chromosome 1q42 (fumarate hydratase)
    - Chromophobe (7q31): familial leiomyomatosis
    - Hereditary papillary RCC (papillary type 1—chromosomal locus 6p12.2) expressed via Potter’s sequence: VH1 (75%); TSC, 60% (75% TSC gene loss next to FH1; medullary cystic kidney disease (MCDK) (chromosome 3p21), McCRD (chromosome 16q12).
  - WT: WT1 (11p13)/WT2 (11p15), tumor suppressor gene, associated with AMHR, Deny-Brock, Beckwith-Wiedemann (BW), mixed pentalogy dysplasia (MDM), retinoblastoma.

PATHOPHYSIOLOGY

- Renal cysts: Structural abnormalities in the nephron causing fluid to accumulate.
- WT encodes a zinc-finger transcription factor that is expressed in the kidney and gonads and is necessary for urogenital development and nephrogenesis. Considered tumor suppressor gene but only 20% of Wilms have identifiable WT1 mutation. Unidentified breastalna, epithelial, or stroma leads to cancer.
- VHL: HIF-1–mediated VEGF angiogenesis upregulated because normal VHL protein-mediated degradation of HIF-1 decreased due to mutation in VHL.
- AML: Component vessel does not have normal wall and prone to bleeding when mass size > 3 cm (prophylactic intervention at 3.4–4 cm).
  - RCC: Clear cell 80% (proliferal tubule), papillary 15% (proliferal tubule), chromophobe 5% (collecting duct), collecting duct carcinoma < 1%, medullary renal carcinoma < 1% (malignant cell).
  - Unreacted small renal masses (<2 cm), <4 cm, unreliable to metastatize (<1%) at 3 yr but size and growth rates are variable and not predictive.
  - RCC size at diagnosis can predict subsequent mets:
    - <3 cm, 0.2% (2–5 cm), 2% (5–7 cm), 7% (>7 cm), 20%.

ASSOCIATED CONDITIONS

- Kidney failure (APN), papillary RCC.
- Congenital diseases (Wilms, AMHR, TCC, BWS, BLS, Li–Fraumeni, Cowden syndrome).
- Von Hippel–Lindau (blue cell RCC).
- Cerebellar lesions (APNDS).
- Sickle cell disease (medullary RCC).
- Hereditary kidney polycystic (RCC).

GENERAL PREVENTION

- Early screening if genetic predisposition high.
- In VHL remove only tumors (>7 cm).
- Consider CT chest no contrast in patients at risk for RCC.

DIAGNOSIS

- Most RCC patients asymptomatic when imaging detected incidentally.
- Cough or bone pain (mets).
- Flank pain, hematuria (2 of RCC triad of flank pain/hematuria/mass).<10% of patients with RCC.

PHYSICAL EXAM

- Skin (VN: TSC adenoma sebaeum & 2nd leaf spot; schist and papules; finger & hair nail deformities).
- With BHD manifestations.
- Lung exam (BHD associated with pneumothorax).
- Neuraxial or Venenomeat bias (VHL): arterial and venous system.
- Renal mass (most of RCC, >10%), more common in Wilms tumor.
- Signs of comorbid conditions that will increase peri-op surgical risk (CVA, CAD, HTN, DM, COPD).
- Paraneoplastic signs:
  - Hypertension (RCC, and Pheo too).
  - Cachexia, weight loss (check albumin).
  - Hypothyroidism (also part of TSC & VHL).
- Signs of anemia.

DIAGNOSTIC TESTS & INTERPRETATION

- Lab:
  - Urine analysis: Hematuria keeps RCC, AML, AML in the differential diagnosis; nitrite and leukocyte esterase positive suggest infection (renal abscess, etc.)
  - Voided urine cytology: May detect TCC of urinary tract (not useful if “atypical”).
  - BUN & creatinine in RCC, renal function tests (BUN and creatinine).
  - Increased LFTs (Stauffer syndrome: Reversible hepatic dysfunction not due to liver mets).
  - Serum calcium: May be elevated in RCC secondary to parathyroid suppression.

- Imaging:
  - CT scan with and without contrast is gold standard for renal masses (10 Houndfield unit = 1 mm of tissue; enhancement = 80% neoplasms) (25–35 mSv effective radiation).
  - CT scan with above plus delayed excretory phase for upper tract neoplasms.
  - Bone scan CT classification (1 and 2 benign, no follow-up; 3F indeterminate, CT > 6 mm/malignant.
  - CIN risk at delayed nephrogenesis: 1 in 60.
  - CIN risk at follow-up: 0.6% if GFR < 30; 60 if GFR < 15; 75 if GFR < 10.
  - CIN risk for contrast-induced nephropathy (CIN) leading to dialysis if GFR < 30.
  - CIN risk increase if GFR < 30.
  - CIN risk increase if GFR < 15.
  - CIN risk increase if GFR < 10.

- Renal masses:
  - Bosniak CT classification (1 and 2: benign, no follow-up; 3F indeterminate, CT > 6 mm/malignant).
  - 3F: Malignant.
  - 4F: Malignant (surgical).

- Biopsy:
  - Staging CT classification.
  - CT whole abdomen.

- HYPOUSIA:
  - VT scan.

- Nephron sparing (ARN, BPH, VHL).
  - Patients on dialysis can get CT without need for immediate dialysis.
  - Consider CT chest no contrast in patients at risk for mets (CIR misses 10%).
Renal Carcinoma

Differential Diagnosis

Ref: 2012 EAU Guidelines; http://www.uroweb.org/guideline/10_Renal_Carcinoma_L.pdf

ICD10: C64.9 Malignant neoplasm of unsp kidney, except pelvis

ICD9: 189.0 Malignant neoplasm of kidney, except pelvis

Patient Monitoring

- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Resources

Kidney Cancer Association www.kidneycancer.org

Additional Reading


Renal Infarction

Renal Lesions Suspect for RCC are treated surgically (laparoscopically or open) usually with radical nephrectomy or partial nephrectomy (PNx). Phb use dependent on surgeon experience and location of tumor to hilar; most 3–4 cm (T1).

PNx decreases long-term risk of CVD mortality and ESRD vs. nephrectomy

Most recommended surgery for Borisak II (50% malignant) at IV cysts (>100%) TCC, of the renal pelvis; by endoscopic ablation for small superficial lesions (low-grade Ta), or radical nephronectectomy

Asymptomatic AML: 3.5 cm or small symptomatic lesions are treated by embolization, partial nephrectomy, or nephrectomy

Painful simple renal cysts and infertile cysts: Percutaneous aspiration and sclerotherapy

Although cytodiagnostic nephrectomy is debated in path-0–2,3A, FDA approval of TKI & mTOR inhibitors based on studies where almost half patients had received a nephrectomy

First Line

- Usually used for advanced mRCC
- Sunitinib or sunitinib – 5 Ph: 1st line in low/intermediate risk
- Temsirolimus: 1st line in high risk
- Pazopanib: 1st line and after cytokine failure

Second Line

- Stabilized: 2nd line after cytokine failure
- Everolimus: 2nd line after TKI

Additional Treatment

Radiation Therapy

- Radiation used in gynecologic tumors: Wilms stage 3–4, all clear cell and rhabdoid stages
- Metastatic RCC for aiv/CNS in adults

Additional Therapies

- RCC: Embolization prior to nephrectomy not beneficial but can be palliative for pain and/or bleeding if nonsurgical candidate
- Aldosterone (or radio frequency) of smaller renal masses (< 3 cm) may be considered in selected cases (elderly, poor surgical risk) (1)

Algorithms

- RCC, General Considerations
- Renal Cell Neoplasms
- Renal Mass, Algorithm
- RCC, Neoplasms
- Renal Mass, Algorithm
- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Monitoring

- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Resources

Kidney Cancer Association www.kidneycancer.org

REFERENCE


Additional Reading

- 2012 EAU Guidelines; http://www.uroweb.org/guideline/10_Renal_Carcinoma_L.pdf

See Also (Topic, Algorithm, Media)

- RCC, General Considerations
- Renal Cell Neoplasms
- Renal Mass, Algorithm
- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Monitoring

- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Resources

Kidney Cancer Association www.kidneycancer.org

REFERENCE


Additional Reading

- 2012 EAU Guidelines; http://www.uroweb.org/guideline/10_Renal_Carcinoma_L.pdf

See Also (Topic, Algorithm, Media)

- RCC, General Considerations
- Renal Cell Neoplasms
- Renal Mass, Algorithm
- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Monitoring

- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Resources

Kidney Cancer Association www.kidneycancer.org

REFERENCE


Additional Reading

- 2012 EAU Guidelines; http://www.uroweb.org/guideline/10_Renal_Carcinoma_L.pdf

See Also (Topic, Algorithm, Media)

- RCC, General Considerations
- Renal Cell Neoplasms
- Renal Mass, Algorithm
- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Monitoring

- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.

Patient Resources

Kidney Cancer Association www.kidneycancer.org

REFERENCE


Additional Reading

- 2012 EAU Guidelines; http://www.uroweb.org/guideline/10_Renal_Carcinoma_L.pdf

See Also (Topic, Algorithm, Media)

- RCC, General Considerations
- Renal Cell Neoplasms
- Renal Mass, Algorithm
- AML: Renal US every 6–12 mo
- Poor surgical candidate with STM imaging every 6 mo alternating with renal US and CT scan with yearly CBF or chest CT
- Stage 1–3 RCC, 20–30% relapse, lung most common (50–60%), median relapse 1–2 yr: evaluate every 6 mo for 2 yr, then annually.
- Stage 4: RCC flu dependent on primary treatment and provider dependent.
RENAL MASS, INTRAOPERATIVE CONSULTATION

Mark R. Anderson, MD, MSc
Anthony T. Corcoran, MD
Robert G. Uzzo, MD

BASICS

DESCRIPTION
• Most renal masses are incidentally found preoperatively on routine axial imaging (eg, CT or MR of the abdomen).
• Although rare today, some renal masses are now identified preoperatively.
  – Typically associated with trauma or urgent cases where preoperative imaging was either not done or inadequate for renal visualization

EPIDEMIOLOGY
Incidence
• Renal cell carcinoma (RCC) – 62,933 estimated new cases in 2014 (US data) – Primarily occurs in 6th or 7th decade – Male > female (3:2) – 4% of RCC are familial; majority are sporadic – 10–20% higher incidence in African Americans

Prevalence
N/A

RISK FACTORS
• RCC
  – Family history, smoking, obesity, hypertension, and end stage renal disease (ESRD)
  – Intraoperative renal mass consult, risk factors include:
    – Pre-existing nonrenal primary cancer
    – Positive metastatic lesion on kidney
    – Inheritable tumor syndrome
    – Associated renal tumor component
  – Renal insufficiency preventing use of contrast during imaging
  – Centrally located or small tumors initially missed on imaging

PATOPHYSIOLOGY
N/A

ASSOCIATED CONDITIONS
• Polycystic kidney disease
  – Autosomal dominant (autosomal dominant polycystic kidney disease) or recessive (autosomal recessive polycystic kidney disease)
  – Inheritable tumor syndromes with renal and extrarenal manifestations
  – von Hippel–Lindau (VHL) gene (17p11)
    – Cystadenoma, lung cysts, spontaneous pneumothorax, colonic polyps, or cancer
  – Hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC) gene, 1q42 (aka: Reed’s syndrome)
    – Uterine leiomyoma and leiomyosarcoma
  – Cystic fibrosis affects renal and extra renal manifestations
  – Hereditary hyperparathyroidism (parathyroid adenoma or parathyroid cancer)
    – Parathyroid hormone (PTH)
    – Fibrous dysplasia and mandibular and maxillary tumors
    – Uterine tumors
    – Papillary thyroid carcinoma with associated papillary renal neoplasm
    – Papillary thyroid cancer, nodular thyroid disease
    – Tuberculosis (TBC), TB43
  – Familial angiomyolipoma, subcutaneous fibroma, hypoglycemia and café au lait spots, cardiac rhabdomyoma, scoliosis, mental retardation, CNS tubers, lymphangiomyomatosis

  – VHL (VHL gene, 3p25)
    – Renal and CNS hemangioblastomas, pheochromocytoma, pancreatic cyst and endocrine tumor, endolymphatic sac tumor, epididymal and broad ligament cystadenomas

GENERAL PREVENTION
N/A

DIAGNOSIS

HISTORY
• Obtain history from operative team and review available medical and endocrine records
  – Prior or current cancers
  – Inheritable tumor syndromes
  – History of renal or abdominal trauma

PHYSICAL EXAM
• Intraoperative evaluation—location of mass
  – Check adrenal
  – Intravenous
  – Extrarenal within Gerota fascia
  – Percutaneous
  – Renal pelvis

DIAGNOSTIC TESTS & INTERPRETATION

Lab
  – Serum creatinine and eGFR

Imaging
• Review all preoperative ultrasound (US), contrast-enhanced CT, and/or MR if available
  – If serial images available, determine growth rate to help define risk (1.0)
  – Average yearly linear growth rate of 0.3 cm for all masses vs. 0.8 cm found in patients with progression
  – Masses with no growth under surveillance unlikely to metastasize

• Intraoperative US with color Doppler (use laparoscopic or finger probe in open surgery)
  – Features suggesting malignant pathology
    – Purely cystic lesions without septation can be observed
    – Renal lesions with solid elements
    – Color Doppler also useful to:
      – Assess flow to (splenolateral and contralateral kidney
      – Differentiate an isoechoic lesion with renal parenchyma since vessels are displaced around solid renal masses
      – Identifies deep vessels near the wall of the lesion that may be encountered during excision

DIAGNOSTIC PROCEDURES/SURGERY

ALERT
• Obtain all available information on renal function.
  – Calculate overall renal function (GFR— Cockcroft–Gault equation; calculators available online) and classify CKD status
  – Status of contralateral renal unit presence, flow, and function

GENERAL ALERT
• Renal function—can estimate percent functional volume preservation if partial nephrectomy planned as volume loss correlates well with ultimate renal function after partial nephrectomy (3%)

Renal biopsy and frozen section analysis
  – Obtain core biopsy with biopsy gun
  – ~20% of intraoperative frozen sections of renal lesions nondiagnostic (4)
  – Management options include active surveillance, ablation, or extirpation (Note: Renal biopsy and frozen section analysis yield poor tumor grade information)

DIAGNOSTIC PROCEDURES/SURGERY

Pathologic Findings
• Approximately 14% of incidentally found renal masses are benign depending on size (10)
  – 68% clear cell RCC
  – Positive association between tumor size and:
    – Rates of clear cell RCC
    – Appearance grade for clear cell RCC
    – Tumor stage

DIFFERENTIAL DIAGNOSIS

Lab
  – Blood glucose, electrolytes, calcium, creatinine, and/or eGFR

IMAGING
• Renal ultrasound
  – Assess for hydronephrosis, cystic lesions, or solid renal masses

DIAGNOSTIC PROCEDURES/SURGERY

ALERT
• Obtain all available information on renal function.
  – Calculate overall renal function (GFR— Cockcroft–Gault equation; calculators available online) and classify CKD status
  – Status of contralateral renal unit presence, flow, and function

DIAGNOSTIC PROCEDURES/SURGERY

Pathologic Findings
• Approximately 14% of incidentally found renal masses are benign depending on size (10)
  – 68% clear cell RCC
  – Positive association between tumor size and:
    – Rates of clear cell RCC
    – Appearance grade for clear cell RCC
    – Tumor stage

DIFFERENTIAL DIAGNOSIS

Lab
  – Blood glucose, electrolytes, calcium, creatinine, and/or eGFR

IMAGING
• Renal ultrasound
  – Assess for hydronephrosis, cystic lesions, or solid renal masses

DIAGNOSTIC PROCEDURES/SURGERY

ALERT
• Obtain all available information on renal function.
  – Calculate overall renal function (GFR— Cockcroft–Gault equation; calculators available online) and classify CKD status
  – Status of contralateral renal unit presence, flow, and function

DIAGNOSTIC PROCEDURES/SURGERY

Pathologic Findings
• Approximately 14% of incidentally found renal masses are benign depending on size (10)
  – 68% clear cell RCC
  – Positive association between tumor size and:
    – Rates of clear cell RCC
    – Appearance grade for clear cell RCC
    – Tumor stage
SURGERY/OTHER PROCEDURES

Avoid the following:
- If no films, and cannot postpone intervention,
- If unable to defer treatment—assess presence, function, and anatomy of both kidneys and consider biopsy
- Look at available films to see if pre-contrast post phases available
  - If preoperative imaging suggests a solid enhancing mass amenable to partial nephrectomy
  - Consider intraoperative biopsy and frozen section analysis
  - Reasonable to perform partial nephrectomy if no family discussion (if present)
  - Do not get fooled by hyperdense cyst or pseudotumor—can appear on CT
- If no films, and cannot postpone intervention, consider biopsy
- If solid elements with flow on Doppler US, normal consider biopsy
- If preoperative imaging suggests a solid, enhancing mass amenable to partial nephrectomy
- Do not get fooled by hyperdense cyst or pseudotumor—can appear on CT

Surgical approach
- ± Radical nephrectomy
- Partial nephrectomy
- Assume presence, flow, or function of contralateral kidney
- Perform a radical nephrectomy because technically easier
- Unless absolute indication for radical nephrectomy, then intervene
- Consider intraoperative biopsy and frozen section analysis
- Major complications, including urine leak, increase with increasing tumor complexity
  - Low complexity—4%
  - Moderate complexity—11%
  - High complexity—22%

FOLLOW-UP

Patient Monitoring
- NCCN guidelines (level of evidence 2B—lower level but consensus recommended)
  - Every 6 mo for 2 yr, then annually for 5 yr
  - History and physical exam
  - Comprehensive metabolic panel
  - At 2 yr as indicated based on recurrence risk
  - Chest and abdominal MRI pelvic imaging
- Risk-based follow-up clinical practice guidelines operationalized at www.cancermonograms.com

Patient Resources
N/A

REFERENCES

ADDITIONAL READING
- NCCN guidelines: http://www.nccn.org/
- See Also (Topic, Algorithm, Media)
  - Birt-Hogg-Dube Syndrome
  - Renal Cell Carcinoma, General
  - Renal Cell Carcinoma, Locally advanced (T3–T4)
  - Renal Cell Carcinoma, Metastatic (T5, M+)
  - Renal Cell Carcinoma, Pediatric
  - Renal Mass
  - Renal Mass, Intraoperative Consultation Algorithm
  - Renal Masses, Benign, WHO Classification
  - Von Hippel-Lindau Disease/Syndrome

TREATMENT

GENERAL MEASURES
- What to do if called to the operating room emergen-
  - If patient unstable and involved kidney unjured, defer to later date
  - If films unavailable, safely defer if possible

Extirpative procedures
- Avoid the following:
  - If no films, and cannot postpone intervention,
  - If unable to defer treatment—assess presence, function, and anatomy of both kidneys and consider biopsy
  - Look at available films to see if pre-contrast post phases available
  - If preoperative imaging suggests a solid enhancing mass amenable to partial nephrectomy
  - Consider intraoperative biopsy and frozen section analysis
  - Reasonable to perform partial nephrectomy if no family discussion (if present)
  - Do not get fooled by hyperdense cyst or pseudotumor—can appear on CT
- If no films, and cannot postpone intervention, consider biopsy
- If solid elements with flow on Doppler US, normal consider biopsy
- If preoperative imaging suggests a solid, enhancing mass amenable to partial nephrectomy
- Do not get fooled by hyperdense cyst or pseudotumor—can appear on CT

Surgical approach
- ± Radical nephrectomy
- Partial nephrectomy
- Assume presence, flow, or function of contralateral kidney
- Perform a radical nephrectomy because technically easier
- Unless absolute indication for radical nephrectomy, then intervene
- Consider intraoperative biopsy and frozen section analysis
- Major complications, including urine leak, increase with increasing tumor complexity
  - Low complexity—4%
  - Moderate complexity—11%
  - High complexity—22%

FOLLOW-UP

Patient Monitoring
- NCCN guidelines (level of evidence 2B—lower level but consensus recommended)
  - Every 6 mo for 2 yr, then annually for 5 yr
  - History and physical exam
  - Comprehensive metabolic panel
  - At 2 yr as indicated based on recurrence risk
  - Chest and abdominal MRI pelvic imaging
- Risk-based follow-up clinical practice guidelines operationalized at www.cancermonograms.com

Patient Resources
N/A

REFERENCES
**GENERAL PREVENTION**

No preventative strategies have been described. Relatives of those with genetic syndromes may be screened.

**ASSOCIATED CONDITIONS**

- Most usually sporadic
- BHD
- Autosomal dominant
- Mutation in gene for folliculin
- Renal tumors
- Chromophobe/oncocytoma
- Spontaneous pneumothorax, lung cysts
- Fibrofolliculomas, especially on face

**DIAGNOSTIC PROCEDURES/SURGERY**

- Percutaneous biopsy
- May be useful to include metastasis to kidney based on patient history
- May guide management of poor surgical candidates
- Pitfalls of biopsy
- Difficult to distinguish oncocytoma from chromophobe RCC
- Coexistence of RCC and oncocytoma in up to 10% cases

**DIAGNOSIS**

**HISTORY**

- Most patients asymptomatic
- Incidentally detected
- Gross hematuria/painful flank mass rare
- Family history of renal tumors, fibrofolliculomas, lung cysts/pneumothorax—rule out BHD

**PHYSICAL EXAM**

- No specific findings for sporadic oncocytoma
- Polypoid flank mass rare
- Dermatological exam if suspected BHD

**DIAGNOSTIC TESTS & INTERPRETATION**

- No lab test can identify renal tumor as oncocytoma
- Laboratory panel as with any newly diagnosed renal mass
- Cannot be used to reliably distinguish oncocytoma from RCC
- CT with and without IV contrast
- Usually not helpful in evaluation of renal mass
- MRI
- Resist enhancement of mass ± central scar
- May guide management of poor surgical candidates
- Cannot be used to reliably distinguish oncocytoma from RCC
- US
- Test of choice with IV contrast allergy, renal insufficiency
- Renal angiogram
- Test of choice with IV contrast allergy, renal insufficiency
- ROC for solid renal mass
- Central scar within mass often seen in oncocytoma, but this can be confused with necrosis, commonly seen with RCC
- Lab
- CBC, chemistry panel, LFTs
- Colloidial iron stain positive in chromophobe RCC but not oncocytoma
- Chromophobe RCC is aldesleukin, cytokeratin 7 positive
- CD82 and epithelial-related antigen (MOC31) may be helpful in the distinction between chromophobe RCC and renal oncocytoma
- Gene expression differences are being explored
- The World Health Organization (2004) renal tumor classification indicates renal oncocytomas are benign neoplasms. In the past some renal oncocytomas were classified as malignant.
- This may have resulted from confusion with clear cell renal carcinomas with eosinophilic component or due to eosinophilic chromophobe RCC (low metastatic potential)

**DIAGNOSIS**

**HISTORY**

- Most patients asymptomatic
- Incidentally detected
- Gross hematuria/painful flank mass rare
- Family history of renal tumors, fibrofolliculomas, lung cysts/pneumothorax—rule out BHD

**PHYSICAL EXAM**

- No specific findings for sporadic oncocytoma
- Polypoid flank mass rare
- Dermatologic exam if suspected BHD

**DIAGNOSTIC TESTS & INTERPRETATION**

- No lab test can identify renal tumor as oncocytoma
- Laboratory panel as with any newly diagnosed renal mass
- Cannot be used to reliably distinguish oncocytoma from RCC
- CT with and without IV contrast
- Usually not helpful in evaluation of renal mass
- MRI
- Resist enhancement of mass ± central scar
- May guide management of poor surgical candidates
- Lab
- CBC, chemistry panel, LFTs
- Colloidial iron stain positive in chromophobe RCC but not oncocytoma
- Chromophobe RCC is aldesleukin, cytokeratin 7 positive
- CD82 and epithelial-related antigen (MOC31) may be helpful in the distinction between chromophobe RCC and renal oncocytoma
- Gene expression differences are being explored
- The World Health Organization (2004) renal tumor classification indicates renal oncocytomas are benign neoplasms. In the past some renal oncocytomas were classified as malignant.
- This may have resulted from confusion with clear cell renal carcinomas with eosinophilic component or due to eosinophilic chromophobe RCC (low metastatic potential)

**DIAGNOSTIC TESTS & INTERPRETATION**

- No lab test can identify renal tumor as oncocytoma
- Laboratory panel as with any newly diagnosed renal mass
- Cannot be used to reliably distinguish oncocytoma from RCC
- CT with and without IV contrast
- Usually not helpful in evaluation of renal mass
- MRI
- Resist enhancement of mass ± central scar
- May guide management of poor surgical candidates
- Lab
- CBC, chemistry panel, LFTs
- Colloidial iron stain positive in chromophobe RCC but not oncocytoma
- Chromophobe RCC is aldesleukin, cytokeratin 7 positive
- CD82 and epithelial-related antigen (MOC31) may be helpful in the distinction between chromophobe RCC and renal oncocytoma
- Gene expression differences are being explored
- The World Health Organization (2004) renal tumor classification indicates renal oncocytomas are benign neoplasms. In the past some renal oncocytomas were classified as malignant.
- This may have resulted from confusion with clear cell renal carcinomas with eosinophilic component or due to eosinophilic chromophobe RCC (low metastatic potential)
Ongoing Care

**PROGNOSIS**

- Oncocytoma is uniformly considered a benign tumor and surgical removal is curative.
- Multiple series report no metastases or death from oncocyotma on long-term follow-up.
- Older, rare reports of metastasis may represent unrecognized, low-grade RCC (6,7).
- Risk of metachronous oncocytoma 4–6%.

**COMPLICATIONS**

- Pelvic and/or extrapelvic complications uncommon.
- Pelvis may be spared with partial nephrectomy whenever feasible based on size and location.
- Long-term surveillance required for partial nephrectomy.
- Chronic renal insufficiency/dialysis may be needed.

**FOLLOW-UP**

- Patient monitoring
  - Long-term surveillance of renal units for metachronous tumor development and coexistent RCC.
- Serum creatinine, urinalysis, chronic renal insufficiency/dialysis.

**PATIENT RESOURCES**

- Kidney Cancer Association
  - www.kidneycancer.org/
- Patient Monitoring
  - Recommended annually to semiannually.

**EXERCISES**

- Pelvic and/or extrapelvic complications uncommon.
- Pelvis may be spared with partial nephrectomy whenever feasible based on size and location.
- Long-term surveillance required for partial nephrectomy.
- Chronic renal insufficiency/dialysis may be needed.

**ADDITIONAL READING**


**REFERENCES**


**CODES**

ICD9

237.0 Benign neoplasm of kidney, except pelvis

ICD10

-D30.0 Benign neoplasm of unspecified kidney
-D30.1 Benign neoplasm of right kidney
-D30.2 Benign neoplasm of left kidney

**CLINICAL/SURGICAL PEARLS**

- Oncocytoma is a benign solid renal lesion.
- No imaging study reliably differentiates oncocytoma from RCC. The CT finding of a central scar, previously felt to be specific for oncocytoma, has been found with RCC, and this finding is not specific.
Sarcomas exhibit aggressive local growth with high rate of local recurrence, even in the event of negative surgical margins, due to a tendency for "skip lesions."
Primary renal sarcoma is extremely rare. Primary renal sarcoma (such as leiomyosarcoma or liposarcoma) with secondary renal invasion is the more common clinical presentation.

**TREATMENT**

**GENERAL MEASURES**
- In adults, the lesions are usually approached as for RCC, with surgical excision being 1st-line therapy, as the histology of lesion is rarely known preoperatively [38].
- Masses tend to be quite large, presumably due to rapid growth pattern.
- The primary treatment of renal sarcomas is surgical excision. Local recurrences should be resected when feasible.
- The role of adjuvant and neoadjuvant therapy in the adult population is poorly understood.

**MEDICATION**

**First Line**
- Doxorubicin and vincristine are used for more favorable stages of Wilms, with the addition of doxorubicin and abdominal radiation for more advanced stages.
- Doxorubicin, vincristine, and etoposide have been used with adult sarcomas; however, response rates at best are poor.

**Second Line**

**SURGERY/OTHER PROCEDURES**
- Mainstay of treatment for all sarcomas involving the kidney is radical nephrectomy with excision of entire tumor mass, which may require resection of adjacent organs. In some cases, partial nephrectomy may be possible [39].
- Wide excision is the preferred approach due to sarcoma’s tendencies toward skip lesions.
- Sarcomas tend to surround the renal vasculature as well as surrounding vascular structures.
- No defined role for lymphadenectomy.
- Preoperative chemotherapy is given in advanced cases of Wilms to downstage prior to surgery, usually with external radiation therapy. In bilateral disease, nephron sparing is indicated.

**ADDITIONAL TREATMENT**

**Radiation Therapy**
- Sometimes employed in management of Wilms tumor postoperatively. Radiation of the tumor bed is indicated if the tumor extended beyond the renal capsule to involve adjacent organs or lymph nodes.
- Radiation therapy after surgery in adult sarcomas may reduce local recurrences.

**Additional Therapies**
- N/A

**COMPLEMENTARY & ALTERNATIVE THERAPIES**
- N/A

**ONGOING CARE**

**PROGNOSIS**
- Adult sarcoma, especially high grade, have a generally poor prognosis, with 5-yr survival rates of approximately 50%.
- Poor prognostic variables include high-grade histology, metastases at presentation, large tumor size, and incomplete resection/margin positivity.
- Local recurrence alone is associated with a better survival rate than local recurrence with concomitant metastasis.
- Pediatric patients with Wilms tumors can expect a >90% cure rate, but prognosis for clear cell sarcoma and especially rhabdoid tumors is much worse.

**COMPLICATIONS**
- Children should be monitored for long-term effects of radiation and/or chemotherapy (such as cardiac dysfunction, HTN, secondary malignancies, endocrinologic abnormalities, and ovarian or testicular failure).

**FOLLOW-UP**
- Careful patient monitoring is essential due to the high recurrence rate.
- Adults: Close follow-up for 2–5 yr
  - CBC every 3–6 moths
  - Abdominal CT every 3–6 moths
  - No specific tumor markers to follow
- Children: Same as adults. Try to limit studies such as CT due to long-term ionizing radiation risks.

**Patient Resources**
- Kidney Cancer Association (www.kidneycancer.org/)

**ICD9**
- 171.5 Malignant neoplasm of connective and other soft tissue of abdomen
- 236.91 Neoplasm of uncertain behavior of kidney and ureter

**ICD10**
- D41.0 Neoplasm of uncertain behavior of kidney

**REFERENCES**
RENAL TRAUMA, ADULT
Lee C. Zhao, MD, MS
Allen F. Morey, MD, FACS

BASICS
DESCRIPTION
- Renal injuries can occur by either blunt or penetrating trauma
- Renal contusions, renal laceration, and renal vascular injury are the general categories
- Renal injury classification: Based on American Association for the Surgery of Trauma (AAST) renal injury grading system (1)
  - Grade I: Subcapsular hematoma
  - Grade II: Laceration < 1 cm deep into cortex, small hematoma with Gerota's fascia
  - Grade III: Laceration > 1 cm into medullary, no collecting system injury
  - Grade IV: Laceration into collecting system, vascular segmental vein or artery injury, renal pelvis laceration and/or complete ureteral pelvic disruption
  - Grade V: Main renal artery or vein injury or thrombosis
- Most commonly injured GU organ: Kidneys are well protected in the retroperitoneum.
- 1–3% of all traumatic injuries
- Renal injury classification: Based on American Association for the Surgery of Trauma (AAST) renal injury grading system (1)

ASSOCIATED CONDITIONS
- Rib fractures
- Injury to other organ systems

DIAGNOSIS
HISTORY
- Blunt trauma history:
  - Allergies
  - Medications
  - Past medical history
  - Last meal
  - Event
  - Contrast allergy, previous renal surgeries, stones, trauma, cancer

PHYSICAL EXAM
- Primary survey
- Tachycardia and hypotension suggest major bleeding
- Abdominal tenderness
- Flank contusion
- Medial/complex laceration

DIAGNOSTIC TESTS & INTERPRETATION
- Indications for imaging
- Basic labs: Hgb, Hct, Cr, electrolytes
- Urinalysis
- Imaging
- Clinical indicators of renal injury from
- Consider placement of ureteral stent for persistent urine extravasation

PATHOPHYSIOLOGY
- Kidneys are well protected in the retroperitoneum
- Deceleration can lead to intimal tearing of renal artery and thrombosis

ASSOCIATED CONDITIONS
- Rib fractures
- Injury to other organ systems

GENERAL PREVENTION
- General trauma preventative measures
- Injuries to other organs

DIFFERENTIAL DIAGNOSIS
- Spontaneous hematuria in patients with renal mass: Traumatic or atraumatic
- Spontaneous hematuria in patients with renal mass: Traumatic or atraumatic
- Nonoperative management: Blunt trauma
- Hemodynamically stable patients with well-staged renal injury may be managed nonoperatively
- 97% blunt renal injuries can be managed nonoperatively
- Nonoperative management: Blunt trauma
- Hemodynamically stable patients with well-staged renal injury may be managed nonoperatively
- Nonoperative management: Blunt trauma
- Monitor with serial Hct and imaging
- Contrast allergy, previous renal surgeries, stones, trauma, cancer
- Contrast allergy, previous renal surgeries, stones, trauma, cancer
- CT
- Contrast enhanced is best
- Delayed films to evaluate urine leak and collecting system
- Medial urine extravasation
- IV urography (IVP)
- While mostly replaced by CT scan, single shot intraoperative IVP when pre-op imaging is not available before abdominal exploration in the OR with a film under patient on OR table
- Monitor with serial Hct and imaging
- Contrast allergy, previous renal surgeries, stones, trauma, cancer

GENERAL MEASURES
- Nonoperative management: Blunt trauma
- Hemodynamically stable patients with well-staged renal injury may be managed nonoperatively
- Nonoperative management: Blunt trauma
- Monitor with serial Hct and imaging
- Consider angiography and embolization as alternative to renal exploration
- Large perinephric hematoma and extravasation of contrast predictive for need of angiographic embolization (SIE)
- Isolated renal injuries
- Most managed nonoperatively except for grade V pedicle avulsion
- Large perinephric hematoma and extravasation of contrast predictive for need of angiographic embolization (SIE)
- Isolated renal injuries
- Most managed nonoperatively except for grade V pedicle avulsion
- Consider placement of central device for persistent urine extravasation

Epidemiology
Incidence
- 1–3% of all traumatic injuries
- Most commonly injured GU organ

Prevalence
- Estimated 245,000 cases of traumatic renal injuries per year worldwide

RISK FACTORS
- Blunt trauma
  - Rapid deceleration
  - Motor vehicle
  - Falls
  - Direct strike to abdomen or flank (sports injury related, bicycle accident, pedestrian in motor vehicle accident [MVA])
- Penetrating trauma
  - Upper abdominal
  - Stab, gunshot, or industrial injury
  - iatrogenic injury
  - Laparoscopic, endourologic, renal biopsy, percutaneous procedures
Nonoperative management: Penetrating injury

- Broad-spectrum antibiotics for penetrating injury and blunt trauma with urinary extravasation or large retroperitoneal hematoma

MEDICATION

- Renal reconstruction
- Renal exploration: Transperitoneal approach

SURGERY/OTHER PROCEDURES

- Indications for operative management
  - Relative: Urine extravasation, urinoma, nonviable parenchyma, delayed diagnosis, segmental arterial pulsatile retroperitoneal hematoma
  - Absolute: Persistent bleeding, expanding and retroperitoneal hematoma
  - Nonviable tissue
  - Isolated urine extravasation can be managed nonoperatively with expectation of 90% resolution (4)

- Early isolation of vessels
- Nonoperative management of renal injuries.

- BST for continued hematuria
- Repeat CT scan
- Serial Hct
- Hypertension
- Hydronephrosis
- Calculus formation
- Sepsis
- Perinephric abscess
- Fistula
- Pseudoaneurysm

Patient Monitoring

- Bed rest for continued hematuria
- Repeat CT scan
- Serial Hct
- Hypertension
- Hydronephrosis
- Calculus formation
- Sepsis
- Perinephric abscess
- Fistula
- Pseudoaneurysm

Patient Resources

- Urology Care Foundation: Kidney (renal) Trauma

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Bladder Trauma
- Renal Trauma, Adult Algorithm
- Renal Trauma, Adult Images
- Renal Trauma, Pediatric
- Retroperitoneal Hematoma
- Uriner, Trauma
- Wunderlich Syndrome

CODES

ICD9

- 866.00 Injury to kidney without mention of open wound into cavity, unspecified injury
- 866.01 Injury to kidney without mention of open wound into cavity, hematoma without rupture of capsule
- 866.02 Injury to kidney without mention of open wound into cavity, laceration

ICD10

- S37.009A Unspecified injury of unspecified kidney, unspecified degree, initial encounter
- S37.019A Minor contusion of unspecified kidney, unspecified degree, initial encounter
- S37.029A Puncture of unspecified kidney, unspecified degree, initial encounter
- S37.039A Laceration of unspecified kidney, unspecified degree, initial encounter

CLINICAL/SURGICAL PEARLS

- CT with IV contrast is single best study.
- Most blunt renal trauma is managed nonoperatively.
- Angiembolization should be considered for stable patients with isolated renal laceration and renal vascular laceration.
- Renal vascular avulsions should be explored.
- Grade IV renal injuries may be substratified by additional findings of active vascular extravasation, perinephric hemATOMA, medial/complex laceration.
BASICS

DESCRIPTION

- Traumatic injury overall is the leading cause of childhood death in the United States.
- Pediatric renal trauma is subdivided into blunt and penetrating mechanisms of injury.
- The pediatric kidney is believed to be more susceptible to trauma vs. the adult kidney.
- Over the past 2 decades, the management of pediatric renal trauma has shifted from operative intervention to conservative management.

EPIDEMIOLOGY

Incidence
- 10–20% of all abdominal blunt trauma involves a renal injury.
- 60% of GU injuries are from blunt trauma.
- Nearly 90% of patients with GU injuries have coexisting injuries to the thorax, spine, pelvis, or intra-abdominal organs.

Prevalence
- N/A

RISK FACTORS

- Frequent GU abnormalities (ur, ureteropelvic junction obstruction horseshoe kidney vs. pelvic kidney).
- Injuries that are 5–10 times more common in pediatric patients undergoing CT for trauma.
- Classically presents with a history of hematuria disproportionate to the severity of trauma.

Decrease in physical renal protective mechanisms:
- Move pliable thoracic cage and weaker abdominal muscles.
- Less renal fat.
- Position of the kidney within the abdomen

Genetics

Disorders that lead to an increase in GU anomalies may have a greater risk for traumatic injury.

PATHOPHYSIOLOGY

- Tissue or organ injury from external source of energy.

- Grading system:
  - Grade I: Subcapsular hematoma, microscopic or gross hematuria, normal radiographic studies.
  - Grade II: Nonexpanding perirenal hematoma or cortical laceration (< 1 cm deep).
  - Grade III: Laceration – 1 cm in parenchyma without collecting system rupture or urine extravasation.
  - Grade IV: Parenchymal laceration through renal cortex, medulla, collecting system, contained main renal artery or vein hemorrhage.
  - Grade V (shattered kidney): Renal pedicle avulsion, multiple parenchymal lacerations, major injury to the renal vessels, urinary extravasation.

ASSOCIATED CONDITIONS

- Injury to other organ systems.

GENERAL PREVENTION

Measures that decrease traumatic injury in general, such as seat belts, air bags.

DIAGNOSIS

HISTORY

- Mechanism of Injury: Degree of actual traumatic injury may not correlate with the mechanism – Blunt trauma, automobile collision, sporting injuries, etc.
- Penetrating: Gunshot wound, stabwound, etc.
- Vital signs in the field:
  - Hypovolemia: Children will often have a normal BP despite a significant blood loss.
  - Up to 70% of children with grade 4 or higher renal injury may have neither gross nor microscopic hematuria.
- Medical history: Any acute or chronic medical conditions and any prior renal injury.
- Surgical history: Previous urologic procedure for reflux, stone, hypospadias, etc.
- Intra- or extravascular shunts.
- Position of consciousness.

PHYSICAL EXAM

- Vital signs and ABCD of resuscitation to stabilize patient.
- BP is often normal in severely hypovolemic children.
- Exposure: Observe for obvious signs of abdominal or thoracic trauma.
- DRE: Observe for perineal ecchymosis.
- Consider perineal ecchymosis.
- Loss of consciousness.

ALERT

- Degree of hematuria does not correlate with degree of injury.

DIAGNOSTIC TESTS & INTERPRETATION

- Lab:
  - CBC, basic metabolic profile, coagulation profile.
  - Urinalysis:
    - Unreliable in determining the extent of GU trauma.
    - Up to 70% of children with grade 4 renal trauma will have neither gross nor microscopic hematuria.
- Imaging:
  - Indications for radiographic imaging: All penetrating abdominal trauma or blunt trauma victims with 1 of the following criteria (1):
    - Significant deceleration or high-velocity injury: MVA, fall from > 15 ft.
    - Trauma resulting in fracture of the thoracic cage, spine, pelvis, or femur or bruising of the suprarenal.
    - Acute peritonitis.
    - Gross hematuria.
    - Microscopic hematuria (≥ 50 RBC/HFP) associated with shock: SBP < 90 mm Hg.
    - Delayed hemorrhage following renal trauma.

- CT:
  - Currently the most commonly used imaging modality in these patients.
  - Three-phase CT (abdomen and pelvis) ideal.
  - Clinically stable patients; most sensitive method for diagnosing and classifying GU trauma, precontrast phase, nephrographic phase after injection of contrast, and delayed images at 15–72 h.
  - Delayed hemorrhage following renal injury.
  - Follow-up images:
    - Three-phase CT. Clinically stable patients; allows for determination of renal perfusion and major renal fracture. This can be followed by a KUB to assess renal integrity.
  - Delayed CT: Obtained postoperatively after patient is stabilized or after patient is resuscitated in the ICU for full trauma evaluation; used to assess grade 3–5 renal injuries. 2–3 days post trauma to assess for baseline hematuria or urinoma.

  - Focused assessment with sonography for trauma (FAST):
    - Often combined with serial physical exams as a screening modality after blunt trauma.
    - Sensitivity ranges from 90–95% and specificity ranges from 93–100%; operator dependent.
  - Opinions vary with limited radiologic resources.
  - Angiography:
    - Used for diagnosis of arteriovenous fistula in the setting of delayed hemorrhage following renal trauma.
  - Retrograde pyelography:
    - Rule out presence of partial/traveling ureteral disruption.
    - Management of symptomatic urinoma with placement of ureteral stent.

  - Single-shot IVP:
    - Increasingly limited role.
    - Rarely used.
  - Contrast-enhanced CT:
    - Three-phase CT is indicated for patients with suspected renal injury.
    - Single-phase CT: Clinically unstable patients; allows for visualization of functioning contralateral kidney when considering unilateral nephrectomy.

  - DMSA scan:
    - Allows for quantification of renal function for grade 3–5 injuries; obtain at least 1 wk after blunt injury, also indicated.

  - Follow-up imaging:
    - Three-phase CT is indicated for patients with persistent fever, worsening flank pain, or gross hematuria > 72 h after injury.

Differential Diagnosis

Injury to other major abdominal organs in the setting of acute trauma.
TREATMENT

GENERAL MEASURES

- The major challenge facing the urologist in evaluating pediatric renal trauma is in determining when to surgically intervene. The decision to intervene operatively is based on clinical indicators: Hemodynamic stability, accurate radiographic staging, presence of associated organ injuries (2).

- In general:
  - Irrespective of the mechanism of injury and provided there are no absolute indications for abdominal exploration then all renal trauma can be observed.
  - Renal exploration and nephrostomy for grade III or higher renal injuries should be carried out if laparotomy is necessary for coexisting intra-abdominal injuries.
  - Renal exploration may be excluded in patients with concurrent intra-abdominal injuries if the urinary tract is separated from the anatomic tract by omentum or other tissue, and adequate drains are left in place.

- Renal injury classification: Based on American Association for the Surgery of Trauma (AAST) renal injury grading system (see “Renal Trauma, Adult”).

MEDICATION

First Line

- Broad-spectrum antibiotics for penetrating injury.

Second Line

- N/A

SURGERY/OTHER PROCEDURES

- Absolute indications for renal exploration:
  - Hemodynamically unstable from a renal source
  - Inability to stop persistent or delayed hemorrhage
  - Expanding or pulsatile retroperitoneal hematoma
  - Hemodynamic instability from a renal source

- Relative indications for renal exploration:
  - Known grade III or higher renal injury during blunt trauma with urinary extravasation or large retroperitoneal hematoma
  - Radiographic staging, presence of associated organ injuries (2).

- The decision to intervene operatively is based on three clinical indicators: Hemodynamic stability, accurate radiographic staging, presence of associated organ injuries (2).

- In general:
  - Irrespective of the mechanism of injury and provided there are no absolute indications for abdominal exploration then all renal trauma can be observed.
  - Renal exploration and nephrostomy for grade III or higher renal injuries should be carried out if laparotomy is necessary for coexisting intra-abdominal injuries.
  - Renal exploration may be excluded in patients with concurrent intra-abdominal injuries if the urinary tract is separated from the anatomic tract by omentum or other tissue, and adequate drains are left in place.

- Renal injury classification: Based on American Association for the Surgery of Trauma (AAST) renal injury grading system (see “Renal Trauma, Adult”).

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

N/A

PEARLS

- N/A

CODES

ICD9

- 866.00 Injury to kidney without mention of open wound
- 866.01 Injury to kidney without mention of open wound
- 866.02 Injury to kidney without mention of open wound

ICD10

- S37.039A Laceration of unsp kidney, unspecified
- S37.019A Minor contusion of unspecified kidney,
- S37.009A Unspecified injury of unspecified kidney,
- 866.02 Injury to kidney without mention of open wound

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Bladder Trauma
- Renal Trauma, Adult
- Renal Trauma, Adult Algorithm
- Renal Trauma, Adult Images
- Retroperitoneal Hematoma
- Urinary, Trauma
- Wunderlich Syndrome

ONGOING CARE

PROGNOSIS

- Based on the overall renal function following the traumatic injury
  - Renal vascular HTN
  - Usually develops within 36 mo after injury
  - DMSA scan is indicated to determine differential renal function
  - CT angiogram may be necessary to rule out arteriovenous fistula as the source of HTN
  - End stage renal disease
  - Bilateral renal injury
  - May require peritoneal or hemodialysis

FOLLOW-UP

Patient Monitoring

- Repeat CT of the kidney 2–3 days after trauma for grade III or higher renal injuries
- Repeat CT if patient has decreasing hemoglobin/HCT despite blood transfusion or if fistula is hemodynamically unstable
- Ambulation should resume when gross hematuria resolves.
- Strenuous physical activity should be avoided for 6 wk.

- N/A

- N/A

- N/A

433

CLINICAL/SURGICAL

PEARLS

- Hemodynamically stable patients can be managed conservatively.
Renal Tubular Acidosis

Steve Dong, MD

**BASICS**

**DESCRIPTION**

- Renal tubular acidosis (RTA) is a metabolic condition characterized by abnormal urinary acidification due to a defect in renal tubules, resulting in hyperchloremic non-anion gap metabolic acidosis, increased pH of the urine.
- 4 major types of RTA are now considered to be only 3:  
  - Type I (distal): Defective distal tubular H+ secretion  
  - Type II (proximal): Defective proximal tubular bicarbonate reabsorption  
  - Type III (mixed): No longer considered as a distinct entity  
  - Type IV: Aldosterone deficiency/resistance

**EPIDEMIOLOGY**

- Most RTAs are sporadic occurring at any age. Familial RTA are rare and usually occurs in childhood.
- RTA II: Usually more predominant in males
- RTA I: More common in adults (2/3 adults; 1/3 children) and women; endemic in certain regions of Thailand
- Acquired RTA type IV:
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Lupus nephropathy
  - Hypertension
  - Diabetic nephropathy
  - Addison disease
  - Interstitial renal disease:
    - Fanconi syndrome due to toxin-related or hereditary tubular defects
    - Osteomalacia
    - Nephrolithiasis
    - Nephrocalcinosis

**ASSOCIATED CONDITIONS**

- Acquired RTA type I:  
  - Autoimmune disease: Systemic lupus erythematosus (SLE), Sjögren syndrome, primary biliary cirrhosis, chronic active hepatitis  
  - Chronic pyelonephritis
  - Diabetes mellitus
  - Hypothyroidism

- Acquired RTA type II:  
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Tubulointerstitial nephritis and interstitial fibrosis
  - Gordon syndrome
  - Sickle cell nephropathy
  - Diabetic nephropathy

**DIAGNOSIS**

**HISTORY**

- Failure to thrive, rickets, and osteomalacia in children
  - Anorexia, nausea, vomiting
  - Weakness and polyuria due to potassium loss
  - Constipation
  - Polydipsia
  - History of hematuria, urinary tract infections (UTIs), passage of stones in urine
  - History of recurrent, familial, or childhood renal stone disease
  - Ask about systemic diseases causing RTA

**PHYSICAL EXAM**

- Urologic exam of genitalia, suprapubic area for swelling and tenderness
- Exam for osteomalacia, hypokalemic muscle weakness, and growth retardation
- Exam for other systemic diseases

**DIAGNOSTIC TESTS & INTERPRETATION**

- Urine pH (fasting, under 6, pH water):  
  - pH < 5.5: Complete type I RTA  
  - pH > 5.5, but systemic acidosis mild or absent: Ammonium chloride loading test and measure urinary bicarbonates; failure of urine pH to go below 5.5 is diagnostic of RTA type III

- RTA II is diagnosed by bicarbonate loading test:
  - After IV bicarbonate infusion, fractional excretion of bicarbonate may be less than 15%.

**PATHOPHYSIOLOGY**

- Type I (distal) tubular acidosis: Secondary to impaired ability to secrete hydrogen ions into the distal tubule or collecting duct. Urine pH may be < 5.5.
- Type II (proximal) tubular acidosis: Impaired bicarbonate absorption in the proximal tubule. Urine pH may be < 5.5.
- Type IV: Presence of aldosterone resistance or deficiency leading to hyperkalemia (not seen in type I and II) along with acidosis. Urine pH may be < 5.5.

**GENERAL PREVENTION**

**RISK FACTORS**

- Genetic disorders
- Secondary to systemic disease. See “Commonly Associated Conditions.”

**GENETICS**

- Familial RTA I (1):  
  - Autosomal dominant (AD) form is associated with mutation in the vacuolar H+ATPase (V-ATPase) gene and associated with sensorineural deafness
  - Familial RTA II: Associated with pseudohypoaldosteronism type I

- Familial RTA III:  
  - Autosomal recessive (AR) form is due to a mutation in the B1 or H+ATPase (V-ATPase) gene and associated with sensorineural deafness
  - Autosomal dominant (AD) form is associated with cerebral calcification

- Familial RTA IV: Associated with pseudohypoaldosteronism type I

- Acquired RTA type I:
  - Autoimmune disease: Systemic lupus erythematosus (SLE), Sjögren syndrome, primary biliary cirrhosis, chronic active hepatitis
  - Chronic pyelonephritis
  - Diabetes mellitus
  - Hypothyroidism

- Acquired RTA type II:
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Tubulointerstitial nephritis and interstitial fibrosis
  - Gordon syndrome
  - Sickle cell nephropathy

- Acquired RTA type III:
  - Fanconi syndrome due to toxin-related or hereditary tubular defects
  - Osteomalacia
  - Nephrolithiasis
  - Nephrocalcinosis

- Acquired RTA type IV:
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Tubulointerstitial nephritis and interstitial fibrosis

- Acquired RTA type V:
  - Sickle cell nephropathy

**ASSOCIATED CONDITIONS**

- Acquired RTA type I:  
  - Autoimmune disease: Systemic lupus erythematosus (SLE), Sjögren syndrome, primary biliary cirrhosis, chronic active hepatitis
  - Chronic pyelonephritis
  - Diabetes mellitus
  - Hypothyroidism

- Acquired RTA type II:  
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Tubulointerstitial nephritis and interstitial fibrosis
  - Gordon syndrome
  - Sickle cell nephropathy

- Acquired RTA type III:  
  - Fanconi syndrome due to toxin-related or hereditary tubular defects
  - Osteomalacia
  - Nephrolithiasis
  - Nephrocalcinosis

- Acquired RTA type IV:  
  - Tubulointerstitial nephropathies
  - Obstructive nephropathy
  - Tubulointerstitial nephritis and interstitial fibrosis
  - Gordon syndrome
  - Sickle cell nephropathy

- Acquired RTA type V:  
  - Sickle cell nephropathy

**PATHOLOGIC FINDINGS**

- Nephrolithiasis
- Nephrocalcinosis
- Osteomalacia

**IMAGING**

- Plain x-ray and computed tomography (CT) urogram:
  - Likely to demonstrate nephrocalcinosis and nephrolithiasis
DIFFERENTIAL DIAGNOSIS
- Other causes of metabolic acidosis (215C)
  - Lactic and ketoadidosis, chronic renal failure, chronic diarrhea, etc.
- Azotemia
- Bilateral stones
- Calcium phosphate stones
- Chronic pyelonephritis
- Hypochloremia < 0.5 mmol/L
- Hypokalemia
- Medullary nephrocalcinosis
- Medullary sponge kidney
- Recurrent stones: >2yr

TREATMENT
GENERAL MEASURES
- Identifiable causes, such as obstructive uropathy or drug-induced RTA, should be corrected or eliminated
- If there is no identifiable etiology, then direct treatment to correction of acidosis

MEDICATION
First Line
- Alkali therapy decreases stone formation and growth, prevents nephrocalcinosis, normalizes growth retardation in children, and corrects hypokalemia in most cases.
- Oral alkali therapy: In both type I and type II RTA with the goal of treatment to restore urinary citrate to high-normal levels, and not simply correct the metabolic acidosis (315C).
  - Sodium bicarbonate (17.7 mmol/L)
  - Bictra (1 mmol Na, 1 mmol citrate)
  - Polytra (1 mmol Na, 1 mmol K, 2 mmol citrate)
  - Type II RTA generally requires lifelong treatment:
    - 1–4 mmol/g of oral bicarbonate or citrate in 2–3 divided doses in adults (405C)
    - May require potassium supplementation for hypokalemia
  - Type II (proximal) RTA:
    - 5–20 mmol/g in 4–6 doses due to the severe bicarbonate wasting.
    - Adults with bicarbonate levels > 10 mmol/L and no evidence of bone disease may not require treatment.
    - Supplemental potassium, calcium, vitamin D, and phosphate may become necessary.
  - Type IV (proximal) RTA: directed toward correction of hypokalemia rather than acidosis
    - Dietary potassium restriction
    - Thiazide or loop diuretics
    - Mineralocorticoid replacement in cases of adrenal disease or hyporeninemia (Hydrocortisone 0.1 mg/d)

Second Line
FKA

SURGERY/OTHER PROCEDURES
- Management of stone by shock wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, and rarely, open surgery
- Management of obstructive uropathy

ADDITIONAL TREATMENT
Radiation Therapy
FKA

Additional Therapies
FKA

COMPLEMENTARY & ALTERNATIVE THERAPIES
FKA

ONGOING CARE

PROGNOSIS
- Primary RTAs: Although a permanent disease, prognosis is excellent if diagnosis and treatment initiated early.
- Prognosis of other RTAs depends on associated disease

COMPLICATIONS
- Hypercalciuria
- Hyperkalemia or hypokalemia
- Nephrocalcinosis
- Nephrolithiasis
- Osteomalacia/osteoporosis

FOLLOW-UP

Patient Monitoring
- Spot urine testing for NAG (<0.05 mmol/g of creatinine in adults).
- Spot urine calcium and citrate.
- Monitoring of serum ions and growth curves in children.
- Weekly monitoring of serum ions in adults.

Patient Resources
- National Kidney and Urologic Diseases Information Clearinghouse (NIDDK) http://kidney.nih.gov/koaidney/Pub/TubularAcidosis

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Calcium, Renal
- Fanconi Syndrome
- Nephrocalcinosis
- Osteopenia and Osteoporosis, Urologic Considerations
- Urolithiasis, Renal

CODES
ICD9
- 255.42 Mineralocorticoid deficiency
- 276.40 Hypokalemia
- 588.89 Other specified disorders resulting from impaired renal function

ICD10
- E87.40 Unspecified adrenocortical insufficiency
- E87.5 Hyperkalemia
- N26.89 Other disorders resulting from impaired renal tubular function

CLINICAL/SURGICAL PEARLS
- Type I RTA is the only type associated with increased stone formation, nephrocalcinosis.
- Potassium levels should be monitored during alkali therapy for RTA and replaced appropriately.
- A young person with multiple stones with systemic acidosis and high urine pH, a diagnosis of type I RTA should be considered.
RENAL VEIN THROMBOSIS, ADULT AND PEDIATRIC
Adonteng A. Kivakye, MD

BASICS
DESCRIPTION
• Renal vein thrombosis (RVT) is an acute or chronic thrombosis in the renal vein leading to a reduction in venous drainage of the kidney.
• In infants, RVT typically presents as a severe illness, occasionally with shock.
• Asynchronous events are: 60% have enlarged kidneys on physical exam; gross hematuria and microangiopathic hemolytic anemia and thrombocytopenia can also be present.
• In the adult, RVT presentation depends on onset of RVT:
  • Acute RVT: Triad of sudden flank pain
  • Costovertebral angle tenderness
  • Gross hematuria
• Chronic RVT: Generally asymptomatic.
• Can have proteinuria and microscopic or gross hematuria.
EPIDEMIOLOGY
Incidence
• Neonates and infants:
  • Commonly associated with hypoglycaemia, dehydration, shock, and/or sepsis
  • Usually acute and unilateral; more common on the left side; although 30% bilateral
  • Male-to-female ratio 3:1
  • Accounts for approximately 10% of venous thrombosis in newborns
  • Most common form of thrombosis not associated with a vascular catheter
• Adults:
  • Associated with nephrotic syndrome
  • Reported incidence of RVT in patients with nephrotic syndrome ranges from 6–62%.
  • Nephrotic syndrome, renal vein thrombosis
  • More often chronic and unilateral

Prevalence
N/A
RISK FACTORS
• Neonates/infants:
  • Acute hypoglycaemia
  • Birth trauma
  • Genetics
• Adults:
  • Abdominal tumor, especially renal cell carcinoma
  • Insulin/hyperglycaemia
  • Intrinsinc hypercoagulability (eg, Factor V Leiden deficiency)
  • Nephrotic syndrome
  • Membranous nephropathy
  • Leukemia
  • Acute leukemic crisis
  • Neoplastic disease
  • Use of oral contraceptives, steroids
  • Contraceptive use
  • Membranous nephropathy
  • Intrinsic hypercoagulability (eg, Factor V Leiden deficiency)
  • Hemolytic anemia
  • Nephrotic syndrome
  • Preterminal course

PATHOPHYSIOLOGY
• Newborn/infant:
  • Diminished intravascular blood flow due to hypovolemia (sufficient dehydration, diarrhea)
  • Causes prothrombotic state
  • Oliguria
  • Marked elevation in LDH with normal transaminases
• Adult:
  • Abdominal tumor, especially renal cell carcinoma
  • Nephrotic syndrome
  • Use of oral contraceptives, steroids
  • Hypothyroidism
  • Pregnancy
  • Pregnancy
  • Pregnancy
  • Pregnancy

ASSOCIATED CONDITIONS
• DVT in patients with nephrotic syndrome
  • Pulmonary embolus

GENERAL PREVENTION
• Adults: Long-term anticoagulation is appropriate if RVT has recurred when patients discontinued anticoagulation.

DIAGNOSIS
HISTORY
• Newborn/infant:
  • Stenotic or bilateral, flank masses
  • Evidence of dehydration
  • Evidence of early postnatal course
  • Dehydration
  • Gross hematuria
  • Microangiopathic hemolytic anemia
  • Nephrotic syndrome

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Newborn/infant:
  • Hemolytic anemia
  • Hypothyroidism
  • Pregnancy
  • Pregnancy
  • Pregnancy
  • Pregnancy

Imaging
• Newborn/infant:
  • Ultrasound, Doppler
  • Abdominal ultrasound

RENAL VEIN THROMBOSIS, ADULT AND PEDIATRIC
Adonteng A. Kivakye, MD

436
Adult:  
- Inferior vena cavaography with selective catheterization of the renal vein is the gold standard for the diagnosis.  
- CT findings are similar in noninvasive evaluation of acute RVT.  
- Sensitivity of CT angiography approaches 100%; considered current imaging modality of choice  
- Low attenuation within the renal veins proximal venous enlargement  
- Capular venous collaterals, thickened Gerota’s fascia and pericapsular streaking  
- Doppler ultrasonography is helpful, especially in a transplanted kidney.  
- MRI: Excellent imaging, avoids iodinated contrast, but concerns with radiation in patients with renal insufficiency  
- IOP  
- faint or absent excretion of contrast  
- Enlarged kidney due to congestion  
- Collateral circulation may cause collecting system obstruction and/or twisting of ureter  
- Renal pelvic is often distorted

Pathologic Findings:  
- Membranous nephropathy is the most common finding in the setting of nephrotic syndrome and RVT confirms etiology and may guide therapy

TREATMENT  

GENERAL MEASURES  
- Evaluate and treat all underlying causes  
- Aggressive hydration and treatment of septic, diuretic, and electrolyte abnormalities

MEDICATION  

First Line  
- Newborn/Infant:  
  - Use of thrombolytic agents is reported, but controversial  
  - Systemic heparization:  
    - Prevents thrombus propagation into vena cava (risk of propagation low with fluid and electrolyte repletion)  
    - Used in neonates with bilateral RVT

Second Line  
- Heparin

SURGERY/OTHER PROCEDURES  
- Infants: no role for surgical thrombectomy  
- Thrombectomy in adults:  
  - Rarely used, because neither renal preservation nor improvement in survival demonstrated  
  - Surgical thrombectomy (either open or percutaneous) in patients with acute bilateral RVT with poor prognosis  
  - Percutaneous post-thrombolytic RVT  
  - Nephrectomy in highly selected patients for blurring measures  
  - Radical nephrectomy and thrombectomy in renal cell carcinoma

ADDITIONAL TREATMENT  
- Infants with renal failure—dialysis if needed  
- RVT filters are indicated in high-risk adult patients for pulmonary embolism.

Radiation Therapy
- N/A

Additional Therapies
- Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS  
- Neonates: Mortality rate of 3%  
- The kidney may recover completely, atrophy, or remain enlarged due to congestion  
- The kidney may recover completely, atrophy, or remain enlarged due to congestion

COMPlications (S)  
- Consumptive coagulopathy  
- Pulmonary embolism  
- Renal failure  
- Loss of graft in transplant patient

FOLLOW-UP  

Patient Monitoring  
- Neonates/Infant:  
  - Renal function may be followed using nuclear scanning. Atrophy is often detected long term. About 5% of affected neonates progress to diastasis or transplantation.  
  - Monitor blood pressure, as renovascular hypertension may occur after RVT in ~20%, even with normal renal function.  
- Adult:  
  - Treat cause of nephrotic syndrome  
  - Long-term anticoagulation as preventive measure in nephrotic syndrome not supported  
- Because RVT may be asymptomatic, all patients with nephrotic syndrome should be monitored for symptoms of RVT

Patient Resources  

REFERENCES  

ADDITIONAL READING  
- See Also (Topic, Algorithm, Media)  
- Renal Cell Carcinoma with Tumor Thrombus  
- Renal Vein Thrombosis, Adult and Pediatric Image  
- Renal Vein, Lymphangioma

ICD9  
- 406.3 Other venous embolism and thrombosis of renal vein  
- 581.9 Nephrotic syndrome with unspecified pathologic lesion in kidney  
- 788.0 Renal colic

ICD10  
- R32.8 Embolism and thrombosis of renal vein  
- N04.9 Nephrotic syndrome with unspecified morphologic changes  
- N23 Unspecified renal colic

CLINICAL/SURGICAL PEARLS  
- Renal vein thrombosis (RVT) is associated with nephrotic syndrome in adults.  
- Membranous nephropathy is most common pathology in RVT with nephrotic syndrome.  
- Neonates and infants more likely than adults to have bilateral RVT.
Retrograde Ejaculation
Pravin K. Rao, MD

PATHOPHYSIOLOGY

- Normal ejaculation requires:
  - Central control in multiple brain regions
  - Sympathetic (T12–L3):
    - Contract bladder neck, seminal vesicles, ejaculatory ducts
  - Parasympathetic (S2–S4):
    - Contract ischiocavernosus
  - Dorsal nerve of penis

- Neurologic control:
  - Sensory (S2–S4):
    - Pelvic nerve
  - Motor (S2–S4):
    - Efferents from sacral cord
  - Sympathetic (T12–L3):
    - Hypepogastric nerves
  - Neural disruption:
    - Spinal cord injury (SCI)
    - Diabetes mellitus (DM)
  - Medication side effects
    - Selective serotonin reuptake inhibitors

ASSOCIATED CONDITIONS

- Idiopathic
- Neurotrophic
- Medication side effects
- Selective serotonin reuptake inhibitors

PATHOLOGY

- Normal ejaculate:
  - Seminal vesicles
  - Prostate
  - Vas deferens

DIAGNOSIS

HISTORY

- Presence of erectile dysfunction
- Cloudy urine after sex
- Symptoms of hypogonadism
- Medical history
- Symptoms of retrograde ejaculation
- Medication side effects
- History of Mendelian conditions

DIAGNOSTIC TESTS & INTERPRETATION

LAB

- Normal ejaculate:
  - Seminal vesicles
  - Prostate
  - Vas deferens

PHYSICAL EXAM

- Normal physical exam:
  - Absent ejaculation

DIAGNOSTIC PROCEDURES/SURGERY

- Retrograde ejaculation:
  - Bladder neck closure
  - Prostate volume
  - Vicarious semen

IMAGING

- Retrograde ejaculation:
  - Bladder neck closure
  - Prostate volume

Pathologic Findings

Pharmacologic Findings
RETROGRADE EJACULATION

DIFFERENTIAL DIAGNOSIS
- Anejaculation
- Anorgasmia (inability to reach orgasm)
- Aspermia due to failure of emission
- Congenital bilateral/lateral absence of the vas deferens
- ED
- Erectile dysfunction
- Failure to reach orgasm
- Poor expulsion of ejaculate through flaccid penile urethra
- Hypogonadism
- Semen spillage in lab
- Poor semen collection technique

TREATMENT
GENERAL MEASURES
- Treatment typically reserved for fertility purposes
- Treat reversible causes
- Modify causative medications
  - Change or discontinue causative medications
  - Some clinicians favor alfuzosin for BPH (possibly less RE than other α-blockers)

MEDICATION
First Line
- α-adrenergic agents
  - Dosing structure highly variable:
    ◦ Pseudoephedrine 60 mg
    ◦ Ephedrine 25–50 mg
    ◦ Imipramine 25–50 mg (may cause dizziness and nausea)
  - Frequency ranges from QD to QID
  - Duration ranges from 2–14 days
  - Side effects: HTN, tachycardia
- Author recommendation: Pseudoephedrine 60 mg QID × 2–7 days prior to ejaculation (titrate to effectiveness)
- Medical therapy less likely to be effective after bladder neck injury or surgery

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Spinal fluid leakage
  - For use with assisted reproductive techniques
  - IVF (in vitro fertilization)
  - ICSI (intracytoplasmic sperm injection)

ADDITIONAL TREATMENT
- Radiation Therapy
- Additional Therapies
- N/A
- Complementary & Alternative Therapies
- N/A

ONGOING CARE
- Patient Monitoring
  - Follow-up semen analysis to determine effectiveness of medical therapy
- Patient Resources
  - MedlinePlus: Retrograde Ejaculation

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
  - Anorgasmia/Dysorgasmia
  - Ejaculatory Disturbances
  - Infertility, Urologic Considerations
  - Semen Analysis, Abnormal Findings and Terminology
  - Semen Analysis, Technical and Normal Value

CODES
- ICD9
  - 355.9 Mononeuritis of unspecified site
  - 608.87 Retrograde ejaculation
  - 606.9 Male infertility, unspecified

- ICD10
  - G62.9 Polyneuropathy, unspecified
  - G64.6 Other male infertility
  - N55.14 Retrograde ejaculation

CLINICAL/SURGICAL PEARLS
- In men with spinal cord injury (SCI) or history of retroperitoneal surgery, men may have failure of seminal emission, so sperm retrieval from the bladder may not be feasible.
**PATHOPHYSIOLOGY**

- **Secondary infection if spread is from infected adjacent organs (78% enteric bacteria).**
- **Most common source from renal diseases accounting for 47% of retroperitoneal abscesses.**
- **Infection seeds a contained space in retroperitoneum:**
  - Depending on the source, aerobic and anaerobic organisms may be present.
  - **Usual source:** normal flora from a nearby organ site (eg, GI, GU, female reproductive tract).
  - **Multimicrobial infections are common.**
  - **Malignancy:** frequently violates fascial barriers, whereas abscesses tend to be contained by the fascia.
  - **Hypoxia and lack of appropriate blood supply limit effective immune response.**
  - **If untreated, bacteremia, followed by shock ensues.**
  - **TB and Staphylococcus (skin source) were previously major pathogens, but are less common today.**
  - **Proteus and Escherichia coli are the most commonly cultured bacteria in retroperitoneal abscesses.**
  - **Common pathogens (aerobic and anaerobic):**
    - Enterobacteriaceae
    - E. coli
    - Klebsiella pneumoniae
    - Proteus spp.
    - Pseudomonas aeruginosa
    - Anaerobes:
      - Peptostreptococcus sp.
      - Bacteroides fragilis
      - Prevotella sp.
      - Clostridium sp.
      - Enterococcus sp.
      - Streptococcus sp.
      - S. aureus
    - **Site-specific pathogens:**
      - Pancreatic abscess:
        - E. coli
      - K. pneumonia
      - F. necrophorum
      - Peptococcus sp.
      - Streptococcus sp.
      - **Anterior retroperitoneal:**
        - F. nucleatum
      - **S. aureus**
  - **Unlike peritoneal cavity, retroperitoneum is relatively avascular:**
    - **Usual source:** normal flora from a nearby organ site.
    - **Virulence factors:** Mucoid substances and capsule enhance spread.
  - **Common retroperitoneal abscesses:**
    - Pancreatic abscess
    - Retroperitoneal abscess
    - **Common sites:**
      - **Prevesical, retrovesical, presacral, perirectal**
      - **Pelvic retroperitoneal:**
      - **Retrofascial (aka iliopsoas):**
      - **Posterior retroperitoneum (aka epidural):**
      - **Anterior retroperitoneum:**
      - **Pancreatic abscess:**
      - **Fusobacterium nucleatum**

**ASSOCIATED CONDITIONS**

- **Diabetes, liver disease, renal insufficiency, immunosuppression, retroperitoneal hematoma:**
- **GU specific:** Urinary tract infection (UTI), urethral stenosis, instrumentation/surgery, malignancy
- **GI specific:** Malignancy, surgery, paraneoplastic pathologies

**GENERAL PREVENTION**

Perioperative antibiotic prophylaxis

**DIAGNOSIS**

- **Abdominal or flank pain (60–75%)**
- **Swelling, fever, and chills (30–90%)**
- **Malaise (15–30%)**
- **Nausea/vomiting**
- **Anorexia**
- **Weight loss (12%)**
- **Duration of symptoms is typically longer than 1 wk**
- **Recent instrumentation/surgery/truma**
- **Recent treatment for UTI**
- **History of urolithiasis, inflammatory bowel disease, pancreatitis, diverticulitis, appendicitis, osteomyelitis, malignancy, TB**
- **Medical comorbidities:** Diabetes, renal insufficiency, immunosuppression (ie, HIV)

**PHYSICAL EXAM**

- **General vital signs:**
  - Fever
  - Tachypnea
  - Tachycardia
  - Tachycardia
- **Unlike peritoneal cavity, retroperitoneum is relatively concealed on exam.**
  - **Assess for:***
    - Tenderness: Usually localized, dull, and mild
    - Costovertebral angle tenderness
    - **Palpable flank/abdominal mass:**
      - Lower abdominal, groin, and/or upper thigh
      - **Retroperitoneal abscess:**
        - Flank pain/abdominal mass
        - Lower abdominal, groin, and/or upper thigh
        - **Referred pain due to irritation of retroperitoneal nerves:**
      - **Fossa sign:** Increased pain when flexing patient’s thigh against examiner’s hand; suggests involvement of psoas muscle

**DIAGNOSTIC TESTS & INTERPRETATION**

- **Lab:**
  - Findings often nonspecific (ie, elevated ESR)
  - Obtain CBC (leukocytosis)
  - **BNP:** Serum glucose often elevated
- **Imaging:**
  - **Approximately 30% will have microscopic hematuria.**
  - **Pyuria is also very common.**
- **Urine/blood cultures:**
  - Evaluates surrounding organs (ie, possible sources)

**IMAGING**

- **Cross-sectional CT or MRI is most helpful:**
  - **CT (100% sensitivity, 77% specificity):**
  - **Low-density mass in retroperitoneum with surrounding inflammation**
  - **Gas may be present in approximately 33% of cases.**
  - **Evaluates surrounding organs (ie, possible sources).**

**DIAGNOSIS**

- **Abdominal or flank pain (60–75%)**
- **Swelling, fever, and chills (30–90%)**
- **Malaise (15–20%)**
- **Nausea/vomiting**
- **Anorexia**
- **Weight loss (12%)**
- **Duration of symptoms is typically longer than 1 wk**
- **Recent instrumentation/surgery/truma**
- **Recent treatment for UTI**
- **History of urolithiasis, inflammatory bowel disease, pancreatitis, diverticulitis, appendicitis, osteomyelitis, malignancy, TB**
- **Medical comorbidities:** Diabetes, renal insufficiency, immunosuppression (ie, HIV)

**PHYSICAL EXAM**

- **General vital signs:**
  - Fever
  - Tachypnea
  - Tachycardia
  - Tachycardia
- **Unlike peritoneal cavity, retroperitoneum is relatively concealed on exam.**
  - **Assess for:**
    - Tenderness: Usually localized, dull, and mild
    - Costovertebral angle tenderness
    - **Palpable flank/abdominal mass:**
      - Lower abdominal, groin, and/or upper thigh
      - **Retroperitoneal abscess:**
        - Flank pain/abdominal mass
        - Lower abdominal, groin, and/or upper thigh
        - **Referred pain due to irritation of retroperitoneal nerves:**
      - **Fossa sign:** Increased pain when flexing patient’s thigh against examiner’s hand; suggests involvement of psoas muscle

**DIAGNOSTIC TESTS & INTERPRETATION**

- **Lab:**
  - Findings often nonspecific (ie, elevated ESR)
  - Obtain CBC (leukocytosis)
  - **BNP:** Serum glucose often elevated
- **Imaging:**
  - **Approximately 30% will have microscopic hematuria.**
  - **Pyuria is also very common.**
- **Urine/blood cultures:**
  - Evaluates surrounding organs (ie, possible sources)

**IMAGING**

- **Cross-sectional CT or MRI is most helpful:**
  - **CT (100% sensitivity, 77% specificity):**
  - **Low-density mass in retroperitoneum with surrounding inflammation**
  - **Gas may be present in approximately 33% of cases.**
  - **Evaluates surrounding organs (ie, possible sources).**
**RETROPERITONEAL ABSCESS**

**SURGERY/OTHER PROCEDURES**
- Early percutaneous drainage (if)
  - Essential in lesions >3 cm
  - May consider antibiotics only in abscesses <3 cm
- Surgical drainage must be considered if:
  - Safe percutaneous drainage not possible
  - Perinephric/perirenal abscess
  - Ruptured aortic aneurysm
  - TB
  - Ruptured viscus (ie, duodenal ulcer)
  - Pancreatitis
  - Osteomyelitis
  - Necrotizing fasciitis
  - Malignancy
  - Consider sending for AFB culture

**Diagnosis**
- Tailor duration of treatment to clinical progress
- Refine antibiotic coverage based on culture results
- Metronidazole (4)

**Pathologic Findings**
- Nonspecific signs and symptoms frequently lead to a delay in diagnosis and treatment.
- Obtain cultures
- Avoid multi-loculated abscesses
- Percutaneous drainage has failed
- Safe percutaneous drainage not possible
- May not show calcifications or gas collections
- Edema in surrounding fat seen as high signal on T2-weighted images
- May not show psoas muscle, fistulization to the skin
- Essential in lesions >3 cm
- Percutaneous drainage has failed
- Multiloculated abscesses
- Perinephric/perirenal abscess
- Perforated viscus (ie, duodenal ulcer)
- Pancreatitis
- Osteomyelitis
- Necrotizing fasciitis
- Malignancy

**Prognosis**
- Mortality is considerable (5–50%) despite modern management that combines antibiotics, drainage, and intensive care support.
- High success with antibiotics and percutaneous drainage (>80%)
- Only 1–4% recurrence with percutaneous drainage
- If abscess is not drained and only antibiotics are used, mortality approaches 100%

**Complications**
- Abscess crossing the midline to opposite side or tracking into the ipsilateral thigh
- DVF
- GI bleed
- Organ failure
- Pneumonia
- Secondary infections: Osteomyelitis, involvement of major muscle, fatalization to the skin

**Follow-Up**
- Patient Monitoring
  - Repeat imaging
  - CT or MRI (if MRSA, clostridial)
  - Timing depends on clinical progress
  - Discharge
  - Must be monitored carefully and irrigated appropriately
  - Can be removed when:
    - Patient is clinically improved
    - Drainage stops (>10 mL/d) or becomes serous
    - Abscess cavity involutes is documented on imaging

**Patient Resources**
- N/A

---

**REFERENCES**

---

**ADDITIONAL READING**

---

**CODES**
- ICD9 – 567.31 Psoas muscle abscesses
- 567.38 Other retroperitoneal abscesses
- 998.59 Other postoperative infection
- ICD10 – K68.19 Other retroperitoneal abscess
- K68.12 Psoas muscle abscesses
- K68.19 Other retroperitoneal abscesses

---

**CLINICAL/SURGICAL PEARLS**
- Non-specific signs and symptoms frequently lead to a delay in diagnosis and treatment.
- Early percutaneous drainage is essential in lesions >3 cm.
Retroperitoneal Fibrosis (RPF, Ormond Disease)

Leonard G. Gomella, MD, FACS

BASICS

PATHOPHYSIOLOGY

Mechanical obstruction of the ureters is usual

HALLMARK IS MEDIAL DEVIATION OF THE URETERS ON IMAGING WITH OR WITHOUT HYDROPEEJYSIS.

Epidemiology

Incidence

- In Finland, incidence is 0.1-1,000/yr
- Unknown, but estimated at 1.200,000-1,500,000/yr

Prevalence

1:18 per 100,000

Risk Factors

- Adverse exposure
- Associated with autoimmune disorders
- Abdominal artery aneurysm
- Male > female (2:1:1)
- RPF most common in the 5th-6th decades, but can occur at any age
- Use of implicated medications (see below)
- Malignancy

Genetics

- Evidence supports an immunogenic role with certain HLA alleles:
  - HLA-DRB1*04 and HLA-B8*08

PATHOPHYSIOLOGY

- Idiopathic RPF recently identified as a retromesenteric disease (6,4 related disease IgG4-RD)
- And is a multisystem, fibroinflammatory condition
- Most commonly, the retroperitoneal thickening is located between L2 and T1, close to the aortic bifurcation
- Mechanical obstruction of the ureters is usual presentation; may also cause venous or arterial occlusion
- Primary RPF
  - 70% of cases are idiopathic, and the exact etiology is unknown
- Mitchell and Parises classify idiopathic RPF in a range of diseases collectively termed chronic pancreatitis
  - Immune-mediated reaction to antigens (cereal and low-density lipoprotein) within autoimmune pancreatitis
  - Often have autoantibodies, and thus overlap with the pathogenesis of RPF

- Secondary RPF: 30% of patients with RPF have an identifiable cause of their RPF:
  - Medications:
    - Prolonged therapy with ergot alkaloids such as methylergometrine (once widely used for migraine headaches)
    - Others include LSD, methyldopa, phenacetin, pht-blockers, amphetamines, hydralazine, and anticoagulants
  - Malignancy:
    - Longest (most common), multiple myeloma, carcinoma, pancreatic tumor, prostate cancer, testicular tumor, and sarcoma
  - Radiotherapy for malignancies such as seminoma, colon, or pancreatic cancer
  - Infections:
    - Tuberculosis, actinomycosis, histoplasmosis
  - Others: Trauma (hemorrhage, urinary extravasation), surgical injury

Diagnosis

- Presentation may include sclerosing mediastinitis, scarring of the kidneys, orbital pseudotumor, and myositis

Associated Conditions

- Atherosclerotic disease (abdominal aortic aneurysm)
- Celiac disease
- Arthritis (rheumatoid arthritis)
- Bronchiectasis
- Sclerosing cholangitis
- Orbital pseudotumor
- Periarteritis nodosa
- Immunoglobulin G4-related disease (IgG4-RD) and autoimmune polyglandular syndrome
- Certain HLA haplotypes:
  - HLA-DRB1*04
- Polygenetic genetic risk

Diagnosis

- A positive family history of autoimmune disease
- Autoimmune markers
- History of smoking
- Use of ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Medication history especially ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Infections
  - Tuberculosis, actinomycosis, histoplasmosis
- Malignancy:
  - Presentation may include sclerosing mediastinitis, scarring of the kidneys, orbital pseudotumor, and myositis

Associated Conditions

- Atherosclerotic disease (abdominal aortic aneurysm)
- Celiac disease
- Arthritis (rheumatoid arthritis)
- Bronchiectasis
- Sclerosing cholangitis
- Orbital pseudotumor
- Periarteritis nodosa
- Immunoglobulin G4-related disease (IgG4-RD) and autoimmune polyglandular syndrome
- Certain HLA haplotypes:
  - HLA-DRB1*04
- Polygenetic genetic risk

Diagnosis

- A positive family history of autoimmune disease
- Autoimmune markers
- History of smoking
- Use of ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Medication history especially ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Infections
  - Tuberculosis, actinomycosis, histoplasmosis
- Malignancy:
  - Presentation may include sclerosing mediastinitis, scarring of the kidneys, orbital pseudotumor, and myositis

Associated Conditions

- Atherosclerotic disease (abdominal aortic aneurysm)
- Celiac disease
- Arthritis (rheumatoid arthritis)
- Bronchiectasis
- Sclerosing cholangitis
- Orbital pseudotumor
- Periarteritis nodosa
- Immunoglobulin G4-related disease (IgG4-RD) and autoimmune polyglandular syndrome
- Certain HLA haplotypes:
  - HLA-DRB1*04
- Polygenetic genetic risk

Diagnosis

- A positive family history of autoimmune disease
- Autoimmune markers
- History of smoking
- Use of ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Medication history especially ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Infections
  - Tuberculosis, actinomycosis, histoplasmosis
- Malignancy:
  - Presentation may include sclerosing mediastinitis, scarring of the kidneys, orbital pseudotumor, and myositis

Associated Conditions

- Atherosclerotic disease (abdominal aortic aneurysm)
- Celiac disease
- Arthritis (rheumatoid arthritis)
- Bronchiectasis
- Sclerosing cholangitis
- Orbital pseudotumor
- Periarteritis nodosa
- Immunoglobulin G4-related disease (IgG4-RD) and autoimmune polyglandular syndrome
- Certain HLA haplotypes:
  - HLA-DRB1*04
- Polygenetic genetic risk

Diagnosis

- A positive family history of autoimmune disease
- Autoimmune markers
- History of smoking
- Use of ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Medication history especially ergot alkaloids
- History of malignancies, other autoimmune or collagen vascular disorders
- Infections
  - Tuberculosis, actinomycosis, histoplasmosis
- Malignancy:
  - Presentation may include sclerosing mediastinitis, scarring of the kidneys, orbital pseudotumor, and myositis

Diagnostic Procedures/Surgery

- Retroperitoneal biopsy may be indicated in patients with severe azotemia prohibiting the use of contrast-enhanced imaging. Usually shows medial deviation of ureters.
- CT-guided biopsy may be necessary to rule out a malignant process.
Pathologic Findings
- Gross findings secondary RPF:
  - Smooth, flat, firm, grayish-tan-colored mass
- Extends from the origin of the renal vessels to the distal extent of the common iliac vessels
- May also involve the thoricacic aorta and other arterial areas
- Microscopic findings: Collagen bundles with capillary proliferation and inflammatory cells
- Later xanthomatous and vascular mass with sheets of hyscocellular collagen
- Vacuoles of small retroperitoneal vessels with plasma cells staining for IgG (polyclonal IgG subclass)

DIFFERENTIAL DIAGNOSIS
- Medial deviation of the ureters
  - Malignancies, aneurysms, bladder diverticulum, and prior surgery
  - 20% of normal individuals have medial deviation of the ureters, especially on the right
- Retroperitoneal mass: See also Section I
  - "Retroperitoneal masses, fluid, and cysts"
  - Malignant processes, inflammatory xerophibrotic tumors
  - Declined type fibromatoses, associated with osteal syndrome
  - Presents as soft tissue mass with mass effect

TREATMENT
- Discontinue any offending medications
- Relieve urinary obstruction:
  - Monitor for postobstructive diuresis after the urinary system is decompressed
- Biopsy to rule out malignancy
- C.I.L.
  - If clear, discontinuation of steroids
  - Immediate ureterolysis may also be helpful:
    - Immunosuppressive agents (e.g., cyclophosphamide or azathioprine for 6–12 mo)
      - Prednisone 60 mg every other day for 2 mo, then tapered over the next 2–3 mo to 10 mg/d for a total of 1 yr
      - Tapered over 5 mo to 5 mg/d
- Observation:
  - May be a role in patients on methylsergide after discontinuation of the medication if normal renal function.
  - These patients should be monitored for resolution of hydronephrosis. If the hydronephrosis does not resolve, then the standard combination of medical and surgical therapy should be administered.
- Tenofovir has been used;
- Low-protein, sodium-restricted diet

Ongoing Care
PROGNOSIS
- Prognosis is excellent with combined medical and surgical therapy.

COMPLICATIONS
- Recurrence of RPF:
  - Typically in the 1st yr, usually limited to those treated with medical therapy
  - Urinary injury, requiring further surgical management
  - Vascular injury
  - Postoperative adhesions due to peritoneal irritation

FOLLOW-UP
- Patient Monitoring:
  - Patients can be monitored at regular intervals with symptom check, ESR/CRP levels, creatinine, and degree of hydronephrosis on US
  - CT/MR is usually performed 2–4 mo after the beginning of the steroid treatment (1)
- Patients treated with definitive surgical intervention require less frequent follow-up

Patient Resources
- Medline Plus: Retroperitoneal Fibrosis

REFERENCES

ADDITIONAL READING

CODES
- ICD9
  - 590.80 Pyelonephritis, unspecified
- 590.90 Pyelonephritis, unspecified (diabetes mellitus, medical) (590.90 diabetes mellitus, unspecified)
- 599.60 Urinary obstruction, unspecified
- 599.60 Urinary obstruction, unspecified

CLINICAL/SURGICAL PEARLS
- Although no tests are diagnostic of RPF, most will present with medid deviation of the ureters on imaging.
  - CT is the image modality of choice
  - Stents are often placed for relief of obstruction
  - Patients who fail steroid treatment without evidence of malignancy should undergo ureterolysis.
Retroperitoneal Masses, Fluid, and Cysts

Mark R. Anderson, MD, MSc
Judd W. Moul, MD, FACS

Description

Retroperitoneal masses and cysts can originate from retroperitoneal organs or nonorgan tissue. The latter are relatively rare.

- 70–80% of primary retroperitoneal neoplasms are malignant in nature, and these account for 0.1–0.2% of all malignancies in the body.
- Most cystic lesions within the retroperitoneum are benign; unless the lesion is mostly solid then suspect malignancy.
- Metastatic disease is the most common etiology of a solid retroperitoneal mass.
- Liposarcomas are among the most common of primary retroperitoneal tumors and are distinguished by their large dimensions and range of subtypes.

Prevalence

N/A

Risk Factors

Primary, solid cystic retroperitoneal mass: Previous radiotherapy (dose dependent), chemical exposure (lynyd chlorite, arsenic), HIV/AIDS

Primary, cystic retroperitoneal mass: Parasitic infection, embryonic remnants, prior lymphadenectomy

Genetics

- Tubulenc sclerosis (TSC), 75 mutation, tumor suppressor loss
- Werner syndrome (chromosome 8 alteration, premature aging)
- Li–Fraumeni syndrome (p53 mutation, tumor suppressor loss)
- Neurofibromatosis (NF1, NF2 mutation)

Malignant neoplasms are being reclassified based on a molecular basis. Well-differentiated and de-differentiated lesions are a continuum of lesions based on the genetic abnormality of giant and ring chromosomes usually involving chromosome 12.

Gene amplification, particularly of \( MDM2 \), chromosomes usually involving chromosome 12.

Pathophysiology

- The retroperitoneum extends from the diaphragm superiorly to the pelvis inferiorly and is situated between the posterior parietal peritoneum anteriorly and the transversalis fascia posteriorly. (1)
- The anterior pararenal space is bordered anteriorly by the posterior parietal peritoneum, posteriorly by the anterior renal fascia (Gerota fascia), and laterally by the posterior parietal peritoneum and transversus fascia. (1)
- The perirenal space is situated within the anterior renal fascia (Gerota fascia) and the transversalis fascia. 
- The great vessel space is the fat-containing region that surrounds the aorta and the inferior vena cava (IVC) and lies anterior to the vertebral bodies and psoas muscles.
- Below the kidneys, the anterior and posterior pararenal spaces merge to form the infrarenal retroperitoneal space, which communicates inferiorly with the presacral space and extraperitoneal compartments of the pelvis. 
- Due to the loose connective tissue in the retroperitoneum, tumors can have widespread growth and extension before clinical presentation.

Associated Conditions

N/A

General Prevention

N/A

Diagnosis

History

- Headaches, palpitations, etc. for hypertension
- Unexplained weight loss
- Constitutional symptoms
- Night sweats
- History of chemotherapy, radiation therapy
- Back or bone pain
- Abdominal swelling
- Malignant: Metastases, methylenetetrahydrofolate, L150Q, p16, p14, p10, p9, p8, p7, p6, p5, p4, p3, p2, p1, p0
- Sporadic gastrointestinal stromal tumor activating kinase mutations KIT or PDGFRA

Physical Exam

- Vital signs for hypertension
- Carnes
- Lymphadenopathy
- Neurologic deficits from paraneoplastic syndrome
- Lower extremity lymphedema
- Breast exam
- Neurologic exam
- Testicular exam
- Abdominal mass
- Signs of visualization

Diagnostic Tests & Interpretation

- CBC: Lactate dehydrogenase (infection or lymphoma), leukopenia, anemia
- Serum chemistry: Elevated serum creatinine, azotemia (obstructive uropathy), transaminisms (biliary obstruction), and elevated alkaline phosphatase (bone involvement).
- AFP, L-MY, p-HCG: Testicular tumor markers
- EBL: Elevated in retropertioneal infection
- U MR: Hematuria, pyuria
- Urology: Evidence of a malignant urothelial source
- Blood and urine culture
- Adrenal mass: Phaeochromocytoma screen
- CT urogram for RCC and urothelial carcinoma
- CT can show enhancement, fat density, water density to help characterize underlying components
- MRI better at defining local invasion
- Ultrasonound can differentiate between solid and fluid-filled masses but not good at determining malignant potential or regional mets
- CT with contrast has relative contraindication if GFR <60, MRI has relative contraindication if GFR <30.
- NAG-3 dimeric renal scan can determine relative differential function between each kidney and urine obstruction.
- CT urogram for mass
- Bone scan, mammogram if needed
- Cytocentrifuge pelvic/prostatic

Diagnostic Procedures/Surgery

- Image-guided biopsy: CT or US-guided fine-needle aspiration is usually feasible, but core-needle biopsy improves diagnostic capability
- Open surgical biopsy (first option if the mass is small and inconvenienced located for needle biopsy
- Be prepared to complete the resection if carcinoma identified
- Aspiration of cyst: Fluid for cytology, culture, creatine
- Angiogram: To delineate relationship of tumor to vascular anatomy or to determine extent of aneurysm

444
Pathologic Findings
- Metastatic pathology is consistent with primary tumor pathology.
- Determination of benign vs. malignant tissue is not always possible, leaving final determination to the surgical pathology.
- Well-differentiated liposarcomas mostly resemble lipomas and are typically low grade.
- Rhabdomyosarcomas comprise 10–15% defined as high-grade malignant variants with very bizarre nuclei and huge lipoblasts and carry poor prognosis.
- Liposarcoma is most common (35%), followed by malignant fibrous histiocytoma (20%), rhabdomyosarcoma, and peripheral nerve neoplasm.
- Hemangioma: Diffuse, monomorphous proliferation of capillaries.
- Lymphangioma
- Pancreatic cyst and pseudocyst
- Lymphocele
- Urinoma
- Hematoma
- Cystic teratoma
- Mesothelioma
- Malignant lymphoma, extramedullary
- Germ cell tumors; choriocarcinoma, malignant teratoma, dysgerminoma, seminoma, nonseminoma germ cell tumors
- Paraganglioma, pheochromocytoma
- Schwannoma, neurofibroma
- Rhabdomyosarcoma, ganglioneuroblastoma (neuroblastoma)
- Chordoma
- Myxoma (myxosarcoma)
- Perivascular epithelioid cell tumor (PECT)
- Pleomorphic adenoma
- Hemangioma (angiosarcoma)
- Lipoma (liposarcoma)
- Angiomyolipoma, lymphangioleiomyomatosis, von Hippel-Lindau syndrome
- Myxofibrosarcoma (malignant fibrous histiocytoma)
- Giant cell tumor of tendon sheath
- Hackney's tumor (bizarre giant cell tumor)
- Carcinosarcoma
- Postoperative seroma

TREATMENT

GENERAL MEASURES
- Need tissue diagnosis via primary excision or needle biopsy
- Core biopsy better than fine needle if possible

PROGNOSIS
- RCC has good prognosis though is most lethal GU tumor
- Pheochromocytoma has good prognosis.
- Adrenal carcinoma typically presents late stage and has poor prognosis even with complete resection.
- Poorly differentiated (liposarcoma metastasize.)
- Complexly reacted, nonmetastatic, and low-grade sarcomas are associated with improved survival.
- Liposarcoma is an independent predictor of poor outcome.
- Adrenal carcinoma typically presents late stage and has poor prognosis even with complete resection.
- Hemangioma has good prognosis.
- RCC has good prognosis though is most lethal GU cancer and present with mets ~25% of time.

COMPLICATIONS
- Bleed injury
- Adenocarcinoma (liver, spleen, pancreas)
- Lymphocele
- Deep vein thrombosis
- Wound infection
- Transfusion-dependent anemia

FOLLOW-UP

Patient Monitoring
- Schedule imaging that is intensive during 1st 2 yr (q3–6mo) followed by biannual, migrating to annual by year 5 is generally recommended for most retroperitoneal masses.

Patient Resources
- N/A

REFERENCES

ADDITIONAL READING
- N/A
- See Also (Topic, Algorithm, Media)
  - Retroperitoneal Abscess
  - Retroperitoneal Fibrosis (RPF, Ormond Disease)
  - Retroperitoneal Hematoma
  - Retroperitoneal Liposarcoma
  - Retroperitoneal Lymphoma
  - Retroperitoneal Masses, Fluids, and Cysts Image
  - Retroperitoneal Rheumatoid Nodules
  - Retroperitoneal Sarcoma
  - Retroperitoneum, Fat Necrosis

CODES
- ICD9
  - 191.0 Malignant neoplasm of retroperitoneum
  - 568.89 Other specified disorders of peritoneum
- ICD10
  - C48.0 Malignant neoplasm of retroperitoneum
  - C66.8 Other disorders of retroperitoneum

CLINICAL/SURGICAL PEARLS
- Most solid retroperitoneal masses are malignant.
RHYTHMOLYSIS
Sanjay S. Kasturi, MD
Leonard G. Gomella, MD, FACS

BASICS

DESCRIPTION
Rhabdomyolysis is muscle necrosis resulting in the egress of cellular muscle particles (mainly myoglobin, calcium, creatine kinase [CK], and lactic acid dehydrogenase [LDH]) into the blood stream.

In particular, myoglobin is harmful to the kidney and often causes acute kidney injury:

– Up to 15% of patients who have rhabdomyolysis can have renal failure.

There are many causes for rhabdomyolysis; this section primarily focuses on operative causes.

EPIDEMIOLOGY

– 2,600 cases per year (likely underreported)

Overall incidence of 0–4.9% in the laparoscopic nephrectomy data

RISK FACTORS

– Trauma and immobilization [1]

– Lying unconscious on hard surface under the influence of alcohol or drugs

– Crush injury

– Prolonged compression as seen in excessive operating times (esp. males)

– Laparoscopic, robotic, and open

– Dorsal lithotomy positioning

– Elevated BMI (esp. muscle mass)

– Seizs and shock

– Toxins (spider and snake venom [mostly in South America, Asia, Africa])

Medications [local anesthesia, itocain (MDMA), LSD, myoglobin, calcium, creatine kinase (CK), and lactic acid dehydrogenase (LDH)]

– Electrolyte and endocrine abnormalities

– Excessive muscle use (status epilepticus, prolonged exercise)

– Cardiac arrest (hypokalemia)

– Disseminated intravascular coagulation (DIC)

– Activation of the coagulation cascade by the substances released from damaged muscle cells

– Hepatic dysfunction

– Myoglobinuria acute renal failure

GENERAL PREVENTION

– Avoid immobilization or prolonged operating times

– Appropriate patient positioning in the operating room

– Some reports of using pulse oximetry monitoring of lower extremity to monitor for compartment syndrome

– Monitor for malignant hyperthermia

PATHOPHYSIOLOGY

– Muscle cell destruction

– Pressure or crush

– Cellular hypoxia

– Reparation injury results in large quantities of potassium, phosphate, myoglobin, CK, and urine leak into the circulation

– Electrolele abnormalities further impact cellular integrity

– Normal plasma myoglobin is very low (0–200 ng/mL)

– With > 100 g of skeletal muscle damaged, serum haptoglobin binding capacity becomes saturated

– At this point circulating myoglobin increases “free” and is filtered by the glomerulus

– Myoglobin precipitates in the kidney and causes renal tubular obstruction, potentially leading to acute kidney injury

– Myoglobin levels return to normal values in 1–6 hr after injury due to hepatic metabolism and renal excretion

– Up to 12 L of fluid may be sequestered in the neerosis muscle tissues

– This relative hypervolemia is an additional cause of renal failure in rhabdomyolysis

– Free iron, which catalyzes the production of free radicals, further enhances ischemic renal tubule damage

– Compartment syndrome

– Caused by insufficient blood supply to muscles due to increased pressure within a body compartment (arm, leg, any enclosed space within the body)

– 6 “Ps” associated with compartment syndrome:

– Pain out of proportion based on exam (arm, leg, any enclosed space within the body)

– Pain out of proportion to exertion

– Pain out of proportion to exercise

– Pain out of proportion to previous injury

– Pain out of proportion to treatment

– Pain out of proportion to activity

– Pain out of proportion to exam

– Myoglobin levels only appear in the urine when serum level > 1,000 U/L

– Myoglobin only appears in the urine when serum level > 100 mg/dL

– Red-brown urine

– Cyanotic discoloration

– Myoglobinuria

– Muscle pain and swelling

– Symptoms may be absent in 50% of patients

– Skin discoloration

– Muscular pain and swelling (symptoms may be out of proportion with exam)

– Muscle weakness

– Symptoms may be absent in 50% of patients

– Reddish-brown urine

– Classic triad of muscle pain, weakness, and dark urine

DIAGNOSTIC TESTS & INTERPRETATION

LAB

– Myoglobinuria

– Myoglobinuria only appears in the urine when serum level > 1,000 U/L

– Red-brown urine when urine levels > 100 mg/dL

– Positive for blood on urine dribble but no RBCs suggests myoglobinuria [5]

– Urine must be collected in ratios of 2:3:1, so it may return to normal if muscle damage is limited

– Elevated CK levels (5× upper limit of normal which is about 1,000 IU)

– CK–1/3 level of 26 hr and remains elevated longer than myoglobin, peaks at 1–3 days and declines at 3–5 days after all muscle injury has stopped

– Basic metabolic panel

– Monitor for acute renal failure and hyperkalemia

– Calcium level

– Can be hypercalcemic early, then hypercalcuric later

– Urine acid

– Conversion of purines from lysed muscle cells

– CBC/differential studies (for DIC)

– UFL, ABG

– Micorosopic urine: Pigmented casts, dysmorphic red cells

IMAGING

– Rarely necessary

– MRI with gadolinium best modality for muscle injury

– Sensitivity of 100% vs. 42% for US and 62% for CT scan

DIAGNOSIS

HISTORY

– Trauma

– Seizs

– New medication

– Toxic exposures, drug use or infection

– Excessive muscle use

– Electrolyte or endocrine disorder

– Prolonged operating room time—most common reason

– Needling (2.3.4)

– Most commonly reported in the laparoscopic nephrectomy data when patients are in flank or modified flank position for > 6 hr but also seen in exagerated lithotomy and steep Trendelenburg

– May see predominates

– Elevated BUN, reported mean BUN of 33.2 in review of the laparoscopic nephrectomy data

PHYSICAL EXAM

– Generalized fatigue, nausea, fever

– Mental status changes

– Skin discoloration

– Muscular pain and swelling (symptoms may be out of proportion with exam)

– Muscle weakness

– Symptoms may be absent in 50% of patients

– Reddish-brown urine

– Classic triad of muscle pain, weakness, and dark urine

446
Rhabdomyolysis

SURGERY/OTHER PROCEDURES

Chest x-ray imaging. 

The classic triad of muscle pain, weakness, and dark urine suggests rhabdomyolysis.

Limit operative times especially in obese and muscular patients. Consider high BMI as a risk factor for intraoperative rhabdomyolysis.

Some advocate not using a kidney rest/bar during laparoscopic surgery to help prevent rhabdomyolysis.

Appropriately pad all pressure points in the operating room.

Early recognition and aggressive hydration (better outcomes within the 1st 6 hr of presentation).

References


Additional Reading


See Also (Topic, Algorithm, Media)

Acute Kidney Injury, Acute

Acute Tubular Necrosis (ATN)

Compartment Syndrome, Urologic Considerations

Myoglobin Nephrotoxity

Urinal, Abnormal Color

Icd9

729.88 Rhabdomyolysis

907.9 Crushing Injury of unspecified site

958.5 Traumatic anuria

Icd10

N92.82 Rhabdomyolysis

T79.5XXA Traumatic anuria, initial encounter

T79.6XXA Traumatic ischemia of muscle, initial encounter

Clinical/Surgical Pearls

The classic triad of muscle pain, weakness, and dark urine suggests rhabdomyolysis.

Limit operative times especially in obese and muscular patients. Consider high BMI as a risk factor for intraoperative rhabdomyolysis.

Some advocate not using a kidney rest/bar during laparoscopic surgery to help prevent rhabdomyolysis.

Appropriately pad all pressure points in the operating room.

Early recognition and aggressive hydration (better outcomes within the 1st 6 hr of presentation).
RHABDOMYOSARCOMA, PEDIATRIC (SARCOMA BOTRYOIDES)

Nicholas G. Cost, MD
Paul H. Noh, MD, FACS, FAAP

**DIAGNOSIS**

**HISTORY**
- Family history of malignancy or genetic syndromes
- Li–Fraumeni syndrome
- Neurofibromatosis
- Bezold tumor
- Autosomal dominant polycystic kidney disease
- 5q31 suppressor gene
- 11p15.5 suppressor gene
- 11p deletion
- 11p deletion

**RISK FACTORS**
- Incidence
- Epidemiology
- Incidence
- Bimodal age distribution
- 0.5–0.7 cases per million children
- Of all types of pediatric RMS15–20% involve GU
- Sarcoma botryoides describes a polypoid variant of RMS
- That tends to occur mostly in children
- Sometimes also called Embryonal Rhabdomyosarcoma
- Most common soft tissue sarcoma in children
- Incidence
- Epidemiology
- Incidence
- Bimodal age distribution
- 0.5–0.7 cases per million children
- Of all types of pediatric RMS15–20% involve GU
- Sarcoma botryoides describes a polypoid variant of RMS
- That tends to occur mostly in children
- Sometimes also called Embryonal Rhabdomyosarcoma
- Most common soft tissue sarcoma in children

**PATHOPHYSIOLOGY**
- The Latin word "botryoides" refers to the polypoid or "grape-like lesion" appearance of the tumor beneath the mucosa
- Some sources refer to this as "embryonal RMS"
- Rapid-growth with local invasion
- Can spread by lymphatic and hematogenous routes
- Thought to arise from immature cells that are destined to form striated skeletal muscle
- However, may arise in locations where skeletal muscle is not typically found, such as the bladder
- Defect in regulatory mechanism that controls proliferation and differentiation of skeletal muscle
- Prognosis and pattern of spread depend on histologic subtype and clinical staging
- Lymph nodes (LNs) and lungs are the most common sites of distant metastasis

**ASSOCIATED CONDITIONS**
See Genetics

**GENERAL PREVENTION**
None

**BASICS**

**DESCRIPTION**
- Rhabdomyosarcoma (RMS) (sarcoma botryoides) is a malignancy arising from embryonal mesenchyme that tends to occur mostly in children (Sometimes also called Embryonal Rhabdomyosarcoma)
- Most common soft tissue sarcoma in children
- Sarcoma botryoides describes a polypoid variant of RMS originating in a hollow viscus (vagina, bladder)
- Of all types of pediatric RMS15–20% involve GU system
- Paratesticular
- Bladder
- Prostate
- Uterus
- Vagina

**EPIDEMIOLOGY**
- Incidence
- Bimodal age distribution
- 1st peak: 2–4 yr
- 2nd peak: 15–19 yr
- 3rd most common solid tumor in children (behind neuroblastoma and Wilms tumor)
- Prevalence
- N/A

**RISK FACTORS**
- Genetics
- Li–Fraumeni syndrome
- Neurofibromatosis
- Bezold tumor
- Autosomal dominant polycystic kidney disease
- 5q31 suppressor gene
- 11p15.5 suppressor gene
- 11p deletion
- 11p deletion

**DIAGNOSTIC TESTS & INTERPRETATION**
- Laboratory investigations
- Complete blood count
- Basic metabolic panel
- Serum electrolytes
- Liver function tests
- Coagulation profile
- Tumor markers
- Cytogenetic abnormalities
- Loss of heterozygosity on chromosome 11
- 1;13 translocation (favorable prognosis)
- 2;13 translocation (unfavorable prognosis)
- X–Y translocation
- Cytogenetic abnormalities
- Loss of heterozygosity on chromosome 11
- 1;13 translocation (favorable prognosis)
- 2;13 translocation (unfavorable prognosis)
- X–Y translocation

**PHYSICAL EXAM**
- General
- Localized
- Abnormal masses
- Prolapse of ureterocele, urethra, vagina
- Ureteral obstruction
- Vaginal discharge/bleeding
- Scrotal swelling or pain
- Hematuria
- Urinary retention
- Stranguria
- Urinary frequency

**DIFFERENTIAL DIAGNOSIS**
- Benign adnexal mass
- Primary testicular tumor
- Nephrogenic adenoma of bladder
- Inflammatory pseudotumor of bladder
- Urothelial carcinoma
- Leiomyosarcoma
- Leiomyoma
- Ureteral or bladder diverticulum
- Wilms tumor
- Neuroblastoma
- Neurofibroma
- Neurofibrosarcoma
- Polypoid adenoma of bladder
- Sarcoma botryoides
- Other pediatric RMS

**TREATMENT**

**GENERAL MEASURES**
- Pre- and post-op staging and risk classification are critical in evaluation and treatment planning
- Prognostic staging: Intergroup Rhabdomyosarcoma Study (IRS) staging classification system based on TNM and primary location
- Prognostic grouping: IRS grouping based on primary resection
- TNM classification: Combines stage, group, and histology—helps determine therapy and prognosis
- Preoperative staging: TNM system
- T1: Confined to organ of origin
- T2: Extends to adjacent organs
- T3: Advanced, not systemically metastatic
- T4: Metastasis present
- N: Regional lymph node involvement
- M: Distant metastases
- Stage 1: Limited disease
- Stage 2: Intermediate disease
- Stage 3: Advanced disease
- Stage 4: Metastatic disease

**DIAGNOSTIC PROCEDURES/SURGERY**
- Biopsy
- Image-guided needle biopsy
- Preoperative staging: IRS staging classification system based on TNM and primary location
- Preoperative grouping: IRS grouping based on primary resection
- TNM classification: Combines stage, group, and histology—helps determine therapy and prognosis
- Prognostic staging: IRS system
- T1: Confined to organ of origin
- T2: Extends to adjacent organs
- T3: Advanced, not systemically metastatic
- T4: Metastasis present
- N: Regional lymph node involvement
- M: Distant metastases
- Stage 1: Limited disease
- Stage 2: Intermediate disease
- Stage 3: Advanced disease
- Stage 4: Metastatic disease

**Pathologic Findings**
- Embryonal:
- Accounts for majority of GU RMS
- embryonal variants associated with excellent prognosis
- Sarcoma botryoides
- Spindle cell rhabdomyosarcoma
- Alveolar:
- Less common in GU RMS
- More common in truncal/radial RMS
- Higher rates of local recurrence, LN spread, and distant metastasis
- Pleomorphic:
- Undifferentiated/anaplastic variant
- Poor prognosis

**RISK FACTORS**
- Genetics
- Li–Fraumeni syndrome
- Neurofibromatosis
- Bezold tumor
- Autosomal dominant polycystic kidney disease
- 5q31 suppressor gene
- 11p15.5 suppressor gene
- 11p deletion
- 11p deletion

**LABORATORY INVESTIGATIONS**
- Complete blood count
- Basic metabolic panel
- Serum electrolytes
- Liver function tests
- Coagulation profile
- Tumor markers
- Cytogenetic abnormalities
- Loss of heterozygosity on chromosome 11
- 1;13 translocation (favorable prognosis)
- 2;13 translocation (unfavorable prognosis)
- X–Y translocation

**DIFFERENTIAL DIAGNOSIS**
- Benign adnexal mass
- Primary testicular tumor
- Nephrogenic adenoma of bladder
- Inflammatory pseudotumor of bladder
- Urothelial carcinoma
- Leiomyosarcoma
- Leiomyoma
- Ureteral or bladder diverticulum
- Wilms tumor
- Neuroblastoma
- Neurofibroma
- Neurofibrosarcoma
- Polypoid adenoma of bladder
- Sarcoma botryoides
- Other pediatric RMS

**TREATMENT**

**GENERAL MEASURES**
- Pre- and post-op staging and risk classification are critical in evaluation and treatment planning
- Preoperative staging: Intergroup Rhabdomyosarcoma Study (IRS) staging classification system based on TNM and primary location
- Prognostic grouping: IRS grouping based on primary resection
- TNM classification: Combines stage, group, and histology—helps determine therapy and prognosis
- Preoperative staging: TNM system
- T1: Confined to organ of origin
- T2: Extends to adjacent organs
- T3: Advanced, not systemically metastatic
- T4: Metastasis present
- N: Regional lymph node involvement
- M: Distant metastases
- Stage 1: Limited disease
- Stage 2: Intermediate disease
- Stage 3: Advanced disease
- Stage 4: Metastatic disease

**DIAGNOSTIC PROCEDURES/SURGERY**
- Biopsy
- Image-guided needle biopsy
- Preoperative staging: IRS staging classification system based on TNM and primary location
- Preoperative grouping: IRS grouping based on primary resection
- TNM classification: Combines stage, group, and histology—helps determine therapy and prognosis
- Prognostic staging: IRS system
- T1: Confined to organ of origin
- T2: Extends to adjacent organs
- T3: Advanced, not systemically metastatic
- T4: Metastasis present
- N: Regional lymph node involvement
- M: Distant metastases
- Stage 1: Limited disease
- Stage 2: Intermediate disease
- Stage 3: Advanced disease
- Stage 4: Metastatic disease

**Pathologic Findings**
- Embryonal:
- Accounts for majority of GU RMS
- embryonal variants associated with excellent prognosis
- Sarcoma botryoides
- Spindle cell rhabdomyosarcoma
- Alveolar:
- Less common in GU RMS
- More common in truncal/radial RMS
- Higher rates of local recurrence, LN spread, and distant metastasis
- Pleomorphic:
- Undifferentiated/anaplastic variant
- Poor prognosis
RHABDOMYOSARCOMA, PEDIATRIC (SARCOMA BOTRYOIDES)

- Postoperative grouping
  - Group I: Localized disease, completely excised, no microscopic residual
  - Group II: Infiltrating beyond site of origin, completely resected
- Vagina/uterine (1)
- Paratesticular
- Risk grouping
  - Low risk
    - Embryonal histology, Stage I, all groups
    - Embryonal histology, Stage II/III, Group I
    - Intermediate risk
      - Embryonal histology, Stage II/III, Group II
      - Alveolar histology, Stage I/II, Group I/II
    - High risk
      - Any histology, Stage IV
- All sites of GU RMS require a multidisciplinary approach to curative therapy including appropriate surgical excision, chemotherapy, and radiation (1)
- For bladder/prostate and vaginal/uterine RMS, chemotherapy is 1st-line therapy after biopsy and before radiation or extirpative surgery in all cases except rare instances amenable to immediate partial cystectomy with negative margins
- For paratesticular RMS, retroperitoneal staging is critical. Any boys <10 yr should have radiologic evidence of enlarged retroperitoneal LNs, and all patients >10 yr should have an ipsilateral retroperitoneal LN dissection (RPLND). This should be done to complete staging and must be done before chemotherapy or radiation (1).

MEDICATION
- First Line
  - Bladder/prostate
    - Low risk: Vincristine, actinomycin-D (VAC)
    - Low-risk N1, intermediate risk: VA + Cyclophosphamide (VAC)
  - Paratesticular
    - VA: Stage I, <10 yr, no evidence of LN involvement on imaging (1)
    - VAC: Positive LNs on RPLND
  - Vaginal/uterine (1)
    - VAC: Chemotherapy followed by repeat biopsy to assess residual disease
- Second Line
  - 2nd-line chemotherapy with addition of carboplatin, etoposide, vinblastine, or topotecan
  - Phase I studies

SURGERY/OTHER PROCEDURES
- Bladder/prostate
  - Partial cystectomy: Primary treatment in rare cases at descending urethra where adequate margins can be obtained
  - Radical cystectomy: Referred after chemotherapy or chemoradiation if tumor not amenable to bladder sparing options
  - Urinary diversion: Both temporary and permanent reconstructive options
- Radical prostatectomy: Performed for isolated prostate tumors after chemoradiation
- Paratesticular
  - Radical inguinal orchiectomy: All cases should be approached inguinally with radical resection
  - All >10 yr regardless of imaging
  - All >10 yr if evidence of LN involvement on imaging, prior to chemotherapy
- Vaginectomy: If evidence of residual disease on postchemotherapy biopsy

ADDITIONAL TREATMENT
- Radiation Therapy
  - Bladder/prostate: Postdiagnostic biopsy in addition to chemotherapy. Most cases (Group I)
    - Following initial attempted resection initial resection with residual margins, in addition to chemotherapy: Group I
  - Paratesticular
    - Positive LNs on RPLND
    - Vaginectomy
    - After chemotherapy or surgical resection unless an initial upfront resection (Group I)

Additional Therapies

ONGOING CARE

PROGNOSIS
- bladder/prostate: 3-yr disease-free survival (81%) (3)
- Vagina/uterine: 83% (Botryoid variant: 92%) (4)
- Embryonal: 83% (Botryoid variant: 92%) (4)
- Paratesticular: 3-yr disease-free survival: 81% (3)
- Overall survival: 96%
- Overall survival: 96% (3)
- 5-yr disease-free survival 68% (3)
- Overall survival: 8% (94%) for those <10 yr, 76% in those >10 yr (3)

COMPLICATIONS
- Bladder/prostate: Bowel obstruction
- Paratesticular: Complications of RPLND
- Vagina/uterine: Infertility
- Sexual dysfunction
- Chemotherapy-related toxicity
- Secondary malignancy

FOLLOW-UP
- Patient Monitoring
  - Postdiagnostic biopsy to assess for recurrent disease
  - Assessment of residual bladder/vaginal function

Patient Resources
http://www.curesearch.org/

REFERENCES

ADDITIONAL READING
N/A

See Also (Topic, Algorithm, Media)
- Bladder Mass, Differential Diagnosis
- Bladder Tumor, Benign and Malignant, General Considerations
- IRS (Intergroup Rhabdomyosarcoma Study) Clinical Considerations
- Rhabdomyosarcoma, Pediatric (Sarcoma Botryoides) (1)
- Testis, Tumor, and Mass, Pediatric, General
- Vaginal Mass, Neonatal

CODES
ICD-9
- 171.6 Malignant neoplasm of connective and other soft tissue of pelvis
- 171.9 Malignant neoplasm of connective and other soft tissue, site unspecified
- 174.9 Malignant neoplasm of female genital organ, site unspecified

ICD-10
- C49.8 Malignant neoplasm of connective and other soft tissue of pelvis
- C49.9 Malignant neoplasm of connective and other soft tissue, unspecified
- C57.9 Malignant neoplasm of female genital organ, unspecified

CLINICAL/SURGICAL PEARLS
- Radical urothelial surgery should be avoided with the goal of organ preservation
- Small residual masses may not require resection if such surgery would lead to morbidity.
SACRAL AGENESIS, UROLOGIC CONSIDERATION

Paul H. Noh, MD, FACS, FAAP
Nicholas G. Cost, MD

ASSOCIATED CONDITIONS
- Tethered cord/hydronephrosis
- VACTERL/VATER association
- Curative syndrome
- Hemivertebra, anorectal malformations, and a presacral mass

GENERAL PREVENTION
Avoid material exposure to potentially causative agents

DIAGNOSIS

HISTORY
- Urinary tract infections (UTIs) in 75% of affected children
- Genetic/birth history
- Maternal drug exposure
- Gestational diabetes
- Urinary incontinence
- Constipation

PHYSICAL EXAM
- Lower extremity strength is usually normal
- Sacral dermatome sensation is usually intact
- Bowel function/constipation

DIAGNOSTIC TESTS & INTERPRETATION
- Magnetic resonance imaging (fetal or postnatal)
- Prenatal/postnatal ultrasound (US)
- Lateral x-ray of lower spine

BASICS

DESCRIPTION
- The partial or complete absence of 2 or more lower vertebral bodies
- May be occult or associated with voiding dysfunction

EPIDEMIOLOGY
Incidence
- 1 in 25,000 live births
- 16% of children with sacral agenesis (SA) have a diabetic mother
- 80% of cases are detected during infancy
- 20% of cases go undetected until difficulty with toilet training (at 3–4 yr of age)

Prevalence
- 1 in 25,000 live births
- 80% of cases are detected during infancy
- 16% of children with sacral agenesis (SA) have a diabetic mother
- Maternal insulin-dependent diabetes
- Maternal drug exposure (Minoxidil noted in case reports)

RISK FACTORS
- Genetic predispositions, see "Genetics"
- Failure of fusion or formation of lower vertebral bodies
- Spectrum of anomalies including meningocele and anorectal malformations
- Spectrum of anomalies including meningocele and anorectal malformations
- Urologic manifestations (5):
  - Spectrum of anomalies that include myelomeningocele and other spinal dysraphisms
  - Failure of fusion or formation of lower vertebral bodies
  - Spectrum of anomalies including meningocele and anorectal malformations

PATHOPHYSIOLOGY
- Failure of fusion or formation of lower vertebral bodies
- Spectrum of anomalies including meningocele and anorectal malformations
- Urologic manifestations (5):
  - Spectrum of anomalies that include myelomeningocele and other spinal dysraphisms

ASSOCIATED CONDITIONS
- Tethered cord/hydronephrosis
- VACTERL/VATER association
- Curative syndrome
- Hemivertebra, anorectal malformations, and a presacral mass

DIAGNOSIS

HISTORY
- Urinary tract infections (UTIs) in 75% of affected children
- Genetic/birth history
- Maternal drug exposure
- Gestational diabetes
- Urinary incontinence
- Constipation

PHYSICAL EXAM
- Lower extremity strength is usually normal
- Sacral dermatome sensation is usually intact
- Bowel function/constipation

DIAGNOSTIC TESTS & INTERPRETATION
- Magnetic resonance imaging (fetal or postnatal)
- Prenatal/postnatal ultrasound (US)
- Lateral x-ray of lower spine

GENERAL MEASURES

Bladder management
- Consideration for clean intermittent catheterization regimen depending on status of ability to empty bladder and low pressure, state of the upper urinary tracts, and renal function status
- Potentially utilizing anticholinergics in the setting of high-pressure neurogenic bladder
- Bowel management
- Identity and treat constipation
- Anorectal manometry
- Orthopedic consultation

MEDICATION

First Line
- Oxybutynin (Ditropan)
  - Infants: 0.2 mg/kg PO TID
  - Children: 0.5 mg PO TID

Second Line
- Oxybutynin
  - Alternate anticholinergics, many not approved for children but used "off label"
SACRAL AGENESIS, UROLOGIC CONSIDERATION

SURGERY/OTHER PROCEDURES

- **UMN Lesions**
  - May require reconstructive surgery for the bladder outlet if there is concomitant incontinence from an open bladder neck.
  - Endoscopic injections of bulking agents to help with bladder neck continence
  - May require reconstructive surgery for the bladder outlet if there is concomitant incontinence from an open bladder neck.

- **LMN Lesions**
  - Endoscopic injections of bulking agents to help with bladder neck continence
  - May require reconstructive surgery for the bladder outlet if there is concomitant incontinence from an open bladder neck.
  - May require continent catheterizable channel (ie, Mitrofanoff)

- **Ureteral reimplantation or endoscopic bulking agent at the ureteral orifices for persistent VUR**

- **Bowel management may require enemas and even include the creation of a continent catheterizable channel for antegrade enemas (MACE [Malone antegrade continence enema])**

ADDITIONAL TREATMENT

- **Radiation Therapy**
  - N/A

- **Additional Therapies**
  - N/A

- **Complementary & Alternative Therapies**
  - N/A

ONGOING CARE

- **PROGNOSIS**
  - Best prognosis for successful toilet training and management of incontinence is when defect is detected early and when the child has normal lower extremity function.

- **COMPLICATIONS**
  - Renal function deterioration
  - Potential for high-pressure urinary storage transmitted to the kidneys which is deleterious for renal function.
  - Scarring from VUR and recurrent UTI
  - Social and developmental difficulties associated with fecal/urinary incontinence

FOLLOW-UP

- **Patient Monitoring**
  - Renal/bladder US at regular intervals
  - Monitor status of upper urinary tracts
  - Basic metabolic panel
  - Voiding cystourethrogram to follow status of VUR as needed
  - Urodynamics every year or every other year to ensure bladder is of a safe capacity and compliance to avoid a setup detrimental to renal health

- **Patient Resources**
  - The International Sacral Agenesis Caudal Regression Association (IASCRA)
  - https://sites.google.com/site/ caudalregressionsyndrome/

REFERENCES


ADDITIONAL READING

- **See Also (Topic, Algorithm, Media)**
  - Caudal Regression Syndrome
  - Myelodysplasia (Spinal Dysraphism), Urologic Considerations
  - Neurogenic Bladder, General
  - Sacral Agenesis Image
  - Spina Bifida/Spina Bifida Occulta, Urologic Considerations
  - Tethered cord/Tethered Cord Syndrome
  - VACTERL/VATER Association

CODES

- **ICD9**
  - 344.61 Cauda equina syndrome with neurogenic bladder
  - 566.55 Detrusor sphincter dyssynergia
  - 756.13 Absence of vertebra, congenital

- **ICD10**
  - N32.81 Cauda equina syndrome with neurogenic bladder
  - N32.89 Other specified disorders of bladder
  - Q76.49 Other congenital malformations of spine, not associated with scoliosis

CLINICAL/SURGICAL PEARLS

- **There is variability in the level of neurologic insult and resulting in bladder dysfunction. This ranges from a UMN lesion with bladder hyperreflexia to an LMN lesion with areflexia.**
- **Aggressive medical management with anticholinergics and CIC may prevent renal damage and the need for major reconstructive surgery.**
SARCOIDOSIS, UROLOGIC CONSIDERATIONS
Jay Simhan, MD
Michael A. Pontari, MD

PATHOPHYSIOLOGY
- The cause of sarcoidosis is unknown. Symptoms are extensive and can involve pulmonary, arthritic, skin lesions, and manifestations relative to specific organ involvement.
- It is suspected that the granulomas of sarcoidosis are caused by an abnormal immunologic response to a stimulus.
- The most common presentation is pulmonary: Blalatral hilar adenopathy (40%). Less common is bilateral hilar adenopathy and pulmonary infiltrate (25%) and pulmonary infiltrate alone (15%). Other presenting manifestations include cough, wheezing, fever, malaise, fatigue, hepatosplenomegaly, splenomegaly, night sweats, and sweats.
- Hypercalcemia: Present in at least 20–30% of patients with sarcoidosis.
- Sarcoidosis may cause neoplastic hypercalcitria and uraemia.
- The sarcoid granuloma produces 1,25(OH)2D3 (calcitriol), causing increased intestinal absorption of calcium. Hypercalcemia: 60% develop hypercalcitria (HAs).
- Pulmonary alveolar cells and lymph node in patients with sarcoidosis are capable of synthesizing vitamin D; this is usually a function limited to the kidney.
- Most patients with sarcoidosis have a suppressed level of PTH secondary to hypercalcemia.
- Secondary hypercalciuria can be seen.
- Most sarcoidosis stones are calcium oxalate.
- Glomerular involvement is very rare and may include:
  - Membranous nephropathy, IgA nephropathy, minimal change disease, proliferative or crescentic glomerulonephritis, and local glomerulonecrosis.
  - Interstitial nephritis with granuloma formation is relatively common in sarcoidosis.
- Tubulointerstitial nephritis and uveitis (TNU) syndrome is lipodystrophic; these patients should be evaluated for sarcoidosis and lipogranuloma syndrome.
- Prostatic involvement has been reported.

ASSOCIATED CONDITIONS
Erythema nodosum

GENERAL PREVENTION
N/A

DIAGNOSIS
HISTORY
- Sarcoidosis can involve any organ system; the clinical presentation is variable and insidious.
- Patients most commonly present in winter and early spring, which suggests a possible environmental trigger.
- Cutaneous involvement is seen in 25% of patients with sarcoidosis. It may accompany systemic involvement.
- Fever, anemia, and polyarthralgia.
- Dyspnea on exertion, cough, chest pain, and occasionally hemoptysis.

PHYSICAL EXAM
- Cutaneous involvement may be present (bipapperm, erythema nodosum)
- Most common sites are face, upper back, trunk, or extremities (BIA)
- Wheezing
- Adenopathy
- Some cases of involvement of tests and epididymis, range from induration to painless mass
- Neurologic symptoms

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Erythrocyte sedimentation rate and mild proteinuria
- Leukopenia and/or lymphocytosis are common.
- Eosinophilia: 24%
- Anemia: 5%
- Hypercalcemia: 49%
- Hypercalciuria: 13%
- Elevated calcium levels
- Serum ACE level is elevated in 60% of patients; therefore, this test is not sensitive in diagnosing sarcoidosis.
- 90% and 2 C may be elevated if there is renal involvement.

Imaging
- Chest imaging may demonstrate hilar adenopathy or pulmonary infiltrate present in 90% of sarcoidosis patients.
- Abdominal imaging may show hepatomegaly, peripancreatic adenopathy, and perirenal fibrosis.
- Stones and nephrolithiasis secondary to hypercalciuria can be seen on CT.
- Sarcoid renal pseudotumors can mimic renal cell carcinoma, and more diffuse enlargement may mimic lymphoma. Retroperitoneal lymph nodes may enlarge sufficiently in sarcoidosis to cause obstruction.
- In rare cases of urinary involvement, underdiagnosis may be seen from urolithiasis or obstruction.
SARCOIDOSIS, UROLOGIC CONSIDERATIONS

TREATMENT

GENERAL MEASURES
- Sarcoidosis remains a diagnosis of exclusion. Before a definitive diagnosis can be made, multiple other conditions that can share similar symptomatology and pathologic findings must be ruled out (See “Differential diagnosis”) above.
- Coordination of care is suggested with experts in the management of the systemic and pulmonary manifestations of the disease.
- Corticosteroids are the mainstay of therapy for most manifestations of sarcoidosis.
- For sarcoidosis-related renal disease, the primary management is steroid therapy. Although many have poor renal function on presentation, patients may respond dramatically to steroid therapy. The steroids are given at high dose for 1–2 mo then reduced for the remainder of the course, which should be at least 1 yr.
- Hydration and limiting sodium intake can reduce hypercalcemia.

MEDICATION

First Line
- Oral corticosteroids are the treatment of choice for patients with hypercalcemia and systemic involvement.
- Initial prednisone 40 mg PO which is tapered to every other day over several weeks for long term therapy, typically 10–15 mg PO every other day
- Nephropathy due to sarcoidosis appears to respond to steroid therapy.

Second Line
- Wilks steroids
- Methotrexate
- Chloroquine

SURGERY/OTHER PROCEDURES
- Biopsy is necessary for diagnosis.
- Obstruction may require diversion.
- Surgical management of urolithiasis

ADDITIONAL TREATMENT

Radiation Therapy
- may

Additional Therapies
- N/A
- Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS
- The course of the disease is variable.
- Spontaneous remission occurs in 50% of patients.
- 1/3 of patients have eventual improvement.
- 10–30% of patients have chronic or progressive disease.

COMPLICATIONS
- Renal failure, interstitial nephritis, ureteral obstruction, neurogenic bladder dysfunction
- Nephropathy is rare and is due to hypercalcemic nephropathy.

FOLLOW-UP

Patient Monitoring
- History, physical exam, chest x-ray, pulmonary function tests, and serum chemistry

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Hematologic, Urologic Considerations
- Urolithiasis, Adult, General
- Hypercalcemia, Urologic Considerations
- Urolithiasis, Adult, General
- Hypercalcemia, Urologic Considerations
- Urolithiasis, Adult, General

ICD9
- 105 Sarcoidosis
- 275.40 Unspecified disorder of calcium metabolism
- 952.0 Calculus of kidney

ICD10
- D86.9 Sarcoidosis, unspecified
- E83.52 Hypercalcaemia
- N32.0 Calculus of kidney

CLINICAL/SURGICAL PEARLS
- Sarcoidosis may cause urologic manifestations and hypercalcemia.
- Rapheovenous lymph nodes may enlarge sufficiently in sarcoidosis to cause obstruction.
- Consider a diagnosis of sarcoidosis in patients presenting with nephrolithiasis of unknown etiology, especially in an African American female.
- For sarcoidosis-related renal disease, oral corticosteroids is the mainstay of treatment.
SCROTUM AND TESTICLE, MASS
Jay Simhan, MD
Jack H. Mydlo, MD

BASICS

DESCRIPTION
A mass in the scrotum or testicle can be noted by the patient or during physical exam

• Location can be in scrotal wall, testicle, or paratesticular tissue

• Testicular masses can be distinguished from other common intrascrotal masses (Hydrocele, varicocele, spermatocoele, epididymal cyst, hematocele) based on exam or imaging studies

• Most palpable testicular tumors in adults are malignant: 80% nonpalpable lesions are benign.

• Children with testicular tumors are more likely to have benign lesions (20–40% benign).

EPIDEMIOLOGY

Incidence
9.837 cases of testicular cancer in the US in 2014 with 380 deaths

Prevalence
• Testicular tumors: 0.05–2/100,000 children

• Lifetime risk 1/270

RISK FACTORS

• Malnutrition, Cryptorchidism, prior testicular neoplasm or hematopoietic malignancy, HH family history of testicular cancer, marijuana use

• Benign mass: Recent trauma, UTI, STDs, viral illness, urethral instrumentation, congenital anomalies, previous history of scrotal surgery

Genetics

• Chromosome 12 alterations in testicular cancer: – Genetics associated in 33% of cases

– 2.2% incidence in brothers of patients with previous history of scrotal surgery

PATHOPHYSIOLOGY

• Depends upon the etiology of the mass

• Differential diagnosis can be narrowed based on patient’s age and history

ASSOCIATED CONDITIONS

Inguinal hernia in pediatric population

GENERAL PREVENTION

Note: testicular self-exam may help diagnosis

DIAGNOSIS

HISTORY

• Age of the patient

• Testicular tics are age-specific

• Torsion usually in prepubertal age group

• Description of the mass

• Small, discrete mass commonly neoplastic

• Diffuse enlargement with tenderness seen with infection, torsion, or trauma

• Associated pain

– Testicular: Sudden, severe, unilateral pain with nausea and vomiting. If torsion intermittent, pain may wax and wane, may have pain during sleep

– Neoplasms rarely cause severe pain, usually described as dull ache or fullness

– Orchitis pain may gradually increase as infection causes increased inflammation

• Referred pain to the scrotum without a mass can be due to renal colic, or nerve root irritation

• Prior scrotal surgery: Orchidectomy for cryptorchidism: increased risk of cancer; malignancy; posthitis granulomata

• History of trauma, surgery, any radiation

• Previous U/I or current lower U/I complaints suggests orchitis: epididymitis

• Urinal discharge suggests STD: concurrent epididymo-orchitis (Chlamydia and gonorrhea are most common in men <35 yr of age)

• Urinal instrumentation: Acquiring infection

• Current disease: Mumps, U/I

• Medical problems: Diabetes mellitus, immunodeficiencies, neurologic disorders, autoimmune disorders, others

• Fever, weight loss, nausea, vomiting, hemoptysis, shortness of breath, and back pain can all be clues to possible metastatic testicular neoplasm

• Nausea and vomiting in torsion or orchitis

ALERT

• Evaluate scrotal swelling and testicular masses urgently

• Solid, firm testicular mass must be considered testicular cancer until proven otherwise

• Patients may present with complaint of testicular mass when they have paratesticular mass instead.

PHYSICAL EXAM

• Never can be ruled out for infection, tumor necrosis, or testicular necrosis

• Mumps orchitis: 30% with mumps parotitis, onset 3–7 days following the parotitis

• Gynecomastia: Germ cell or Leydig cell tumor

• Abdomen:

– Focal tenderness or masses suggest metastasis

• Palpation:

– Retroperitoneal lymphadenopathy from metastatic tumors can sometimes be palpated

– Palpate for signs of hernia

Tumors:

- Size:

– Most early-stage neoplasms or cysts are palpable

– Evaluate if testicular vs. paratesticular mass

– Palpate for signs of hernia

- Temperature:

– Thawing testis and scrotum with flashlight

- Physical examination:

– Assess scrotal swelling and testicular masses

– Palpate for signs of hernia

- Palpate for signs of orchiectomy

Fever can be marker for infection, tumor necrosis, or testicular necrosis

Small, discrete mass commonly neoplastic

Torsion usually in prepubertal age group

Tumor types are age-specific

2.2% incidence in brothers of patients with previous history of scrotal surgery

Genetics associated in 33% of cases

Lab

- CBC to evaluate for anemia associated with malignancy

- Urine analysis and urine culture: May suggest the diagnosis of orchitis or epididymitis

- Hematologic and proteinase: Viral infection

- Pyuria and bacteriuria: Bacterial infection

- Tumor markers:

– AFP: Elevated in embryonal cell carcinomas, metastatic carcinomas, pink cell tumors, or combined tumors, but never increased in pure seminomas

– HCG: Elevated in all choriocarcinomas and some embryonal cell carcinomas, pink cell carcinomas, and seminomas

– LDH: Non-specific, elevated in metastatic disease

- Ultrasound: Rule out gonadoblastoma

Imaging (1)

- Ultrasonography: US (diagnostic procedure of choice): – 95% sensitivity for testicular tumor diagnosis

– Specificity for malignancies is lower since US detects benign lesions as well

- Most testicular tumors have hypoechoic areas, but overall heterogeneity of the lesion is common

- Color Doppler essential for the differentiation of torsion from epididymo-orchitis

– Decreased blood flow with torsion

– Increased blood flow with epididymo-orchitis

– Will also sometimes show increased vascularity in testicular neoplasms
DIFFERENTIAL DIAGNOSIS
See specific Section I and II topics.

Differential Diagnosis

- Adenocarcinoma of the rect testis
- Chylorch. Usually associated with visceral
- Fibrous pseudotumor of the tunica albuginea
- Hydrocele, primary or due to trauma, torsion, tumor, epididymo:hydrocele of the cord
- Orchiectomy of tunica vaginalis
- Paratesticular sarcoma: Rhabdomyosarcoma, mesothelioma, leiomyosarcoma, liposarcoma
- Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
- Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcifications, fat necrosis, malignancy
- Spem granuloma following vasectomy
- Spermatocoele (epidermal cyst)
- Testicular cysts (simple, tunica albuginea, epididymo)
- Testicular tumor: Germ cell tumors (95% of testicular malignancies) are: Sertoli cell, granulosa cell tumors
- Metastatic tumors: Prostatic, lung, and GI tract
- Rare kidney: malformation, melanoma, parvocell, badder, and thyroid
- Mixed germ cell and stromal tumor
- Angioma, blepharochromocytoma, hemangioma, GCHS, melano, and neurofibrom
- Maligant fibrohistiocytoma (most common soft tissue cancer in late adult life)
- Lymphoma or lymphoma
- Varicocele
- Pediatric painless mass: Similar to adult list; most common are: Hydrocele, hemangi, scrococele, testicular teratoma, adrenal rest tumor, rhabdomyosarcoma

TREATMENT

GENERAL MEASURES
- Scrotal ultrasound is indicated in most cases of scrotal mass
- Testicular torsion is an emergency and requires immediate evaluation

MEDICATION

First Line
- Cause-specific treatment, as well as supportive care, should be applied to cases of orchitis. Bed rest, scrotal support, ice bags, and antibiotics.
- Broad-spectrum antibiotics should be administered if a bacterial source is suspected.
- A patient’s sexual partners should be treated if STD is the case.

Second Line
- N/A

SURGERY/OR OTHER PROCEDURES
- Testicular neoplasms: Radical orchietomy with high ligation of the spermatic cord, inguinal incision.
- Testicular biopsy or orchietomy through a scrotal approach is contraindicated if there is the possibility of neoplasm.
- Cystic lesions are difficult to differentiate from neoplastic lesions and are usually removed as above for testicular neoplasms.
- In children, tests: spacing surgery for benign lesions such as teratoma, Leydig cell tumor, and epithelial cyst based on frozen biopsy findings.

ADDITIONAL TREATMENT

Radiation Therapy
Seminoma or some sarcomas

Additional Therapies
Chemotherapy for advanced testicular tumors
Complementary & Alternative Therapies
- N/A

PROGNOSIS

In prepubertal patients, epididymo-orchitis

COMPLICATIONS

Infection, complications secondary to radiation or chemotherapy

FOLLOW-UP

Patient Monitoring
- Patients should be advised to perform monthly testicular self-exams.
- Patients diagnosed with cancer should have disease-specific follow-up.

CONTACTS

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Parasitic Tumors, General
- Spermatic Cord Mass and Tumors, Adult, General
- Spermatic Cord Mass and Tumors, Pediatric, General
- Scrotum and Testicle, Mass Image
- Scrotum and Testicle, Mass, General
- Scrotum and Testicle, Mass, Algorithm
- Spermatic Cord Mass and Tumors
- Testis Tumors
- Testis Tumor (Benign)
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General
- Testis, Testicle or Testicular/Epididymal Appendages

CODES

ICD9
- 185.9 Malignant neoplasm of other and unspecified tests
- 222.0 Benign neoplasms of tests
- 208.89 Other specified disorders of male genital organs

ICD10
- C62.98 Malignant neoplasm of unspecified tests, unspecified
- D09.20 Benign neoplasms of unspecified tests
- N08.89 Other specified disorders of male genital organs

CLINICAL/SURGICAL PEARLS
- Evaluate acute scrotal swelling or testicular masses urgently
- A solid, firm testicular mass in an adult is cancer until proven otherwise.

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Parasitic Tumors, General
- Spermatic Cord Mass and Tumors, Adult, General
- Spermatic Cord Mass and Tumors, Pediatric, General
- Scrotum and Testicle, Mass Image
- Scrotum and Testicle, Mass, General
- Scrotum and Testicle, Mass, Algorithm
- Spermatic Cord Mass and Tumors
- Testis Tumors
- Testis Tumor (Benign)
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General
- Testis, Testicle or Testicular/Epididymal Appendages

CODES

ICD9
- 185.9 Malignant neoplasm of other and unspecified tests
- 222.0 Benign neoplasms of tests
- 208.89 Other specified disorders of male genital organs

ICD10
- C62.98 Malignant neoplasm of unspecified tests, unspecified
- D09.20 Benign neoplasms of unspecified tests
- N08.89 Other specified disorders of male genital organs

CLINICAL/SURGICAL PEARLS
- Evaluate acute scrotal swelling or testicular masses urgently
- A solid, firm testicular mass in an adult is cancer until proven otherwise.

Patient Resources

REFERENCES
SCROTUM AND TESTICLE, TRAUMA

Lee C. Zhao, MD, MS
Allen F. Morey, MD, FACS

ASSOCIATED CONDITIONS

- Associated injuries
  - Urethra, corpora spongiosum
  - Corpus cavernosa
  - Testicular torsion
  - Testicular tumor

GENERAL PREVENTION

- Protective equipment during contact sports
  - Male雅 competing in boxing should wear the appropriate protective gear

DIFFERENTIAL DIAGNOSIS

- Trauma
  - Determine type of injury and magnitude of force
  - Investigate contamination of objects used in stab injuries

PHYSICAL EXAM

- Timing, severity, progression of pain, swelling, discoloration

DIAGNOSIS

- Testicular rupture is usually immediately painful followed by acute onset of swelling
- Torsion typically has more insidious progression of symptoms

PHYSICAL EXAM

- For testicular injury
  - Surgical exploration recommended for penetrating trauma

DIAGNOSTIC TESTS & INTERPRETATION

- Lab
  - Urinalysis
  - Blood culture if infection suspected

- For delayed presentation with abscess formation, culture abscess contents

DIAGNOSTIC TESTS & INTERPRETATION

- Imaging
  - Scrotal ultrasound
    - Highly sensitive and specific for hematocele, avulsion, and rupture
  - Evaluate integrity of tunica albuginea
  - Heterogeneous areas within testicular parenchyma is suggestive of testicular rupture
  - Doppler US may rule out torsion

DIFFERENTIAL DIAGNOSIS

- Trauma of the testicle or one of its appendages
  - Infection (epididymitis, orchitis)
  - Ruptured varicocele resulting in discoloration or tenderness
  - Pelvic fracture resulting in scrotal swelling

TREATMENT

- First Line
  - Narcotics as needed: Oral and IV
  - Protract testicular torsion
  - Pelvic fracture resulting in scrotal swelling

SURGERY/OTHER PROCEDURES

- Blunt trauma: Ruptured testis, expanding hematocele
  - Ruptured varicocele resulting in discoloration or tenderness

SELECTED REFERENCES

- Military services are developing devices for ballistic protection of the external genitalia

ADDITIONAL RESOURCES

- Proper safety training for industrial machinery
- Protective equipment during contact sports
- Testicular tumor
- Corpora cavernosa
- Urethra, corpora spongiosum
- Corpora cavernosa
- Testicular torsion
- Testicular rupture
- Scrotal ultrasound
- Heterogeneous areas within testicular parenchyma
- Highly sensitive and specific for hematocele, avulsion, and rupture
- Evaluate integrity of tunica albuginea
- Doppler US may rule out torsion
- Infection (epididymitis, orchitis)
- Ruptured varicocele resulting in discoloration or tenderness
- Pelvic fracture resulting in scrotal swelling
SCROTUM AND TESTICLE, TRAUMA

FOLLOW-UP
Patient Monitoring
- Repeat US for conservatively managed patients
- Serum testosterone and fertility testing for patients with bilateral testicular injury

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Burns, External Genitalia and Penile
- Edema, External Genitalia
- Penile, Trauma
- Scrotum and Testicle, Trauma Algorithm
- Scrotum and Testicle, Trauma Images
- Testes Pain
- Torsion, Testes, and Testicular Appendages
- Urethra, Trauma (Anterior and Posterior)

CODES
ICD9
- 878.2 Open wound of scrotum and testes, without mention of complication
- 902.4 Contusion of genital organs
- 993.14 Other injury of external genitals

ICD10
- S30.22XA Contusion of scrotum and testes, initial encounter
- S31.31XA Laceration w/o foreign body of scrotum and testes, initial
- S39.94XA Unspecified injury of external genitals, initial encounter

CLINICAL/SURGICAL PEARLS
- Sonogram is the best technique to evaluate for testicular rupture.
- Heterogeneous areas within testicular parenchyma are more often suggestive of testicular rupture than defect in tunica albuginea on ultrasound.
- Repair testicular rupture whenever possible.
- Early exploration and repair of testicular injury is highly efficacious. Rupture of tunica albuginea of testicle in as many of 50% of blunt scrotal trauma presenting for evaluation. Prompt exploration and repair leads to improved salvage rates.
- In pediatric patients, painless hematocele after abdominal injury is a concern for ruptured viscera (especially spleen).
SCROTUM, SQUAMOUS CELL CARCINOMA

Lydia T. Laboccetta, MD
James S. Rosoff, MD

BASICS

DESCRIPTION
- Squamous cell carcinoma (SCC) of the scrotum is a very rare, environmentally induced cancer with high metastatic potential
- The first reported occupational cancer
  - Initially described in 1775 by Sir Percivall Pott in chimney sweeps
- Synonyms: Chimney sweeps cancer, Mule-spinners’ disease, Pott cancer

EPIDEMIOLOGY

Incidence
- 1.5-3/10 million men in US/1 similar rates noted in Dutch series (2)
- Increasing incidence in US may be related to increases in HPV infection, Psoralen plus ultraviolet light A (PUVA) treatment for psoriasis, and also due to improved reporting
- Lower incidence among black men in older series, though increased risk in black men in more recent SEER database analysis (1)
- Most reported in men > 50 yr; median age in SEER series: 68

Prevalence: N/A

RISK FACTORS
- Chemical/mechanical irritation
  - Classically described in chimney sweeps: Related to soot or chemical exposure, poor hygiene
- Oil/petroleum: Machine workers (lathe workers, spinning machines)
- Repeated trauma
- Rarely in patients with prior scrotal incision/scar
- Poor hygiene
- Oil/petroleum: Machine workers (lathe workers, spinning machines)
- Repeated trauma
- Poor hygiene

GENETICS
- N/A

PATHOPHYSIOLOGY

SCC: A malignant tumor of epidermal keratinocytes
- Usually a solitary, slow-growing nodule with or without ulceration usually on the anterolateral aspect of the scrotum
- Starts as a small pimple or nodule which gradually develops ulceration, raised or rolled edges, purulent discharge
- Lesion may persist for 6 mo before ulcerating
- May have associated condylomata of penis, scrotum, perianal region
- May lead to lymphadenopathy due to malignancy or infection
- 30-40% have palpable lymphadenopathy at presentation
- 25% have inguinal metastases at presentation

DIAGNOSIS

HISTORY
- Occupational exposure to chemical and/or mechanical irritants
- History of treatment for psoriasis
- History of HPV 16
- History of scrotal trauma, scrotal surgery
- Inflammatory conditions involving the scrotum
- Change in size of lesion or ulceration
- Fever
- Nonhealing nodule or ulcer

PHYSICAL EXAM
- Exam of external genitalia, inguinal and distant lymph nodes:
  - Usually a solitary, slow-growing nodule with or without ulceration
  - Lesion may persist for 6 mo before ulcerating
  - May have associated condylomata of penis, scrotum, perianal region
  - May lead to lymphadenopathy due to malignancy or infection
  - 30-40% have palpable lymphadenopathy at presentation
  - 25% have inguinal metastases at presentation

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- WBC count to rule out acute infection
- Urimalys and urine culture if indicated

IMAGING
- CT may help to assess size, extent of lymphadenopathy but cannot differentiate inflammation vs. malignancy
- MRI
  - Improved accuracy in diagnosis and staging
  - Can assess infiltrative vs. inflammatory process
  - Lymphangiography is accurate in delineating metastatic vs. inflammatory nodes, but cannot detect micrometastases

Pathologic Findings
- SCC
  - Most are well or moderately differentiated and contain focal areas of keratosis
  - Surrounding epidermis demonstrates hyperkeratosis, acanthosis, dyskeratosis
  - Diffuse lymphocytic infiltrate may be present
  - Staging staging for all scrotal carcinoma, not only SCC, no TNM classification exists (3)
  - Stage A1: Localized to scrotal wall
  - Stage A2: Locally invasive involving adjacent structures (testis, spermatic cord, penis, pubis, and perineum)
  - Stage B: Metastatic disease to the inguinal lymph nodes only
  - Stage C: Metastatic disease to the pelvic or lymph nodes without evidence of distant spread
  - Stage D: Metastatic disease beyond the pelvis including distant organs
- In SEER series, 76% presented with localized disease, 20% with regional metastases, and 4% with distant metastases (4)

DIFFERENTIAL DIAGNOSIS
- Benign scrotal lesions:
  - Condyloma
  - Eczema
  - Hidradenits suppurativa
  - Folliculitis
  - Nevus
  - Periurethral abscess
  - Psoriasis
  - Tuberculosis epidemic inclusion cyst
  - Sebaceous cyst/epidermal inclusion cyst
  - Tuberculosis: epididymitis with a draining sinus
  - Syphilis
  - Sebaceous cyst
  - Malignant melanoma
  - Basal cell carcinoma
  - Paget disease
  - Marjolin ulcer: Cancer arising from site of prior inflammation
- Tuberculosis: epididymitis with a draining sinus
- Malignant scrotal lesions:
  - Basal cell carcinoma
  - Malignant melanoma
  - Paget disease
  - Malignant scar: Cancer arising from site of prior inflammation
- Kaposi sarcoma: A purple, papular, plaque-like, or nodular lesion on the penis or scrotum
- Sarcoma: Lymphangioma from the Darts layer of the scrotum is most common, though still very rare

ASSOCIATED CONDITIONS
- HPV/condylomata
- Psoriasis
- Associations with many other carcinogens have been described

DIAGNOSTIC PROCEDURES/SURGERY
- Excisional biopsy of primary lesion

ASSOCIATED CONDITIONS
- HPV/condylomata
- Psoriasis
- Associations with many other carcinogens have been described

DIAGNOSTIC PROCEDURES/SURGERY
- Excisional biopsy of primary lesion
SCROTUM, SQUAMOUS CELL CARCINOMA

TREATMENT
GENERAL MEASURES
• Management is primarily surgical.
• Local wide excision is diagnostic and therapeutic.
MEDICATION
First Line
• Broad-spectrum antibiotics for 4–6 wk in patients with lymphadenopathy
• Chemotherapy has not demonstrated success for primary treatment (single agent or combination therapy)
  – Methotrexate, bleomycin, and cisplatin have been used with radiotherapy in 1 case report, but the patient later required surgical resection
  – Bleomycin has been reported as successful in 2 cases
  – Multiple case reports exist in the literature of combined adjuvant chemotherapy and radiotherapy
• Topical 5-FU has not been successful in treating carcinoma in situ of the scrotum
Second Line
• N/A
SURGERY/OTHER PROCEDURES
• Primary lesion:
  – Wide local excision of lesion with a 2-cm margin of skin and dartos fascia.
  – Small lesions may be closed primarily.
  – Large lesions may require split-thickness skin grafting or local flaps.
  – If hemiscrotectomy is performed, the ipsilateral testis may be placed in a thigh pouch or moved to the contralateral hemiscrotum.
  – Excision of all scrotal contents is required only when structures are directly involved by tumor.
• Regional lymph nodes
  – If palpable adenopathy resolves after antibiotics or was never present, then a superficial inguinal lymph node biopsy should be performed:
    ○ Ipsilaterally if lesion is lateral
    ○ Bilaterally if lesion at the median raphe
  – If palpable lymphadenopathy persists after antibiotics, then a bilateral superficial lymph node biopsy should be performed.
  – Full bilateral lymphadenectomy should be performed only on the side of the positive biopsy:
    ○ If performing a unilateral lymphadenectomy, a contralateral superficial inguinal lymph node biopsy should also be performed.
  – If there is a positive frozen section, then perform a bilateral lymphadenectomy.
• Laser vaporization of the primary lesion has been used in poor surgical candidates or those who refused surgery.
• Mohs micrographic surgery has also been used for primary lesions.

ADDITIONAL TREATMENT
Radiation Therapy
• Has not been effective and is reserved for recurrences and poor surgical candidates.
• Has been described in multiple case reports as adjuvant therapy.
Additional Therapies
• N/A
Complementary & Alternative Therapies
• N/A

ONGOING CARE
PROGNOSIS
• Scrotal cancer survival is worse for SCC histology than all other histologies except melanoma
  – Survival at 5 yr (1):
    ▪ Stage A: 70–80%
    ▪ Stage B: 40–50%
    ▪ Stage C: Rare
    ▪ Local recurrence rates:
      ▪ 21–40%
      ▪ May require additional excision
      ▪ Patients with industrial exposure may be at higher risk for recurrence
COMPLICATIONS
• Femoral hernias after ilioinguinal lymphadenectomy
• Lymphedema
• Lymphoceles
• Wound infections
FOLLOW-UP
Patient Monitoring
• Self-exams for local recurrence of lesion or lymphadenopathy
• Periodic follow-up by physician for monitoring of local recurrence or lymphadenopathy
• Follow-up is required for life
Patient Resources
• N/A

REFERENCES

ADDITIONAL READING
• N/A
See Also (Topic, Algorithm, Media)
• Scrotum and Testicle Mass
• Scrotum, Epidermal Inclusion Cyst
• Scrotum, Hemangiomata
• Scrotum, Lymphatic Carcinoma
• Scrotum, Tumors, Benign and Malignant
• Seborrhoeic Dermatitis
• Skin Tags, External Genitalia (Acrochordon, Pedunculated Papilloma)

CODES
ICD9
187.7 Malignant neoplasm of scrotum
ICD10
C63.2 Malignant neoplasm of scrotum

CLINICAL/SURGICAL PEARLS
A nonhealing ulcer or nodule on the scrotum should raise suspicion for squamous cell carcinoma.

459
SEMINAL VESICLE, CYSTS AND MASSES

Mark W. Ball, MD
Arthur L. Burnett, II, MD, MBA, FACS

PATHOPHYSIOLOGY

Genetics

RISK FACTORS

Prevalence

N/A

DIAGNOSIS

HISTORY

Most SV cysts are asymptomatic

When symptomatic, typical symptoms are:

- Dysuria, irritative voiding
- Hematuria
- Hematospermia
- Intersitial

Diagnose other malignancy such as prostate cancer

PATHOPHYSIOLOGY

Normal anatomy:

- SVs are elongated, flat, paired structures that lie between the rectum and bladder, superior to the prostate.
- Mean normal length is 3.1 cm and width is 1.5 cm; contributes 50–80% of total seminal ejaculatory volume
- Blood supply: Vascular/venous network; artery, branch of the umbilical artery
- Cysts disease of the SVs can be either congenital or acquired; congenital cysts are associated with anomalies of the ipsilateral mesonephric duct.
- Acquired SV cysts result from ejaculatory duct obstruction, inflammation, or other abnormality.
- Cysts are filled with seminal fluid (nonmotile spermatozoa, red and white blood cells, and epithelial cells).

Congenital SV cysts are typically associated with an ipsilateral ectopic center and/or (ipsilateral renal abnormalities):

- Lesions <5 cm are slowly symptomatic.
- Lesions >12 cm have been described as giant cysts and are often associated with symptoms related to bladder outlet or colonic obstruction.

In men, 30% of ectopic centers insert into the SV.

3 patterns of spread of prostate cancer into SV

1. Direct spread along the ejaculatory duct
2. Prostatic capsule perforation followed by extension into the prostatic tissue and the SV
3. Isolated deposits

Direct invasion of the SVs can also occur in malignancies of the bladder and rectum

ASSOCIATED CONDITIONS

Bladder cancer
Ectopic ureter
Bilateral renal dysplasia or agenesis
Prostatic cancer
Rectal cancer

GENERAL PREVENTION

N/A

DIAGNOSTIC TESTS & INTERPRETATION

Lab

PSA elevation may suggest prostate cancer.

IMAGING

TRUS (transrectal ultrasound):

- Tomography for suspected SV abnormality or SV mass on DRE

- SV cystic lesion: Echogenic center with echogenic peripheral halo

- SV tumors: Isoechoic to the prostate, but hyperechogenic to normal SV

CT:

- SV tumors: Enlarged SV with a high attenuation lesion and a normal bladder and prostate. Can be cystic if there is significant tumor necrosis

- Cannot distinguish benign from malignant tumors. Dilated tissue planes suggest a secondary tumor by direct extension

MRI:

- Cannot distinguish benign from malignant tumors
- SV cyst: T1; low signal intensity, T2; unidirectional smooth wall with uniform high intensity and well-defined margin

- Hemorrhagic SV cyst: High intensity on both T1 and T2; heterogeneous intensity

Diagnostic Procedures/Surgery

Cystoscopy

- Hematospermia with absent or reduced orifice

- Intracystic cyst aspiration and noted with congenital SV cyst

TRUS-guided needle placement for SV aspiration or biopsy for pathologic diagnosis

Uroscopy. Limited value and use today in imaging the SV. Can help determine duct obstruction in azoospermic men; also helps distinguish SV cyst from a mullerian or other wolffian duct cyst

Pathologic Findings

Most primary SV masses are benign and rarely neoplastic
**SEMINAL VESICLE, CYSTS AND MASSES**

- **SV cysts**
  - Symptomatic: SV infection is uncommon.
  - May occur as a consequence of prostatitis or epididymitis.
  - SV abscess: Best imaged on MRI or US.
  - Presumably factors include diabetes or chronic infection.
- **SV calculi**: Often present with pain, infection, or hematospermia; usually the result of infection and ejaculatory duct obstruction.
- Congenital cysts: Congenital cysts are typically associated with ipsilateral epididymal, seminal vesicular, and/or ipsilateral renal dysplasia.
- Benign SV tumors:
  - Papillary adenoma or cystadenoma: Middle-aged men, minimally invasive cyst in presentation and on imaging.
  - Arteriovenous malformations of the SV: Usually presents in the elderly.
  - Often coexistent with bladder or prostate cancer.
- **Other rare tumors**:
  - Carcinoid.
  - Mixed SV tumors are extremely rare:
    - Only 15 cases reported.
    - Variously described as cystadenoma, cystomyoma, low-grade phyllode tumor, benign mesenchymoma, adenomyoma, and mesonephric hamartoma.
- Malignant SV tumors:
  - SV neoplasms are from secondary invasion from prostate, bladder, or rectal cancer, or from other sites.
  - Direct extension into the SV can often be mistaken for primary SV cancer.
  - Primary adenocarcinoma of the SV:
    - Age >50 yr, incidence is rare.
    - Serum PSA and PAP are normal, and CA125 elevated.
    - Tumors positive for CA125 and negative for PSA.
  - Primary carcinoma:
    - Extremely rare aggressive tumor, usually diagnosed late in disease course.
    - Tumors: Leydigoma, angiosarcoma, and mesenchymal adenocarcinoma.
- **SV invasion by another malignancy**: Direct involvement of SV by prostate, bladder, or rectal cancer, or from other sites.
- **SV invasion by another malignancy**: Extensively described as cystadenoma, cystomyoma, low-grade phyllode tumor, benign mesenchymoma, adenomyoma, and mesonephric hamartoma.
- **Malignant SV tumors**:
  - Most SV neoplasms are from secondary invasion from prostate, bladder, or rectal cancer, or from other sites.
  - Direct extension into the SV can often be mistaken for primary SV cancer.
  - Primary adenocarcinoma of the SV:
    - Age >50 yr, incidence is rare.
    - Serum PSA and PAP are normal, and CA125 elevated.
    - Tumors positive for CA125 and negative for PSA.
  - Primary carcinoma:
    - Extremely rare aggressive tumor, usually diagnosed late in disease course.
    - Tumors: Leydigoma, angiosarcoma, and mesenchymal adenocarcinoma.
  - SV invasion by another malignancy: Directed at the primary tumor type.
- **Additional treatment**
  - Radiation Therapy.
  - Chemotherapy.
  - Immunotherapy.
  - Targeted therapy.
  - Hormone therapy.
  - Surgery.
- **Prognosis**
  - Primary SV malignancies due to their rarity, typically present at an advanced stage and are diagnosed late.
  - SV invasion by another malignancy: Directed at the primary tumor type.
  - SV invasion by another malignancy: Diagnosis and management of seminal vesical cysts associated with ipsilateral renal agenesis.
- **Follow-up**
  - Asymptomatic benign tumors: Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Monitoring**
  - Asymptomatic benign tumors:
    - Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Resources**
  - N/A.
- **ADDITIONAL READING**
- **CODES**
  - 198.82 Secondary malignant neoplasm of general organs.
  - 608.6 Benign vesicles.
  - 608.89 Other specified disorders of male genital organs.
- **ICD9**
  - 198.82 Secondary malignant neoplasm of general organs.
  - 608.6 Benign vesicles.
  - 608.89 Other specified disorders of male genital organs.
- **ICD10**
  - C79.82 Secondary malignant neoplasm of general organs.
  - N49.3 Inflammatory disorders of seminal vesicle.
  - N60.8 Other specified disorders of male genital organs.
- **CLINICAL/SURGICAL PEARLS**
  - Hematospermia can be a sign of underlying malignancy.
  - SV calculi are typically associated with ipsilateral renal agenesis.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
- **ONGOING CARE**
  - SV calculi: Often concomitant with bladder or prostate cancer.
  - SV duct stones: Lithotripsy is feasible in select patients via a ureteroscope.
  - SV tumors:
    - All solid or noncystic SV masses on TRUS should undergo a US-guided biopsy.
    - If tumor is confirmed: Further stage with CT and MRI.
  - Enlarging asymptomatic benign tumors are treated with simple seminal vesiculectomy.
  - Historically, small benign tumors were excised transperitoneally or retroperitoneally, and large tumors, transvasically or transcotally.
  - Today, excisions are typically by transperitoneal laparoscopy (case series are small).
  - A diagnosis of malignancy (large in size or poorly differentiated) warrants radical cystoprostatectomy and regional lymph node dissection, en bloc with adherent surrounding structures.
- **ADDITIONAL TREATMENT**
  - Radiation Therapy.
  - Chemotherapy.
  - Immunotherapy.
  - Targeted therapy.
  - Hormone therapy.
  - Surgery.
- **Prognosis**
  - Primary SV malignancies due to their rarity, typically present at an advanced stage and are diagnosed late.
  - SV invasion by another malignancy: Diagnosis and management of seminal vesical cysts associated with ipsilateral renal agenesis.
- **Follow-up**
  - Asymptomatic benign tumors: Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Monitoring**
  - Asymptomatic benign tumors:
    - Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Resources**
  - N/A.
- **ADDITIONAL READING**
- **CODES**
  - 198.82 Secondary malignant neoplasm of general organs.
  - 608.6 Benign vesicles.
  - 608.89 Other specified disorders of male genital organs.
- **ICD9**
  - C79.82 Secondary malignant neoplasm of general organs.
  - N49.3 Inflammatory disorders of seminal vesicle.
  - N60.8 Other specified disorders of male genital organs.
- **CLINICAL/SURGICAL PEARLS**
  - Hematospermia can be a sign of underlying malignancy.
  - SV calculi are typically associated with ipsilateral renal agenesis.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
- **ONGOING CARE**
  - SV calculi:
    - Often concomitant with bladder or prostate cancer.
    - SV duct stones: Lithotripsy is feasible in select patients via a ureteroscope.
    - SV tumors:
      - All solid or noncystic SV masses on TRUS should undergo a US-guided biopsy.
      - If tumor is confirmed: Further stage with CT and MRI.
  - Enlarging asymptomatic benign tumors are treated with simple seminal vesiculectomy.
  - Historically, small benign tumors were excised transperitoneally or retroperitoneally, and large tumors, transvasically or transcotally.
  - Today, excisions are typically by transperitoneal laparoscopy (case series are small).
  - A diagnosis of malignancy (large in size or poorly differentiated) warrants radical cystoprostatectomy and regional lymph node dissection, en bloc with adherent surrounding structures.
- **ADDITIONAL TREATMENT**
  - Radiation Therapy.
  - Chemotherapy.
  - Immunotherapy.
  - Targeted therapy.
  - Hormone therapy.
  - Surgery.
- **Prognosis**
  - Primary SV malignancies due to their rarity, typically present at an advanced stage and are diagnosed late.
  - SV invasion by another malignancy: Diagnosis and management of seminal vesical cysts associated with ipsilateral renal agenesis.
- **Follow-up**
  - Asymptomatic benign tumors: Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Monitoring**
  - Asymptomatic benign tumors:
    - Close follow-up with DRE and TRUS. Other radical surgery for malignancy, no clear follow-up consensus exists.
- **Patient Resources**
  - N/A.
- **ADDITIONAL READING**
- **CODES**
  - 198.82 Secondary malignant neoplasm of general organs.
  - 608.6 Benign vesicles.
  - 608.89 Other specified disorders of male genital organs.
- **ICD9**
  - C79.82 Secondary malignant neoplasm of general organs.
  - N49.3 Inflammatory disorders of seminal vesicle.
  - N60.8 Other specified disorders of male genital organs.
- **CLINICAL/SURGICAL PEARLS**
  - Hematospermia can be a sign of underlying malignancy.
  - SV calculi are typically associated with ipsilateral renal agenesis.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
  - If secondary malignancy is present, treatment should be directed at the primary tumor type.
**SEXUAL ABUSE, PEDIATRIC**

Monica M. Metzdorf, MD
Julia S. Barthold, MD, FACS

**BASICS**

**DESCRIPTION**
- Sexual activity involving a child or a minor
- Spectrum of pediatric sexual abuse includes intercourse, fondling, pornography, and exhibitionism

**EPIDEMIOLOGY**
- Incidence:
  - ∼1% of children sexually abused each year
- Prevalence:
  - 12–20% of girls and 8–10% of boys have been sexually abused by age 18 (12–40% overall)
  - Of girls reporting abuse (1):
    - 12–25% of girls and 8–10% of boys have been sexually abused by age 18 (12–40% overall)
    - 53% reported that the abuse occurred at home

**RISK FACTORS**
- Occurs in all socioeconomic levels
- Gender:
  - Girls more likely to be abused
- Parental abuse:
  - Increased risk with:
    - Physical abuse
    - Emotional abuse
    - Sexual abuse
- Parents who were abused:
  - Increased risk
- Poor hygiene:
  - Increased risk
- Mental illness:
  - Increased risk
- Poverty:
  - Increased risk
- Multiple child caretakers:
  - Increased risk
- Teen parents:
  - Increased risk

**PATHOPHYSIOLOGY**
- American Academy of Pediatrics definition (2):
  - Sexual abuse is the engaging of a child in sexual activities that the child cannot comprehend, and cannot give informed consent, and that violates the social taboos of society.
- Children cannot consent to any sexual activity, but can be sextually abused if they are developmentally unprepared and cannot give informed consent, and that violates the social taboos of society.

**ASSOCIATED CONDITIONS**
- Physical abuse
- Emotional abuse

**GENERAL PREVENTION**
- Education
- Social services

**DIAGNOSIS**

**ALERT**
- Findings in the evaluation of children with possible injuries to the external genitalia that should raise concern for sexual abuse include:
  - Presence of other nonurogenital trauma.
  - Patient < 9 yo.
  - Perianal, rectal injury without history of penetrating trauma.
  - Findings of more extensive or severe trauma.
  - Lack of correlation between reported history and physical findings.

**HISTORY**
- Child may make a statement of abuse, or abuse is witnessed
- Child brought by law enforcement/social services for evaluation for possible abuse as part of investigation
- Caregiver suspects child may have been abused
  - Suspicious findings on routine exam
- Suspicious complaints:
  - Rectal or vaginal bleeding or discharge, especially in prepubertal child
  - Presence of semen, sperm, or acid phosphatase;
    - When severe rectal injury suspected, persistent bleeding or full-thickness lacerations, consider exam under anesthesia.
  - Exam findings of concern:
    - Abnormal discharge or bleeding of genitalia.
    - Acute or healed tear in posterior aspect of hymen.
    - Hemorrhage or swelling of hymen.
  - Injury or scarring of posterior fourchette, fossa navicularis, or hymen.
  - Anal bruising or lacerations.

**DIFFERENTIAL DIAGNOSIS**

**LAB**
- Culture for gonorrhea and Chlamydia.
- Vaginal foreign body
- Blood in urine
- Premenarchal females should have pregnancy test.
- Presence of semen, sperm, or acid phosphatase:
  - Positive culture for gonorrhea or Chlamydia, or a positive test for syphilis or HIV
- All postmenarchal females should have pregnancy test.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Imaging**
- Imaging should be performed if suspicious physical findings are noted.

**DIFFERENTIAL DIAGNOSIS**

**Surgical Procedures**
- Consider exam under anesthesia.

**CONSIDER EXAM UNDER ANESTHESIA**

**PHYSICAL EXAM**
- Be familiar with the normal appearance of the prepubertal introitus and hymen (image).
- Do not force exam on uncooperative children.
- Do not use speculum in prepubertal child.
- Do not touch hymen with swabs or other objects.
- Do not perform a digital rectal exam (DRE).
- Educate caretaker and patient that most sexually abused children have a normal physical exam.
- Absence of physical findings does not exclude abuse
- Perform complete physical exam including skin, oropharynx, genitalia, and anal area.

**ALERT**
- Use frog-leg position with gentle labial traction to visualize female anatomy.
- Consider exam in chest-knee position to confirm suspected abnormalities.
- Consult specialists as appropriate.
- Document thoroughly exam findings and descriptions, using drawings or photos if feasible.
- When severe rectal injury suspected, persistent bleeding or full-thickness lacerations, consider exam under anesthesia.
- Exam findings of concern:
  - Abnormal discharge or bleeding of genitalia.
  - Acute or healed tear in posterior aspect of hymen.
  - Hemorrhage or swelling of hymen.
  - Injury or scarring of posterior fourchette, fossa navicularis, or hymen.
  - Anal bruising or lacerations.

**SEXUAL ABUSE, PEDIATRIC**

**BASICS**

**DESCRIPTION**
- Sexual activity involving a child or a minor
- Spectrum of pediatric sexual abuse includes intercourse, fondling, pornography, and exhibitionism

**EPIDEMIOLOGY**
- Incidence:
  - ∼1% of children sexually abused each year
- Prevalence:
  - 12–20% of girls and 8–10% of boys have been sexually abused by age 18 (12–40% overall)
  - Of girls reporting abuse (1):
    - 12–25% of girls and 8–10% of boys have been sexually abused by age 18 (12–40% overall)
    - 53% reported that the abuse occurred at home

**RISK FACTORS**
- Occurs in all socioeconomic levels
- Increased risk with:
  - Physical abuse
  - Emotional abuse
  - Sexual abuse
- Parents who were abused:
  - Increased risk
- Mental illness:
  - Increased risk
- Poverty:
  - Increased risk
- Multiple child caretakers:
  - Increased risk
- Teen parents:
  - Increased risk

**PATHOPHYSIOLOGY**
- American Academy of Pediatrics definition (2):
  - Child sexual abuse is the engaging of a child in sexual activities that the child cannot comprehend, and cannot give informed consent, and that violates the social taboos of society.
  - Children cannot consent to any sexual activity, but can be sextually abused if they are developmentally unprepared and cannot give informed consent, and that violates the social taboos of society.

**ASSOCIATED CONDITIONS**
- Physical abuse
- Emotional abuse

**GENERAL PREVENTION**
- Education
- Social services

**DIAGNOSIS**

**ALERT**
- Findings in the evaluation of children with possible injuries to the external genitalia that should raise concern for sexual abuse include:
  - Presence of other nonurogenital trauma.
  - Patient < 9 yo.
  - Perianal, rectal injury without history of penetrating trauma.
  - Findings of more extensive or severe trauma.
  - Lack of correlation between reported history and physical findings.

**HISTORY**
- Child may make a statement of abuse, or abuse is witnessed
- Child brought by law enforcement/social services for evaluation for possible abuse as part of investigation
- Caregiver suspects child may have been abused
  - Suspicious findings on routine exam
- Suspicious complaints:
  - Rectal or vaginal bleeding or discharge, especially in prepubertal child
  - Presence of semen, sperm, or acid phosphatase;
    - When severe rectal injury suspected, persistent bleeding or full-thickness lacerations, consider exam under anesthesia.
  - Exam findings of concern:
    - Abnormal discharge or bleeding of genitalia.
    - Acute or healed tear in posterior aspect of hymen.
    - Hemorrhage or swelling of hymen.
    - Injury or scarring of posterior fourchette, fossa navicularis, or hymen.
    - Anal bruising or lacerations.

**DIFFERENTIAL DIAGNOSIS**

**LAB**
- Culture for gonorrhea and Chlamydia.
- Vaginal foreign body
- Blood in urine
- Premenarchal females should have pregnancy test.
- Presence of semen, sperm, or acid phosphatase:
  - Positive culture for gonorrhea or Chlamydia, or a positive test for syphilis or HIV
- All postmenarchal females should have pregnancy test.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Imaging**
- Imaging should be performed if suspicious physical findings are noted.

**DIFFERENTIAL DIAGNOSIS**

**Surgical Procedures**
- Consider exam under anesthesia.

**CONSIDER EXAM UNDER ANESTHESIA**

**PHYSICAL EXAM**
- Be familiar with the normal appearance of the prepubertal introitus and hymen (image).
- Do not force exam on uncooperative children.
- Do not use speculum in prepubertal child.
- Do not touch hymen with swabs or other objects.
- Do not perform a digital rectal exam (DRE).
- Educate caretaker and patient that most sexually abused children have a normal physical exam.
- Absence of physical findings does not exclude abuse
- Perform complete physical exam including skin, oropharynx, genitalia, and anal area.

**ALERT**
- Use frog-leg position with gentle labial traction to visualize female anatomy.
- Consider exam in chest-knee position to confirm suspected abnormalities.
- Consult specialists as appropriate.
- Document thoroughly exam findings and descriptions, using drawings or photos if feasible.
- When severe rectal injury suspected, persistent bleeding or full-thickness lacerations, consider exam under anesthesia.
- Exam findings of concern:
  - Abnormal discharge or bleeding of genitalia.
  - Acute or healed tear in posterior aspect of hymen.
  - Hemorrhage or swelling of hymen.
  - Injury or scarring of posterior fourchette, fossa navicularis, or hymen.
  - Anal bruising or lacerations.
GENERAL MEASURES
- Mental health evaluation is essential (3)
- Acute evaluation and treatment of injuries

MEDICATION
First Line
- Varies with presentation
- Pain medication as appropriate
- Prophylaxis (PPE) for prevention of pregnancy and STIs should be offered to adolescents
- PPE generally not indicated for prepubertal children

Second Line
N/A

SURGERY/OTHER PROCEDURES
- Consider exam under anesthesia
- Depends upon findings/injuries

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Need for mental health support, especially in:
  - Patients reporting suicidal or self-injurious thoughts
  - More intrusive forms of assault
  - More violent assaults
  - Longer period of molestation
  - Closer relationship of perpetrator to victim

COMPlications
- Psychological
  - Eating disorders
  - Depression and anxiety
  - Suicidal behaviors
  - Self-injury
- Posttraumatic stress disorder
- Sexual dysfunction
- Pregnancy
- STIs/STI's

FOLLOW-UP
Patient Monitoring
- Follow-up exams for healing of injuries
- Evaluation for development of STIs
- Evaluation for development of pregnancy and discussion of this possibility with the postpubertal child
- Emotional support/therapy

Patient Resources
- Barlow to Light: National Resources Related to Child Sexual Abuse. http://www.J2I.org/site/4Ig707t56U7PV44v3QdHw4k4

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
Sexual Abuse, Pediatric Image

CODES
ICD9
- 995.33 Child sexual abuse
- 715.41 History of physical abuse

ICD10
- T74.22XA Child sexual abuse, confirmed, initial encounter
- T76.22XA Child sexual abuse, suspected, initial encounter

CLINICAL/SURGICAL PEARLS
- Pediatric providers should always alert to signs and symptoms that suggest the possibility of sexual abuse.
- The clinician is obligated to report any suspected case of childhood sexual abuse.
- Sensitivity during the history and exam and providing the victim access to psychological and social work support are key factors in the case of children who have been sexually abused.
SEXUAL DYSFUNCTION, FEMALE

Samuel Walker Nickles, MD
Nima Baradaran, MD
Eric S. Roener, MD, FACS

BASICS

DESCRIPTION
Sexual dysfunction is a disorder involving sexual desire, orgasm, arousal, or sexual pain in females that results in significant personal distress. It includes the following:
- Hypoactive sexual desire disorder
- Subjective sexual arousal disorder
- Sexual pain disorder
- Combined genital and subjective arousal disorder
- Persistent sexual arousal disorder
- Sexual anorgasmic disorder
- Menopause
- Vasculogenic
- Neurogenic
- DSM-IV defines female sexual dysfunction (FSD)
- Dyspareunia
- Women's orgasmic disorder
- Sexual aversion disorder
- Persistent sexual arousal disorder
- Combined genital and subjective arousal disorder
- Subjective sexual arousal disorder

ASSOCIATED CONDITIONS
- Depression
- Endometriosis, vulvodynia, etc.
- Urinary incontinence
- Intercourse
- Menopause
- Multiple sclerosis
- Any disease that causes decreased estrogen or androgens

GENERAL PREVENTION
- Lifestyle modification to reduce CV disease or premature aging affect sexual desire and response
- Medications
- Previously prescribed medications can decrease sexual desire and function
- Prior pelvic surgery such as hysterectomy or cystectomy can disrupt the autonomic nerve plexus, thus contributing to sexual dysfunction
- OCP, biogenic estrogens

PHYSICAL EXAM
- A thorough physical and pelvic/manual exam:
  - Assess for vaginal atrophy, labia minora, vaginal depth, genitopelvic sensation
  - Examine for trigger points, scarring, or narrowing from prior surgery or genital infection
  - Assess for prolapse, masses
- If neurologic signs are present, a more detailed neurologic assessment is then warranted including anal and vaginal tone, bulbocavernosal reflex, and voluntary tightening of the anus

DIAGNOSTIC TESTS & INTERPRETATION
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Imaging
- Vaginal and clitoral phthlymography, duplex US, and selective pudendal angiography can be used to assess genital blood flow.

DIFFERENTIAL DIAGNOSIS
- Vascular causes of decreased estrogen or androgen action
- Neurogenic causes due to multiple sclerosis, spinal cord injury, or pelvic trauma
- Neuropathic causes (diabetes, peripheral vascular disease, etc.)
- Medication-related effects

LAB
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Pathologic Findings
- Vascular
- Neurologic
- Psychogenic

PHYSICAL EXAM
- A thorough physical and pelvic/manual exam:
  - Assess for vaginal atrophy, labia minora, vaginal depth, genitopelvic sensation
  - Examine for trigger points, scarring, or narrowing from prior surgery or genital infection
  - Assess for prolapse, masses
- If neurologic signs are present, a more detailed neurologic assessment is then warranted including anal and vaginal tone, bulbocavernosal reflex, and voluntary tightening of the anus

DIAGNOSTIC TESTS & INTERPRETATION
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Imaging
- Vaginal and clitoral phthlymography, duplex US, and selective pudendal angiography can be used to assess genital blood flow.

Diagnostic Procedures/Surgery
- Genital/vaginal sensation threshold testing, genital temperature sensation, and the bulbocavernosal reflex can be evaluated to rule out associated neurologic dysfunction

Pathologic Findings
- Vascular
- Neurologic
- Psychogenic

PHYSICAL EXAM
- A thorough physical and pelvic/manual exam:
  - Assess for vaginal atrophy, labia minora, vaginal depth, genitopelvic sensation
  - Examine for trigger points, scarring, or narrowing from prior surgery or genital infection
  - Assess for prolapse, masses
- If neurologic signs are present, a more detailed neurologic assessment is then warranted including anal and vaginal tone, bulbocavernosal reflex, and voluntary tightening of the anus

DIAGNOSTIC TESTS & INTERPRETATION
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Imaging
- Vaginal and clitoral phthlymography, duplex US, and selective pudendal angiography can be used to assess genital blood flow.

Diagnostic Procedures/Surgery
- Genital/vaginal sensation threshold testing, genital temperature sensation, and the bulbocavernosal reflex can be evaluated to rule out associated neurologic dysfunction

Pathologic Findings
- Vascular
- Neurologic
- Psychogenic

PHYSICAL EXAM
- A thorough physical and pelvic/manual exam:
  - Assess for vaginal atrophy, labia minora, vaginal depth, genitopelvic sensation
  - Examine for trigger points, scarring, or narrowing from prior surgery or genital infection
  - Assess for prolapse, masses
- If neurologic signs are present, a more detailed neurologic assessment is then warranted including anal and vaginal tone, bulbocavernosal reflex, and voluntary tightening of the anus

DIAGNOSTIC TESTS & INTERPRETATION
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Imaging
- Vaginal and clitoral phthlymography, duplex US, and selective pudendal angiography can be used to assess genital blood flow.

Diagnostic Procedures/Surgery
- Genital/vaginal sensation threshold testing, genital temperature sensation, and the bulbocavernosal reflex can be evaluated to rule out associated neurologic dysfunction

Pathologic Findings
- Vascular
- Neurologic
- Psychogenic

PHYSICAL EXAM
- A thorough physical and pelvic/manual exam:
  - Assess for vaginal atrophy, labia minora, vaginal depth, genitopelvic sensation
  - Examine for trigger points, scarring, or narrowing from prior surgery or genital infection
  - Assess for prolapse, masses
- If neurologic signs are present, a more detailed neurologic assessment is then warranted including anal and vaginal tone, bulbocavernosal reflex, and voluntary tightening of the anus

DIAGNOSTIC TESTS & INTERPRETATION
- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hypothyroidism
- Hormonal profile
- Serum total and free testosterone
- Estradiol level
- LH, FSH, prolactin
- Sex hormone binding globulin (SHBG)

Imaging
- Vaginal and clitoral phthlymography, duplex US, and selective pudendal angiography can be used to assess genital blood flow.

Diagnostic Procedures/Surgery
- Genital/vaginal sensation threshold testing, genital temperature sensation, and the bulbocavernosal reflex can be evaluated to rule out associated neurologic dysfunction

Pathologic Findings
- Vascular
- Neurologic
- Psychogenic
**SEXUAL DYSFUNCTION, FEMALE**

**TREATMENT**

**GENERAL MEASURES**
- Attempt to identify a correctable cause and treat when present.
- Exercise and pelvic floor training/massage can improve sexual function.

**MEDICATION**
- Treat prolapse and incontinence in affected patients, as female sexual dysfunction may be in part related to its inhibition due to leakage during sexual relations.

**First Line**
- Hormone replacement therapy (HRT) is the mainstay of treatment in postmenopausal women or oophorectomized women (4).
  - Oral estrogen or topical vaginal estrogen may improve libido and ameliorate symptoms of dysosmia or irritation.
  - Oxytocin is an estrogen agonist/antagonist indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.
  - One tablet (60 mg) taken orally once daily with food.
  - Do not use estrogens or estrogen agonist/antagonist or fluconazole concomitantly.
- Topical steroids for genital edema.
- Androgen replacement therapy can be considered in patients with androgen deficiency.
  - Combined estrogen and testosterone replacement therapy can be used or testosterone alone can be applied topically or with a patch (counsel patient on risks of virilization including: Acne, hirsutism, male pattern baldness, and clinical hypertrichosis).
- Testosterone replacement is controversial and not FDA approved despite being one of the most commonly prescribed off label drugs for desire disorders.
- Tibolone (synthetic steroid) is commonly used in Europe in postmenopausal women with desire and arousal disorders.

**Second Line**
- Androgen replacement therapy can be considered in patients with androgen deficiency.
- Computerized and testosterone replacement therapy can be used or testosterone alone can be applied topically or with a patch (counsel patient on risks of virilization including: Acne, hirsutism, male pattern baldness, and clinical hypertrichosis).

**ADDITIONAL TREATMENT**

**Radiation Therapy**

**Additional Therapies**
- Eros Critical Therapy Device is a handheld mechanical device that has been FDA approved for the treatment of sexual arousal and orgasmic disorders in women.
- Several other pharmacologic agents are under investigation for treatment of female sexual dysfunction.
- PDE-5 inhibitors are thought to enhance vaginal lubrication and enjoyment in postmenopausal women; however, the benefit is not well established.
- α-Adrenergic antagonists such as phentolamine and yohimbine produce vasodilatation of the smooth muscle, increasing vaginal blood flow and lubrication.

**Complementary & Alternative Therapies**
- Education, sex therapy, psychotrapey, and cognitive behavioral therapy are also important in the multidisciplinary management of sexual dysfunction including those with a history of sexual abuse.
- Currently there are limited studies on the effectiveness of herbal remedies to aid female sexual dysfunction.

**ONGOING CARE**

**PROGNOSIS**
- Outcome is improved if a specific cause can be identified.

**COMPLICATIONS**
- Patients on HRT should be appropriately counseled on its risks and benefits.

**FOLLOW-UP**
- Patient Monitoring
  - Close monitoring of progress and compliance is necessary.

**ADDITIONAL READING**
- See Also (Topic, Algorithm, Media)
  - Dysspareunia, Female
  - Erectile Dysfunction/Impotence, General Considerations
  - Female Hypoactive Sexual Desire Disorder
  - Female Sex Function Index (FSFI)
  - Incontinence, Urinary, Adult Female
  - Libido, diminished, female
  - Pelvic Organ Prolapse (Cystocele and Enterocele)
  - Pelvic Pain, Female
  - Vaginal Atrophy, Urologic Considerations

**ICD9**
- 302.70 Psychosocial dysfunction, unspecified
- 302.73 Female orgasmic disorder

**ICD10**
- F52.22 Female sexual arousal disorder
- F52.31 Female orgasmic disorder
- N94.1 Dyspareunia

**CLINICAL/SURGICAL PEARLS**
- FSD is a complex condition with many etiologies.
  - A multidisciplinary approach is often necessary.
  - Search for reversible cause such as incontinence or prolapse and treat accordingly.

**REFERENCES**
PATHOPHYSIOLOGY

- Transmission is primarily via sexual contact.
- Nonsexual transmission: Mother–infant, blood transfusions, accidental needle injury.

RISK FACTORS

- Prevalence

EPIDEMIOLOGY

- Incidence
- Prevalence
- Risk factors

Gender

- CCR5 mutation provides relative protection against HIV infection (2C1)

STI

- Ulcerative lesions
- Exposure at delivery and/or in utero
- Low socioeconomic status, drug abuse
- Multiple sex partners, sexual contact with infected person

Prevalence

- 20 million new infections yearly (1A)
- Relative frequency of cases by disease: HPV > Chlamydia > Trichomonas > Gonorrhea > HSV-2 > syphilis > HIV > Hep B
- 50% of new STIs in patients 15–24 yr old

110 million STIs estimated by the Centers for Disease Control and Prevention (CDC) (1A)

Most prevalent STI is human papilloma virus (HPV)

- 25% STIs are incurable (HIV, HSV-2, Hep B)

25% of women are symptomatic, and can have a mucopurulent cervical discharge

40% of untreated women will develop pelvic inflammatory disease (PID), PID is associated with infertility and ectopic pregnancy

Associated conditions

- HPV 6 and 11 tend to cause warts, HPV 16, 18, 31, 33, and 35 are high risk for cellular dysplasia and increase cancer risk
- Condyloma acuminate (HPV)
- Condyloma lata (Trichomonas)
- Serologic: Nonspecific treponemal test (STFT) or fluorescent treponemal antibody absorption test (FTA-ABS)

- Cytologic detection (Tzanck smear) is not sensitive and should not be relied upon

- Growth of HSV in culture with acridine staining is gold standard

- Rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) sensitivity is 6% in primary syphilis, 100% in secondary, and over 95% in tertiary syphilis

- Must confirm with a specific treponemal test

- Excellent for early syphilis

- Positive for life
## General Measures

- **Screen for co-infection including HIV**
- **Educate for prevention of transmission**
- **Screen partners**

### Differential Diagnosis

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Types</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized lichen planus (GLP)</td>
<td>Lesions genital (papillary)</td>
<td>Ulceration is painless</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>Genital ulcers</td>
<td>Painful and pruritic</td>
</tr>
</tbody>
</table>

### Diagnostic Procedures/Surgery

- **Specialized tests** are required for visualization of dark-staining Donovan bodies in sample

### Pathologic Findings

- **Screen partner**
- **Educate for prevention of transmission**
- **Screen for coinfection (including HIV)**

### Nonulcerative STDs

- **Genital ulcer: Other causes**
- **Genital ulcer mnemonic (CHISEL)**
- **Questionable utility**: Not validated

### Imaging

- **N/A**

### Medication

- **First Line**
  - HIV: [Abillice](https://www.gilead.com) 400 mg PO TID for 7–10 days, or tamsulosin 250 mg PO TID for 7–10 days (SJA)
  - Chlamydia: Azithromycin 1 g PO in 1 dose or doxycycline 200 mg IM in 1 dose
  - Syphilis: Primary—Benzathine penicillin G 2.4 million units IM in 1 dose  
    - Latent—Early—Benzathine penicillin G 2.4 million units IM once. Late—Benzathine penicillin G 2.4 million units IM weekly × 3 wk
  - Tertiary—Neurosyphilis—Benzathine penicillin G 2.4 million units IM weekly × 3 wk
  - Syphilis—denosumab crystalline penicillin G, 3–4 million units IM q4h for 10–14 days
  - Granuloma Inguinale: Doxycycline 100 mg PO BID for 21 days or until all lesions are healed
  - LGV: Doxycycline 100 mg PO BID for 3 wk
  - Gonorrhea: Ceftriaxone 250 mg IM in 1 dose, or ofloxacin 400 mg PO in 1 dose; also treat Chlamydia
  - Chlamydia: Azithromycin 1 g PO in 1 dose or doxycycline 100 mg PO BID for 7 days
  - Trichomonas: Metronidazole 2 g PO 1 dose
  - Genital warts (condyloma): Ablation with laser, electrocautery, or cryotherapy
  - HIV: Kaposi sarcomas
  - Genital ulcers: Ablation with electrocautery, electrosurgery, or surgery
  - HIV: Medical management portends long survival
  - HSV: Outbreaks reduced by prophylactic therapies
  - Many STIs cured with treatment

### Follow-up

- **Patient Monitoring**
  - Screen nonpregnant females <25 yr old for gonorrhea/chlamydia. Screen nonpregnant females with risky behavior for gonorrhea/chlamydia.

### Patient Resources

- CDC: [http://www.cdc.gov/std](http://www.cdc.gov/std)

### references


### ADDITIONAL READING

- N/A
- See Also (Topic, Algorithm, Media)
  - **Genital ulcers**
  - **Lymphadenopathy, inguinal**
  - **Sexually Transmitted Infections (STIs)** (Sexually Transmitted Diseases [STDs]), General Images
  - **See Section I and Section II “Specific STDs/STIs”**

### CODES

- **ICD9**
  - D42 Human immunodeficiency virus [HIV] disease
  - 019.1 Other nonviral sexually transmitted infections

### CLINICAL/PEARLS

- **When treating gonorrhea treat for chlamydia as these often coexist.**
- **HIV vaccine recommended for Either HIV vaccine is recommended by the CDC for 11–12-year-old girls. Quadrivalent HPV vaccine is recommended for 11–12-year-old boys. Start series at age 9 years.**
- **Vaccination is also recommended for 13–16-year-old females and 13–21-year-old males who have not completed the vaccine series. Quadrivalent HPV vaccine may be given to 22–26-year-old males and is routinely recommended for both men who have sex with men (MSM) and immunocompromised persons aged 22 through 26 years.**
- **Immunization may lead to urethral stricture in men.**
SICKLE CELL DISEASE, UROLOGIC CONSIDERATIONS

Philip J. Dorsey, Jr., MD, MPH
Benjamin R. Lee, MD, FACS

DESCRIPTION

Sickle-cell SC disease is a chronic hemoglobinopathy transmitted genetically and marked by severe chronic hemolytic anemia and periodic acute painful episodes.

Genetics

SC trait (heterozygote) usually asymptomatic
SC disease: Inheritance of 2 alleles, all RBCs contain HbS tetramer: The deoxygenated state polymerizes
Several haplotypes; allelic with β-thalassemia
Allele is on chromosome 11
Autosomal codominant inheritance pattern

Prevalence

25–30% of Western Africans have SC trait
8–10% of African Americans have SC trait
Prevalence estimated at 8% of African Americans
∼1:500 African American births
1:1,000 Hispanic American births

RISK FACTORS

Renal papillary necrosis due to ischemia; may cause secondary infection or obstruction
Hematuria is due to chronic papillary infarctions
Decreased renal concentrating ability is common
SC trait (heterozygote) usually asymptomatic

ASSOCIATED CONDITIONS

Anaemia
Anemia
Hepatitis C and HIV (increased risk for these and other transfusion-associated infections)
Priapism
Renal medullary carcinoma
Hypothyroidism (Urine with low specific gravity)
Urinary tract infections

GENERAL PREVENTION

Avoid situations that precipitate sickling episodes
Pathologic Findings

Peripheral blood smear: Presence of sickled or deformed RBCs

PHYSICAL EXAM

HTN is unusual.
Nocturnal enuresis
Timing of sexual maturation (delayed puberty)

ASSOCIATED CONDITIONS

Anemia
Acute papillary necrosis

DIAGNOSIS

HISTORY

Prior episodes of SC complications and outcomes
Timing of sexual maturation (delayed puberty)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Complete blood count (CBC). Note degree of anemia
Peripheral blood smear. Presence of sickled or deformed RBCs with high reticulocyte count
Hb electrophoresis: Types and percentage of Hb present

Lab

SC prep: Rapid determination of SC disease vs. trait vs. normal. Check fetal Hb level
Urinary analysis: Hematuria, proteinuria, or infection
Urinal culture: Infection if indicated by urinary analysis or symptoms
Serum creatinine
Monitor for renal insufficiency, and calculate GFR as needed. The creatinine clearance may overestimate the GFR.

TREATMENT

GENERAL MEASURES

Hematuria (see Section I topic)
Priapism (see Section I topic)

DIAGNOSTIC PROCEDURES/SURGERY

CT urogram using low-osmolar contrast, as indicated for hematuria
Ureteroscopy: For hematuria as indicated

IMAGING

CT urogram using low-osmolar contrast, as indicated for hematuria
– May not be useful in progressive renal insufficiency
– May not be useful in progressive renal insufficiency
– May not be useful in progressive renal insufficiency

PHYSICAL EXAM

HTN is unusual.
Nocturnal enuresis
Timing of sexual maturation (delayed puberty)

ASSOCIATED CONDITIONS

Anemia
Acute papillary necrosis

DIAGNOSIS

HISTORY

Prior episodes of SC complications and outcomes
Timing of sexual maturation (delayed puberty)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Complete blood count (CBC). Note degree of anemia
Peripheral blood smear. Presence of sickled or deformed RBCs with high reticulocyte count
Hb electrophoresis: Types and percentage of Hb present

Lab

SC prep: Rapid determination of SC disease vs. trait vs. normal. Check fetal Hb level
Urinary analysis: Hematuria, proteinuria, or infection
Urinal culture: Infection if indicated by urinary analysis or symptoms
Serum creatinine
Monitor for renal insufficiency, and calculate GFR as needed. The creatinine clearance may overestimate the GFR.

TREATMENT

GENERAL MEASURES

Hematuria (see Section I topic)
Priapism (see Section I topic)
SICKLE CELL DISEASE, UROLOGIC CONSIDERATIONS

MEDICATION

First Line

- Simple transfusion:
  - Transfusion performed to increase proportion of RBCs with normal Hb to decrease sludging
  - Blood transfusion performed less frequently than in the past because of risks of exposure to antigens
- Antibiotics: As needed for infections
- Hematuria:
  - Divided with IV hydration is standard
  - Alkalization decreases sludging and control persistent and threatening hematuria, but can cause clot formation in the urinary tract
- Persistent or threatening hematuria may rarely necessitate nephrectomy
- High-dose uro in selected cases
- Priapism (see Section 4.1 "Priapism").
  - Prompt corporal irrigation to induce detumescence and remove old clotted blood
  - Use an adrenergic medication for corporal injection to decrease infusate for detumescence
  - Impotence due to fibrosis can be managed with penile prosthesis after 6 mo
- Delayed sexual maturation:
  - Caution supplemented of testosterone
  - Second Line

Surgery/Other Procedures

May be needed in the acute setting for priapism
- Radiation Therapy

NA

Additional Therapies

- Follow-up and monitoring by hematologist
- Folic acid and penicillin in pediatrics

Genetic counseling

Complementary & Alternative Therapies

NA

ONGOING CARE

PROGNOSIS

Several factors aside from genetic inheritance determine prognosis, including frequency, severity, and nature of specific complications.

COMPLICATIONS

- Nephropathy:
  - Renal insufficiency
  - Vas-class renal medulla secondary to hyperosmolality, inducing RBCs sludging
  - Progressive cortical infarction leads to CRF, average age of onset is 23 yr
  - Hypertension: inability to maintain systolic urine in the face of dehydration or vasopressin
  - Usually associated with renal insufficiency, able to dilute urine
  - Associated impairment of K excretion
  - Renal biopsy:
  - Fibrotic and segmental glomerulosclerosis, membranous glomerulopathy, or MPGN
  - Proteasia may progress to full-blown nephrotic syndrome

- Hematuria:
  - Microscopic or gross hematuria, mechanism unknown. Source rarely identified, possibly due to papillary necrosis
  - Usually unilateral (left-sided)
  - May be female
  - Usually rectum with contraceptive (e.g., sperm, condoms, hydration) with 50% recurrence
  - Associated with nephrotic syndrome
  - Papillary necrosis:
  - Due to medullary ischemia from sludging in vasa recta (see in 40% of patients with SCD)
  - Radiologic diagnosis: can be difficult due to poor concentrating ability of kidneys
  - Can cause hematuria
  - Can obstruct, if sloughed papilla blocks the UPJ or ureter
  - Priapisms:
  - Affects ~66% of SC disease patients
  - 2 age peaks: onset usually after puberty is 5–13 yr, then at 21–29 yr
  - Initiating factors: Nocturnal penile tumescence and sexual arousal
  - Typically, biopsoral involvement
  - Pathophysiology: Engagement and sludging of the corpora, with no outflow and low flow
  - Major risk in fibrosis and subsequent impotence; children have greater chance of recovery and subsequent erectile function
  - Impotence:
  - Fibrosis from recurrent episodes of priapism
  - Delayed sexual maturation:
  - Primary hypogonadism, due to testicular ischemia or infarction, hypothyroidism, or hypothalamic insufficiency
  - Correlates with severity of sickle disease
  - Infertility:
  - Complication of hypospermatism and direct testicular insult by ischemia or infarction
  - UT:
  - Usually escherichia coi, or other gram-negative bacteria
  - Can lead to more serious infections or bacteremia

PRO Academy 

- Incomplete distal RTA type I (from progressive medullary infarction
  - Inability to lower urine pH to <5
  - Compensatory hyperchloremic metabolic acidosis in SC disease and renal insufficiency
  - Not associated with nephrotic

- Acute urinary retention:
  - Related to acute, painful SC, transient, resolves with resolution of the acute episode
  - Renal medullary carcinoma:
    - Median age 13 yr
    - High mortality

Follow-Up

Patient Monitoring

- Renal function over time
- Regular follow-up

Patient Resources


References


Additional Reading

- See Also (Topic, Algorithm, Media)

- Fajos N, Grazioli A, et al. Sickle cell disease and renal insufficiency
- Bissell A, et al. AUA Update Series

Codes

ICD9

- 599.70 Hematuria, unspecified
- 599.70 Nephropathy, unspecified
- 599.70 Priapism
- 599.70 Renal medullary carcinoma
- 599.70 Ureteral carcinoma

ICD10

- D57.1 Sickle cell disease without crisis
- K88.89 Priapism, unspecified
- K88.89 Hematuria, unspecified
- K88.89 Ureteral carcinoma
- K88.89 Renal medullary carcinoma

Clinical/Surgical Pearls

Urologic complications are common in SC disease.
SPERMATIC CORD MASS AND TUMORS
Nima Baradaran, MD
James S. Rosof, MD

DESCRIPTION
• The spermatic cord extends from the internal inguinal ring to the testicle, passing through the inguinal canal.
• Cord structures consist of vas deferens, internal and external spermatic arteries, artery to the testicle, pampiniform plexus, lymphatic, nerves, investing layer of fascia, and cremaster muscle.
• Considered paratesticular tissue.
• Masses or swelling can be cystic or solid:
  - Most cystic (75-80%)
  - Usually asymptomatic
  - Most solid spermatic cord masses are also benign.

EPIDEMIOLOGY
Incidence
Variates by type (see Pathophysiology).
Prevalence
Variates by type (see Pathophysiology).

RISK FACTORS
Variates by type (see Pathophysiology).

GENETICS
Variates by type (see Pathophysiology).

PATHOPHYSIOLOGY
• Cord mass can arise from cord contents or from structures above or below the cord:
  - Generally noncute and benign
  - Most common malignant tumors are sarcoma
  - Varicocele
  - Hydrocele
  - Generally nonacute and benign
  - Cord mass can arise from cord contents or from structures above or below the cord.
  - Considered paratesticular tissue
  - Rare congenital anomaly from abnormal closure of the processus vaginalis
  - Palpable, grade II: Palpable without Valsalva maneuver.
  - Generally nonacute and benign
  - May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
  - Painful groin mass contiguous with the cord structures that transilluminates.

Hydrocele:
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.

Varicocele:
• Enlarged, tortuous spermatic veins above the testis; most common on the left side.
• Varicocele:
  - Rare inflammation of spermatic cord, epididymis, and paratesticular soft tissue, from muscle, adipose, or connective tissue
  - More common in young, sexually active males
  - Presents as TBJ, epithelial, difficult to differentiate from acute epididymoorchitis
  - Usually secondary to infection of epididymis via direct extension.
  - Scrotal:
    - Systemic granulomatous disease, increased intestinal absorption of calcium, hyperparathyroidism, and hypercalcemia
  - Varicocele:
    - Inflammation of spermatic cord secondary to severe epididymitis or due to trauma
  - Flail Harlequin:
    - Caused by Wuchereria bancrofti, often with a thickened spermatic cord and epididymis
  - Undescended testicle
  - Retroperitoneal tumors:

ASSOCIATED CONDITIONS
• Renal tumor invading renal vein or retroperitoneal mass compressing right gonadal vein with ischemia.
• Spasmatic cord:
  - Cloudy fluid and sperm filled cyst arising from epididymal tubules.

HISTORY
• Patients present with symptoms or asymptomatic mass with or without swelling.
• Most masses are painless or at onset.
• Presence or absence of pain does not differentiate benign or malignant mass.
• Scrotal elevation may provide relief.
• Recumbent position may resolve mass and pain in varicocele and communicating hydrocele.
• History of cryptorchidism is important.

ALERT
• Always rule out torsion of cord if pain is acute.

PHYSICAL EXAM
• Examine patient in warm room in both upright and supine positions.
• Cord mass can be palpated in the inguinal region or the upper scrotum.
• Palpate mass with thumbs and 1 to 2 fingers of both hands and note character (hard, firm, cystic).
• Transillumination signifies cystic mass: cystic mass may not transilluminate if thick wall, chronic inflammation, or blood present.
• Spermatic cord can be followed to the internal inguinal ring by palpation.
• Verify both testicles present in scrotum.
• The vas deferens can be felt in the scrotum by 1st encircling the cord with the fingers and allowing small amounts of cord to pass through.
• Testicular biopsy may be appropriate.
• Palpation can determine superior and inferior extent of mass.
• Testicular tissues may be atrophic.

DIAGNOSIS

BASICS
• swims toward synovial and parietal layers of tunica vaginalis.
• Palpable, grade II: Palpable without Valsalva maneuver.
• Generally nonacute and benign
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Palpable, grade II: Palpable without Valsalva maneuver.
• Generally nonacute and benign
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Palpable, grade II: Palpable without Valsalva maneuver.
• Generally nonacute and benign
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Palpable, grade II: Palpable without Valsalva maneuver.
• Generally nonacute and benign
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoogenesis.
• Painful processus vaginalis causes collection of peritoneal fluid between the vaginal and parietal layers of tunica vaginalis.
• May cause infertility: likely increasing scrotal temperature, impairing spermatozoegen
DIFFERENTIAL DIAGNOSIS
- Cellularity arrangement: occasional or absent mitotic figures and uniform
distinguish leiomyosarcoma from leiomyoma based on
- Solid masses: Biopsy (mostly excisional) with surgical
Diagnostic Procedures/Surgery
- Imaging
- Lab
- Diagnostic Tests & Interpretation

Vasitis and vasitis nodosa (usually associated with
Varicocele
- Testis tumor
- Sperm granuloma, spermatocele
- Undescended/retractile testicle, polyorchidism
- Malignant tumor: Liposarcoma, rhabdomyosarcoma,
inguinal lymphadenopathy – Cannot differentiate benign or malignant mass
- Inguinal hernia
- Adenomatoid tumor of the cord (1,2)
- MRI or CT in certain clinical scenarios
- Scrotal US: Solid vs. cystic mass (2)

Adenomatoid tumors found on routine exam:
- Lipoma of the cord is palpated as smooth, firm mass
- Torsion of the cord or incarcerated/strangulated
- Lipoma, leiomyosarcoma, and
- rhabdomyosarcoma may recur; closely monitor
- (physical exam, imaging)

In children, repair hydrocele by age 2 if it does not
- Communicate hydrocele often involves in
- children within 1st yr
- Inguinal hernia (adults): Herniorrhaphy
- Communicating hydrocele often resolves in
- Varicocele:
- – Varicocelectomy may relieve pain and improve fertility
- – Standard tests: volume measurements are
- Standard tests: volume measurements are
- mainstay of assessing need for surgical
- management of varicocele
- Explore solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected
- – Inguinal hernia: (adults): Hemorraphy
- Communicating hydrocele with hernia:
- – Explore all solid masses for malignancy.
- – Explore solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected
- – Explore all solid masses for malignancy:
- – Exploration of asymptomatic contralateral inguinal
- canal in children with inguinal hernia or
- communicating hydrocele is controversial
- Varicocele:
- – Varicocelectomy may relieve pain and improve fertility
- – Explore solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected
- – Communicating hydrocele with hernia:
- – Explore all solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected
- – Communicating hydrocele with hernia:
- – Explore all solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected
- – Communicating hydrocele with hernia:
- – Explore all solid masses for malignancy:
- – Inguinal incision; testis is delivered and inspected

GENERAL MEASURES
- Distinguish tests and epididymitis (physical exam, transillumination, social DoS).
- Most cutaneous masses do not need treatment.
- Investigate pain as presenting feature; sarcoma is often misdiagnosed as inflammatory lesion.

MEDICATION

First Line
- Anti-TB short course for 6–9 mo for TB (tuberculoma) in spermatic cord

Second Line
- N/A

SURGERY/OTHER PROCEDURES
- Surgical Excision: if choice of procedure
- Elective exploration of asymptomatic contralateral inguinal

– Biopsy to confirm diagnosis
– Early control of cord at internal ring
– Inguinal incision; testis is delivered and inspected
– Standard tests: volume measurements are
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected
– Explore solid masses for malignancy:
– Inguinal incision; testis is delivered and inspected

ADDITIONAL TREATMENT
Radiation Therapy
- Retroperitoneal lymphadenopathy with adjacent
- radiation or chemotherapy indicated for malignant

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

PEARLS
- Pain may be attributed to emergencies such as
torsion,
- Ultrasound is a valuable diagnostic tool.

PROGNOSIS
- Excellent for benign lesions

COMPLICATIONS
- Risk of infertility in varicocele

FOLLOW-UP
- Patient Monitoring
- None for benign masses.
- Liposarcoma, leiomyosarcoma, and
- rhabdomyosarcoma may recur; closely monitor
- Ager 2 if it does not

Patient Resources
- N/A

REFERENCES
- 1. Eble JN, Sauter G, Epstein JI, et al., eds. Pathology
- of tumors of the urinary system and
- male genital organs. World Health Organization
- classification of tumours. Lyon, France: IARC Press;
- 2. Dogra V, Gottlieb RH, Oka M. Sonography of the
- scrotum.

ADDITIONAL READING
- 68-year-old male with left spermatic cord mass. Rev

See Also (Topic, Algorithm, Media)
- Genitourinary Male, Male and Female
- Lipoma, Spermatic Cord
- Paratesticular Tumors
- Scrotum and Testicle, Mass
- Scrotum and Testicle, Mass Images
- Spermatic Cord Mass and Tumors Images
- Vascular, Adult
- Vascular, Pediatric

CODES
- ICD9
- 200.8 Benign neoplasm of other specified sites
of male genital organs
- 608.9 Unspecified disorder of male genital organs
- ICD10
- C49.5 Malignant neoplasm of connective and soft
- tissue of pelvis
- D29.8 Benign neoplasm of other specified male
genital organs
- N50.9 Disorder of male genital organs, unspecified

CLINICAL/SURGICAL

PEARLS
- Pain may be attributed to emergencies such as
torsion,
- Ultrasound is a valuable diagnostic tool.
SPERMATOCELE
Irvin H. Hirsch, MD
Leonard G. Gomella, MD, FACS

**PATHOPHYSIOLOGY**
- Main concern is usually that of confusion with a true testicular mass.
- Precise mechanism is unknown.
- Cystic dilatations of tubules of the epididymis
- The efferent ductules in the head of the epididymis
- The distinction between a spermatocele and an epididymal cyst is based on size, epididymal cystic masses >2 cm are spermatoceles
- Spermatoceles are always located superior to the testis and are palpable as distinct from the testis, which differentiates them from hydroceles
- Spermatocele generally range in size from 2 to 5 cm
- Trauma and inflammation may result in obstructed efferent ductules or epididymal tubules, resulting in a dilated spermatocele
- No effect on fertility
- Most are idiopathic
- Most <5 cm in size

**ASSOCIATED CONDITIONS**
- Epididymal obstruction may rarely be present
- Prior vasectomy
- High association with tubular ectasia of the rete testes

**DIAGNOSIS**

**HISTORY**
- Typical presentation is a painless, asymptomatic, intratesticular mass found on testicular self-exam or on routine office exam.
- Occasionaly may present with orchialgia or scrotal heaviness
- No associated urinary symptoms

**PHYSICAL EXAM**
- Palpation shows a smooth, soft, nontender mass at the head (caput) of the epididymis
- Less palpable posterior to the testis but is distinct from testis
- A cystic mass above the testis is usually demonstrated on scrotal transillumination

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urine analysis

**Imaging**
- Scrotal US is diagnostic
  - Lesion is hypoechogenic with posterior acoustic enhancement
  - May have internal echoes
- MRI if US is indeterminate

**Differential Diagnosis**
- Adenoma tumor of the epididymis
  - Most common solid tumor of the epididymis
  - Enlarged epididymis
- Epidermoid cyst
  - Most common solid tumor of the epididymis
  - Hydrocele, the other common cystic lesion is devoid of spermatozoa
- Fibromuscular wall lined by cuboidal epithelium

**BASICS**

**DESCRIPTION**
- Spermatocele is a benign, fluid-filled cystic mass most often in the head (caput) of the epididymis
- The spermatocele can occur in other areas of the epididymis, rete testis, or along the vas deferens
- Sometimes referred to as a “spermatic cyst” or an “acquired epididymal cyst.”
- Clinically, spermatocele is differentiated from a hydrocele in that the spermatocele may contain viable or nonviable spermatozoa.
- Usually not a cause of epididymal obstruction
- Also called an epididymal cyst or acquired epididymal cyst in the literature (1)
- Some sources state that the epididymal cyst is congenital and represents the most common epididymal mass.
- The origin of the epididymal cyst is thought to be lymphatic.
- Epididymal cyst fluid does not contain spermatozoa.
- Clinical management is similar, so the differentiation between spermatocele and epididymal cyst may not be significant.

**EPIDEMIOLOGY**
- Incidence
  - Peak incidence in 4th–5th decades
  - Rare in children
  - No racial or ethnic predilection
  - Rare in children
  - Peak incidence in 4th–5th decades

**RISK FACTORS**
- Diethylstilbestrol (DES) exposure in utero
- Inflammation
- VHL syndrome: Von-Hippel Lindau (VHL) syndrome
- Mutations of the VHL suppressor gene on 3p
- VHL syndrome
  - Increased incidence of epididymal cysts and papillary cystadenomas of the epididymis
  - Clinical management is similar, so the differentiation between spermatocele and epididymal cyst may not be significant
  - On US, most common appearance is 15–20-mm solid mass with small cystic components
  - Epidermoid Epididymis/Epiploicae
    - Acute, very tender on exam
    - Chronic, may have secondary calcification
    - Common cause of epididymal pain

**ASSOCIATED CONDITIONS**
- High association with tubular ectasia of the rete testis

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urine analysis

**Imaging**
- Scrotal US is diagnostic
  - Lesion is hypoechogenic with posterior acoustic enhancement
- MRI if US is indeterminate

**DIFFERENTIAL DIAGNOSIS**
- Adenoma tumor of the epididymis
  - Most common solid tumor of the epididymis
  - Enlarged epididymis
- Epidermoid cyst
  - Most common solid tumor of the epididymis
  - Hydrocele, the other common cystic lesion is devoid of spermatozoa
- Fibromuscular wall lined by cuboidal epithelium

**BASICS**

**DIAGNOSIS**

**HISTORY**
- Typical presentation is a painless, asymptomatic, intratesticular mass found on testicular self-exam or on routine office exam.
- Occasionaly may present with orchialgia or scrotal heaviness
- No associated urinary symptoms

**PHYSICAL EXAM**
- Palpation shows a smooth, soft, spherical nontender mass at the head (caput) of the epididymis.
- Less palpable posterior to the testis but is distinct from testis
- A cystic mass above the testis is usually demonstrated on scrotal transillumination

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Urine analysis

**Imaging**
- Scrotal US is diagnostic
  - Lesion is hypoechogenic with posterior acoustic enhancement
  - May have internal echoes
- MRI if US is indeterminate

**DIFFERENTIAL DIAGNOSIS**
- Adenoma tumor of the epididymis
  - Most common solid tumor of the epididymis
  - Enlarged epididymis
- Epidermoid cyst
  - Most common solid tumor of the epididymis
  - Hydrocele, the other common cystic lesion is devoid of spermatozoa
- Fibromuscular wall lined by cuboidal epithelium
Surgey should be deferred in men seeking fertility
Ligation of spermatocele at its stalk
Performed by magnified or microsurgical dissection
Spermatocelectomy is elective and indicated for
Supportive care is usually sufficient:
Most do not require treatment unless symptomatic.
Varicocele
TB of the epididymis
Sperm granuloma:
Sarcoid
Polyorchidism
Papillary cystadenoma:
Malignant epididymal tumor:
Epithelial and transitional cell cancers
Gastrointestinal tumors: Pancreatic, rectal, colon
Gynecologic cancers: Cervical, uterine
Melanoma
Adenocarcinomas: Cervix, breast, prostate, bladder
Lymphomas: Non-Hodgkin lymphoma, Hodgkin disease
Malignant germ cell tumors: Testicular germ cell tumors
Seminoma, non-seminomatous germ cell tumors
Chemotherapy: For systemic disease
Radiotherapy: For localized disease
Orchidectomy: For local disease
Prognosis: 5-year survival rates
Additional treatment
Surgical therapy: Epididymectomy, sperm cystectomy
Non-surgical therapy: Vasectomy, intratesticular chemotherapy
Future fertility
Testicular biopsy: Biopsy of the testis to evaluate spermatogenesis
Testicular self-exam: A method to detect testicular masses
Sperm banking: Storing sperm for future use
Sperm retrieval: Technique to retrieve sperm from infertile men
Sperm injection: Intrauterine insemination, intracytoplasmic sperm injection
Prognosis
Typical cases
Non-seminomatous germ cell tumors
Seminoma
Other tumors
Close follow-up
Surgical management
Radiation therapy
Chemotherapy
Fertility preservation
Orchidectomy
Adjuvant therapy
Follow-up
Patient monitoring
Patient resources
Additional reading
Clinical/surgical pearls
• A common pitfall is the failure to distinguish between hydrocele and spermatocele preoperatively.
• Spermatoceles are always located superior to the testis and are palpable as distinct from the testis, which differentiates them from hydroceles.
• Ideal surgical approach: Incise the tunica albuginea testis to maintain the spermatocele definition throughout its excision.

Additional treatments
• Transcutaneous aspiration with or without sclerotherapy:
  • Agents used have included tetracycline, fibrin glue, phentol, talc powder, and others
  • Not usually recommended due to high recurrence rate and chemical epididymitis
  • Spermatocele aspiration may provide a sperm source for azoospermic men treated by IVF or ICSI

Additional therapies
N/A

Prognosis
• Most require no intervention and do not lead to epididymal obstruction.
• Recurrence rate is low postoperatively.

Complications
• Orchalgia
• Concern for cancer
• Postoperative spermatocele
• Vascular injury during spermatocelectomy causing testicular atrophy
• Infection
• Epididymal obstruction: Very concerning in cases of bilateral spermatocele surgical repair. Some authors recommend sperm cryopreservation in this setting

Follow-up
• Periodic scrotal self-exam
• Sperm count and motility
• Continued testosterone self-exam

Ongoing care
• Periodic scrotal US if symptoms recur
• Sperm count and motility

References
SPINAL CORD INJURY, UROLOGIC CONSIDERATIONS
Jessica Wetterlin, MD
Derek Matoka, MD

BASICS

DESCRIPTION
- Spinal cord injury (SCI) may result from damage to the spinal column secondary to trauma, vascular injury, infection, or disc prolapse
- SD can impact lower urinary tract and sexual function and varies based on level and completeness of injury
- Upper and lower urinary tract dysfunction due to SCI can lead to significant morbidity and mortality
  - Increased risk for renal failure, UTI (urinary tract infection), small/badder candidiasis, and malignancy

EPIDEMIOLOGY
- Incidence
  - 40 cases per million in US; 12,000 new cases per year

DESCRIPTION
- Derek Matoka, MD

ASSOCIATED CONDITIONS
- Bladder wall thickening and fibrosis common
- Pathologic Findings
- Diagnostic Tests & Interpretation

DIAGNOSIS

HISTORY
- Onset, duration, etiology of injury
- Voiding symptoms
- - Incontinence or obstructive
- - Inconce: Stress, urge, overflow
- Method of urinary management
- Voluntary voiding, closed intermittent catheterization (OIC), indwelling catheter or urethral catheter

PHYSICAL EXAM
- Temperature, blood pressure
- Palpable flank mass/tenderness
- Suprapubic fullness: Distended bladder
- Evaluate instincion, spontaneity or with stress maneuvers
- GU exam for testicular or prostate abnormality
- Complete Neurologic exam: Sensation, tone, and bladder activity

GU exam for testicular or prostate abnormality
- Evaluate instincion, spontaneity or with stress maneuvers
- Complete Neurologic exam: Sensation, tone, and bladder activity

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Blood studies:
    - Serum chemistry: Basic metabolic panel (BMP) (assess renal function and acidosis), CBC
    - Urinalysis
  - Imaging:
    - Renal US (ultrasound): To screen for calculi, urolithiasis episodes, interventions, calculus
    - VCUG (voiding cystourethrogram):
      - Trabeculation, diverticulum, incomplete emptying, vesicoureteral reflux
      - Nuclear medicine renal scan:
        - Performed to evaluate for compromised function or presence of obstructive element

Diagnostic Procedures/Surgery
- PVR: To ensure complete bladder emptying
- Video urodynamics: Essential to assess and follow bladder and urodynamic dysfunction
- Video urodynamics: Essential to assess and follow bladder and urodynamic dysfunction

Diagnosis
- Injury
  - Intervertebral disc disease
  - Malignancy (metastasis)
  - Spinal cord vascular disease
  - Traumatic
  - Ventral body injury

DIFFERENTIAL DIAGNOSIS
- Intervertebral disc disease
- Malignancy (metastasis)
- Spinal cord vascular disease
- Traumatic
- Ventral body injury
TREATMENT

GENERAL MEASURES
- Goal of treatment: Optimize intravesical bladder pressures to protect upper urinary tract
- Spontaneous voiding with continence
- Indwelling catheterization should be avoided when possible to avoid complications (urethral strictures, UTI, calciﬁcation, malignancy)
- Indwelling urethral catheter or suprapubic tube (SPT)
- Immobile self-catheterization: Most effective treatment, requires manual dexterity
- If unable to self-catheterize urethra
- Male: External catheter, cutout obstruction procedure, urinary diversion, or creation of continent catheterizable stoma
- Female: Urinary diversion or creation of continent catheterizable stoma
- Incontinence between catheterizations may suggest elevated intravesical pressure due to poor compliance or DO
- Reduce storage pressure. Increase frequency of catheterization, anticholinergics, or augmentation cystoplasty
- Lower urinary tract that cannot be reconstructed require urinary diversion with or without continent ileovesicostomy
- Incontinent urostomy
- Continent urinary reservoir

MEDICATION
First Line
- Anticholinergics improve urinary storage pressure and decrease involuntary contraction
- Oxybutynin 5 mg PO BID-TID
- Tolterodine 2 mg PO BD, others
- α-adrenergic blockers: Decrease internal sphincter function, lower voiding pressures, ineffective for DO
- Agents include: doxazosin 1–8 mg PO QD, tamsulosin 1–10 mg PO QHS, tamsulosin 0.4 mg PO QD

Second Line
- Botulinum toxin injected into detrusor

SURGERY/OTHER PROCEDURES
- Spina bifida requires external catheter
- Augmentation cystoplasty: Use of internal segment to enlarge the bladder, increasing bladder volume to decrease intravesical pressure
- Usually requires clean intermittent catheterization (CIC)
- Neuropathy
- Useful for those unable to perform CIC
- Social reeducation
- Deafferentation with dedenervation abolishes spontaneous detrusor contraction, improving urinary storage
- Nerve root stimulation allows for control over detrusor contraction

ADDITIONAL TREATMENT
Radiation Therapy
HIV

Additional Therapies
Sacral nerve root stimulator

Complementary & Alternative Therapies
- Vanillin agents (capsaicin and wakameferon) suppress uninhibited detrusor contraction

ONGOING CARE

PROGNOSIS
- Poor urologic care improves morbidity, mortality, and quality of life in SCI individuals
- Early data suggested renal disease was major cause of death in the paraplegic patient. However, more recent data has revealed that pneumonia, sepsis, heart attack, accidents, and suicides are now leading causes of mortality (2)

COMPLICATIONS
- Urosepsis (3)
- Ulceration
- Due to urinary tract, chronic infection, acidosis associated with immobility, bladder calculi related to chronic indwelling catheters
- Upper urinary tract deterioration
- Hydroureteronephrosis due to elevated intravesical pressure
- Lower urinary tract deterioration
- Detrusor hypertrophy, decreased compliance
- Urinary-erosion, fistula with chronic catheterization

Autonomic dysreflexia
- Can occur with SCI at T6 level or higher with complete/incomplete spinal cord lesions
- Triggered by a noxious stimuli below the level of the lesion, bladder and bowel dysfunction are the most common causes
- Unopposed sympathetic activity results in vasoconstriction and HTN (hypertension)
- HTN sensed by baroreceptors in carotid and aortic arch activating parasympathetics above lesion to counter the sympathetic response. However, the SCI inhibits parasympathetics activity below the level of the lesion
- Signs and symptoms include HTN, headache, bradycardia, flushing, diaphoresis, blurred vision
- Treatment: Remove offending stimuli
- Address HTN with rapid onset/short duration agent (nifedipine, captopril, hydralazine)

Detrusor hypertrophy
- Associated with chronic catheter
- Depression
- Skin complications (related to incontinence)

Felty’s Syndrome
- Urologic complications (related to infection)

FOLLOW-UP

Patient Monitoring
- UTS screening: Routine urine cultures are unnecessary in healthy, asymptomatic individuals
- UDS: Completed periodically. However, no consensus exists regarding frequency. Obtain UDS after resolution of spinal shock and every 5 yr in stable patients. If a change in bladder-related symptoms (incontinence) is noted, UDS should be repeated to evaluate for change in bladder dynamics
- UTI: Useful, noninvasive screening tool to monitor upper and lower tracts
- Recommended initially and annually for 5–10 yr, then every other year

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
- Autonomic Dysreflexia
- Bladder Anuria (Detrusor Areﬂexia)
- Detrusor-Sphincter Dyssynergia (DSD)
- Neurogenic Bladder, General
- Neuropathic Detrusor Overactivity (NDO)
- Spinal Cord Injury, Urologic Considerations
- Augmentation
- Urinary-Stomal, Indications and Normal Values

COMMENTS

CLINICAL/SURGICAL PEARLS
- Suprasacral lesions generally result in an upper motor neuron deﬁcit with NDO
-Sacral lesions generally produce a lower motor neuron deﬁcit with resulting detrusor areﬂexia
- UDS should be obtained at least 6 wk after injury and repeated when appropriate

REFERENCES
STRESS URINARY INCONTINENCE, FEMALE
Nima Baradaran, MD
Samuel Walker Nickles, MD
Eric S. Rovner, MD, FACS

BASICS

DESCRIPTION
- Stress urinary incontinence (SUI) is subjectively defined by the International Continence Society as the “true complaint of involuntary leakage on effort or exertion, or on sneezing or coughing” (1)
- Urinary incontinence (UI) should be further described by specifying: Type, frequency, severity, precipitating factors, social impact, effect on hygiene and quality of life, the measures used to contain the leakage and whether or not the individual seeks or desires help because of urinary incontinence (1)

EPIDEMIOLOGY
Incidence
Annual incidence of any type of new UI ranges from 3 to 11% and increases with age, with approximately 50–70% attributed to SUI alone or in association with urge incontinence (mixed urinary incontinence or MUI)

Prevalence
~30% of women aged 30 to 60 have urinary incontinence, with approximately 50–70% attributed to SUI alone or in association with urge incontinence (mixed urinary incontinence or MUI)

Significant variation is seen in specific populations, eg, incontinence, with approximately 50–70% attributed to SUI alone or in association with urge incontinence (mixed urinary incontinence or MUI)

Incidence
Annual incidence of any type of new UI ranges from 3 to 11% and increases with age, with approximately 50–70% attributed to SUI alone or in association with urge incontinence (mixed urinary incontinence or MUI)

Prevalence
~30% of women aged 30 to 60 have urinary incontinence, with approximately 50–70% attributed to SUI alone or in association with urge incontinence (mixed urinary incontinence or MUI)

Significant variation is seen in specific populations, eg, community dwelling vs. long-term facility occupants, and nulliparous vs. postpartum females.

RISK FACTORS
Aging, obesity, smoking, pregnancy, and child birth

Genetics
Deficient collagen structures

PATHOPHYSIOLOGY
Anteriorly: Weakness of urethral supportive structures (vaginal wall and surrounding connective tissue) leads to hypermobility and loss of urethral compression (1)

Intrinsic sphincter deficiency: Loss of intrinsic urethral closure, coaptation, and function

Neurogenic: Rarely, loss of spinal sympathetic reflex and/or pudendal nerve efferents leading to relaxation of the external and intrinsic closure forces of the urethra.

ASSOCIATED CONDITIONS
- Chronic cough, COPD, obesity
- Pelvic organ prolapse (cystocele, rectocele) and/or anal incontinence
- 40% of women with urethral sphincter incompetence will have a cystocele
- Occult incompetence: Urethral sphincteric incompetence masked by the presence of pelvic prolapse

GENERAL PREVENTION
See treatment

DIAGNOSIS

HISTORY
- Subjective characterization of UI (aggravating factors)
- Duration of symptoms
- Impact on life
- Diaphoresis vs. nocturnal UI
- Urinary frequency, urgency, nocturia
- UI history
- Pad use
- Past medical/surgical history
- Neurologic (Parkinson, MS, back surgery, etc.)
- Medical conditions (DIAB, dementia, etc.)
- Radiation and trauma
- Gynecologic history (parity, hormonal status)
- Previous pelvic surgery
- Medications (psychotropics and diuretics)

PHYSICAL EXAM
- Cough stress test to be negative.

DIAGNOSTIC TESTS & INTERPRETATION

BASICS

Lab
- Routine renal function evaluation unnecessary
- Pad test
- Postvoid residual measurement
- Voiding diary
- Quality of life questionnaires
- Urodynamics
- Urodynamics indicated especially in patients who have failed previous pelvic floor reconstruction or with mixed incontinence, urinary urgency, or obstructive symptoms, and in those who have elevated PVRs or neurologic disease

Pathologic Findings
- Sphincter muscle deficiency is the main pathology.

DIFFERENTIAL DIAGNOSIS

- Enuresis means any involuntary loss of urine. If it is used to denote incontinence during sleep, it should always be qualified with the adjective “nocturnal”
- Richter: Vesicovaginal, rectovaginal
- Mixed urinary incontinence (MUI) is the complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing, or coughing
- Neurogenic bladder (CVD and spinal cord lesions)
- Pelvic organ prolapse
- Polyuria/polydipsia
- Potentially reversible conditions (DIAPERS):
  - Drugs
  - Infection
  - Atonic vaginitis
  - Psychological (depression, delirium, dementia)
  - Endocrine (hyperglycemia, hypercalcemia)
  - Restricted mobility
  - Fluid intake
  - Situation specific: eg, the report of incontinence during sexual intercourse, origgie incontinence
  - Urethral abnormalities (diverticulum)
  - Urge vs. stress vs. overflow incontinence
  - Urethral incontinence: Involuntary leakage accompanied by or immediately preceded by urgency
  - Urinary leakage may need to be distinguished from sweating or vaginal discharge
  - Urethral fist infection
  - Vaginal vaulting

- Cystoscopy in the presence of urinary urgency, hematuria, UTI, or other irritative symptoms, particularly if they have previously undergone a previous anti-incontinence procedure, pelvic radiation, or pelvic prolapse repair

- Urodynamics indicated especially in patients who have failed previous pelvic floor reconstruction or with mixed incontinence, urinary urgency, or obstructive symptoms, and in those who have elevated PVRs or neurologic disease
STRESS URINARY INCONTINENCE, FEMALE

TREATMENT

GENERAL MEASURES
- Initial therapy includes behavioral modification and pelvic floor exercise
- Lifestyle modifications
- Weight loss, smoking cessation, moderation of fluid intake, caffeine and/or alcohol

ADDITIONAL TREATMENT
- Pelvic floor muscle training (PFMT)
- Transurethral injectable bulking agents

SURGERY/OTHER PROCEDURES
- In rare cases an α-adrenergic receptor antagonist (phenylpropanolamine) or tricyclic antidepressant (imipramine) may be utilized but this is an off-label use
- Duloxetine is a serotonin and norepinephrine reuptake inhibitor approved for major depression and is approved for treatment of SUI in Europe but not in US

Medication
- Inhibits detrusor contractions
- Strong pelvic floor contraction increases intra-abdominal pressure
- Patient compliance and periodic reinforcement are essential
- Timed voiding
- Fluid and dietary management
- Patient education and periodic reinforcement are essential
- Pelvic floor muscle training (PFMT)
- Vaginal cones and weights
- Biofeedback: Helps patients identify and isolate correct pelvic muscles
- Pelvic floor electrical stimulation
- Magnetic therapy
- Wire- or extravesical and intravaginal support and occlusive devices (pessaries, plugs, urethral inserts, etc.)

Complications
- Untreated SUI may result in skin rash and chronic irritation
- Vaginal, urethral, and intravesical erosion of the synthetic suburethral sling
- Complications of sling procedures include:
  - Urinary retention following stress incontinence
  - Dyspareunia
  - Voiding dysfunction (due to obstruction), UTI, pain, and dyspareunia
  - Vaginal, urethral, and intravesical erosion of the intravesical and intravaginal support, voiding dysfunction (due to obstruction), UI, UTI, and dyspareunia
  - Vascular injury or intestinal perforations are rare and associated with slings, as well as open abdominal approaches

Follow-up
- Patient Monitoring
- Conservative management requires regular reinforcement and education

Patient Resources
- National Association for Continence
- http://www.nafc.org

REFERENCES

Ongoing Care
- Medication
- Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2010(11):CD003654.

Additional Reading
- Dmochowski RR, Blaivas JM, Gormley EA, et al. Second Line

Addendum
- Pelvic floor muscle training training versus no treatment, or inactive control treatments, for urinary incontinence in women.


See Also
- Topic, Algorithm, Media
- ICD (International Classification of Incontinence Questionnaire), ICQ-MIUTS
- Incontinence Impact Questionnaire (IIQ-7)
- Incontinence, Urinary, Adult Female
- Pad Test
- SUI (Stress Urinary Incontinence)
- Stress Urinary Incontinence, Female Images

Codes
- ICD9: 593.3 Stress incontinence, female
- ICD10: N39.3 Stress incontinence (female) (male)

Clinical/Surgical Pearls
- It is imperative to distinguish different types of urinary incontinence in female.
- Lifestyle modification and conservative treatment is the 1st step in management.
- Midurethral slings are the standard surgical treatment and are highly effective in properly selected patients.
STRESS URINARY INCONTINENCE, MALE

Jack Matthew Zuckerman, MD
Kurt A. McCammon, MD, FACS

PATHOPHYSIOLOGY

Male continence relies on an intact internal and external urinary sphincter and a compliant bladder for storage of urine.

Internal sphincter:
- Bladder neck and prostate
- Smooth muscle/involuntary
- Internal sphincter
- Detrusor/propulsive

External sphincter:
- Contraction of the external sphincter is required for SUI to be present

Genetics
N/A

DIAGNOSIS

HISTORY

- Incontinence history
- Duration
- Severity (pads, diapers, tissues, etc.)
- The nature of the absorptive device helps with the assessment of the degree of leakage
- Precipitating events (cough, sneeze, etc.)
- Presence/absence of urge symptoms
- Suggests pharmacologic therapy may benefit
- Frequency of urination
- Fluid intake, including use of caffeine, alcohol
- Use of medications such as diuretics or antihypertensive medications
- Neurologic or spinal cord disease or injury
- Voiding diary
- Prior pelvic surgery or other urologic surgery
- Prior pelvic radiation
- Prior anti-incontinence procedures
- AKU symptom score
- ICIQ (International Consultation on Incontinence Questionnaire), ICS-MULTIS

PHYSICAL EXAM

- Abdominal exam
- Urinalysis and urine culture
- Frequency of urination
- Presence/absence of urge symptoms
- Use of medications such as diuretics or antihypertensive medications
- Anticholinergics
- Antidepressant medications
- Anxiety
- Depression
- Unusual abdominal wall pain
- Inguinal hernia
- Spinal deformity
- Skin breakdown or fungal/bacterial infection
- Surgical scars
- Digital rectal exam for assessment of the prostate
- Neurologic or spinal cord disease or injury

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis and urine culture
- PSA if known history of prostate cancer or has had a prostatectomy

Imaging
- Prostate residual urine (PVR) measurement to rule out urinary retention
- Other routine imaging not indicated
STRESS URINARY INCONTINENCE, MALE

**DIAGNOSTIC PROCEDURES/SURGERY**
- Pressure flow studies are helpful to confirm stress incontinence and rule out other complicating factors such as urge incontinence/detrusor overactivity, detrusor underactivity, bladder outlet obstruction, and poor bladder compliance.
- Cystoscopy to rule out uncorrectable anatomic stenosis (most often after radical prostatectomy) or urethral stricture is essential prior to any planned surgical intervention.

**PATHOLOGIC FINDINGS**

**DIFFERENTIAL DIAGNOSIS**
- Stress urinary incontinence
- Urge urinary incontinence: involuntary leakage accompanied by or immediately preceded by urgency
- Mixed urinary incontinence
- Overflow incontinence: urinary retention
- Postvoid dribbling (urine retained in the urethra)
- Stress urinary incontinence: eg, the report of incongruous leakage resulting from sexual intercourse
- Urethral atrophy
- Urinary leakage may need to be distinguished from sweating

**MEDICATION**

- Lifestyle changes: Decreasing certain activities that cause SUI
- Limiting fluid intake
- Efficacious following RP to allow quicker return of continence (7)

**GENERAL MEASURES**

- Pelvic floor physical therapy (eg, “Kegel” exercises)
- Self-reported pad counts are easier to obtain, but not as accurate as a pad weight test.
- Patients may also be followed with 1-hr or 24-hr diaries which can be obtained regularly in the office.

**TREATMENT**

**GENERAL MEASURES**

- Pelvic floor physical therapy (“Kegel” exercises): Efficacious following RP to allow quicker return of continence, though not found to improve overall continence (7).
- May also be used in men with SUI from other causes to strengthen the pelvic floor
- Lifestyle changes: Limiting fluid intake, Decreasing certain activities that cause SUI
- Perineal dressings
- Condom catheter

**MEDICATION**

- Incretin: physical therapy (eg, “Kegel” exercises)
- Effective following RP to allow quicker return of continence, though not found to improve overall continence (7).
- May also be used in men with SUI from other causes to strengthen the pelvic floor
- Lifestyle changes: Limiting fluid intake, Decreasing certain activities that cause SUI
- Perineal dressings
- Condom catheter

**GENERAL MEASURES**

- Pelvic floor physical therapy (“Kegel” exercises): Efficacious following RP to allow quicker return of continence, though not found to improve overall continence (7).
- May also be used in men with SUI from other causes to strengthen the pelvic floor
- Lifestyle changes: Limiting fluid intake, Decreasing certain activities that cause SUI
- Perineal dressings
- Condom catheter

**MEDICATION**

- Anticholinergic agents: Mitralis, Carbidopa
- Skin breakdown
- Candidiasis
- Dermatitis

**DIAGNOSTIC PROCEDURES/SURGERY**

- Prostatectomy history or complications: Report from the Standardization Sub-committee of the International Continence Society.

**ADDITIONAL TREATMENT**

**RADIATION THERAPY**

- N/A

**ADDITIONAL THERAPIES**

**COMPLEMENTARY & ALTERNATIVE THERAPIES**

- N/A

**ONGOING CARE**

**PROGNOSIS**

- General speaking SUI is stable or progressive in nature. It is not likely spontaneously resolved.
- PH differs from other causes of SUI in that it has been shown to improve over time. However, a plaque is seen after approximately 2 yr and further improvements are not anticipated (6).
- With surgical treatment, and occasionally medical management, male SUI can be expected to improve dramatically in most cases.

**COMPLICATIONS**

- Urinary incontinence
- Skin breakdown
- Urinary tract infection
- Decreasing certain activities that cause SUI
- Efficacious following RP to allow quicker return of continence

**FOLLOW-UP**

- Patient Monitoring: Following surgical or medical treatments patients should be followed with standardized questionnaires, such as the International Consultation on Incontinence Questionnaire Short Form.
- Patients may also be followed with 1-hr or 24-hr pad weight testing, but this can be burdensome to obtain regularly in the office.
- Self-reported pad counts are easier to obtain, but not as accurate as a pad weight test.
- No routine labs or imaging are required unless complicating factors in the initial history and physical were identified.

**PATIENT RESOURCES**


**REFERENCES**


**ADDITIONAL READING**


**SEE ALSO**

- Topic, Algorithm, Media
- Baking Agents, Injectable
- Incontinence, Urinary, Adult Male
- Incontinence, Urinary, Following Radical Prostatectomy
- Incontinence, Sphincteric Deficiency
- ICD-10 (International Classification of Diseases, 10th Revision)
- Overactive Bladder (OAB)

**CODES**

- C90.32 Stress incontinence, male
- C91.03 Incontinence (female) (male)

**CLINICAL/SURGICAL PEARLS**

- SUI is uncommon in young men, but becomes more common with age as more patients are undergoing urologic procedures.
- Most effective treatments are surgical, though medical therapy may be helpful in men with mild incontinence.
- The artificial urinary sphincter (AUS) remains the gold standard procedure for male SUI, however urethral slings are now commonly used with success approaching that of the AUS with proper patient selection.
STROKE (CVA), UROLOGIC CONSIDERATIONS
Katie S. Murray, DO
Tomas L. Griebling, MD, MPH, FACS

GENERAL PREVENTION
- Stroke prevention measures
  - Smoking cessation
  - Blood pressure control
  - Cholesterol control
  - Diabetic control
  - Atrial fibrillation therapy in older women
  - Identify and control arterial fibrillation
  - Balanced diet and exercise
  - Low-dose aspirin if appropriate

DIAGNOSIS
- Based on diagnosis of CVA
- Evaluate for previous or underlying urologic issues or complaints
- Obtain medication history
- Detailed past surgical history

PHYSICAL EXAM
- Abdominal exam for bladder distention
- Neurologic exam (usually already done by primary team during initial diagnosis)
- Digital rectal exam (DRE) to evaluate rectal tone and prostate size in males
- Pelvic exam in females

DIAGNOSTIC TESTS & INTERPRETATION
- Urinalysis with or without urine culture as clinically appropriate
- Cystourethrogram to evaluate renal function
- Postvoid residual bladder scan
- Abdominal imaging
  - Renal/bladder ultrasound
  - KUB

Diagnostic Procedures/Surgery
- Voiding/fill/void studies
  - Bladder capacity
  - Daily weights
- Urodynamic studies: Should not be performed until stability in neurologic symptoms following stroke (not immediately)
  - Typically 3–6 mo following stroke
  - Evaluate bladder function and detrusor function vs. bladder outlet obstruction
  - May be used for surgical guidance and management if necessary

Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS
- Urinary Retention (see Section I “Urinary Retention, Adult Male,” “Urinary Retention, Adult Female”)
  - Urge incontinence
  - Stress incontinence
  - Mixed incontinence
  - Low bladder compliance resulting in overflow incontinence

TREATMENT
GENERAL MEASURES
- General stroke rehabilitation interventions (3)
  - Physical therapy
  - Occupational therapy
  - Initially and short term
    - Urinary bladder dysfunction with Foley catheter vs. clean intermittent catheterization (CIC)
  - Long term
    - CIC, Foley or suprapubic catheter for urinary retention and elevated post-void residuals
    - Caution to avoid long-term indwelling urethral catheter to avoid risk of bladder neck erosion or urethral injury
    - Bladder overactivity
    - Behavioral modifications regarding voiding
    - Use medication therapy below

MEDICATION
First Line
- Antimuscarinics or α1 blockers: Decrease detrusor overactivity (DO) that is demonstrated as urinary frequency and urgency
  - α1 antagonists
  - Side effects
    - Dry mouth, blurred vision, confusion
    - Use cautiously in geriatric patients secondary to potential central nervous system effects

Second Line
- α1-blockers for prostatic hyperplasia and retention related to BPH if necessary
- 5α-reductase inhibitors for BPH especially in those men with large prostate glands
STROKE (CVA), UROLOGIC CONSIDERATIONS

SURGERY/OTHER PROCEDURES
- Suprapubic catheter placement if long-term urinary retention
- Intravesical Botulinum toxin injections for DO
  - Temporary effect and may require patients to perform CIC
- Neuromodulation
  - Transurethral resection of prostate if concomitant BPH with clinical obstruction
- Urinary diversion

ADDITIONAL TREATMENT RADIATION THERAPY
- Additional Therapies
- Psychological support and re-enforcement
- Complementary &Alternative Therapies
  - Absorbent pads and products
  - Pelvic floor physical therapy with or without biofeedback
  - Acupuncture

ONGOING CARE

PROGNOSIS
- Health-related quality of life is impaired in general those with urgency incontinence post neurologic event (481)
- Urinary symptom outcome is proportional to the extent of resolution of other stroke sequelae
  - Those who resolve cognitive and/or motor function often resolve urinary issues

COMPLICATIONS
- Short term
  - Acute renal failure if acute urinary retention
  - Urinary tract infection if not draining bladder appropriately
- Long term
  - Renal dysfunction and possible renal failure
  - Urinary tract infections—recurrent
  - Decreased quality of life
  - Depression

FOLLOW-UP

PATIENT MONITORING
- Detrusor overactivity (DO): yearly checkups, medication monitored
- Neuromodulation and performing CIC
  - Evaluate renal function with yearly (or more often if clinically indicated) creatinine and renal ultrasound
  - Urodynamic evaluation for significant change in clinical symptoms
  - If revolving catheter dependent, needs regular cystoscopy to visualize bladder and monitor for cancer or stones
  - Increased risk of bladder cancer is secondary to chronic foreign body in urinary tract

PATIENT RESOURCES

REFERENCES


ADDITIONAL READING
- www.stroke.org (National Stroke Association)

CODES

ICD9
- 434.91 Cerebral artery occlusion, unspecified with cerebral infarction
- 788.29 Other specified retention of urine
- 788.38 Overflow incontinence

ICD10
- I63.9 Cerebral infarction, unspecified
- R33.8 Other retention of urine
- N39.490 Overflow incontinence

CLINICAL/SURGICAL PEARLS

- Important to determine residual urinary effects after near full recovery from stroke.
- Prior to operation, ensures stability of urinary function.

ADDITIONAL READING

- Detrusor Overactivity
- Neurogenic Bladder, General Considerations
- Urinary Retention, Adult Female
- Urinary Retention, Adult Male
- Urinary Retention, Pediatric
ASSOCIATED CONDITIONS

- BPH with urinary retention
- IC/PBS
- Prostatitis
- UTI
- Urinary retention

RISK FACTORS

- History of urinary tract infections (UTIs)
- BPH as it may cause urinary retention
- Urinary tract obstruction
- Immunosuppressed patients have increased susceptibility to infections
- Pelvic radiation treatment
- Chronic pain syndromes
- Stressful athletic activity

PHYSICAL EXAM

- Rectal exam: Tenesmus, swelling, or boggy prostate during palpation may indicate prostatitis
- Pelvic masses
- Pelvic exam: Palpable bladder suggests urinary retention
- Evidence of masses or blood with GI tract disease
- Pyuria, nitrite, and bacteria with infection
- Pyelonephritis
- Acute appendicitis
- Bladder perforation
- Prostatitis including acute bacterial, chronic nonbacterial, inflammatory and noninflammatory (NIH CP/CPPS III A and B)
- Prostatitis
- Urolithiasis
- Urethral stricture and IC/PBS (may see inflammatory lesions or Hunner’s ulcers)
- Acute urosepsis
- Acute urologic sepsis
- Urinary bladder perforation
- Urethral injury
- Urethral stricture
- Urolithiasis
- Urologic: CT cystogram
- Urologic: Urethral catheterization
- Urologic: Urinary REI
- Urologic: Urgency and stress urinary incontinence
- Urologic: Urinary tract infection
- Urologic: Urethral biopsy
- Urologic: Urinary retention
- Urologic: Urethral stricture
- Urologic: Urinary tract disease

IMAGING

- Plain x-ray: Important for evaluation of bowel, urachus, or foreign body
- CT pelvic: Useful for diagnosing GI etiology, urachus, or pelvic masses. Has no role in uncomplicated infections of the GU tract.
- US bladder: Assess posterior residual volume, calculi, or mass
- Pelvic US: Useful for genitourinary causes. Transvaginal US is best for uterine or ovarian evaluation.

DIAGNOSTIC PROCEDURES/SURGERY

- Cystoscopy:
  - Evaluate for bladder tumor, stone, outlet obstruction, urethral stricture and IC/PBS (may see inflammatory lesions or Hunner’s ulcers)
  - Comorbidized during acute GU infection such as UTI or prostatitis
  - Mears–Stamey 4-glass test for prostatitis evaluation
- Urodynamics:
  - Assess bladder capacity, bladder contraction, pressure, and outlet obstruction. Not indicated for acute suprapubic pain.

PATHOLOGIC FINDINGS

- Based on the specific entity

DIFFERENTIAL DIAGNOSIS

- Urologic:
  - UTI
  - Pyelonephritis
  - Urethral stricture
  - Urinary tract infection
  - Urolithiasis
  - Urethral biopsy

- Gynecologic:
  - Ovarian torsion/ovarian vein thrombosis
  - Ovarian fibroma
  - Ovarian vein thrombosis
  - Submucous fibroid

- Gastrointestinal:
  - Acute appendicitis
  - Celiac disease
  - Crohn’s disease
  - Diverticulitis
  - Inflammatory bowel disease
  - Ulcerative colitis

- Inflammatory:
  - Acute appendicitis
  - Celiac disease
  - Crohn’s disease
  - Diverticulitis
  - Inflammatory bowel disease
  - Ulcerative colitis

- Urologic:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis

- Urinary:
  - Acute pyelonephritis
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary retention
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Miscellaneous:
  - Acute appendicitis
  - Celiac disease
  - Crohn’s disease
  - Diverticulitis
  - Inflammatory bowel disease
  - Ulcerative colitis

- Other:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- General:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Urologic:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Gynecologic:
  - Ovarian torsion/ovarian vein thrombosis
  - Ovarian fibroma
  - Ovarian vein thrombosis

- Gastrointestinal:
  - Acute appendicitis
  - Celiac disease
  - Crohn’s disease
  - Diverticulitis
  - Inflammatory bowel disease
  - Ulcerative colitis

- Inflammatory:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Urinary:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Miscellaneous:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- Other:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection

- General:
  - Acute appendicitis
  - Bladder perforation
  - Bladder perforation
  - Bladder stricture
  - Cystitis
  - Prostatitis
  - Pyelonephritis
  - Urolithiasis
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
  - Urinary tract infection
Interstitial cystitis/painful bladder syndrome  
BPH/urinary retention  

- Complicated UTI: Treat for 7–14 days with  
- Acute uncomplicated UTI in women (3,4):  
- The focus of this discussion is on urologic pathologic  

- First Line  
- r  
- r  
- Interstitial cystitis/painful bladder syndrome  
- BPH/urinary retention  

- Acute uncomplicated UTI in women (3,4):  
- Nitrofurantoin monohydrate/macrocrystals  
- Trimethoprim–sulfamethoxazole (160/800 mg  
- Antibiotics empirically for 2 wk. If cultures are  
- Culture-specific antibiotics.  
- Risk factors that make a UTI complicated include:  
- Indwelling catheter  
- Male sex  
- Functional or anatomical abnormality of the  
- Prophylaxis:  
- Antibiotics empirically for 2 wk. If cultures are  
- BPH/Urinary retention  
- Bladder calculi  
- Often require surgical removal. Medical therapy  
- Transurethral resection of prostate or other  
- Superficial tumors:  
- TURBT  
- Invasive tumors: Radical cystectomy with urinary  

- Second Line  
- SURGERY/OTHER PROCEDURES  
- • BPH/Urinary retention  
- • Transurethral resection to relieve acute  
- obstruction; if unable to perform then suprapubic  
- catheterization should be considered.  
- • Transurethral resection of prostate or other  
- ablative procedure (laser, microwave) if  
- appropriate.  
- • Bladder calculi:  
- • Remove transurethraly and fragment manually  
- with lithotrite or with Holmium laser  
- • Open cystolithotomy rarely needed  
- • IC/PBS  
- - 2nd-line treatment includes manual physical  
- therapy techniques that resolve pelvic, abdominal  
- and hip muscular trigger points, and lengthen  
- muscle contractions.  
- • Antispasmodics, cholinergic, hydroxyurea or pentam  
- polysulphone may be used as 2nd-line oral  

- Ongoing Care  
- Patient monitoring and follow-up is dependent on  
- the specific pathologic process.  
- Assessment of postobstructive diuresis following  
- relief of urinary obstruction includes measurement  
- of serum electrolytes.  
- Urine culture following treatment of complicated  
- UTI should be performed to ensure adequate treatment.  
- This is not needed for uncomplicated UTI in women.  

- Second Line  
- SUPRAPUBIC PAIN, GENERAL CONSIDERATIONS  

- Treatment  
- • The focus of this discussion is on urologic pathologic processes.  
- • Some common urologic conditions and interventions are noted below. Other conditions are beyond the scope of this section.  

- Medication  
- First Line  
- • Acute uncomplicated UTI in women (3,4):  
- • Nitrofurantoin monohydrate/macrocrystals  
- (100 mg twice daily for 5 days is appropriate due to  
- minimal resistance and propensity for collateral  
- damage)  
- • Trimethoprim–sulfamethoxazole (160/800 mg  
- [1 double-strength tablet] twice daily for 3 days)  
- given its efficacy in numerous clinical trials.  
- • Complicated UTI: Treat for 7–14 days with  
- culture-specific antibiotics.  
- • Risk factors that make a UTI complicated include:  
- • Indwelling catheter  
- • Immunosuppression  
- • Male sex  
- • Functional or anatomical abnormality of the  
- urinary tract  
- • History of urinary tract surgery  
- • Prophylaxis:  
- • Antibiotics empirically for 2 wk. If cultures are  
- positive or the patient has improved clinical  
- symptoms then continue antibiotics for 4–6 wk.  
- Antibiotics with excellent prostatic penetration  
- can be considered for uric acid stones.  
- • Alpha-blockers, such as tamsulosin, may be used.  
- • Alpha-blockers, such as tamsulosin, may be used.  
- • Bladder calculi  
- • Often require surgical removal. Medical therapy  
- can be considered for uric acid stones.  
- • Interstitial cystitis/painful bladder syndrome  
- (IC/PBS) (5)  
- • 1st-line treatment is behavioral modifications,  
- counseling and stress management, and coping  
- techniques.  
- • 2nd-line treatment includes manual physical  
- therapy techniques that resolve pelvic, abdominal  
- and hip muscular trigger points, and lengthen  
- muscle contractions.  
- • Antispasmodics, cholinergic, hydroxyurea or pentam  
- polysulphone may be used as 2nd-line oral  

- Other:  
- • Trauma  
- • Sexual abuse  
- • Osteitis pubis  
- • Abdominal wall myofascial pain  
- • In athletics (2):  
- • Sports hernia (athletic pubalgia, Sportsman’s  
- hernia)  
- • Adductor strain  
- • Muscle tears  
- • Avulsion injuries  
- • Stress fractures.  
- • Tears of acetabular labrum  

- Follow-up  
- Assessment of postobstructive diuresis following  
- relief of urinary obstruction includes measurement  
- of serum electrolytes.  
- Urine culture following treatment of complicated  
- UTI should be performed to ensure adequate treatment.  
- This is not needed for uncomplicated UTI in women.  

- Prognosis  
- Good prognosis with treatment of a clearly identified  
- problem. Patients with IC/PBS often have a chronic  
- course with flares that can last days to weeks to  
- months. These patients require a multimodal  
- treatment approach.  

- Follow-up  
- Patient Monitoring  
- • Patient monitoring and follow-up is dependent on  

- Codes  
- ICD9  
- • 592.9 Urinary calculus, unspecified  
- • 592.9 Urinary tract infection, site not specified  
- • 789.09 Abdominal pain, other specified site  

- Additional Reading  
- Edwards, B. Diagnostic and management of benign  

- See Also (Topic, Algorithm, Media)  
- • Bladder Calculi  
- • Cysts, General  
- • Interstitial cystitis  
- • Prostate, Benign Hyperplasia/Hyper trophy  
- • Prostatitis, General  
- • Stamey Test (Shires-Stamey Test)  
- • Urethra Stricture, Male  
- • Urinary Stress/Friction, Female  
- • Urinary Retention, General  

- References  
- 1. Sellas RA, Sabab R. Urinary retention in adults:  
- Diagnosis and Initial Management. Am Fam  
- 3. Wagnerlehner PM, Wurth P, Petket G.  
- Antimicrobials in uncomplicated infections.  
- 4. Hummers-Pradier E, Kochen MW. Urinary tract  
- infections in adult general practice patients. Br J  
- 5. Feudale SS, Moster DT, Bhadra AR. Recognition  
- and management of nonrelaxing pelvic floor  

- Clinical/Surgical Pearls  
- • Multiple organ systems can cause suprapubic pain  
- including urologic, gastrointestinal, gynecologic,  
- neurovascular and other rare causes.  
- • Bacterial cystitis typically causes a sharp and  
- stabbing pain that is worse at the end of micturition.  
- This is secondary to inflammation of the urethra.  
- • Acute urinary retention causes suprapubic pain by  
- overdistention of the bladder.  
- • CT imaging can be useful for diagnosing (i)  
- stricture, urethritis or pelvic masses, but CT has  
- no role in uncomplicated infections of the GU  
- tract.  
- • Cystoscopy can be used to evaluate for bladder  
- tumors, stone, outlet obstruction or urethral  
- stricture.  
- • 1st-line treatment for interstitial cystitis/painful  
- bladder syndrome (IC/PBS) involves behavioral  
- modifications, counseling and stress management  
- and coping techniques.
SYPHILIS
John L. Phillips, MD, FACS
Dawdu Lankford, MD, MPH

DESCRIPTION
- "Syphilis", coined by Fracastoro in 1500s
- Describes infection by the spirochete Treponema pallidum, 1st discovered in 1905 by Hoffman

RISK FACTORS
- Other sexually transmitted conditions
- "Syphilis" coined by Fracastoro in 1500s

ASSOCIATED CONDITIONS
- Other sexually transmitted conditions
- "Syphilis" coined by Fracastoro in 1500s

DIAGNOSTIC TESTS & INTERPRETATION
- "Syphilis" coined by Fracastoro in 1500s

BASICS
- "Syphilis", coined by Fracastoro in 1500s
- Describes infection by the spirochete Treponema pallidum, 1st discovered in 1905 by Hoffman

PATHOPHYSIOLOGY
- Contact inoculation through fluids, in utero; rare dissemination through transfusion
- Incubation: 10–90 days
- "Syphilis", coined by Fracastoro in 1500s

HISTORY
- "Syphilis", coined by Fracastoro in 1500s

DIAGNOSIS
- "Syphilis", coined by Fracastoro in 1500s
- Describes infection by the spirochete Treponema pallidum, 1st discovered in 1905 by Hoffman

PREVENTION
- "Syphilis", coined by Fracastoro in 1500s
- Describes infection by the spirochete Treponema pallidum, 1st discovered in 1905 by Hoffman
SYPHILIS

SURGERY/OTHER PROCEDURES
Acute graft replacement has been used for late syphilitic aortic dissection.

ADDITIONAL TREATMENT

Immunotherapy

Additional Therapies

- Penicillin: 2.4 MU Benzathine PCN G IM q4w
- Azithromycin 1 g PO (single dose)

Ongoing Care

- Excellent in primary syphilis
- Good in asymptomatic neurosyphilis
- Poor if symptomatic tabes dorsalis
- Syphilitic aneurysms can cause death within 6 mo
- Poor if symptomatic tabes dorsalis
- Good in asymptomatic neurosyphilis
- Excellent in primary syphilis

Follow-Up

- Yearly thereafter
- Repeat serologic testing q3mo
- FTA-ABS by 36 mo
- Tuberculin testing
- Check HIV status
- Check CNS/spinal fluid

PEARLS

- Patients with a history of syphilis should be counseled to undergo HIV testing.
- Late syphilis may be asymptomatic.
- Condyloma lata are highly infectious and must be differentiated from HPV-related condyloma acuminate largely on physical exam.

CLINICAL/SURGICAL PEARS

- Screen pregnant women for syphilis (USPSTF grade B recommendation).
- Screen people at-risk for syphilis (USPSTF grade A recommendation).
- Pregnancy is an absolute contraindication for doxycycline or azithromycin.
- Nonpenicillin, Nontetracycline alternatives are inferior to PCN but include ceftriaxone.

CODES

ICD9 - 059.9 Syphilis, unspecified
093.9 Syphilis, unspecified
A51.49 Other secondary syphilitic conditions
59/No. RR-12.

ADDITIONAL READING


REFERENCES


ADDITIONAL MEASURES

- Antimicrobial therapy is maintained.
- Serologic monitoring thereafter
- Contact public health service

MEDICATION

First Line

- Penicillin, 2.4 MU Benzathine PCN G IM × 1 (4)
- PCN-allergy: Tetracycline 500 mg PO q6h or doxycycline 100 mg PO q12h × 2 wk
- If pregnant: Ceftriaxone 1 g IM

Second Line

- Tetracycline 250 mg PO q6h and Doxycycline 100 mg for 14 days
- Azithromycin (Zithromax) 1 g PO × 1

Treatment failure: 4-fold increase in titer
- Treatment is supportive
- Under treatment and development of late disease
- Tabes dorsalis (poor prognosis)
- Aortic aneurysm rupture

FOLLOW-UP

Patient Monitoring

- Repeat serologic testing q6mo × 4 then qmo × 2
- Yearly thereafter
- 4-fold decrease should be seen in 12–24 mo
- Treatment failure: 4-fold increase in titer

Patient Resources

**TESTIS CANCER, ADULT GENERAL CONSIDERATIONS**

Brett S. Carver, MD

**BASICS**

**DESCRIPTION**
- Testicular cancer is a malignancy of germ cell origin originating in the testis and is the most common malignancy in males, 15–35 yr of age.
- Testicular cancer may always be considered in males presenting with testicular swelling.
- Patients with testicular cancer may present with a testicular mass, gynaecomastia, infertility, abdominal mass, or symptoms related to metastatic disease such as back pain or cough.

**EPIDEMIOLOGY**

**Incidence**
- It is estimated that in US, 8,820 new cases of testicular cancer would be diagnosed and 380 men would die of this disease in 2014.
- Germ cell tumors (GCTs) of the testis occur predominantly in Caucasian males.
- Lifetime risk of developing testis cancer is ~1 in 270, and the lifetime risk of dying of testicular cancer is ~1 in 5,000.

**Prevalence**

**RISK FACTORS**
- Risk factors associated with the development of testicular cancer:
  - Cryptorchidism
  - Family history of testicular cancer or other malignancies
  - Testicular atrophy
  - Klinefelter syndrome
  - Cannabinoid use controversy

**Genetics**
- Identification of isochromosome 12p amplification.

**PATHOPHYSIOLOGY (1)**
- GCTs of the testis can be divided into 2 major subgroups based on histology: Seminoma and nonseminomatous germ cell tumor (NSGCT).
  - Seminoma: ~50% of all testicular cancers most frequently appear in the 4th decade of life.
  - ~10–15% of patients will produce the serum tumor marker human chorionic gonadotropin (HCG).
  - The remainder of GCTs is comprised of nonseminomatous histology (embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma) and frequently present in the 3rd decade of life.
  - ~50–70% of nonseminomas will produce α-fetoprotein (AFP) and/or HCG.

**Histologic findings of seminoma, embryonal carcinoma, choriocarcinoma, yolk sac tumor, teratoma.**

**ALERT**
- Markers must be drawn prior to radical orchiectomy.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Serum tumor markers (AFP, HCG) should be obtained prior to orchiectomy.
- The serum tumor markers are necessary for diagnosis, staging, and risk classification.
- Tumor markers obtained prior to orchiectomy:
  - 1 or more elevated in 85–90% of NSGCT
  - HCG:
    - Half-life: 24–36 hr
    - Elevated in 40–60% with testis cancer; 100% of choriocarcinomas
  - AFP:
    - Half-life: 5–7 days
    - Produced by yolk sac tumors, embryonal cell carcinoma, and teratocarcinomas
    - Not produced in pure seminoma or pure choriocarcinoma
  - If AFP elevated in case of pure seminoma, NSGCT elements are present.

**Associated Conditions**
- Infertility
- Cryptorchidism
- Gynaecomastia

**GENERAL PREVENTION**
- Possible early orchiectomy for undescended testicle
- USPSTF: Against routine screening for testicular cancer in asymptomatic adolescent and adults including routine testicular self-exams.
- American Cancer Society suggests that men with family history do monthly self-exams.

**DIAGNOSIS**

**HISTORY**
- The most common symptom at the time of diagnosis is painless swelling or enlargement of the testis.
- Acute testicular pain is reported to occur in ~10% of patients with testicular cancer and often represents infarction or hemorrhage within the tumor.
- At initial presentation, symptoms manifesting secondary to metastatic disease occur in ~20% of patients and include:
  - A mass in the left neck, pulmonary complaints such as hemoptysis or dyspnea, an abdominal mass, or back pain that can often be disabling.
  - In ~5% of patients, gynaecomastia or tenderness of the breast is reported.

**PHYSICAL EXAM**
- The most common finding on physical exam is a solid intratesticular mass or swelling.
- Patients should undergo a complete physical exam with emphasis on palpation of the cervical lymph nodes (lymphadenopathy), breasts (gynecomastia), abdomen (lymphadenopathy, liver masses), and the contralateral testis (bilaterally testicular tumors).

**ALERT**
- Baseline ultrasonography is the initial imaging modality of choice with a ~95% specificity in identifying intratesticular lesions.
- Testicular ultrasonography often reveals a solid hypoechoic mass present within the testis.
- The contralateral testis should also be imaged as ~2% of patients will have bilateral testicular cancers.
- The initial staging evaluation should include a CT scan of the chest, abdomen, and pelvis with and without contrast.
- CT is the most effective radiographic technique for identifying metastatic disease both above and below the diaphragm.
- No evidence of metastases in ~70% of patients with seminoma and 35% of patients with nonseminoma.

**Diagnostic Procedures/Surgery**
- A radical orchietomy with high ligation of the spermatic cord at the level of the inguinal ring provides histopathologic diagnosis, primary tumor staging, and excellent local control of the tumor, with minimal morbidity and no mortality.

**Pathologic Findings**
- Histologic findings of seminoma, embryonal carcinoma, choriocarcinoma, yolk sac tumor, teratoma.
- Documentation of lymphovascular invasion.
- Pathologic and clinical staging follows the TNM classification and risk assessment if performed using the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification.

**ALERT**
- 18–33% of patients with testicular cancer were initially treated for epididymitis resulting in a delay in diagnosis of testicular cancer.
DIFFERENTIAL DIAGNOSIS

- Benign lesions
  - Epididymitis/orchitis
  - Bacterial, STD, mumps
  - Testicular trauma: Usually blunt; contusion, rupture, usually associated hematoma
  - Torsion (testicle or appendix)
  - Intratesticular neuroepithelial hamartoma
  - Cysts (simple, tubular, albino, epidemoid)
  - Adrenal rest tumors: In general benign, but can contribute to infertility in patients with congenital adrenal hyperplasia.
  - Fibrous pseudotumor of the testis/epididymis
  - Parakeratinized squamous metaplasia
  - Eosinophilic granuloma
  - Malignant lesions
    - Testicular primary tumors (GCT, stromal and mixed as discussed above)
    - Leukemia involving testis: Tests can be a site of solitary recurrence of leukemic postmortem (sanitary site). Biopsy to confirm diagnosis. Treat with testis-sparing radiation, treat bilaterally.
    - Symptoms involving testis: Usually represents extension from extratesticular sites, rarely can represent a primary (lymphoma 1% of lymphoma cases). Can present bilaterally one-third of the time; mostly involves older men >60 yrs; constitutional symptoms common present (fever, chills, night sweats, weight loss).
    - Metastatic solid tumors: Common: Prostate, lung, GI tract; more rare: Kidney, malignant melanoma, parotid, bladder, and thyroid.
    - Adenocarcinoma of the testis: Arises in the testis collecting system, high-stage presentation, poor response to chemotherapy and radiation, with median survival of 1 yr.
    - Mesothelioma of testicle/vaginalia: Rare, similar to the more common pleural histology, associated with asbestos exposure.
    - Paratesticular sarcomas: Rhabdomyosarcoma, malignant fibrous histiocytoma (most common soft tissue sarcoma in late adult life).

TREATMENT

GENERAL MEASURES

- Inguinal radical orchiectomy/high ligation of the spermatic cord is diagnostic and therapeutic.
- Patients are then staged based on TNM classification (see Section VII: “Reference tables: TNM. Testis Cancer”).

ALERT

Discuss sperm banking prior to treatment.

MEDICATION

First Line (1,2)

- Regardless of histology, patients with advanced GCTs (III–IV) and with persistently elevated tumor markers following radical orchiectomy (UII), are initially treated with platinum-based chemotherapy according to the IGCCCG risk stratification.
  - Good-risk disease: 3 cycles of bleomycin, etoposide, and cisplatin (BEP) or 4 cycles of etoposide and cisplatin (EP).
  - Intermediate-risk or high-risk disease: 4 cycles of BEP — 10–40% of patients with poor-risk disease fail to achieve a durable response to conventional chemotherapy

Second Line

Second-line chemotherapeutic regimens are reserved for advanced testicular cancer in whom serum tumor markers do not normalize following initial therapy.

SURGERY/OTHER PROCEDURES

- Radical orchiectomy should be performed for diagnostic and treatment of the primary tumor.
- In US, the preferred management for patients at high risk for relapse in the retroperitoneum, ie, placental site primary carcinoma, lymphovascular invasion, or extension into the tunica or scrotum, is primary RPLND if serum tumor markers have normalized.
- Postchemotherapy RPLND (PC-RPLND) and resection of residual masses should be done. Following chemo, 40% undergoing RPLND will have teratoma; 10–15% have GCT.

ADDITIONAL TREATMENT

Radiation Therapy

In US, radiation therapy to the retroperitoneum remains the treatment of choice for patients with clinical stage I and IIa seminoma.

Additional Therapies

- Surveillance, with serial imaging and tumor markers, in well-selected low-risk patients.
- Stage I seminoma:
  - Stage I NSGCT:
  - No teratomatous elements, no lymphovascular invasion, and no embryonal cell carcinoma in the primary specimen. Patients must be reliable

Complementary & Alternative Therapies

Discuss sperm banking before therapy.

ONGOING CARE

PROGNOSIS

- Prognosis is dependent on initial clinical stage, risk stratification, and histology.
- The multidisciplinary approach to GCT has survival rates at >90%.

COMPLICATIONS

- Radical orchiectomy: Wound infection, scrotal and/or retroperitoneal hematoma
- RPLND: Wound infection, parapneumonic, venous thrombosis, chylous ascites, anejaculation, and small-bowel obstruction.
- Chemotherapy: Neutropenia, gastrointestinal symptoms, alopecia, pulmonary fibrosis, and cardiovascular events.

FOLLOW-UP

Patient Monitoring

Physical and/or chest CT imaging of the chest, abdomen, and pelvis is needed follow-up according NCCN guidelines.

Patient Resources


REFERENCES


ADDITIONAL READING

NCCN Guidelines for the Treatment of Testis Cancer (www.nccn.org)

See Also (Topic, Algorithm, Media)

- International Germ Cell Cancer Collaborative Group (IGCCCG)
- Reference Tables: TNM: Testis Cancer
- Testis Cancer: Adult General Considerations
- Testis Cancer, Seminoma
- Testis Cancer, Seminoma
- Testis Cancer, Nonseminomatous Germ Cell Tumors, General
- Testis, Leydig Cell Tumor
- Testis, Seminoma
- Testis, Torsion, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral
- Testis, Testiculoma, Maturation and Immaturity
- Testis, Testicular and Urethral

CODES

ICD9

- 186.9 Malignant neoplasm of unspecified testes
- 185.9 Malignant neoplasm of other and unspecified testes
- 608.3 Atrophy of testis

ICD10

- C69.0 Malignant neoplasm of unspecified testis
- C69.9 Malignant neoplasm of unspecified testes
- K00.0 Atrophy of testis

CLINICAL/SURGICAL PEARLS

All intrascrotal masses should be assumed to be testicular cancer until proven otherwise.

Elevated AFP is diagnostic for nonseminomatous GCT.

Inguinal radical orchiectomy with high ligation of the spermatic cord is the initial treatment.
TESTIS CANCER, CHORIOCARCINOMA
Brett S. Carver, MD

BASICS

DESCRIPTION
- Choriocarcinoma is a type of germ cell tumor (GCT) composed of syncytiotrophoblastic, cytotrophoblastic, and other trophoblastic cells.
- Histologic cell type for nonseminomatous GCTs.
- Pure choriocarcinomas are commonly associated with metastatic disease and high levels of hCG at the time of presentation.

EPIDEMIOLOGY

Incidence
- It is projected that in US, 8,820 new cases of testicular cancer would be diagnosed and 380 men would die of this disease in 2014.
- Pure choriocarcinoma comprises <1% of testicular GCT.
- Choriocarcinoma is a histologic cell type in ~10% of nonseminomas.

Prevalence

N/A

RISK FACTORS

- Risk factors associated with the development of testicular cancer include:
  - Cryptorchidism, family history, testicular atrophy, infertility.

Genetics

Identification of isochromosome 12p amplification.

PATHOPHYSIOLOGY

- Choriocarcinoma is a histologic subtype of nonseminomatous GCTs composed primarily of syncytiotrophoblastic and cytotrophoblastic.
- Syncytiotrophoblastic cells produce human chorionic gonadotropin (HCG) which may be detected by endocrinology or measurement of serum levels.
- Pure choriocarcinomas are associated with significantly elevated levels of serum HCG. Choriocarcinoma represents a germ cell transformed through extraembryonic differentiation.
- Relationship between size of primary tumor and metastatic disease may seem paradoxical, with widespread disease associated with a relatively small primary tumor.
- Route of metastatic spread is variable compared to other GCTs, which are often stepwise and widespread.
- Choriocarcinoma is associated with a greater propensity for hematogenous dissemination.
- hCG is produced by syncytiotrophoblasts and is elevated in 100% of choriocarcinomas. The serum half-life of hCG is 24–36 h.
- Elevated serum levels of hCG are also noted in 40–60% of embryonal carcinomas and 5–10% of pure seminomas.

ASSOCIATED CONDITIONS

- Infertility
- Cryptorchidism
- Gynecomastia

GENERAL PREVENTION

- Conflicting data; early orchectomy reduces testis cancer risk in cryptorchidism

DIAGNOSIS

HISTORY

- Past medical history focusing on history of cryptorchidism.
- The most common symptom at the time of diagnosis is painless swelling or enlargement of the testis. Acute testicular pain is reported to occur in ~10% of patients with testicular cancer and often represents infection or hemorrhage within the tumor.
- At initial presentation, symptoms manifesting secondary to metastatic disease occur in ~20% of patients and include, a mass in the left neck, pulmonary complaints such as hemoptysis or dyspnea, an abdominal mass, or back pain that can often be disabling.
- Patients with choriocarcinoma may present with gynecomastia or tenderness of the breast secondary to elevated serum HCG.
- Neurologic symptoms related to brain metastases may be present in patients with advanced pure choriocarcinoma.

PHYSICAL EXAM

- The most common finding on physical exam is a solid intratesticular mass or swelling.
- Through exam of both groins — Careful palpation of surrounding spermatic cord structures on involved side to evaluate extent of disease.
- Transillumination of scrotal contents if hydrocele is present.
- Cervical lymph nodes (lymphadenopathy), breasts masses/lymphadenopathy, liver masses.
- Histologic cell type for nonseminomatous GCTs composed primarily of syncytiotrophoblastic, cytotrophoblastic, and other trophoblastic cells.
- Histologic cell type for nonseminomatous GCTs.
- Pure choriocarcinomas are commonly associated with metastatic disease and high levels of hCG at the time of presentation.
- Identification of isochromosome 12p amplification.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Serum tumor markers (AFP, HCG, LDH) should be obtained prior to and following radical orchectomy. The serum tumor markers are necessary for diagnosis, staging, and risk classification. While normal postorchectomy serum tumor markers does not preclude the finding of metastatic disease, an elevation of either AFP or HCG does signify the presence of metastases.
- Pure choriocarcinomas are often associated with significantly high levels of serum HCG.

PHYSICAL EXAM

- The most common finding on physical exam is a solid intratesticular mass or swelling.
- Through exam of both groins — Careful palpation of surrounding spermatic cord structures on involved side to evaluate extent of disease.
- Transillumination of scrotal contents if hydrocele is present.
- Cervical lymph nodes (lymphadenopathy), breasts masses/lymphadenopathy, liver masses.
- Histologic cell type for nonseminomatous GCTs composed primarily of syncytiotrophoblastic, cytotrophoblastic, and other trophoblastic cells.
- Histologic cell type for nonseminomatous GCTs.
- Pure choriocarcinomas are commonly associated with metastatic disease and high levels of hCG at the time of presentation.
- Identification of isochromosome 12p amplification.

DIFFERENTIAL DIAGNOSIS

- There are a delimitation of testicular masses only. For a complete listing of intrascrotal and testicular masses see Section I: “Scrotum and Testicle Mass:”
- Benign lesions:
  - Epididymitis/Orchitis: Bacterial, STD, mumps, TB
  - Testicular trauma: Usually blunt; contusion, hematoma
- Neoplasm:
- Testicular: Various, with seminoma, embryonal carcinoma.
- Adnexal masses:
- Fallopian tube: Benign, malignant

DIFFERENTIAL DIAGNOSIS

- There are a delimitation of testicular masses only. For a complete listing of intrascrotal and testicular masses see Section I: “Scrotum and Testicle Mass:”
- Benign lesions:
  - Epididymitis/Orchitis: Bacterial, STD, mumps, TB
  - Testicular trauma: Usually blunt; contusion, hematoma
- Neoplasm:
- Testicular: Various, with seminoma, embryonal carcinoma.
- Adnexal masses:
- Fallopian tube: Benign, malignant

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Serum tumor markers (AFP, HCG, LDH) should be obtained prior to and following radical orchectomy. The serum tumor markers are necessary for diagnosis, staging, and risk classification. While normal postorchectomy serum tumor markers does not preclude the finding of metastatic disease, an elevation of either AFP or HCG does signify the presence of metastases.
- Pure choriocarcinomas are often associated with significantly high levels of serum HCG.

PHYSICAL EXAM

- The most common finding on physical exam is a solid intratesticular mass or swelling.
- Through exam of both groins — Careful palpation of surrounding spermatic cord structures on involved side to evaluate extent of disease.
- Transillumination of scrotal contents if hydrocele is present.
- Cervical lymph nodes (lymphadenopathy), breasts masses/lymphadenopathy, liver masses.
- Histologic cell type for nonseminomatous GCTs composed primarily of syncytiotrophoblastic, cytotrophoblastic, and other trophoblastic cells.
- Histologic cell type for nonseminomatous GCTs.
- Pure choriocarcinomas are commonly associated with metastatic disease and high levels of hCG at the time of presentation.
- Identification of isochromosome 12p amplification.

DIFFERENTIAL DIAGNOSIS

- There are a delimitation of testicular masses only. For a complete listing of intrascrotal and testicular masses see Section I: “Scrotum and Testicle Mass:”
- Benign lesions:
  - Epididymitis/Orchitis: Bacterial, STD, mumps, TB
  - Testicular trauma: Usually blunt; contusion, hematoma
- Neoplasm:
- Testicular: Various, with seminoma, embryonal carcinoma.
- Adnexal masses:
- Fallopian tube: Benign, malignant

DIFFERENTIAL DIAGNOSIS

- There are a delimitation of testicular masses only. For a complete listing of intrascrotal and testicular masses see Section I: “Scrotum and Testicle Mass:”
- Benign lesions:
  - Epididymitis/Orchitis: Bacterial, STD, mumps, TB
  - Testicular trauma: Usually blunt; contusion, hematoma
- Neoplasm:
- Testicular: Various, with seminoma, embryonal carcinoma.
- Adnexal masses:
- Fallopian tube: Benign, malignant

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Serum tumor markers (AFP, HCG, LDH) should be obtained prior to and following radical orchectomy. The serum tumor markers are necessary for diagnosis, staging, and risk classification. While normal postorchectomy serum tumor markers does not preclude the finding of metastatic disease, an elevation of either AFP or HCG does signify the presence of metastases.
- Pure choriocarcinomas are often associated with significantly high levels of serum HCG.

IMAGING

- Testicular ultrasonography is the initial imaging modality of choice with a >95% sensitivity and specificity in identifying intratesticular lesions.
- Testicular ultrasonography often reveals a solid hypoechoic mass present within the testis.
First Line (2)

TREATMENT

GENERAL MEASURES (1)

- Treatment options are based on clinical staging.

- Prognosis for patients with testicular cancer is based on physical exam, serum tumor markers, and histologic tumor features according to the TNMS staging system.

MEDICATION

First Line (2)

- Bilateral disease can be present. Though contralateral testis should be treated as a potential sanctuary site. Biopsy can be utilized to confirm diagnosis of the primary tumor.

- All intratesticular masses should be assumed to be testicular cancer until proven otherwise.

- All intratesticular masses should be assumed to be testicular cancer until proven otherwise.

- Malignant lesions: Testicular primary tumors (carcinoma and nonseminomatous GCTs) grow in the spermatic cord and are diagnostic and therapeutic.

- Adenocarcinoma of the rete testis: Arises in the mediastinum and is characterized by constitutional symptoms commonly present (fever, chills, night sweats, weight loss).

- Lymphoma involving testis—usually represents a systemic process and is often characterized by a high burden of disease or poor prognosis.

- Leukemia involving testis—testis can be a site of disease relapse and is often a site of initial failure.

- Poor prognosis: Mediastinal primary, nonseminomatous visceral metastases, AFP > 1,000, β-hCG > 5,000, and LDH > 1.5 for upper limit of normal (ULN)

- Intermediate prognosis: Testis or retroperitoneal primary, no nonpulmonary visceral metastases, AFP 1,000–10,000, β-hCG 5,000–50,000, or LDH 1.5–10 ULN

- Good prognosis: Testicular primary, nonseminomatous visceral metastases, AFP > 10,000, β-hCG > 50,000, and LDH ≤ 10 ULN

- Complications of chemotherapy: Neutropenia, gastrointestinal symptoms, alopecia, pulmonary fibrosis, and cardiovascular events; propensity for gastrointestinal symptoms, alopecia, pulmonary fibrosis.

- Complications of RPLND: Wound infection, scrotal hematoma, and retroperitoneal hematoma.

- Choriocarcinoma is often associated with hemoptysis, neurologic and pulmonary monitoring is critical following chemotherapy.

- Second Line chemotherapy is reserved for patients with advanced testicular cancer in whom serum tumor markers do not normalize following initial chemotherapy regimen.

SURGERY/OTHER PROCEDURES

- Radical orchiectomy is performed for diagnosis and treatment of the primary tumor.

- In US, the preferred management for patients at high risk for relapse in the retroperitoneum, ie, predominant embryonal carcinoma, lymphocytic invasion, or extension into the tunica or scrotum, is primary RPLND if serum tumor markers have normalized.

- Postchemotherapy RPLND (PC-RPLND) and resection of residual masses are an integral component in the management of advanced nonseminoma.

ADDITIONAL TREATMENT

Radiation Therapy

Occasionally radiation therapy for cerebral metastases is utilized, but systemic therapy remains the initial treatment of choice for the management of metastatic disease including cerebral metastases.

Additional Therapies

- Complementary & Alternative Therapies

ONGOING CARE

CLINICAL/SURGICAL PEARLS

- All intratesticular masses should be assumed to be testicular cancer until proven otherwise.

- Choriocarcinomas are associated with production of β-hCG.

- Choriocarcinomas have a predilection for brain metastases.

- Inguinal radical orchiectomy with high ligation of the spermatic cord is diagnostic and therapeutic.

- Treatment options are based on clinical staging, through contralateral testis should be treated as a potential sanctuary site.

- Lymphoma involving testis—usually represents a systemic process and is often characterized by a high burden of disease or poor prognosis.

- Leukemia involving testis—testis can be a site of disease relapse and is often a site of initial failure.
TESTIS CANCER, EMBRYONAL CARCINOMA
Nicholas J. Kuntz, MD
Judd W. Moul, MD, FACS

ASSOCIATED CONDITIONS
• Infertility
• Cryptorchidism
• Seminoma

GENERAL PREVENTION
• Possibility early orchectomy for undescended testicle
• Textile self-exam

DIAGNOSIS
• Signs and symptoms
  • Painless testicular mass (50–60%)
  • Testicular pain or dull ache (30–40%)
  • Painless testicular mass (50–60%)
  • Testicular pain or dull ache (30–40%)
  • Testicular self-exam

PHYSICAL EXAM
• Signs and symptoms
  • Pale or vacuolated cytoplasm
  • Epithelioid cells arranged in glands or tubules,

DIAGNOSTIC TESTS & INTERPRETATION
• Tumor markers
  • AFP (alpha fetoprotein)
  • HCG (human chorionic gonadotropin)

PATHOPHYSIOLOGY
• EC is an aggressive GCT subtype
• High associated relapse rate (35–40%)
• Absent in pure seminoma and choriocarcinoma.
• Human chorionic gonadotropin (HCG)
• Normally secreted by placental syncytiotrophoblasts.
• Half-life of ~24–36 hr. Consists of α- and β-chains; α-chain analogous to hCG.

DIAGNOSTIC TESTS & INTERPRETATION
• Lab
  • Alpha fetoprotein (AFP)
  • β-HCG

PATHOPHYSIOLOGY
• EC is an aggressive GCT subtype
• High associated relapse rate (35–40%)
• Absent in pure seminoma and choriocarcinoma.
• Human chorionic gonadotropin (HCG)
• Normally secreted by placental syncytiotrophoblasts.
• Half-life of ~24–36 hr. Consists of α- and β-chains; α-chain analogous to hCG.
• Elevated in 60% of all GCT, 90% of seminomas, and all choriocarcinomas.

DIAGNOSTIC TESTS & INTERPRETATION
• Lab
  • Alpha fetoprotein (AFP)
  • β-HCG
  • Scrotal ultrasound (US) (see “Imaging”)
  • Transillumination test

PHYSICAL EXAM
• Signs and symptoms
  • Painless testicular mass (50–60%)
  • Testicular pain or dull ache (30–40%)
  • Painless testicular mass (50–60%)
  • Testicular pain or dull ache (30–40%)
  • Testicular self-exam

DIAGNOSTIC TESTS & INTERPRETATION
• Tumor markers
  • AFP (alpha fetoprotein)
  • HCG (human chorionic gonadotropin)

PATHOPHYSIOLOGY
• EC is an aggressive GCT subtype
• High associated relapse rate (35–40%)
• Absent in pure seminoma and choriocarcinoma.
• Human chorionic gonadotropin (HCG)
• Normally secreted by placental syncytiotrophoblasts.
• Half-life of ~24–36 hr. Consists of α- and β-chains; α-chain analogous to hCG.
• Elevated in 60% of all GCT, 90% of seminomas, and all choriocarcinomas.
• Lactate dehydrogenase (LDH)
• Normally secreted by placental syncytiotrophoblasts.
• Half-life of ~24–36 hr. Consists of α- and β-chains; α-chain analogous to hCG.
• Elevated in 60% of all GCT, 90% of seminomas, and all choriocarcinomas.
• Lactate dehydrogenase (LDH)
• Normally secreted by placental syncytiotrophoblasts.
• Half-life of ~24–36 hr. Consists of α- and β-chains; α-chain analogous to hCG.
TESTIS CANCER, EMBRYONAL CARCINOMA

ADDITIONAL READING


5. NCCN follow-up protocol:

   Patient Monitoring
   — Primary surveillance:
   — 20% recurrence, most common 1st 2 yr
   — NCCN follow-up protocol:
     Year 1: Tumor markers and chest x-ray every 1–2 mo; abdominal CT every 3–4 mo
     Year 2: Tumor markers and chest x-ray every 2 mo; abdominal CT every 4–6 mo
     Years 3–5: Tumor markers and chest x-ray every 3–6 mo; abdominal CT every 6–12 mo
     After year 5: Tumor markers and chest x-ray every 1–2 yr
   — RPLND:
     Most likely site of recurrence is the chest (3)
     — NCCN follow-up protocol:
       Year 1: Tumor markers and chest x-ray every 2–3 mo; baseline abdominal/pelvic CT
       Year 2: Tumor markers and chest x-ray every 2–3 mo; abdominal/pelvic CT as indicated
       Year 3–5: Tumor markers and chest x-ray every 3–12 mo; abdominal/pelvic CT as indicated
       After year 5: Tumor markers and chest x-ray every 3 yr
   — Chemotherapy and RPLND:
     — NCCN follow-up protocol:
       Year 1: Tumor markers and chest x-ray every 2–3 mo; abdominal/pelvic CT every 6 mo
       Year 2: Tumor markers and chest x-ray every 2–3 mo; abdominal/pelvic CT every 6–12 mo
       Years 3–5: Tumor markers and chest x-ray every 3–12 mo; abdominal/pelvic CT as indicated
       After year 5: Tumor markers and chest x-ray every 3 yr

CODES

ICD9
491.9 Malignant neoplasm of other and unspecified tests
608.3 Atrophy of tests
752.51 Undescended tests
ICD10
C62.90 Malig neoplasm of unsp testis, unsp
carcinoma of the testis
Q53.9 Undescended testicle, unspecified
descended or undescended
Q539.9 Undescended testicle, unspecified
descended or undescended
608.3 Atrophy of tests
752.51 Undescended tests

CLINICAL/SURGICAL PEARLS

1. No evidence testicular mass is testicular cancer until proven otherwise.

2. Transrectal or biopsy is contraindicated.

3. EC is aggressive histologic subtype with increased risk of occult disease.

4. Second opinion of pathologic specimens by experienced pathologists is encouraged.


REFERENCES


ADDITIONAL READING


TESTIS CANCER, ENDODERMAL SINUS TUMORS (YOLK SAC TUMORS)

Elizabeth V. Dray, MD
Marcus L. Quek, MD, FACS

PATHOPHYSIOLOGY
- Associated with gains in chromosome 12p in adults.
- RUX1 promoter methylation on chromosome 1p in children (1)
- ITGCN precursor lesion in adults, unclear relationship in children.
- Lymphatic and hematogenous spread
- Up to 20% of children present with large metastases compared to 4–6% of adults

ASSOCIATED CONDITIONS
- Adults:
  - Cryptorchidism
  - Later age at orchiopexy associated with higher relative risk of cancer
  - Risk also increases with intra-abdominal testis and bilateral cryptorchidism.
- Children:
  - Disorders of sex development

DIAGNOSIS
- Presents as painless testicular mass
- May also present as retroperitoneal mass in mediastinal GCT
- Incidentally associated with trauma in <10% of cases.

PHYSICAL EXAM
- Painless testicular mass
- 15–50% have associated hydrocele

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Serum tumor markers
  - HCG never elevated in pure YST.
  - Tumor markers elevated after appropriate half-life decline.

Imaging
- Sonob US
  - Hepaticor or heterogenous mass with increased blood flow on Doppler

CT
- Stains positive for AFP

Differential Diagnosis
- Adenomatous tumor of testis or epididymis
- Adrenal rest tumors
- Cystic dysplasia of the testis
- Chylous cyst of the mediastinum
- Henoch–Schönlein purpura (usually no mass)

Diagnosis
- Precision of testis-sparing surgery.

Etiology
- In children, anechoic cystic lesions with blood flow on Doppler
- Normal AFP suggestive of benign mass, can attempt testis-sparing surgery.
- CT chest/abdomen/pelvis with PO and IV contrast
- For staging in all age groups.

Genetics
- Heredity unknown

Risk Factors
- General risk for testicular cancer
  - Cryptorchidism
  - Klinefelter syndrome
  - Family History
  - Male infertility
  - Loss of body hair, young maternal age
  - Young paternal age
  - Testicular microcystis

Heredity
- Unknown

RISK FACTORS
- N/A

Prevalence
- 85% of children present with stage I disease, compared to 20% of postpuberal cases

Epidemiology
- Incidence
  - Children:
    - Incidence of pediatric testis tumors is 0.3–1.2 per 100,000
    - YST comprised 62% of all testicular tumors in childhood based on AAP tumor registry.
  - Adults:
    - In US, ~8,820 new cases of testicular cancer would be diagnosed and 380 men would die of this disease in 2014.
    - Lifetime risk of developing testis cancer is ~1 in 270, and the lifetime risk of dying of testicular cancer in US is ~0.003.
    - Pure YST is extremely rare, but found in 4% of mixed GCTs.

Diagnosis
- Presents as painless testicular mass
- May also present as retroperitoneal mass in mediastinal GCT
- Incidentally associated with trauma in <10% of cases.

History
- Presents as painless testicular mass
- May also present as retroperitoneal mass in mediastinal GCT
- Incidentally associated with trauma in <10% of cases.

Differential Diagnosis
- Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
- Spina bifida epidermal cyst
- Testicular cysts
- Testicular tumors:
  - YST, teratoma, seminoma, embryonal, choriocarcinoma, mixed tumors
  - Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors
- Metastatic tumors
  - Mesothelial tumors
  - Hamartoma, carcinoid, and neurofibroma
  - Testis tumor of adrenogenital syndrome
  - Leukemia or lymphoma
  - Yolk sac

Pathologic Findings
- Gross:
  - Endodermal sinus tumors appear firm, yellow-white mass
- Microscopic:
  - Round to oval cells of atoll, yolk sac, mesenchyme
  - Arranged in glandular, papillary, or microcystic pattern with hyaline globules
  - Schiller–Duck bodies characteristic finding
  - Stains positive for AFP

References:
- AAP tumor registry
- APCC guidelines
- National Comprehensive Cancer Network (NCCN) guidelines
- NCI SEER database
TESTIS CANCER, ENDODERMAL SINUS TUMORS (YOLK SAC TUMORS)

TREATMENT

GENERAL MEASURES

- Adults:
  - Management handled as for nonseminomatous GCT. See Section I “Testis Cancer: Nonseminomatous Germ Cell Tumors, General.”

- Children:
  - Inguinal orchiectomy curative in 80% of children with stage I disease.
  - Adjuvant chemotherapy recommended for stage II–IV disease.

MEDICATION

First Line (4)

- Chemotherapy: Bleomycin, etoposide, cisplatin (BEP)
  - Carboplatin may have equivalent outcomes compared to cisplatin with decreased ototoxicity and nephrotoxicity.

Second Line

- Etoposide, ifosfamide, cisplatin (VIP)
  - High-dose chemotherapy regimens for treatment failures.

SURGERY/OTHER PROCEDURES

- In children: Lymph nodes >2 cm and <4 cm in size at diagnosis should undergo excisional or interventional radiology biopsy to confirm histology.

- Postchemotherapy residual retroperitoneal disease should undergo retroperitoneal lymphadenectomy.

ADDITIONAL TREATMENT

Radiation Therapy

No role for radiation in endodermal sinus tumor.

Additional Therapies

- Sperm banking should be offered prior to chemotherapy in adolescents and adults.

- Fertility-sparing procedure for prepubertal boys are controversial, but include Testicular sperm extraction (TESE) and cryopreservation of testicular tissue.

Complementary & Alternative Therapies

N/A

ONGOING CARE

PROGNOSIS

- Adults: See “NSGCT”

- Children:
  - Survival for all stages approaches 100% at 6 yr.
  - 20% of children with stage I disease will relapse during surveillance; however, excellent cure rates with chemotherapy.

COMPLICATIONS

- Chemotherapy toxicity
  - Bleomycin: Pulmonary fibrosis
  - Carboplatin: Ototoxicity, nephrotoxicity, neuropathy
  - Etoposide: Panostytopenia
  - Infertility

FOLLOW-UP

Patient Monitoring

- Children:
  - CXR, CT or MR, AFP, and history and physical exam monthly for 3 mo, then at 6 mo postoperatively, and subsequently every 6 mo for 36 mo.

- Note: Imaging guidelines evolving in light of increasing awareness of the impact of radiation on pediatric populations.

Patient Resources


REFERENCES


ADDITIONAL READING


- See Also (Topic, Algorithm, Media)

- Paratesticular Tumors
- Reference Tables: TNM: Testis Cancer
- Rhabdomyosarcoma, Pediatric
- Scrotum and Testicle, Mass
- Testis Cancer, Adult General Considerations
- Testis Cancer: Endodermal Sinus Tumors (Yolk Sac Tumors) Image
- Testis Cancer: Nonseminomatous Germ Cell Tumors, General
- Torsion, Testis and Testicular Appendages

CODES

ICD9

- 186.9 Malignant neoplasm of other and unspecified testis.
- 608.89 Other specified disorders of male genital organs
- 752.9 Undescended testicle, unspecified

ICD10

- C62.90 Malignant neoplasm of unspecified testis
- C62.89 Other specified disorders of male genital organs
- N50.8 Other specified disorders of male genital organs
- Q53.9 Undescended testicle, unspecified

CLINICAL/SURGICAL PEARLS

- Endodermal sinus tumor is the most common GCT of the epididymis.
- Inguinal orchectomy with high ligation of spermatic cord maintains therapy.
- Excellent prognosis for all stages in children.
## Testis Cancer, Nonseminomatous Germ Cell Tumors, General

Robert H. Blackwell, MD
Marcus L. Quek, MD, FACS

### BASICS

**DESCRIPTION**
- Nonseminomatous germ cell tumors (NSGCTs) are malignant neoplasms of the testicle originating from germ cells, excluding seminoma.
- 4 histologic types: Choriocarcinoma, embryonal cell, teratoma, and yolk sac.
- ~50% of NSGCT have a mixed histology, may also include a seminoma component (mixed GCT).

**RISK FACTORS**
- **Cryptorchidism:** ~7–10% incidence in cryptorchid patients in the US (8,820 new cases will be diagnosed with about 370 deaths).
- **SEER age-adjusted incidence of testicular cancer in US in 2010 was 221,020.**

**EPIDEMIOLOGY**

- **Incidence**
  - SEER prevalence of testicular cancer in US in 2010 was 221,020.
  - In US (2014), ~8,800 new cases will be diagnosed with about 370 deaths.

- **Prevalence**
  - SEER prevalence of testicular cancer in US in 2010 was 221,020.

### RISK FACTORS

- **Family history:** ~1–4% of patients with newly diagnosed GCTs report a family history.
- Sons have a 4–6× increased risk of GCT, siblings have a 5–10× increased risk.

**Cryptorchidism:** ~3–7× increased risk of GCT.
- 3–10% incidence in cryptorchid patients in the ipsilateral undescended testicle, ~5% in the contralateral testicle.

**Environment:** Higher incidence in Northern Europe (8–10×).
- 5% in the Americas, Africa, Asia.

**Prior testicular tumor:** 2% incidence of malignancy.
- 7–10% incidence in cryptorchid patients in the US.

**Family history:**
- ~30–40% of testicular tumors in men with a family history do monthly self-exams.
- Sons have a 4–6× increased risk of GCT; siblings have a 5–10× increased risk of GCT.

**Genetics**
- Identification of isochromosome 12p amplification; found in nearly all GCT.
- 2–3% incidence of bilateral testis tumors may suggest congenital predisposition.

### PATOPHYSIOLOGY

- **ITGCN (Intestinal-type germ cell neoplasia also referred to as CT) is believed to be the precursor lesion of all GCTs, excluding spermatocytic seminoma.**
- ~25% of patients with a GCT will have ITGCN in the contralateral testicle.

- **GCTs typically spread in a predictable manner** via the retroperitoneal (lymph nodes although choriocarcinoma also spreads hematogenously):
  - Right-sided tumors typically spread to retroperitoneal lymph nodes. Tumor may spread right to left, but not left to right.
  - Right-to-left spread of choriocarcinoma via the thoracic duct, and left-sided tumors (usually left) retrograde to the contralateral lymph nodes.
  - Nerve 60% of NSGCT contain ~1 histologic subtype in varying amounts (mixed GCT).

### CHORIOCARCINOMA

- **Expected presenting age:** 20–30 yr
- **Tumor markers:** Markedly elevated HCG, normal AFP.
- **Radiotherapy** may be effective for small tumors.

### EMBRYONAL CELL CARCINOMA

- **Expected presenting age:** 25–35 yr
- **Tumor markers:** Elevated or normal HCG/AFP.
- **ITGCN:** 70% progresses to GCT over 7 yr.

### TERAATOMA

- **Expected presenting age:** 0–10 yr
- **Tumor markers:** Markedly elevated AFP, normal HCG.

### YOLK SAC TUMOR

- **Expected presenting age:** 0–10 yr
- **Absence of yolk sac elements in mixed GCT is a predictor of worse outcome.**

### ASSOCIATED CONDITIONS

- **Choriocarcinoma**
  - Presents as painless mass or swelling testicle.
  - May be initially detected following testicular trauma, but not associated with trauma.
  - **Back or flank pain present in ~10% of cases.**

### PHYSICAL EXAM

- **Scrotal exam including both testes, epididymis, and scrotal contents.**
- **Abdominal exam with attention to palpable lymphadenopathy and/or viscer.**
- **Spermatic/epididymal**
- **Gynecomastia** (present in ~7%).

### DIAGNOSTIC TESTS & INTERPRETATION

**Lab**
- **Tumor markers:** Used preop, postop, surveillance.
  - **HCG:** Produced by syncytiotrophoblasts.
  - **AFP:** Produced by epithelial lining of endodermal sinus.
- **Half-life:** 5–7 days.
- **LDH:** Elevated with increased tumor burden.
- **Half-life:** 4–5 days.

**Imaging**
- **Scrotal US:** Tumors tend to be hypochogenic with blood flow seen within the tumor.
- **Microthorax:** Prevalence of <6% in patients undergoing testicular ultrasound, although controversial if associated with malignancy.

### Histopathology

- **Choriocarcinoma:** Have both syncytiotrophoblasts and endodermal sinus.
- **Embryonal:** Distinct cell arrangements and vascular invasion often present.
- **Teratoma:** At least 2 germ cell layers present.
- **Yolk sac:** May be intra-abdominal, pelvic, or mesenteric.
- **AFP:** Produced by epithelial lining of endodermal sinus.
- **Half-life:** 24–36 hr.
- **HCG:** Produced by syncytiotrophoblasts.
- **Half-life:** 5–7 days.

### DIFFERENTIAL DIAGNOSIS

- See Section I “Testis Cancer, Adult General Considerations” and “Testis Cancer, Pediatric, General Considerations.”

### ALERT

Encourage sperm banking prior to any definitive treatment.
Unlike seminomas, NSGCTs are not treated with SURGERY/OTHER PROCEDURES following initial chemotherapy. Tumor markers do not normalize in disease where serum tumor markers do not normalize and chemotherapy is reserved for patients with advanced disease. RPLND given suspected disseminated disease postorchiectomy without radiographic evidence of metastasis. Surgery is curative for low-volume nodal disease with 95% cure rate if nodes negative, but may be salvaged with subsequent chemotherapy. High-volume disease (pN2–3—risk of relapse >50%) or tumor left behind; adjuvant BEP chemotherapy decreases relapse to <1%.

Stage IS disease: Elevated tumor markers
- Surveillance: In reliable patients with no risk factors for failure
- The templates should not be strictly upheld should future RPLND be needed. Superior boundary: Renal hilum bilaterally
- Inferior boundary: Edge of aorta down to level where it crosses the ipsilateral common iliac artery. The ipsilateral gonadal vessels and spermatic cord stump are included in the specimen.
- Right-sided template medial boundary: Lateral edge of aorta down to level of RPLND, then from aorta down along the right common iliac artery to where the right ureter crosses.
- Left-sided template medial boundary: Lateral edge of the IVC down to level of the IMA, then from the aorta down along the left common iliac artery to left ureter crossing.
- Postchemotherapy: A full bilateral template is utilized with prospective nerve sparing. The templates should not be strictly upheld should future RPLND be needed.

ADDITIONAL TREATMENT
Radiation Therapy
Unlike seminomas, NSGCTs are not treated with radiation (teratoma is radiosensitive).

Additional Therapies
- SEE Section III “Testis Cancer, Nonseminomatous Germ Cell Tumor” for treatment algorithm.
- Stage IIA disease treatment options
- Surveillance: In reliable patients with no risk factors for failure. No teratoma elements, no lymphovascular invasion, and no embryonal cell carcinoma in the primary. Reliable patient; cure rate >95% with close follow-up
- 20–30% relapse rate; these patients can be salvaged with subsequent chemotherapy. RPLND: Modified unilateral template/ nerve-sparing: 70–75% will have no tumor (pN0)
- Perform within 4–6 wk of CT and 7–10 days of tumor for accurate clinical staging
- >95% cure rate if nodes negative, but may be curative for low-volume nodal disease
- 1% relapse rate
- Chemotherapy: 95% cure rate with BEP

Stage IIB disease
- Postorchiectomy tumor markers positive: induction chemotherapy
- Postorchiectomy tumor markers negative: either RPLND or chemotherapy
- No viable tumor (pN0), observe patient
- Low-volume tumor, surgery curative in 60–90%; surveillance or chemotherapy
- High-volume disease (pN2–3—risk of relapse >50%) or tumor left behind; adjuvant BEP chemotherapy decreases relapse to <1%
- Stage IIIa IIb IIIc or IV disease
- Either 3 or 4 cycles of BEP chemotherapy
- Complete response, observe
- Partial response with residual masses, full bilateral RPLND (nerve sparing if applicable)
- Residual masses: 40% fibrosis, 40% teratoma, 20% viable malignancy
- Teratoma/Therios on pathology. Observe
- Viable tumor and tumor markers are elevated or tumor is left behind; consider salvage chemotherapy
- No viable tumor (pN0), observe patient
- Superiority determined by histology
- Testis Cancer, Nonseminomatous Germ Cell Tumor Algorithm

ONGOING CARE
PROGNOSIS
• Has been divided into good, intermediate, and poor prognosis based on stage and risk factors.
• SEE Section I “International Germ Cell Cancer Collaborative Group (ICCCCG)”
  - Good: 5-yr survival 94%
  - Intermediate: 5-yr survival 83%
  - Poor: 5-yr survival 71%

COMPLICATIONS
- Surveillance: Risk of recurrence, risk for secondary malignancy due to repeat CT imaging
- RPLND
  - Iatrogenic dysfunction can impair fertility; a nerve-sparing template can preserve antegrade ejaculation in more than 90% of cases.
  - Mortality (nephrectomy, fea, lymphatic, paracolic, celiac axis) rate 5–25%; tumor bowel obstruction rate 1–2%, mortality rate <1%
- Chemotherapy
  - Bleomycin: Pulmonary fibrosis. Need to limit IV fluid hydration and supplemental oxygenation
  - Cisplatin: Nephrotoxicity, ototoxicity, peripheral neuropathy
  - Secondary malignancy, especially leukemias, skin malignancies, and lymphomas
  - Metabolic syndrome
  - Infertility (50% with normal semen 2 yr after chemotherapy, 25% remain azoospermic)

FOLLOW-UP
Patient Monitoring
- Physical exam, tumor markers, and imaging (CT, abdomen/pelvic CT)
- Frequency of follow-up may be tailored depending on therapy, stage, and disease risk

Patient Resources
NCCN Testicular Cancer Information. www.cancer.gov/cancertopics/types/testicular

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- International Germ Cell Cancer Collaborative Group (ICCCCG)
- Reference Tables: ICD-10-CA Testis Cancer
- Urol Oncol. Testicular cancer.

CODES
ICD9
- 186.9 Malignant neoplasm of other and unspecified testis
- 752.5 Treated testicle, unspecified
- 752.5 Treated testicle, unspecified
- 186.9 Malignant neoplasm of other and unspecified testis

ICD10
- C62.9 Malignant neoplasm of testis, unspecified
- C62.9 Treated testicle, unspecified
- 752.5 Treated testicle, unspecified
- 752.5 Treated testicle, unspecified

CLINICAL/SURGICAL PEARLS
- An atypical inguinal orchiectomy, tap the residual spermatic cord stump with a long sk suture for identification at future RPLND.
- Lymphatic drainage is unpredictable unless there is a history of scrotal/inguinal surgery.
- Tumor marker half-lives can be followed to assess if they fall appropriately after treatment (should nadir after 5 half-lives).
Embryonal carcinoma is capable of differentiating into embryonic structures, such as mature (tissue) or immature (adult) teratomas and extraembryonic structures such as yolk sac and choriocarcinoma tumors.

Seminoma (or spermatocellular seminoma) is a primitive germ cell neoplasm that cannot further differentiate (unusual in childhood, except with gonadal dysgenesis).

Teratoma: Monodermal (epidermoid cyst) or multiple histologic types present (neve, cartilage, intestinal epithelium, etc.). Benign and no prepubertal transformation.

Yolk sac tumors characterized by Schiller–Duval bodies (Yolk sac in appearance, contain AFP).

Leydig tumors which can secrete testosterone are malignant 10% of time. (Rare in children—40%, increased in adults—50% above 20 years old, infants—10% malignant.) can secrete estrogen or testosterone, and granulosa cells (75% diagnosed within 1 mo of birth) have a common embryonic origin from a mesonephric stem cell.

Gonadoblastomas are small benign tumors found in patients with gonadal dysgenesis, including those who have at least a portion of the Y chromosome. Although benign they have high risk of malignant transformation.

15–20% of all RMS arise from the genitourinary system.

– Most common genitourinary sites are the prostate, bladder, and paratesticular (ovaries and uterus are relatively unusual sites).

– Survival rates vary with site (ovary and paratesticular have a better prognosis than bladder/prostate primaries).

2 main histologic types of RMS

– Embryonal RMS is the most common subtype of RMS and accounts for most of the genitourinary neoplasm.

– Alveolar RMS occurs more commonly in the trunk and extratesticular than in GU, worse prognosis than embryonal tumor.

– Epithelial usually not infectious in pediatrics; likely due to refluxing fluid from urethra. Obtain urine culture. If infected need renal ultrasound to rule out urologic etiology.

– Vascular/lymphatic pathogenesis not known. Body habitus (tall, thin), genetics (risk increased if brother or 1st-degree relative has vascular Mayo), or systemic venous anomalies (“nutcracker” by SMA, left renal vein insertion), and rarely central outflow obstruction from tumors.

– In neotens and young children “hematoma” will be used to describe a communicating hydrocele with a “hematoma sac” present though no organ protrusion present: Patient process vasa

ASSOCIATED CONDITIONS

- Hypercalcemia:

  - Testicular tumor: Undescended testis (UOT), gonadal dysgenesis, precocious puberty in non–germ cell tumors (NGCT).

- Hematoma: 1–5% lesions, 3–10% found in preterm infants, 15% bilateral, clinical symptoms hydrocele: 2%, asymptomatic process palpable present—46% of time. (Rare in children—40%, increased in adults—50% above 20 years old, infants—10% malignant.)

- Vascular: ~0–10% old, increasing to 15% through puberty into adulthood.

- Paratesticular tumors: Very rare, bimodal—infancy and adolescence.

- Epididymitis: Less common than adults

GENERAL PREVENTION

- One in three orchidopexy reduces risk in undescended testes.

- USPSTF: Against routine screening for testicular cancer in asymptomatic adolescent and adults including routine testicular self-exams.

- American Cancer Society suggests that men with family history do monthly self-exams.


DIAGNOSIS

- Rationale testicular mass (testicular tumor)

- Acute onset of pain (torsion, epididymitis)

- Symptoms of precocious puberty (tumors—germ cell tumors)

- Painful scrotal mass (testicular tumor)

- Subacute pain (varicocele)

- Abnormal laboratory test (testosterone value)

PHYSICAL EXAM

- Systemic exam identifying intrascrotal structures (testicular mass vs. intraabdominal mass).

- Testicular aspirate from scrotal mass with scrotal US.

- Solid masses do not transilluminate

- Hydrocele transilluminates (communicating if fluid manipulated back into abdomen)

- Solid masses do not transilluminate:

  - Vascular tumors (“bag of worms”)

  - If does not diminish when supine under manual pressure may be due to tumor.

- Lap: Lymphoma or retinoblastoma

- Breast exam, signs of virilization (consider adrenal tumor)

- Breast exam, signs of virilization (consider adrenal tumor) for NGCT tumors

DIAGNOSTIC TESTS & INTERPRETATION

- Core biopsy or fine needle aspiration

- Bulldog biopsy (in pediatrics and extremities)

- Needle biopsy (anywhere including GU)

- Metastatic workup

BASICS

DESCRIPTION

- In contrast to adults, testicular tumors in children are often benign including teratoma, dermoid, and epidermoid cyst.

- The majority of malignant germ cell tumors in children are yolk sac tumors.

- Differentiate testicular mass from scrotal wall and paratesticular mass with scrotal US.

- The most common causes of scrotal swelling or mass in pediatric includes hernia (organ protrusion required) and hydrocele (likely communicating in younger children), with lesions such as varicocele (see scrotal section), scrotal wall swelling (infant bite or nephrotic syndrome), with testicular neoplasms less common (peak incidence at 2 yr old and adolescence).

- Though very rare, most common malignant paratesticular tumor is rhabdomyosarcoma.

EPIDEMIOLOGY

Incidence

- Testicular tumors: (tumor registry data not presented due to reporting bias toward yolk sac). Total 0–3/1,000,000 males, 2% of

  - Testis (well differentiated) — 66%

  - Yolk sac (endothelial sinus) tumor 15%

  - Stromal tumors — 15%

  - Gonadal blastoma — 1%

  - Lymphoma testicular primary: Rare

  - Epidermoid cyst: < 1%

Prevalence

– N/A

RISK FACTORS

- Cryptorchidism: Prepubertal germ cell tumors (5.1%)

- Congenital adrenal hyperplasia (CAH): In boys often presents with precocious puberty. Adrenal excess, commonly present along the spermatic cord and in the testicular bursa, may hypertrophy in patients with CAH, leading to testicular nodules that are clinically indistinguishable from testicular tumors.

- Klinefelter syndrome

- Family history of testicular cancer

- More common in white men than black men

GENETICS

- Gonadal blastoma is associated with gonadal dysgenesis and a 45X0/45XY karyotype.

- Yolk sac tumors: Abnormalities: 1p, 6q, 3p

- Large-cell calcifying Leydig tumors are associated with Peutz–Jeghers syndrome and Carney complex.

- No clear genetic etiology exists for teratoma, dermoid, and granulosa tumor.

PATHOPHYSIOLOGY

- Non–germ cell and germ cell tumors originate from the olfactory epithelium and primordial germ cells, respectively

- Torsion in germ cells can evolve into seminoma or embryonal carcinoma

- Embryonal carcinoma is capable of differentiating into embryonic structures, such as mature (tissue) or immature (adult) teratomas and extraembryonic structures such as yolk sac and choriocarcinoma tumors.

- Seminoma (or spermatocellular seminoma) is a primitive germ cell neoplasm that cannot further differentiate (unusual in childhood, except with gonadal dysgenesis).

- Teratoma: Monodermal (epidermoid cyst) or multiple histologic types present (neve, cartilage, intestinal epithelium, etc.). Benign and no prepubertal transformation.

- Yolk sac tumors characterized by Schiller–Duval bodies (Yolk sac in appearance, contain AFP).

- Leydig tumors which can secrete testosterone are malignant 10% of time. (Rare in children—40%, increased in adults—50% above 20 years old, infants—10% malignant.) can secrete estrogen or testosterone, and granulosa cells (75% diagnosed within 1 mo of birth) have a common embryonic origin from a mesonephric stem cell.

- Gonadoblastomas are small benign tumors found in patients with gonadal dysgenesis, including those who have at least a portion of the Y chromosome. Although benign they have high risk of malignant transformation.

- 15–20% of all RMS arise from the genitourinary system.

- Most common genitourinary sites are the prostate, bladder, and paratesticular (ovaries and uterus are relatively unusual sites).

- Survival rates vary with site (ovary and paratesticular have a better prognosis than bladder/prostate primaries).

- 2 main histologic types of RMS

- Embryonal RMS is the most common subtype of RMS and accounts for most of the genitourinary neoplasm.

- Alveolar RMS occurs more commonly in the trunk and extratesticular than in GU, worse prognosis than embryonal tumor.

- Epithelial usually not infectious in pediatrics; likely due to refluxing fluid from urethra. Obtain urine culture. If infected need renal ultrasound to rule out urologic etiology.

- Vascular/lymphatic pathogenesis not known. Body habitus (tall, thin), genetics (risk increased if brother or 1st-degree relative has vascular Mayo), or systemic venous anomalies (“nutcracker” by SMA, left renal vein insertion), and rarely central outflow obstruction from tumors.

- In neotens and young children “hematoma” will be used to describe a communicating hydrocele with a “hematoma sac” present though no organ protrusion present: Patient process vasa.
DIFFERENTIAL DIAGNOSIS

See Section I and II “Individual Tumor Types”

DIAGNOSTIC PROCEDURES/SURGERY

Biopsy not indicated. The diagnostic procedure of choice is the radical orchiectomy.

Imaging

• Painless scrotal mass: history, CT scan
• Painful scrotal mass: CT scan, ultrasound

Pathologic Findings

See Section I and II “Individual Tumor Types”

DIFFERENTIAL DIAGNOSIS

• Painful scrotum:
  – Varicocele: Fullness and not a firm mass; changes with position
  – Testis tumor of adrenogenital syndrome
  – Metastatic tumors: Unusual in childhood

• Painful perineum:
  – Testicular tumor: Germ cell tumors: Yolk sac tumor
  – Testicular cysts
  – Spermatocele (epididymal cyst): Uncommon

• Scrotal edema (insect bite, nephrotic syndrome, Henoch–Schönlein purpura, Fournier gangrene)
  – Paratesticular rhabdomyosarcoma (bimodal age peak: 3–4 and teens)

• Masses in the scrotum:
  – Testicular tumor: Germ cell tumors: Yolk sac tumor, teratoma, seminoma, embryonal cell carcinoma, choriocarcinoma, Seminial gland tumors; Leydig, Sertoli cell, granulosa cell
  – Metastatic tumors: Unusual in childhood
  – Mixed germ cell and stromal tumor (gonadoblastoma)
  – Hamartoma, carcinoma in situ, neurofibroma

• Testis tumor of adrenogenital syndrome
  – Leukemia or lymphoma
  – Viral infection: Herpes and not a firm mass; changes with position

GENERAL MEASURES

• If concern for tumor obtain tumor markers pre- and postoperatively (1–4 wk)
• Discuss sperm banking, especially if chemotherapy needed
• Do not make incision through scrotum (inguinal incision only)
• Use long tag nonabsorbable suture when ligating spermatic cord
• Do not make incision through scrotum (inguinal incision only)

MEDICATION

• First Line: Chemotherapy for all yolk sac tumor stage 1 or greater or other germ cell tumor
• Platinum based for other nonseminomatous (choriocarcinoma, choriocarcinoma, and thymic cysts)

SURGERY/OTHER PROCEDURES

• Prepubertal teratoma is uniformly benign
• Prepubertal testicular teratomas, Leydig and Sertoli cell tumors are benign; orchiectomy or testicular-sparing surgery is curative and no additional therapy is needed
• Yolk sac tumor or other malignant tumor; radical orchidectomy and observation if low stage
• Retropertitoneal lymph node dissection (RPLND):
  – Ipsilateral RPLND before chemo.
  – Only indicated: 90% of yolk sac tumors are stage I at presentation; 85% 6-yr survival in stage 4 patients

RPLND: Retrograde ejaculation, lymphocele

ADDITIONAL TREATMENT RADIATION THERAPY

Used in rhabdomyosarcoma

ADDITIONAL THERAPIES

N/A

N/A

ADDITIONAL READING

N/A

N/A

CLINICAL/SURGICAL PEARLS

• The presence or absence of pain or tenderness alone cannot reliably rule in or out benign vs. malignant processes in the scrotum
• Acute onset of testicular pain in a child is most likely torsion, and emergent evaluation is indicated, early surgical intervention; do not delay surgery for imaging
• Painless testicular mass is highly suspicious for tumor and should be confirmed with imaging

ICD9

186.8 Malignant neoplasm of other and unspecified testis

608.89 Other specified disorders of male genital organs

T17.15 Malignant neoplasm of connective and other soft tissue of penis

ICD10

C60.80 Malignant neoplasm of unspecified testis, F52.2, ICD-10 Malignant neoplasm of connective and other soft tissue of trunk

N/A

N/A

ICD10

C60.80 Malignant neoplasm of unspecified testis, F52.2, ICD-10 Malignant neoplasm of connective and other soft tissue of trunk

N/A

N/A

N/A

N/A

N/A
TESTIS CANCER, SEMINOMA

Robert B. Den, MD
Mark Hurwitz, MD

**PATHOPHYSIOLOGY**

*Rarely presents as an extragonadal GCT in a site remote from the testicle.*

*Hematogenous dissemination is much less common than in NSGCT.*

*β-hCG elevation can sometimes be seen in seminoma.*

*The presence of elevated AFP during evaluation usually suggests nonseminomatous elements.*

*Due to slower growth pattern, relapses tend to be later than with NSGCT, and many can occur 2–3 yr after chemotherapy.*

**ASSOCIATED CONDITIONS**

*Increased risk in patients with cryptorchidism; risk is >30% times the general population.*

**GENERAL PREVENTION**

*Ultrasound or orchidectomy useful risk in undescended testicles.*

**DIAGNOSIS**

**HISTORY**

*Family history or swelling in the testes.*

*History of undescended testicle or inguinal surgical procedure as a child.*

**PHYSICAL EXAM**

*Palpate the testes bilaterally.*

*Examine the groin for evidence of surgical scar (prior orchidectomy).*

*Inspect for lymphedema of the groin or lower extremities.*

*Lymphatic spread is not typically inguinal; however, prior scrotal surgery may change lymphatic drainage.*

**DIAGNOSTIC TESTS & INTERPRETATION**

*CT of chest, abdomen, and pelvis to evaluate for metastatic disease.*

*Chest x-ray: To rule out metastatic lesions.*

*CBC and chemistry battery.*

*Beta-HCG.*

*Serum AFP.*

*Beta-绒毛膜促性腺激素 elevation can sometimes be seen in seminoma.*

*Cells of varying size that resemble maturing spermatogonia (peak age >50).*

*Does not stain for PLAP.*

**DIFFERENTIAL DIAGNOSIS**

*Adenocarcinoma of the rete testis.*

*Adequate lymphatic drainage.*

*Inguinal lymphadenopathy.*

*Right-sided tumors spread in the following order: The left-sided tumors tend to spread in the following order.*

*The slow growth characteristics of most seminomas result in them most commonly being diagnosed at an early stage (≤50% stage I).*
Radiation Therapy

ADDITIONAL TREATMENT

SURGERY/OTHER PROCEDURES

First Line

Radical inguinal orchiectomy

Radical orchiectomy (cIS), are initially treated with platinum-based chemotherapy according to the IGCCCG risk stratification.

Stage IA,B: Radical orchiectomy and adjuvant RT in persistently elevated tumor markers following stage I or II (B3 bulky) disease.

Stage I: 98–100%

Stage II (B1/B2 nonbulky): 98–100%

Stage II (B1/B2 bulky) and Stage III: >90% complete response rate to chemotherapy and 86% durable response to conventional chemotherapy.

Second Line High dose chemotherapy or clinical trial

Medication

First Line

RPLND is not usually for seminoma.

Carboplatin:

Stage I:

Stage II (B3 bulky) and stage III:

Stage II (B1/B2 nonbulky): 98–100%

Stage II (B1/B2 bulky) and stage III: >90%

Response rates to chemotherapy seem to be slightly better without prior radiation.

COMPLICATIONS

Infertility, GI complications, and possible induction of secondary malignancies are a concern following adjuvant RT.

Involvement of retroperitoneal lymph nodes may produce backache.

Follow-up

Patient Monitoring

Surveillance:

- Hb, AFP, β2-MG, LDH:
  - Every 3–4 mo for yrs 1–2
  - Every 6–12 mo for yrs 3–4, then annually
  - Adenoviral/epidemic CT annually for yrs 1–3, then every 4–6 mo for yrs 4–5
  - ORX as clinically indicated for yrs 1–5

- Carboplatin:
  - Every 3–4 mo for yrs 1–2
  - Every 6–12 mo for yrs 3–4, then annually
  - Adenoviral/epidemic CT annually for yrs 1–3
  - ORX as clinically indicated
  - RT:
    - Every 3–4 mo for yrs 1–2
    - Every 6–12 mo for yrs 3–4
  - Adenoviral/epidemic CT annually for yrs 1–3 (for patients post only para-aortic RT)
  - ORX as clinically indicated

Additional Therapy

- Active surveillance for low-risk, early disease:
  - Avoids unnecessary treatment and related side effects

- CT every 4–6 mo, reduce interval after ~5 yr

- Traditional risk factors that increase the recurrence risk: tumor size >4 cm, invasion of the rete testis, anaplastic features, small vessel invasion

- The role of salvage chemotherapy, surgical removal, or RT of persistent masses detected by CT continues to be controversial.

Complementary & Alternative Therapies

Patients should consider sperm banking prior to treatment to aid in avoiding risk of infertility.

Additional reading


References


Additional reading


See also (Topic, Algorithm, Media)

1. International Germ Cell Cancer Collaborative Group (IGCCCG)

2. Reference Tables: TMM: Testis Cancer

3. Testis Cancer, Pediatric, General Considerations

4. Testis Cancer, Nonseminomatous Germ Cell Tumors, General

5. Testis Cancer, Seminoma Image

6. Testis, Testes, Mature and Immature

7. Testis, Tumor and Mass, Adult, General Considerations

8. Testis, Tumor and Mass, Pediatric, General Considerations

Codes

ICD09

- N00.9 Inflammatory neoplasm of other and unspecified tests

- N82.89 Other specified disorders of male genital organs

ICD10

- C62.90 Idiopathic neoplasm of unsp tests, unsp desc or undeiercogn

- C62.92 Idiopathic neoplasm of left tests, unsp desc or undeiercogn

- N80.8 Other specified disorders of male genital organs

Aplastic seminoma is no longer recognized as distinct entity.
TESTIS, LEYDIG CELL TUMOR

Austin R. Younger, MD
James S. Rosofsky, MD

DESCRIPTION
Leydig cell tumors (LCTs) are hormonally active steroid-secreting tumors that may produce feminizing/virilizing syndromes.

- Most common sex conditional tumors
  - Neoplasms containing (leydig, Sertoli), granulosa, or thal cell (commonly referred to as nonseminomas)
- Usually benign, 10% malignant variants reported in adults only (1)
- TNM staging follows current NCCN Guidelines for Testis Cancer

EPIDEMIOLOGY (1)
- An estimated 8,820 new cases of testicular cancer were diagnosed in 2014
- LCTs represent 1–3% of all testicular neoplasms
- LCTs are not associated with cryptorchidism
- Equal incidence between right and left testis with 4–10% occurring bilaterally
- Bimodal distribution with peak incidences occurring between ages 4–5 and 30–60
- Most common sex cord/stromal tumors
- LCTs usually secrete testosterone, may also secrete other androgens, corticosteroid, estrogen, and progesterone.

PATHOPHYSIOLOGY
- Leydig cells are located in the interstitium of testicle
- Produce testosterone to estrogens from aromatase conversion (seen in animal studies only)
- Hypothalamic–pituitary axis is directly involved in feedback regulation
  - Reinke crystals: Pathognomonic for LCT, rhomboid/cylindrical crystals, pale staining within cytoplasm and nucleus.
  - Malignant LCT: Larger, hemorrhage/necrosis present, replace or spread stromal/tubular architecture
- Vital role in development of male secondary sex characteristics and spermatogenesis
- In neoplasia, feedback regulation is disrupted resulting in uncontrolled hormone production.

DIAGNOSIS
- Low estradiol, increased testosterone, gynecomastia, and hyperplastic lesion on ultrasound are highly suspicious for LCT
- Histopathology confirms diagnosis

HISTORY
- Children commonly present with:
  - Precocious puberty due to androgen secreting tumors; irreversible and profound physical changes—early diagnosis is critical
- Feminization symptoms—low energy, anhedonia, change in penile length, deepened voice, testicular atrophy, gynecomastia, infertility
- Adults commonly present with:
  - Nontender testicular mass/nodule
  - Incidental finding on imaging for other conditions
  - Premature testicular development to identify any deviation in normal growth and maturation

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - All other tests should be within normal limits if malignancy not present
  - Virilization occurs due to unopposed testosterone/estrogen production independent of LH stimulation.
  - Virilizing signs are often not observed in adults.
- Imaging
  - CT chest/abdomen/pelvis: If concern for malignancy, testicular ultrasound preferred imaging if mass is palpable

PHYSICAL EXAM
- A unilateral mass is palpable in 90% of cases with careful exam
- Hypothalamic imbalance responsible for physical changes
  - Virilizing changes
    - Children: Precocious puberty, early growth, early change in penile length, deepened voice, increased muscle mass
    - Adults: Usually asymptomatic
  - Feminizing changes
    - Children: Delayed maturational, testicular atrophy, gynecomastia
    - Adults: Female hair distribution, gynecomastia, testicular atrophy

DIAGNOSTIC PROCEDURES/SURGERY
- Historically, radical inguinal orchietomy was gold standard treatment
- Testis-sparing surgery (TSS): Enucleation of tumor
  - Historically, radical inguinal orchiecetomy was gold standard for treatment
  - Some cases; no evidence of local recurrence or metastases on long-term follow-up (3,5)

PATHOLOGIC FINDINGS
- Gross pathology
  - Benign LCTs: 3–5 cm, sharply delineated, solid mass, embedded within testis, displaces normal stromal/hilar architecture
  - Brown to yellow-white depending on total lipid content
- Malignant LCT: Larger, >5 cm, infiltrative margins, hemorrhage/necrosis present, replace or spread beyond testicular parenchyma
- Microscopic pathology
  - Testicular tumors, large polygonal cells with eosinophilic/clear granular cytoplasm, round regular nuclei, eosinophilic/gray, prominent nucleoli
  - Neoplastic Leydig cells: pathognomonic for LCT
  - Malignant lesions: Lobular, minimally invasive tumor cells with increased lipid inclusions

LITERATURE CITED

• Findings that correlate with malignancy
  – Cytologic/histologic atypia, increased mitotic activity
  – Local invasion of the capsule, lymphovascular invasion
  – Increased expression of androgen receptors
  – Immunoexpression of androgen receptors

DIFFERENTIAL DIAGNOSIS

• Testicular masses (see Section I: “Testis Cancer, Pediatric, General Considerations”)
• Precocious puberty
• Adrenocortical syndromes
• Gynecomastia/feminization
• Pituitary lesions
• Paraneoplastic syndromes

TREATMENT

GENERAL MEASURES

• Management is primarily surgical
• Radical orchiectomy is the gold standard

SURGERY/OTHER PROCEDURES

• Radical orchiectomy
• Testicular sparing surgery

• Testis-sparing surgery (TSS) is a reasonable option in certain cases and has no reported increased risk of local recurrence or metastasis compared with radical orchiectomy.

• Findings that correlate with malignancy
  – Cytologic/histologic atypia, increased mitotic activity
  – Local invasion of the capsule, lymphovascular invasion
  – Increased expression of androgen receptors
  – Immunoexpression of androgen receptors

DIFFERENTIAL DIAGNOSIS

• Testicular masses (see Section I: “Testis Cancer, Pediatric, General Considerations”)
• Precocious puberty
• Adrenocortical syndromes
• Gynecomastia/feminization
• Pituitary lesions
• Paraneoplastic syndromes

ADDITIONAL TREATMENT

Radiation Therapy

• Radiotherapy may be used as a preoperative or postoperative treatment.

ADDITIONAL THERAPIES

• Observation
• Chemotherapy

ONGOING CARE

• Surveillance and follow-up are important for patients with Leydig cell tumors.

CLINICAL/SURGICAL PEARLS

• Leydig cell tumors (LCTs) are hormonally active steroid-secreting tumors that may produce feminizing virilizing syndromes.
• LCTs are usually benign; 10% malignant variants reported in adults only.
• Low estradiol, increased testosterone, andropause, and hypochlonic lesion on ultrasound are highly suspicious for LCT.
• Social exploration with frozen section is reliable in diagnosing LCT.
• Testicular sparing surgery (TSS) is a reasonable option in certain cases and has no reported increased risk of local recurrence or metastasis compared with radical orchiectomy.
No studies exist at this time

DESCRIPTION
- Orchalgia is scrotal or testicular pain
- Acute or chronic
- Intermittent or constant
- Unilateral, bilateral, or alternating
- Characteristics
  - Localized to scrotum
  - May radiate to groin, perineum, back, or legs
  - Chronic orchalgia
  - Lasting >3 mo
  - Concurrent or intermittent pain.
- No specific cause is identified in most cases.
- Secondary gains with malingering
- Depression
- Life stressors
- Current life stressors
- Social support
- Neutropathic conditions
  - Diabetes
  - Polymyalgia rheumatica
  - RSD
- Pain psychology
- Nerve entrapment (ilioinguinal or genitofemoral)
- Inguinal hernia (incarcerated, other)
- Testicular tumors
- Testicular torsion
- Torsion of testicular/epididymal appendices
- Epididymitis and epididymo-orchitis
- Viral orchitis
- Prostatitis
- Epididymal granulomas
- Scrotal/inguinal mass
- Herniated intervertebral disc

ASSOCIATED CONDITIONS
- Often idiopathic (~15%)
- Can be associated with:
  - Previous surgery (vasectomy, hernia repair)
  - Trauma
  - Intermittent torsion
  - Hydrocele, varicocele, spermatocele
  - Tumor
  - Infection
  - Herniated intervertebral disc
  - Vasculitis (polymyalgia rheumatica)

GENERAL PREVENTION
- USPSTF: Against routine screening for testicular cancer in asymptomatic adolescent and adults including routine testicular self-exams.
- American Cancer Society suggests that men with family history do monthly self-exams.

ALERT
- Acute onset of testicular pain in a child is most likely torsion, and emergent evaluation is indicated, early surgical intervention; do not delay surgery for imaging.

TESTS, PAIN (ORCHALGIA)

Alosh Madala, MD
Dmitry Nikolovsky, MD

BASICS

PREVALENCE
- Chronic testicular pain
  - Idiopathic 25–50%
  - Postvasectomy chronic orchalgia
  ~15%

RISK FACTORS
- Organic/physical risk factors
  - Previous trauma or surgery
  - Post-vasectomy pain syndrome in ±43% of men who have undergone this procedure
  - Posthemia repair
  - Sperm granuloma following vasectomy
- Neuropathic conditions
  - Diabetic neuropathy
  - Neurontin withdrawal from migraine
- Psychological risk factors
  - Life stresses
  - Depression
  - Secondary gain with malingering

GENETICS
- No studies exist at this time

PATHOPHYSIOLOGY
- Poorly understood
- Idiopathic in most cases
- Tests involvement
  - Sympathetic nerve supply from T10–T12 segments
  - Accompany the internal spermatic vessels
  - Penetrate the tunica albuginea
  - Accompany the internal spermatic vessels
  - Sympathetic nerve supply from T10–T12 segments
- Secondary gain with malingering
  - Depression
  - Life stressors
  - Social support
  - Neutropathic conditions
  - Diabetes
  - Polymyalgia rheumatica
  - RSD
- Pain psychology
  - Nerve entrapment (ilioinguinal or genitofemoral)
  - Inguinal hernia (incarcerated, other)
  - Testicular tumors
  - Testicular torsion
  - Torsion of testicular/epididymal appendices

DIAGNOSIS

HISTORY
- Onset, location, duration, quality, aggravating (exercise, sexual intercourse, or ejaculation) and relieving factors.
- Visual analog scale (VAS) of 0–10 helps quantify degree of pain (~15%)
- Consult with multiple physicians including urologists
- Multiple treatments (antibiotics, anti-inflammatory drugs)
  - Little or no relief
  - Severe pain
  - Refractory to treatment
  - Referred pain (nerve root irritation)
  - Psychogenic
- Referral (venous occlusion, renal insufficiency)
- Medical causes: Diabetic neuropathy, polyarteritis nodosa
  - Postoperative (vasectomy, inguinal herniorrhaphy)
  - Inguinal hernia (incarcerated, other)
  - Testicular tumor
  - Testicular torsion
  - Testicular vesiculation
  - Testicular tumor
  - Testicular vasovasostomy from sexual arousal without ejaculation
  - Testicular pain with sexual activity
  - Chronic pelvic pain syndrome (CPPS)

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Urine analysis and culture
  - Bacterial and after prostatic massage
  - Serum analysis (for chronic epididymitis)
- Consider STD/STI screening

IMAGING
- Scrotal US with color flow doppler
  - Evaluate scrotal contents
  - Rule out testicular torsion and tumor

DIAGNOSTIC PROCEDURES/SURGERY

Cystoscopy and urodynamics are of limited value

PATHOLOGIC FINDINGS
Based on etiology

DIFFERENTIAL DIAGNOSIS (2)
- Chronic pelvic pain syndrome (CPPS)
- Chronic epididymitis
- Hydrocele, spermatocele
- Idiopathic orchalgia
- Testicular tumors
  - Paratesticular tumor
  - Testicular abscess
  - Epididymal or epididymo-orchitis
  - Urethritis
  - Prostatitis
  - Viral orchitis
  - Testicular abscess
  - Hydrocele, spermatocele
  - Idiopathic orchalgia
  - Testicular tumors
  - Paratesticular tumor
  - Testicular abscess
  - Epididymal or epididymo-orchitis
  - Urethritis
  - Prostatitis
  - Viral orchitis
  - Testicular abscess
  - Hydrocele, spermatocele
  - Idiopathic orchalgia
  - Testicular tumors
  - Paratesticular tumor
  - Testicular abscess
  - Epididymal or epididymo-orchitis
  - Urethritis
  - Prostatitis
  - Viral orchitis
  - Testicular abscess
  - Hydrocele, spermatocele

MEDICATION

GENERAL MEASURES
- For acute testicular pain: See Section 1 “Acute Scrotum”
- For chronic testicular pain
  - Scrotal support
  - Avoid physical activity
  - Hot baths

MEDICATION

FIRST LINE
- NSAIDs
  - Variable and usually temporary relief
- Regimens described include ibuprofen 400–600 mg q PO bid for 1 mo

TREATMENT

502
ADDITIONAL THERAPIES (10,11)

- Antidepressants and anticonvulsants - Demonstrated benefit in chronic idiopathic orchalgia
- Poor response to postvasectomy pain
- Tricyclic antidepressants - Amitriptyline 10–25 mg qhs
- Gabapentin 300 mg titrated up to 6,300 mg daily
- Denervation of spermatic cord - Through surgical or percutaneous means

RADIATION THERAPY

- Sacral nerve stimulation - May be helpful in patients with spinal disk and back problems with nerve root irritation
- Physical therapy
- Vasoavasostomy in the setting of postvasectomy pain
- Epididymectomy
- Denervation of spermatic cord (3,9)

The following are used for the management of acute testicular pain in a child: See Section I

- Tricyclic antidepressants
- Antidepressants and anticonvulsants
- Antibiotics
- - Adrenergic antagonists
- - Doxycycline 100 mg PO BID or ciprofloxin 250–500 mg PO BID for 2–3 wk

SECOND-LINE (5.6)

- Acute testicular pain in a child: See Section I "Torsion, Testis or Testicular/Epidermidal Appendages"
- The following are used for the management of chronic pain in an adult:
  - Minimally invasive treatment options (7,8)
  - Denervation of spermatic cord
  - Block with local anesthetic
- Orchiectomy
- - Testis: May continue to have pain
  - Inguinal approach superior to scrotal
- - 75% patients have relief after surgical removal of varicoceles, hydroceles, spermatoceles, or intermittent torsion.
- Epididymectomy
- - Poor results except in the setting of postvasectomy pain syndrome
- Vasovasectomy in the setting of postvasectomy pain

ADDITIONAL TREATMENT

- Physical therapy
  - May be helpful in patients with spinal disk and back problems with nerve root irritation

RADIATION THERAPY

- NA

ADDITIONAL THERAPIES (10,11)

- Pulsed radiofrequency denervation of the spermatic cord (4)
- Testicular scrotal block with local anesthetic
- Sacral nerve stimulation - 80% decrease in pain

CONCLUSION

- Oral gabapentin or pregabalin (neurontin) treatment for refractory neuropathic testicular pain.
- Consider gabapentin or nortriptyline before considering surgery.
- Psychotherapy
- - Should be strongly considered before surgical intervention
- Pelvic muscle exercises

ONGOING CARE

PROGNOSIS

Depends on etiology

COMPLICATIONS

- Surgery
  - Epididymectomy may result in loss of testicle or infertility

FOLLOW-UP

Patient Monitoring

Periodic follow-up with urology or other providers depending on etiology (if known)

PATIENT RESOURCES

- Urology Care Foundation: Epididymitis and Orchitis.
  - http://www.urologyhealth.org/urology/index.html?article=114&display=1

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Acute Scrotum
- Chronic Pelvic Pain Syndrome (CPPS)
- Epididymitis
- Painful Testicles
- Prostatitis, Chronic Nonbacterial, Inflammatory & Noninflammatory (NH CP/CPPS IA A and B)
- Scrotal Pain Syndrome (Chronic Scrotal Pain Syndrome (CSPS))
- Sperm and Testicle, Mass
- Sperm Granuloma
- Spermatocele
- Testis, Pain (Orchalgia) Image Q
- Testis, Tumor and Mass, Adult, General Considerations
- Torsion, Testis or Testicular/Epidermidal Appendages
- Varicocele, Adult
- Vasectomy and Postvasectomy Pain Syndrome

CODES

ICD-9

367.89 Other pain disorders related to psychological factors
688.89 Other specified disorders of male genital organs
993.14 Other injury of external genitals

ICD-10

P54.81 Pain disorder exclusively related to psychological factors
N80.8 Other specified disorders of male genital organs
S39.94 Other unspecified injury of external genitals, initial encounter

CLINICAL/SURGICAL PEARLS

- The presence or absence of pain or tenderness alone cannot reliably rule in or out benign vs. malignant processes in the scrotum or testes.
- Physical exam is often normal with testicular pain.
- Ultrasound is the most valuable study.
- Surgical options should only be considered after medical and conservative management fails for chronic testicular pain.
TESTIS, SERTOLI CELL TUMOR
Tariq A. Khemees, MD
Ahmad Shabegis, MD, FACS

PATHOPHYSIOLOGY
- Sertoli cells are supporting cells of the testis.
  - During fetal development: Secrete anti-Mullerian hormone, which leads to regression of Mullerian ducts.
  - During adulthood: Promote differentiation of spermatogonia.
- Normally, Sertoli cells do not have aromatase activity (the enzyme that converts testosterone to estradiol); however, neoplastic Sertoli cells may express aromatase.
- Excess estrogen in prespermatogenic boy will lead to accelerated skeletal maturation and gynecomastia.

ASSOCIATED CONDITIONS
- Gynecomastia
  - Carney complex (CNC)
  - Peutz–Jeghers syndrome (PJS)
  - Tuberous sclerosis (TS)
- Breast exam: Look for:
  - Mass
  - Tenderness
  - Feminization, hair pattern, and other signs of estrogen access
  - Bone scan
- Imaging:
  - Testicular US
  - LCCSCT:
    - Bilateral in 20% of reported cases, especially in familial syndromes
    - Usually appear as solid, well-circumscribed, and hypervascularized masses
    - Bilateral increase in testicular volume
    - Occasionally cysts are seen
    - Calcifications: Microcalcifications within the tumor mass
    - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
  - Metastatic workup includes:
    - Chest x-ray
    - CT pelvis and abdomen
    - Bone scan

Diagnostic Procedures/Surgery
- Excisional biopsy usually by radical orchiectomy, can be curative
- Fine needle biopsy or nonexcisional biopsy of mass should never be done due to the risk of spread of the more common malignant tumors such as embryonal cell carcinoma or seminoma
- Partial orchietomy, inguinal approach for patient with familial syndrome

Pathologic Findings
- Gross: Generally well circumscribed, yellow-gray, and lobulated on cut surface
- Histologically:
  - Solid, tubular, or cord-like growth pattern of spermatogonia
  - Neoplastic Sertoli cells may express aromatase.
- Immunophenotype:
  - Neoplastic Sertoli cells do not have aromatase expression.
- Histologic subtypes:
  - Classic or tumors that are not otherwise specified:
    - Large-cell calcifying Sertoli cell tumor
      - Mean age of 45 yr
      - Low malignant potential (around 10–20%)
      - Mostly have benign clinical course, but malignancy can occur especially in older ages
      - Bilateral: Early and late onset
      - Frequently associated with MNS
  - Tuberous sclerosis (TS): Autosomal dominant caused by TSC1 and TSC2 mutations and characterized by:
    - Mental retardation
    - Facial angiofibromas
    - Spotty skin pigmentation
    - Multiple hamartomatous polyps along the whole gastrointestinal tract
    - Malignant renal tumors
    - Cardiac rhabdomyomas
    - Angiomyolipomas
    - Inguinal lymphadenopathy
    - Angiomyofibroblastoma
    - Intrahepatic cholestatic syndrome
    - Synganglium disease
    - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
  - Peutz–Jeghers syndrome (PJS):
    - Malignant tumors frequently occur in gastrointestinal tract
  - Tuberous sclerosis (TS):
    - Malignant tumors frequently occur in renal tract
  - Breast:
    - Breast: Look for:
      - Mass
      - Tenderness
      - Feminization, hair pattern, and other signs of estrogen access
      - Bone scan
- Lab:
  - See steroid: Check for age-appropriate levels of:
    - LH
    - FSH
    - Androgens
    - Estrogen
    - Progesterone
  - Tumor markers:
    - AFP is usually negative
    - hCG is usually negative
    - Paraneoplastic alkaline phosphatase is usually negative

RISK FACTORS
- 40% of LCCSCT are hereditary and are associated with multiple neoplasia syndromes (MNSs) namely:
  - Carney complex (CNC)
  - Peutz–Jeghers syndrome (PJS)
  - Tuberous sclerosis (TS)
- Genetics:
  - Autosomal dominant; mainly caused by STK11 gene mutations and characterized by:
    - Mental retardation
    - Facial angiofibromas
    - Multiple hamartomatous polyps along the whole gastrointestinal tract
    - Angiomyolipomas
    - Intrahepatic cholestatic syndrome
    - Synganglium disease
    - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
- Other causes:
  - Malignant tumors frequently occur in renal tract
  - Breast:
    - Breast: Look for:
      - Mass
      - Tenderness
      - Feminization, hair pattern, and other signs of estrogen access
      - Bone scan

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - See steroid: Check for age-appropriate levels of:
    - LH
    - FSH
    - Androgens
    - Estrogen
    - Progesterone
  - Tumor markers:
    - AFP is usually negative
    - hCG is usually negative
    - Paraneoplastic alkaline phosphatase is usually negative

BASICS
- Genetics:
  - Autosomal dominant; mainly caused by STK11 gene mutations and characterized by:
    - Mental retardation
    - Facial angiofibromas
    - Multiple hamartomatous polyps along the whole gastrointestinal tract
    - Angiomyolipomas
    - Intrahepatic cholestatic syndrome
    - Synganglium disease
    - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
  - Peutz–Jeghers syndrome (PJS):
    - Malignant tumors frequently occur in gastrointestinal tract
  - Tuberous sclerosis (TS):
    - Malignant tumors frequently occur in renal tract
  - Breast:
    - Breast: Look for:
      - Mass
      - Tenderness
      - Feminization, hair pattern, and other signs of estrogen access
      - Bone scan

DIAGNOSIS
- HISTORY
  - Familial history of MNS
  - Growth spurt
  - Fertility
  - Lab:
    - See steroid: Check for age-appropriate levels of:
      - LH
      - FSH
      - Androgens
      - Estrogen
      - Progesterone
    - Tumor markers:
      - AFP is usually negative
      - hCG is usually negative
      - Paraneoplastic alkaline phosphatase is usually negative

IMAGING
- Testicular US
  - Usually appear as solid, well circumscribed, and hypervascularized mass
  - Bilateral increase in testicular volume
  - Occasionally cysts are seen
  - Calcifications: Microcalcifications within the tumor mass
- Chest x-ray
- CT pelvis and abdomen
- Bone scan

Diagnostic Procedures/Surgery
- Excisional biopsy usually by radical orchiectomy, can be curative
- Fine needle biopsy or nonexcisional biopsy of mass should never be done due to the risk of spread of the more common malignant tumors such as embryonal cell carcinoma or seminoma
- Partial orchietomy, inguinal approach for patient with familial syndrome

Pathologic Findings
- Gross: Generally well circumscribed, yellow-gray, and lobulated on cut surface
- Histologically:
  - Solid, tubular, or cord-like growth pattern of spermatogonia
  - Neoplastic Sertoli cells may express aromatase.
- Immunophenotype:
  - Neoplastic Sertoli cells do not have aromatase expression.
- Histologic subtypes:
  - Classic or tumors that are not otherwise specified:
    - Low malignant potential (around 10–20%)
    - Mostly have benign clinical course, but malignancy can occur especially in older ages
    - Bilateral: Early and late onset
    - Frequently associated with MNS
  - Tuberous sclerosis (TS):
    - Autosomal dominant caused by TSC1 and TSC2 mutations and characterized by:
    - Mental retardation
    - Facial angiofibromas
    - Multiple hamartomatous polyps along the whole gastrointestinal tract
    - Angiomyolipomas
    - Intrahepatic cholestatic syndrome
    - Synganglium disease
    - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
  - Peutz–Jeghers syndrome (PJS):
    - Malignant tumors frequently occur in gastrointestinal tract
  - Tuberous sclerosis (TS):
    - Malignant tumors frequently occur in renal tract
  - Breast:
    - Breast: Look for:
      - Mass
      - Tenderness
      - Feminization, hair pattern, and other signs of estrogen access
      - Bone scan

DIAGNOSTIC TESTS & INTERPRETATION
- Lab:
  - See steroid: Check for age-appropriate levels of:
    - LH
    - FSH
    - Androgens
    - Estrogen
    - Progesterone
  - Tumor markers:
    - AFP is usually negative
    - hCG is usually negative
    - Paraneoplastic alkaline phosphatase is usually negative

IMAGING
- Testicular US
  - Usually appear as solid, well circumscribed, and hypervascularized mass
  - Bilateral increase in testicular volume
  - Occasionally cysts are seen
  - Calcifications: Microcalcifications within the tumor mass
  - Christmas tree-like appearance of multiple calcifications in syndromic LCCSCT is almost always pathognomonic for this tumor
- Metastatic workup includes:
  - Chest x-ray
  - CT pelvis and abdomen
  - Bone scan
DIFFERENTIAL DIAGNOSIS
- Always rule out precocious puberty in any child who presents with testicular enlargement and accelerated growth pattern.

- **Adult/pediatric painful mass:**
  - **Testicular trauma:** Usually blunt; contusion, rupture, usually associated hematoma.
  - **Torsion:** (testiculate, epididymal, appendicular).
  - **Henoch–Schönlein purpura** (usually no mass).

- **Adrenal rest tumors:**
  - Rhabdomyosarcoma
  - Schwannoma
  - Calcifying Sertoli cell tumor

- **Sclerosing:**
  - Adrenal rest tumors, rhabdomyosarcoma
  - Malignant fibrous histiocytoma (most common sarcoma)

- **Angioma:**
  - Fibroma, leiomyoma, hamartoma, neurofibroma

- **Mixed germ cell and stromal tumor**
  - Teratoma (1–5%)
  - Teratocarcinoma

- **Gonadal stromal tumors:**
  - Leydig tumor
  - Granulosa cell tumors

- **Germ cell tumors:**
  - Seminoma
  - Embryonal cell carcinoma
  - Carcinoma, choriocarcinoma, yolk sac carcinoma

- **Metastatic tumors:**
  - Lung
  - Prostate
  - Head and neck
  - Gastrointestinal tract

- **Bilateral LCCSTs** can gradually increase in size, block the spermatic cord, and induce gynecomastia.

- **Calcifying Sertoli cell tumors of the testes** in children and young adults are typically benign and can be treated with pharmacotherapy for symptomatic relief of gynecomastia and/or advanced puberty.

MEDICATION
- **Radical inguinal orchectomy:**
  - Used in metastatic disease, but unproven benefit.

- **Postvasectomy syndrome:**
  - Usually no mass.

- **Adrenal rest tumors:**
  - No hormonal imbalances.
  - No hereditary association.
  - Affects young adults mainly.
  - Malignancy has never been reported.

- **Testicular trauma:**
  - Usually blunt; contusion, rupture.
  - No hereditary association.

- **Incarcerated/strangulated hernia**
  - No definite recommendations can be made.

- **Adrenal rest tumors:**
  - Inhibin: Has been proposed as marker for LCCST.
  - Frozen-section biopsy confirms the diagnosis.

- **Infertility/subfertility**
  - Malignant tumors: Uncommon.

- **Metastasis:**
  - Used in metastatic disease, but unproven benefit.

- **Radiation Therapy**
  - Used in metastatic disease, but unproven benefit.

- **Aromatase inhibitors** may be an effective mode of pharmacotherapy for symptomatic relief of gynecomastia and/or advanced pubertal acceleration.

- **Surgical resection**
  - Retroperitoneal lymph node dissection: Reported approach for patient with familial syndrome.

- **LCCSCT in the setting of CNC in children and young adults are typically benign and can be treated with pharmacotherapy for symptomatic relief of gynecomastia and/or advanced pubertal acceleration**.

TREATMENT

- **BRCA1/BRCA2**
  - Breast cancer.
  - Colon cancer.

- **Testis-sparing (partial orchiectomy) inguinal**
  - In prepubertal boys, testis-sparing local excision has thought to be a more common malignancy of the testicle.

- **Radical inguinal orchiectomy**
  - Used in metastatic disease, but unproven benefit.

- **Second Line**
  - **Radiation Therapy**
    - No proven role.
  - **Chemotherapy**
    - Platinum based chemotherapy
    - Used in metastatic disease, but unproven benefit.

- **Platinum-based chemotherapy**
  - Used in metastatic disease, but unproven benefit.

- **First Line**
  - **Radiation Therapy**
    - No proven role.

FOLLOW-UP

- **Patient Monitoring**
  - **Benign tumors:**
    - Routine surveillance.

- **Malignant tumors:**
  - Imaging for metastasis.
  - Periodic screening for conditions associated with MNS is necessary in syndromic LCCST.

- **Patient Resources**

REFERENCES

ADDITIONAL READING

CODES

- **ICD-10**
  - D29.20 Benign neoplasm of unspecified testis.
  - D29.20 Benign neoplasm of testis.
  - D29.22 Benign neoplasm of testis.

- **ICD-O**
  - 8222.2 Benign neoplasm of testis.
  - 8222.2 Benign neoplasm of testis.

CLINICAL/SURGICAL PEARLS

- Consider hereditary syndromes.

- Most Sertoli cell tumors are benign.
Testis, Teratoma, Mature and Immature

John L. Phillips, MD, FACS
Vladimir A. Valera, MD, PhD

**BASICS**

**DESCRIPTION**
- Testicular teratoma (TT) are germ cell tumors (GCTs) which form somatic tissues in varying stages of maturity (karyotype).
  - Mature (M) = well-differentiated endoderm, mesoderm, and/or ectoderm germ cell (GGC) layers
  - Immature (I) = feral or embryonal GC layers
- Most common GCT in childhood
- Adult TT: mature and immature; Consider as malignant
- Pediatric TT: mature and immature; Behave in general as benign lesions

**EPIDEMIOLOGY**
- **Prevalence**
  - 8,820 cases of testicular cancer in the US in 2014
  - 5.5 cases: 100,000 men
- **Incidence**
  - Adults: 2nd to 4th decade
  - Mature: Immature types 10:1 (1)
  - Pure teratoma (T) in 5% of adult GCTs but 35–40% of pediatric GCT
  - T found in retroperitoneum in 80% of cases
- **Pediatric TT, mature and immature:** Behave in general as benign lesions
  - Consider as malignant
  - Typically large and multinodular
  - 80% of children ≥ 2 years
  - 50% of cases

**RISK FACTORS**
- **Developmental**
  - Family history
  - 10% of patients after chemo for NSGCT (2)
- **Environmental**
  - Increased sperm counts and reduced fertility
  - Lower sperm count in patients with congenital adrenal hyperplasia
  - Increased risk of testicular cancer in patients with congenital adrenal hyperplasia
  - Increased risk of testicular cancer in patients with congenital adrenal hyperplasia

**ASSOCIATED CONDITIONS**
- **Gastrointestinal**
  - % of patients with congenital adrenal hyperplasia
  - Increased risk of testicular cancer in patients with congenital adrenal hyperplasia
  - Increased risk of testicular cancer in patients with congenital adrenal hyperplasia

**DIAGNOSIS**

**DIAGNOSTIC TESTS & INTERPRETATION**
- **Laboratory**
  - Tumor markers
  - α-Fetoprotein (AFP) (10%)
  - β-HCG (only elevated if chorio- or seminomatous elements present)
- **Imaging**
  - Ultrasonography is preferable in all cases
  - MRI is more sensitive than ultrasound
  - CT scan with and without contrast
  - PET scan not usually indicated; may have a role in the postchemotherapy setting

**DIFFERENTIAL DIAGNOSIS**
- **Benign lesions**
  - Epidermoid cysts: Common and nonmalignant
  - Fibrous pseudotumor of the testis: Benign
  - Intratesticular and extratesticular lesions:
    - Epithelial tumors: Benign
    - Malignant tumors: Benign
  - Neuroendocrine tumors: Benign
  - Other rare benign lesions: Angioma, fibroma, leiomyoma, hamartoma, carcinoid, neurofibroma
  - Malignant lesions
  - Testicular primary tumors: Benign
  - Nonseminomatous GCT

**GENERAL PREVENTION**
- **Stage patient per TNM**
- **Document tumor markers:** Important for staging
- **Document presence of nonneoplastic elements:** Important for treatment algorithms

**Pathologic Findings**
- **Large (5–10 cm), multinodular, heterogeneous (solid, cystic, mixed)**
- May contain teeth, hair, bone, cartilage
- Cystic areas mixed with solid
- Mature teratoma
  - Tissue of elements of endoderm (ep), mesoderm (eg, md), and ectoderm (eg, bone)
- Immature teratoma
  - Neuropathology with embryonic features:
    - Poorly formed cartilage
    - Primitive glandular structures
    - High grade if microscopically active
  - Dermoid cysts
    - True (benign), no atypia or mitoses
    - Keratin, hair, dermoidocyst

**DIFFERENTIAL DIAGNOSIS**
- **These are a delineation of testicular masses only. For a comprehensive listing of intrascrotal and testicular masses see Section 1: “Scrotum and Testicle Mass”**
- **Benign lesions**
  - Epidermoid cysts: Benign
  - Fibrous pseudotumor of the testis: Benign
  - Intratesticular and extratesticular lesions:
    - Epithelial tumors: Benign
    - Malignant tumors: Benign
  - Neuroendocrine tumors: Benign
  - Other rare benign lesions: Angioma, fibroma, leiomyoma, hamartoma, carcinoid, neurofibroma
  - Malignant lesions
  - Testicular primary tumors: Benign
  - Nonseminomatous GCT
  - Leukemia involving testes—tests can be a site of solitary recurrence of leukemia posttreatment
  - Treatment can be toxic with radiation, though contralateral testes should be treated as bilateral disease can be present.
  - Symptoms from invading testis: Raynaud’s phenomenon
  - Constitutional symptoms commonly present

**DIAGNOSTIC TESTS & INTERPRETATION**
- **Labor**
  - Tumor markers
  - Protin, ferritin, ceruloplasmin
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematoma
  - Testicular (testis and appendages)
  - Nonseminomatous GCT
  - Other rare benign lesions: Angioma, fibroma, leiomyoma, hamartoma, carcinoid, neurofibroma
  - Malignant lesions
  - Testicular primary tumors: Benign
  - Nonseminomatous GCT
  - Leukemia involving testes—tests can be a site of solitary recurrence of leukemia posttreatment
  - Treatment can be toxic with radiation, though contralateral testes should be treated as bilateral disease can be present.
  - Symptoms from invading testis: Raynaud’s phenomenon
  - Constitutional symptoms commonly present

**DIAGNOSIS**

**ALERT**
- Identify symptoms of metastatic disease.

**DIAGNOSTIC TESTS & INTERPRETATION**

**ALERT**
- Markers must be drawn prior to orchiectomy.

**IMAGING**
- Ultrasonography is critical in assessing for intratesticular masses; typically hypoechoic
- Microcalcification in calcified masses should be documented and followed; biopsy of biopsy is controversial, more common in Europe
- Chest x-ray or better chest CT
- Abdomen-pelvis CT scan with and without contrast (if creatinine normal)
- PET scan not usually indicated; may have a role in the postchemotherapy setting

**DIAGNOSTIC TESTS & INTERPRETATION**

**ALERT**
- Identify symptoms of metastatic disease.

**DIAGNOSTIC TESTS & INTERPRETATION**

**ALERT**
- Markers must be drawn prior to orchiectomy.

**IMAGING**
- Ultrasonography is critical in assessing for intratesticular masses; typically hypoechoic
- Microcalcification in calcified masses should be documented and followed; biopsy of biopsy is controversial, more common in Europe
- Chest x-ray or better chest CT
- Abdomen-pelvis CT scan with and without contrast (if creatinine normal)
- PET scan not usually indicated; may have a role in the postchemotherapy setting
Ongoing Care

PROGNOSIS
- Excellent with low stage & complete resection
- 95-100% cure rate in adults
- 100% cure rate in children
- Rare to poor if metastatic/complex resection
- 86-9% 2-yr survival for retroperitoneal disease only
- 40-7% 2-yr survival for retroperitoneal + multiple sites

COMPILATIONS
- Infertility
- Precocious puberty
- Post-RPLND loss of erection (infertility)
- Chemotherapy toxicity
  - Platinum: Renal
  - Bleomycin: Pulmonary toxicity and fibrosis (watch for ARDS)
  - Etoposide: Myelosuppression

FOLLOW-UP
Patient Monitoring
- Surveillance is not good option in primary teratoma because of occult GC elements in retroperitoneum
- If markers elevated, look for occult nonteratoma elements or, rarely, GI elements within teratoma.
- NCCN guidelines for teratoma after RPLND
  - Year 1–2
    - Check β-hCG (but may recur after complete resection or recur in different loci)
    - CT abdomen/pelvis baseline and q3mo
  - Year 3–4
    - β-hCG + markers q3–6mo
    - CT abdominal/pelvis q6mo
    - CT brain q4–12mo

Patient Resources
- Testicular Cancer Awareness Foundation. www.testicularcancerawarenessfoundation.org
- Teratoma Support Foundation. www.Teratoma.weakly.com

Additional Reading

See Also (Topic, Algorithm, Media)
- Growing Teratoma Syndrome
- International Germ Cell Cancer Collaborative Group (IGCCCG)
- Reference Tables: TNM: Testis Cancer
- Tests Cancer, Pediatric, General Considerations
- Tests Cancer, Seminoma
- Tests Cancer, Nonseminomatous Germ Cell Tumors, General
- Tests, Teratoma, Mature and Immature Images
- Tests, Tumor and Mass, Pediatric, General Considerations

Codes
ICD9
- 196.9 Malignant neoplasm of other and unspecified testis
- 222.0 Bening neoplasm of testis
- 752.51 Undescended testis

ICD10
- C62.20 Benign neoplasm of unspecified testis
- D29.20 Benign neoplasm of unspecified testis
- Q36.9 Undescended testicle, unspecified

Clinical/Surgical Pearls
- Teratomas are resistant to chemotherapy and radiotherapy.
- Metastatic embryonal germ cell tumor may mature into teratoma in adult males. Therefore, mature teratomas in adults should be treated aggressively.
- Infertility and mature teratomas in children are benign.
- Pure teratomas do not secrete AFP (but may harbor GI elements that do).
- Pure teratomas do not secrete A-HCG (but may harbor choriocarcinomatous or seminomatous elements that do).
- Prognosis RPLND has double the rate of teratomas than RPLND No stage I tumors.
PATHOPHYSIOLOGY

- Isochromosome 12p amplification seen in the majority of testicular cancer.
- Prevalence and Incidence
  - Incidence rate was 5.5/100,000 men per year.
  - Mortality has dropped from 5.5% today, due to improved imaging, better tumor markers, and multidrug chemotherapy.
- 95% of testicular tumors are germ cell tumors; other types are rare (see conditional conditions).
- While benign lesions can be found in the testis (see Chapter 2), all solid lesions should be considered cancer until definitely proven otherwise.

EPIDEMIOLOGY

- Prevalence
  - Median age of diagnosis was 33 (2006–2010).
- Prevalence and Incidence
  - 5.5/100,000 men per year.
  - By race/100,000: White 6.6, black 1.4, Asian men 1.9; Hispanic men 4.7.

ASSOCIATED CONDITIONS

- In 2010, in US there were 221,020 men alive with history of testicular cancer.

RISK FACTORS (2)

- History of cryptorchidism—7–10% of cases; 4–6 times more likely to develop testicular cancer.
- Seminoma is most common tumor type.
- Orchiepexy reduces relative risk (RR) from 3 to 2 if performed prior to onset of puberty.
- Family history (affected 1st-degree relative).
- History of cryptorchidism:
  - Examine both testes.
  - Examine for gynecomastia (5% of cases).
- History of infertility:
  - Systemic symptoms: Weight loss; abdominal pain/discomfort; fevers; mastodynia or other changes in secondary sex characteristics.
  - Local symptoms: Change in testicular size or texture; testicular pain (uncommon).

DIFFERENTIAL DIAGNOSIS

- Benign lesions
  - Nongerm cell tumors (5–7%): Leydig cell tumors: 2–3% of tumors; not fixed to scrotum, and size of lesion correlates with disease bulk.
  - Invasive cancer of the testis: Malignant germ cell tumors: These are a delineation of testicular masses only. For a complete listing of intracapsular and testicular masses see Section I “Scrotum and Testicle Mass”.
- Nonspecific marker for GCT
  - Elevated in 40–60% with testis cancer; 100% of testis cancer.
  - Half-life: 1 day.
  - Half-life: 24–36 hr.
  - Half-life: 24–36 hr.
- Elevated in 40–60% with testis cancer; 100% of testis cancer.
  - Half-life: 5–7 days.
  - Produced by yolk sac tumors, embryonal cell carcinoma, and teratocarcinoma.
  - Not produced in pure seminoma or pure choriocarcinoma. If AFP elevated in case of pure seminoma, 70% will be choriocarcinoma.
  - Prognosis for pure choriocarcinoma is poor.
- Nonspecific marker for GCT
  - Elevated in 20% of low stage and 50% of high-stage GCT.
  - Half-life: 5–7 days.
  - Serum and urine estrogen may be elevated in Leydig cell tumors.

DIAGNOSIS

- HISTORY
  - Local symptoms: Change in testicular size or texture; testicular pain (uncommon).
  - Systemic symptoms:
    - Weight loss; abdominal pain/discomfort; fevers; mastodynia or other changes in secondary sex characteristics.
    - History: Cryptorchidism, infertility, orchiepexy.
- PHYSICAL EXAM
  - Check all lymph nodes, including supraclavicular lymph nodes.
  - Check all lymph nodes.
  - Check all lymph nodes.
- DIAGNOSTIC TESTS & INTERPRETATION
  - Tumor markers obtained prior to orchiectomy.
  - Lobectomy of testis—testis can be a site of sanctuary for testicular cancer. Biopsy can be utilized to confirm diagnosis in a patient with history of leukemia.
  - Treatment can be tests sparing with radiation, though contralateral testis should be treated as bilateral disease can be present.

TESTIS, TUMOR AND MASS, ADULT, GENERAL CONSIDERATIONS

Srinivas Vourganti, MD
Allan D. Sefer, MD, FACS
SURGERY/OTHER PROCEDURES

Radical orchectomy:  - Indicated in patients with stage I and II NSGCT.  - Follow-up similar to stage IIA seminomas.  - Frequency of follow-up is based on initial stage and cell type and the response to therapy.

SECOND LINE
High-dose chemotherapy with autologous bone marrow transplantation in patients with residual disease and/or recurrent disease or failure, enrollment in a clinical trial.

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Reference Tables: TNM: Tests Cancer
- Scrotum and Testicles, Mass
- Tests Cancer, Adult General Considerations
- Tests Cancer, Choriocarcinoma
- Tests Cancer, Embryonal Carcinoma
- Tests Cancer, Endodermal Sinus Tumors (Yolk Sac Tumors)
- Tests Cancer, Pediatric, General Considerations
- Tests Cancer, Seminoma
- Tests Cancer, Nonseminomatous Germ Cell Tumors, General
- Tests, Leydig Cell Tumor
- Tests, Pain (Dyschialgia)
- Tests, Sertoli Cell Tumor
- Tests, Teratoma, Mature and Immature
- Tests, Testis and Mass, Adult, General Considerations
- Images: Testis, Tumor and Mass, Pediatric, General Considerations
- Images: Testis, Tumor and Mass, Adult, General Considerations
- Images: Testis Cancer, Nonseminomatous Germ Cell Tumors, Adult
- Images: Testis Cancer, Adult General Considerations
- Images: Testis Cancer, Nonseminomatous Germ Cell Tumors, Pediatric
- Images: Testis Cancer, Testis, Tumor and Mass, Pediatric, General Considerations
- Images: Testis Cancer, Testis, Tumor and Mass, Adult, General Considerations

COMPLICATIONS
- Intensity:  - Increased risk of secondary malignancies in patients undergoing chemotherapy or radiation

FOLLOW-UP

Patient Monitoring
- In patients who undergo RPND:  - Serial monitoring with chest x-ray, physical exam, and tumor markers.  - RPND is rare, so imaging of this region is not usually needed.
- Follow-up depends upon initial stage and cell type of primary tumor and response to therapy.
- In patients who did not undergo RPND:  - Follow-up similar, serial monitoring of retroperitoneum using CT scanning.
- Frequency of follow-up is based on initial stage and cell type and the response to therapy.

Patient Resources
- American Cancer Society: http://www.cancer.org/cancer/testicularcancer/index

CLINICAL/SURGICAL PEARLS
- Increased risk of malignancy in patients with history of cryptorchidism and family history of testis cancer.
- Ultrasound should be performed to resolve any concerns of abnormal scrotal swelling.
- Initial diagnosis of radical orchectomy using an inguinal approach to avoid scrotal violation.
- All testis masses in adults should be considered malignant until proven otherwise.
RISK FACTORS

Incidence

- 0.5–2 per 100,000 children/yr
- 25–30% of pediatric tumors are malignant (2).
- Testis accounts for 2% of pediatric tumors.

The most common causes of painless scrotal swelling in a child include hernias, hydroceles, varicocele, and scrotal wall swelling.

- Tests-SPG of 15% of pediatric tumors.

Epidemiology

Prepubertal testicular tumors in children are much more often benign than the postpubertal tumors which are more often malignant.

Must differentiate a true testicular tumor or mass from paratesticular and scrotal masses.

- The most common causes of painless scrotal swelling in a child include hernias, hydroceles, varicocele, and scrotal wall swelling.
- Tests-SG of 15% of pediatric tumors.

RISK FACTORS

- Risk factors for GCTs:
  - Past personal history
  - Family history
  - Gonadal stromal tumors: 10–15% of cases (3), leukemia: <2%, cystic dysplasia: <1%

- Prevalence

GENERAL CONSIDERATIONS

- **YST (also called endodermal sinus tumor):**
  - AFP elevated in 80% of YST, and normally elevated in a neonate (physiologically).
  - AFP half-life is 5–7 days.
  - Elevated after orchectomy implies metastatic disease.
  - Yolk sac elements stain positive for AFP.
  - β-hCG produced by syncytiotrophoblast indicates a mixed GCT.

- **Gonadoblastoma:**
  - Most common tumor in disorders of sexual development; germ cell component prone to malignant degeneration.
  - Seminomas and mixed GCT rare in prepubertal children.

- **Gonadal tumors (3):**
  - Leydig cell tumor:
    - Peak age: 4–5 yr.
    - Decreased testosterone production with normal LH.
  - Differential diagnosis includes pituitary lesions, Leydig cell hyperplasia, CAH based on hormonal production.
  - Reinecke crystals classically described in adults.
  - Rare in children on histology.
  - Malignancy not reported in Leydig cell tumors in children.
  - Sertoli cell tumor:
    - Peak age: <4; most not hormonally active.
    - May serve as a sanctuary site of these tumors.
    - AFP elevated in a neonate (physiologically).
  - Granulosa cell tumor:
    - Rarely metastasizes.
    - Testes tumor of adrenogenital syndrome:
      - Benign, suppressible with glucocorticoids.
    - Gynecomastia when hormonally active.
      - Peak age: 4; most not hormonally active.
      - AFP elevated in 80% of YST, and normally elevated in a neonate (physiologically).
      - β-hCG produced by syncytiotrophoblast indicates a mixed GCT.

PHYSICAL EXAM

- Scrotal asymmetry.
- Abnormality intratesticular vs. intratesticular vs. paratesticular.
- Diffusely enlarged testicle or palpable nodularity in the testicle.
- Does not transilluminate (solid).
- Inguinal canal and cord structures are usually normal in a boy with a testicular tumor.
- Signs of precocious puberty.

DIAGNOSTIC TESTS & INTERPRETATION

- Serum markers AFP and β-hCG.
- Obtain prior to orchiectomy in all patients with a testicular mass.
- Marked AFP elevations present in neonates; may be detectable up to 8 mo of age.
- Serum testosterone, LH, and FSH levels if a gonadal mass is suspected.

Imaging

- Scrotal ultrasound (US)
  - Differentiates intratesticular vs. extratesticular.
  - Does not differentiate benign from malignant.
  - Paratesticular rhabdomyosarcoma (PT-RMS): Does not differentiate benign from malignant.
  - Hypervascular, solid extratesticular mass.
  - Often large, testicle not seen on US.
  - Metastatic disease seen as small, multiple nodules in the retroperitoneum.
  - Metastatic disease seen on US.
  - Normal in a boy with a testicular tumor.
  - Staging:
    - Stage 1: Limited to testis, markers normalize according to half-life. No radiologic evidence of metastatic disease.
    - Stage 2: Transcrotal orchectomy or tumor rupture during orchectomy, persistent elevated markers, residual disease in scrotum or disease on pathology >5 cm from testicular cord margin.
    - Stage 3: Nodes >4 cm, no visceral or distant disease.
    - Stage 4: Distant metastases.
  - Postpubertal GCTs staged and managed according to adult testicular cancer guidelines.

ASSOCIATED CONDITIONS

- Disorders of sexual development with a dysgenetic testis (e.g., DSD).
- Marked AFP elevations present in neonates; may be detectable up to 8 mo of age.
- Serum testosterone, LH, and FSH levels if a gonadal mass is suspected.

DIAGNOSTIC PROCEDURES/SURGERY

- All suspicious testicular and paratesticular lesions should be approached inguinally.
- Prepubertal patients with a primary testicular lesion and normal tumor markers may be considered for tests-sparring surgery (TSS).
- Such approaches require intraoperative assessment including immediate frozen-section analysis to ensure complete resection.
- If frozen-section reveals GCT elements or concern for incomplete resection, radical orchidectomy should be performed.
- Intraoperative US may be helpful.
- Prepubertal patients with a normal contralateral testicle should undergo radical inguinal orchidectomy.
- Paratesticular lesions consistent with malignancy should be managed with radical inguinal orchidectomy.

BASICS

- Important to distinguish prepubertal "pediatric" testes tumors from the postpubertal "adolescent" testes tumors (1).
- Prepubertal testicular tumors in children are much more often benign than the postpubertal tumors which are more often malignant.
- Must differentiate a true testicular tumor or mass from paratesticular and scrotal masses.
- The most common causes of painless scrotal swelling in a child include hernias, hydroceles, varicocele, and scrotal wall swelling.

PATHOPHYSIOLOGY

- GCTs typically develop from a precursor lesion, which, in turn, appears to develop from arrested primordial germ cells or gonocytes.
- Teratoma: Monodermal (epidermoid/cyst) or multiple histologic types present.
- Normal adult testicular neoplasm include tubular ectasia of the rete testis, inflammation, and hematoma.
- Marked AFP elevations present in newborn; may be detectable up to 8 mo of age.
- Serum testosterone, LH, and FSH levels if a gonadal mass is suspected.

TESTIS, TUMOR AND MASS, PEDIATRIC, GENERAL CONSIDERATIONS

Nicholas G. Cost, MD
Paul H. Noh, MD, FACS, FAAP
Pathologic Findings

- GCTs
  - Teratoma: Consists of elements of at least 2 of the 3 germ cell layers of endoderm, mesoderm, and ectoderm.
  - YST: Epithelial cells that form glandular and ductal structures arranged in columns, papillary projections, or solid islands within a primitive mesenchymal stroma. The cells have poorly defined cell borders and vacuolated cytoplasm with glycogen and fat.
  - Seminoma: Islands or sheets of relatively large cells with clear cytoplasm and densely staining nuclei.
  - Embryonal carcinoma: Predominantly epithelial cells arranged in glands or tubules. Cell borders indistinct, cytoplasm pale or vacuolated, and nuclei rounded with coarse chromatin.
  - Choriocarcinoma: Distinct cell types must be demonstrated to satisfy the histologic diagnosis of choriocarcinoma. Syncytiotrophoblasts and cytotrophoblasts.
  - Granulosa cell tumors: Must have 3 elements: Sertoli cells, interstitial tissue, and germ cells.

- Stromal tumors
  - Leydig cell tumors: Uniform, closely packed cells with clear cytoplasm and densely staining nuclei.
  - Sertoli cell tumors: Epithelial elements resembling Sertoli cells and varying stroma.
  - Granulosa cell tumors: Characteristic Call-Exner bodies may be identified, consisting of PAS-positive material similar to that seen in the basement membrane of the tubules.

DIFFERENTIAL DIAGNOSIS

- Painful childhood testicular masses:
  - Epidermoid and squamous cell carcinomas
  - Inguinal hernia
  - Varicocele
  - Henoch–Schönlein purpura (usually no mass)
  - Epididymitis/orchitis; bacterial, mumps

- Other causes of testicular swelling or pain and testicular tumors:
  - Rhabdomyosarcoma (RMS) (bimodal age 3–4 and adolescence)
  - Polyorchidism
  - Lipoma of the cord
  - Hernia
  - Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of cord
  - Fibrous pseudotumor of the tunica albuginea
  - Cystic dysplasia of the testis
  - Adrenal rest tumors
  - Adenomatoid tumor of testis or epididymis
  - Torsion (testicle, testicular or epididymal appendage); more common after puberty
  - Henoch–Schönlein purpura (usually no mass)
  - Epididymitis/orchitis; bacterial, mumps

- Germ cell tumors: Characteristic Call-Exner bodies may be identified, consisting of PAS-positive material similar to that seen in the basement membrane of the tubules.

- Embryonal carcinoma: Malignant epithelioid cells, interstitial tissue, and germ cells

- Choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts

- Teratoma: Contain elements of at least 2 of the 3 germ cell layers of endoderm, mesoderm, and ectoderm.

- Embryonal carcinoma: Malignant epithelioid cells, interstitial tissue, and germ cells

- Choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts

- Teratoma: Contain elements of at least 2 of the 3 germ cell layers of endoderm, mesoderm, and ectoderm.

TREATMENT

GENERAL MEASURES

- N/A

PROGNOSIS

- N/A

ONGOING CARE

- N/A

REFERENCES


ADDITIONAL READING

N/A

See Also (Topic, Algorithm, Media)

- Pathologic Tumors
- Reference Tables: ICD-10, ICD-9

CODES

- N/A

CLINICAL/SURGICAL PEARLS

- N/A

OTHER SPECIFIED DISORDERS OF MALE GENITAL ORGANS

- N/A


- Henoch–Schönlein purpura (usually no mass)

- Epididymitis/orchitis; bacterial, mumps

- Embryonal carcinoma: Malignant epithelioid cells, interstitial tissue, and germ cells

- Choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts

- Teratoma: Contain elements of at least 2 of the 3 germ cell layers of endoderm, mesoderm, and ectoderm.

- Embryonal carcinoma: Malignant epithelioid cells, interstitial tissue, and germ cells

- Choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts

- Teratoma: Contain elements of at least 2 of the 3 germ cell layers of endoderm, mesoderm, and ectoderm.
TESTOSTERONE REPLACEMENT THERAPY, GENERAL PRINCIPLES

Robert L. Segal, MD, FRCS(C)
Arthur L. Burnett, II, MD, MBA, FACS

Basics

Description
Hypogonadism is the clinical syndrome associated with low serum testosterone (T).

- Can occur in early life (eunuchoid), although most commonly seen in aging males.
- Late-onset male hypogonadism may also be referred to as andropause.
- Androgen deficiency in the aging male (andropause) or androgen deficiency syndrome.

Epidemiology
Incidence
- Prevalence: 2–4 million men in U.S.

- Age-related decline (“andropause”)
- Increased serum sex hormone binding globulin
- Dampening in the amplitude of circadian release of T
- Decreased testicular responsiveness to LH
- Overall 5.6–38.7% men are affected, depending on study.

Risk Factors
- Medical conditions (chronic lung disease, chronic renal failure, anorexia nervosa, depression, HIV
- Hypothyroidism (which suppresses the pituitary, testes, adrenal, prostate)
- Increased body fat (visceral obesity)
- Medications (GnRH agonists/antagonists, androgen antagonists, estrogen, opiates, lithium, steroids, amiodarone, thiazide diuretics, omeprazole)
- Low protein diet

Genetics
- Pathologic Findings

Pathophysiology
- At age increases, there is:
  - Decreased number of Leydig cells within the testicle (site of T production)
  - Decreased testicular responsiveness to LH
  - Diminution in the amplitude of circadian release of T
- Increased serum sex hormone binding globulin (SHBG): Concentration of T is therefore less bioavailable (functionally active) T

Associated Conditions
- Metabolic syndrome (obesity, hypertension, diabetes)
- Impaired fasting glucose/insulin resistance/diabetes mellitus type II (OSSA)
- Asthma/chronic obstructive pulmonary disease/obstructive sleep apnea (OSA)
- Disossemiosis

General Prevention
No

History
- Low energy level/daytime sleepiness (2)[B]
- Decreased sexual interest/erectile dysfunction (2)[A]
- Frequent dyshydra (ED)/voidance of spontaneous erections/erectile dysfunction (2)[A]
- Decreased motivation/creativity
- Hot flushes/sweats
- Loss of muscle/massive obesity
- Visual field defects

- Several validated questionnaires to screen for T deficiency have been developed, but are unreliable with low specificity (1)[C]

Physical Exam
- May not be contributory (2)[B]
- Small testicular size/soft consistency (2)[B]
- Hair distribution and pattern (2)[B]
- Gynecomastia (2)[B]
- Digital exam (2)[B] to rule out palpable prostate abnormality

Diagnostic Tests & Interpretation

Lab
- Total serum T (best before 11:00 am) (1)[A]
- Free T
- Bioavailable T
- No universally accepted lower limit of normal serum T
- It is generally agreed that serum T > 12 nmol/L (350 ng/dL) does not usually need replacement (2)[A]
- If T < 8 nmol/L (230 ng/dL), replacement is typically beneficial (2)[B]

- FDA research trial definition: Hypogonadism is total serum T levels of < 300 ng/dL.
- Serum albumin
- SHBG
- If secondary hypogonadism is suspected:
  - Serum prolactin, Serum gonadotropines (LH; FSH)

Imaging
- Imaging (MRI, CT) if prostatomegaly suspected
- Dose scan for the assessment of bone mineral density (note the risk for osteoporosis/osteopenia (1)[B]

Diagnostic Procedures/Surgery
- No

Pathologic Findings
- No

Differential Diagnosis
- Acute critical illness (surgery, head trauma)
- Age-related decline (“andropause”)

- Alcoholism
- Chronic; illness/failures; chronic renal failure; hypertension; hyperlipidemia; diabetes; sleep apnea; obesity, anorexia nervosa, depression, HIV
- Hematologic (sickle cell disease, thalassemia)
- Hemochromatosis of the pituitary, Leydig cells
- Hypothyroidism (hypothyroidism, hypopituitarism
- Kallmann, Klinefelter, or Nelson syndrome
- Medications: GnRH analogues/castration, glucocorticoids, androgens, estrogens, progestins (eg, megestrol), chronic opioids, marijuana (controversial)

- Pituitary infusions, infarction, trauma, radiation (aberrant TRH production)
- Pituitary tumors, macroadenomas, hyperprolactinema

- Syndrome: Prader–Willi and Sertoli only

- Testicular failure (primary): Congenital or acquired anemia, hypothyroidism, mumps orchitis, radiation therapy, chemotherapy
- Testicular tumors

Treatment

General Measures
- Treatment is warranted for men with clinical symptoms associated with objective biochemical findings of low T (2)[C]
- In the context of significant symptoms and normal or borderline T levels, a trial of TRT is acceptable with appropriate follow-up to ensure improvement in symptoms (2)[C]. If no improvement is noted, further workup to delineate cause is warranted

- In the presence of visceral obesity, weight loss through regular exercise and low-calorie intake is recommended (2)[A]
- Appropriate glycemic, blood pressure, and lipid management is recommended
- TRT contraindications include:
  - Known prostate cancer (absolute)
  - Known breast cancer (absolute)
  - Unexplained prostate-specific antigen (PSA) elevation/suspicious DRE finding (absolute)
  - Severe lower urinary tract symptoms (LUTS) associated with BPH
  - Enlarged prostate (50 or greater) (2)[B]
  - Uncontrolled/poorly controlled heart failure
  - Unintended OSA, although no scientific evidence exists demonstrating a direct causal relationship between T and OSA
  - Men seeking fertility

- Improvement is expected in:
  - Reduction of body fat/massive obesity (2)[A]
  - Increase in fat-free mass/muscule strength (1)[A]
  - Insulin resistance/diabetes control in men with DM II (2)[A]
  - Bone mineral density at lumbar spine (1)[A]
  - Hypogonadism with sexual desire/ED/delayed ejaculation (2)[B]

- Considerations in the elderly male: The American Geriatrics Society (AGS) lists T as a medication to generally avoid in older adults because of potential for cardiac problems and men with personal history of prostate cancer.

- TRT agents/options outlined below

- Testicular tumors, macroadenomas, hyperprolactinema

- Syndrome: Prader–Willi and Sertoli only

- Testicular failure (primary): Congenital or acquired anemia, hypothyroidism, mumps orchitis, radiation therapy, chemotherapy
- Testicular tumors

First Line
- Buccal (strimore) 30 mg Tbl 3 times/day
- Dose: 30 mg BD
- Avoids 1st pass effect of hepatic metabolism
- Apply to gum over incisor; do not chew/swallow

- Transdermal (Androgel): Apply to nonshaved skin
- Dose: 5–10 mg/g twice/day, 3 times/day
- Avoid: Brewery, alcohol, hot showers, hot tubs

- Topical agents: Interpersonal transfer possible and should be avoided, especially for women and children

- Gels should be dry before putting on clothes over application site; delay washing

- Brand names provided to avoid patient confusion; see FDA label for details

Medication
**TESTOSTERONE REPLACEMENT THERAPY, GENERAL PRINCIPLES**

- Transdermal gels; product-specific dosing; apply clean dry; Shouder, upper arm, abdomen
- (AndroGel 1%)
- Dosage: Topical daily 5–10 g (max)
- (AndroGel 1.62%)
  - Dosage: Topical 2 pump activations or 40–50 mg patch, adjust from 1 activation 20–25 mg or single 20.25 mg patch, 81 mg (max)
  - Intranasal 10 mg/15 mg per application; apply to inner nasal area only
- Dosage: Scott 4 pump activations (30 mg) QAM; adjust 1–7 pump activations (10 mg–70 mg daily), 70 mg max
- (Testim 1%) 50 mg/1.5 g gel; 50 mg repeat dose taken; apply shoulder or upper arm
- Dosage: Scott 5–10 g patches MAX
  - Transdermal solution
    - (Oseso 1%) 30 mg/5.5 mL of solution
    - Dosage 60 mg T CI pump = 30 mL of T solution to each arm daily; adjust based on levels
  - IM short-acting formulations may be associated with fluctuations in serum T (subcutaneously 2–6 d after injection, subdermal 10–14 d after injection) which may be associated with symptom fluctuation
  - T cypionate (Depo-Testosterone) 200–400 mg IM every 3–4 wk or 100–150 mg every 2 wk preferred
  - T enanthate (Biolostat) 100–400 mg IM every 4 wk or 100–150 mg every 2 wk preferred
  - Nandrolone decanoate: 100–300 mg IM monthly until puberty development occurs
- T implant
  - Pellets (Testopel) (735 mg) 150–450 mg SC implant every 3–4 wk or 2 pellets for each 25 mg T required weekly; in upper buttock with local anesthetic
  - Local symptoms such as pain, bleeding
  - Pellet infection and extrusion (up to 10%)
  - Parenteral T undecanoate (Avodox): 750 mg IM (3 mL) Initially, at 4 wk, then 750 mg every 10 wk
  - T gel (Testim) 2 pump activations or 11 (T10 testosterone) one in each nostril 7D (total 33 mg/day)
- 1 formulations outside the US:
  - Oral T undecanoate: 40–80 mg PO with meals BID to TID
  - T–in–adhesive matrix patch: 2 patches (4.8 mg Tiday) applied every 2 days
  - T gel 2% 3–4 g (60–80 mg) T applied to abdomen or both thighs daily

**SECOND LINE**

- Any agent from the first line medication can be used as second line if the product is ineffective or there are practical use issues with an individual patient

**SURGERY/OTHER PROCEDURES**

- Insertion of subdermal T pellets (see above MEDICATION First line)

**ADDITIONAL TREATMENT**

- **Radiation Therapy**

**ADDITIONAL THERAPIES**

- There may be therapeutic synergism with combined TRT and phosphodiesterase-5 inhibitors in men with low T and ED (2E)
- Other forms of androgen therapy include the usage of dehydroepiandrosterone (DHEA), dihydrotestosterone (DHT), although their use has not been proven effective (2E)
- **Human chorionic gonadotropin (hCG)** may preserve spermatogenesis in young men with hypogonadism (1B) (See Section “Testosterone, Decreased Hypogonadism”)
- Antiandrogens and aromatase inhibitors may raise endogenous T in secondary hypogonadism if the hypothalamic–pituitary–testicular axis is intact
- Selective androgen receptor modulators (SRMs) may have a role in hypogonadism

**COMPLEMENTARY & ALTERNATIVE THERAPIES**

- There are no alternative therapies that will cure low T. Some stress management techniques can relieve the stress and anxiety associated with hypogonadism: yoga, meditation techniques, emotional support/counseling, healthy lifestyle (nutritious diet, active exercise, adequate rest)

**ONGOING CARE**

**PROGNOSIS**

- Goal is for the restoration of serum T within normal lab limits; supraphysiologic levels should be avoided (2E)
- Target serum T should be 40–70% of upper limit of normal serum T (2E)
- There is no evidence of benefit for maintaining a diurnal rhythm of serum T (2E)

**COMPLICATIONS**

- Enlarged prostatic hyperplasia
- Erythrocytosis; gynecomastia; fluid retention
- Other than prostate cancer, no other malignancies have been reported

**FOLLOW-UP**

- Patient Monitoring
  - Clinical and biochemical verification of treatment effect should occur 1–6 mo after initiating TRT (depending on TRT modality) (1C)
  - Repeat assessment of serum T parameters
  - Dosing may be adjusted if TRT suboptimally effective
- Monitor hematocrit 3, 6, and 12 mo after initiating TRT, then annually (1A)
- Monitor prostate health (DRE/PSA) 3, 6, and 12 mo after initiating TRT, then annually (1A)
- In men with known unresponsive or metastatic prostate cancer, bone mineral density should be verified after 6, 12, or 24 mo of TRT (1C)
- Monitoring lipid and glomseria is not routinely required for safety but should be done as part of general health maintenance

**PATIENT RESOURCES**

- Urology Care Foundation AUA, www.urologyhealth.org/urology/index.cfm?article=See Also (Topic, Algorithm, Media)

- **Andropause (Late-Onset Male Hypogonadism)**
  - Erectile Dysfunction/Impotence, General Considerations
  - Peyronie’s disease
  - Hypogonadism, Society Definitions
  - Infertility
  - See Specific Syndromes: Kallmann, Klinefelter, Laurence–Moon–Prader–Willi, Sertoli–only
  - Testosterone (Free and Total) Lab Testing
  - Testosterone Replacement Following Localized Prostate Cancer Therapy
  - Testosterone Replacement Therapy, Prostate Cancer Risk
  - Testosterone, decreased (hypogonadism)
  - Testosterone, decreased (hypogonadism) Algorithm 1

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)

- Andropause (Late-Onset Male Hypogonadism)
  - Erectile Dysfunction/Impotence, General Considerations
  - Peyronie’s disease
  - Hypogonadism, Society Definitions
  - Infertility
  - See Specific Syndromes: Kallmann, Klinefelter, Laurence–Moon–Prader–Willi, Sertoli–only
  - Testosterone (Free and Total) Lab Testing
  - Testosterone Replacement Following Localized Prostate Cancer Therapy
  - Testosterone Replacement Therapy, Prostate Cancer Risk
  - Testosterone, decreased (hypogonadism)
  - Testosterone, decreased (hypogonadism) Algorithm 1

**CODES**

- 107.9 Other subclinical hypogonadism
- 107.8 Androgen deficiency in male hypogonadism

**CLINICAL/SURGICAL PEARLS**

- Treatment is usually indicated for men with both symptoms and lab evidence of low serum T.
- The risks and benefits of each TRT modality should be thoroughly discussed.
- Post TRT initiation, patient monitoring for treatment effect, biochemical resolution, and development of adverse effects is critical.
- Patients who have completed prostate cancer treatment for localized disease cancer treatment may cautiously be initiated on TRT in certain circumstances.
TESTOSTERONE, DECREASED (HYPOGONADISM)
Philip T. Zhao, MD
Allen D. Seftel, MD

BASICS
DESCRIPTION
Hypogonadism is the clinical syndrome associated with low serum testosterone (T).

- Can occur in early age (early onset), although most commonly seen in aging males.
- Late-onset male hypogonadism may also be referred to as andropause, androgen deficiency in the aging male, or androgen deficiency syndrome.
- Usually associated with impaired sperm production, or with an isolated impairment of sperm production or function with normal T production.

- T is essential for:
  - Normal sexual function, growth and development of male sexual organs, and maintenance of male secondary sexual characteristics.
  - Normal levels and function result in:
    - Enhanced libido, increased energy, and production of RBCs; osteoporosis protection.

In utero hypogonadism:
- Ambiguous genitalia, normal female genitalia, microphallus, pseudovaginal perineoscrotal hypospadias, bifid scrotum, cryptorchidism.

Prepubertal hypogonadism:
- Delayed puberty, microphallus, small testes, no male hair pattern, disproportionately long arms/legs, high-pitched voice, poor muscle mass.

Postpubertal/adult hypogonadism:
- Lack of libido, erectile dysfunction (ED), hot flashes/sweats, gynecomastia, spermarche, infertility (azoospermia), increased body fat/BMI, osteopenia/osteoporosis, hypercholesterolemia.

EPIDEMIOLOGY
Incidence
- N/A

Prevalence (1)
- 2–4 million men in US; Hypogonadism increases with age.
  - Overall 5.6–38.7% men are affected, depending on study.
  - 6th decade: 12%; 7th: 19%; 8th: 29%; 9th: 49%.

RISK FACTORS
- Testicular trauma/orchiectomy.
- Medications
  - Decreased T production: Dopamine antagonists, corticosteroids, ethanol, ketoconazole, GnRH analogues/antagonists.
  - Decreased conversion of T to dihydrotestosterone (DHT), see Reductase inhibitors.
  - Androgen receptor blockade: Flutamide, spironolactone, cyproterone, finasteride.
  - Infections (mumps orchitis, HIV).
  - Medical conditions:
    - Iron toxicity to pituitary gonadotrophs, autoimmune diseases, etiologic renal disease (ESRD), uremia, histiocytosis X, pituitary apoplexy.
    - Myotonic dystrophy.

Genetics
- Klinefelter syndrome.
- Kallmann syndrome; mutation in Dax-1.
- Laurence–Moon–Bardet–Biedl syndrome.
- Prader–Willi syndrome.
- Y chromosome microdeletion.
- Congenital androgen resistance/insensitivity.
- Alstrom, Rud, Bloom syndromes; mutations in leptin.

PATHOPHYSIOLOGY
- T is regulated by the hypothalamic–pituitary-testicular axis.
- Gonadotropin-releasing hormone (GnRH) neurons originate in the olfactory placode and migrate through the cribriform plate of the ethmoid to localize in the hypothalamus.
- GnRH pulse amplitude and frequency activate intracellular signalling mechanisms, which results in differential gene expression of the 2 subunits forming LH and FSH.
- LH stimulates Leydig cells to produce T.
- Feedback inhibition by T on the hypothalamus and pituitary maintains hormonal balance.
- FSH stimulates Sertoli cells to support spermatogenesis and sperm inhibition, which provides feedback on the pituitary.
- Week-long night/day shift work does not seem to change T levels.
- T levels decrease 0.8–1.6% per year in men aged 40–70.

ASSOCIATED CONDITIONS
- Increased risk for developing type 2 diabetes mellitus, metabolic syndrome, cardiac events, and a general reduction in survival.
- Impact on cardiac events is controversial with most publications supporting a protective effect of “normal” T levels.

GENERAL PREVENTION
- Screening: The Endocrine Society in US recommends against screening for androgen deficiency in the general population.

DIAGNOSIS
HISTORY
- Development:
  - General abnormalities (eg, hypospadias, microphallus, cryptorchidism), delayed sexual development/growth, need for hormone therapy, family history of delayed puberty or reproductive disorders; psychological impact of delayed puberty or growth, difficulty in school or learning disability, inability or reduced ability to smell.

- Sexual function:
  - Poor erections; reduced spontaneous, nighttime, morning erections; inability to perform sexually; decreased sexual activity; inability to father children despite uncorrected sexual relations (> 1 yr); small or shrinking testes.
Definitions of T levels and hypogonadism are the Food and Drug Administration (FDA) uses a cutoff value of 300 ng/dL to define hypogonadism. There is no consensus among specialists (endocrinologists, urologists, pathologists) as to what lab values define a “low” T level. Society definitions of T levels and hypogonadism are summarized in Section II: “Hypogonadism, Society Definitions”.

**Lab**

- Testicular size: palpation
- Testosterone: serum
- Testosterone precursors: DHEA-S
- Testosterone metabolites: estradiol

**EXTERNAL GENITALIA**: Testes and phallus

- Small, firm suggests Klinefelter syndrome
- Soft and atrophic but normal sized suggestive of hypogonadism

**BRAIN FUNCTION**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**BONE FUNCTION**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Gastrointestinal functions**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Cardiovascular function**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Respiratory function**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Integumentary system**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Musculoskeletal system**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Hypothalamic-pituitary-gonadal (HPG) axis**

- Decreased muscle bulk/strength; reduced physical activity or performance; broad or elongated gait; poor coordination and memory

**Differential diagnosis**

- Hypogonadotropic hypogonadism (primary): Inadequate stimulation of gonadotropin release by the hypothalamus
- Hypergonadotropic hypogonadism (primary): Gonadal failure (chemotherapy or radiotherapy)
- Hypogonadotropic hypogonadism (secondary): Inadequate stimulation of gonadotropin release by the hypothalamus

**Pathological findings**

- Testicular biopsy: Klinefelter syndrome
- FSH and LH: Kallmann syndrome
- Androgen receptor assay (genetic testing):
  - Small testes: Klinefelter syndrome
  - Large testes: Pretibial myxedema, pseudohyppoparathyroidism

**Diagnostic procedures/surgery**

- MRI: Testicular tumor
- Biopsy: Testicular mass
- Ultrasound: Testicular mass

**Treatment**

- Avoid T replacement in a man with infertility seeking to regain fertility.

**General measures**

- General well-being; reduced sexual desire, interest, and motivation (fatigue); poor energy/vitality; excessive fatigue; poor motivation and initiative, passivity, low self-confidence/self-esteem; depressed mood; irritability; difficulty sleeping; hot flashes/sweats, poor concentration and memory

**Physical examination**

- External genitalia: Testis and phallus
- Testes volume
- Measure with a Prader orchidometer (normal adult 15–25 mL)
- ≤ 6 mL: characteristic of prepubertal hypogonadism
- Soft and atrophic but normal sized suggestive of prepubertal hypogonadism
- Small, firm suggests Klinefelter syndrome
- Genital ambiguity, hypoplastic/absent penis

**Diagnostic tests & interpretation**

- There is no consensus among specialists (endocrinologists, urologists, pathologists) as to what lab values define a “low” T level.
- The Food and Drug Administration (FDA) uses a cutoff value of 300 ng/dL to define hypogonadism for clinical trial development and enrollment.
- Society definitions of T levels and hypogonadism are summarized in Section II: “Hypogonadism, Society Definitions”.
- Total T concentrations are affected by alterations in sex hormone binding globulin (SHBG), and T levels may be suppressed sufficiently with illness, certain medications, and some nutritional deficiencies.
**MEDICATION**

## First Line
- **Buccal** (Sialol) 30 mg Titrat-system
  - Dose: 30 mg BID
  - Avoid 1st pass effect of hepatic inactivation
- **Transdermal** (Androderm). Apply to non-scrotal skin (back, abdomen, upper arms, thighs); avoid bony prominence; delivers 2-4 mg/patch
  - Dose: Based on patch; start one 4 mg/patch/24 h; adjust to 1 or more patch combinations for desired effect
- Skin irritation may be noted; remove for MRI
- **Transdermal** pain; product-specific dosing; apply deep dry: Shoulder, upper arm, or abdomen
  - (AndroGel 1%)—Doses: Topical daily 5-10 g (24 h)
  - (AndroGel 1.62%)—Doses: Topical 2 pump activations or 40-55 mg pack; adjust from 1 activation 25-25 mg or single 25-25 mg packs; 81 mg (24 h)
  - (Fortesta) 10 mg 10.5 mg/g per patch; apply to inner thigh area only
  - Dose: Start 4 pump activations (80 mg QAM); adjust 1-2 pump activations (50-70 mg daily; 70 mg max)
- (Dector) 10 g 50 g 1-5 g gels: 50 mg/g dose tube; apply shoulder or upper arm
  - Dose: Topical 5-10 g/2 tubes MAX
- **Transdermal solution**
  - (Aventen) 30 mg/1.5 mL solution
  - Dose 60 mg T (1 pump) = 30 mg of T solution to each area daily; adjust based on levels
- RA short-acting formulations, may be associated with fluctuations in serum T (endocrinologic fluctuations)
  - (Gelone; Testosterone) 200-400 mg IM every 3-4 wk or 100-150 mg every 2 wk preferred
  - 1 anectrate (Deltrostib) 100-400 mg IM every 4 wk or 100-150 mg every 2 wk preferred
  - Pentaject: 50-100 mg IM agent monthly, or 25-50 mg every 2 wk, increase to 50-100 mg every 4 wk and then adult dose over 2-4 yr or until pubertal development occurs

## Second Line
- **T implant**
  - (Omipact) 2 pellets (15 mg/packet) 150-450 mg SC implant every 3-6 mo
  - 2 pellets for each 25-25 mg required weekly, in upper buttock with local anesthesia
  - Local symptoms such as pain, bleeding
  - Pelvic infection and erosion (up to 10%)
  - T nasal gel (Nasltest 2 pumps each nostril; 111 mg testosterone) once in each nostril 110 mg total (113 mg/day)
  - T formulations outside US:
    - Oral T undecanoate: 40-80 mg PO with meals IND to TID
    - Parenteral T undecanoate: 1,000 mg IM initially, at 6 wk, then 1,000 mg every 10-14 wk; long lasting
    - T in-adhesive matrix patch: 2 patches (4.8 mg T) applied every 2 days
    - T gel 2%; 3.4-4.60-80 mg of T) applied to abdomen or both inner thighs daily

### Second Line
- Any of the agents noted as first line can be potentially used a second line alternative agents

## SURGERY/OTHER PROCEDURES
### Pituitary adenoma; Transsphenoidal resection
- **ADDITIONAL TREATMENT**
- **Radiation Therapy**
  - GnRH: 5-25 ng/kg SQ every 2 hr by programmable infusion pump for 6-12 mo or longer
  - FSH/human menopausal gonadotropin (hMG), LHRH agonists, recombinant human FSH (rhFSH): After 6-12 mo of hCG treatment alone
  - Human chorionic gonadotropin (hCG): 500-2,000 IU given SQ 2-3x weekly to maintain serum T levels within the normal range for 6-12 mo
  - Addition to KCS to stimulate sperm production: human chorionic gonadotrophin (hCG): 500-2,000 IU given SQ 2-3x weekly to maintain serum T levels within the normal range for 6-12 mo
  - Added to KCS to stimulate sperm production: FSH/human menopausal gonadotropin (hMG), human FSH (FSH), recombinant human FSH (rHMG)

### Additional Therapies
- **if Hypogonadotropic**: May provide
  - supplemental hormone replacement therapy to stimulate testicular production of androgens
  - Initially stimulate T and sperm production:
    - Human chorionic gonadotrophin (hCG): 500-2,000 IU given SQ 2-3x weekly to maintain serum T levels within the normal range for 6-12 mo
  - Addition to KCS to stimulate sperm production
    - FSH/human menopausal gonadotropin (hMG), human FSH (FSH), recombinant human FSH (rHMG)

### Additional Therapies
- **If Hypogonadotropic**: May provide
  - supplemental hormone replacement therapy to stimulate testicular production of androgens
  - Initially stimulate T and sperm production:
    - Human chorionic gonadotrophin (hCG): 500-2,000 IU given SQ 2-3x weekly to maintain serum T levels within the normal range for 6-12 mo
  - Addition to KCS to stimulate sperm production
    - FSH/human menopausal gonadotropin (hMG), human FSH (FSH), recombinant human FSH (rHMG)

### Ongoing Care
- Radiation therapy to restore T levels to the normal range by adjusting dosage of medication and improve symptoms of hypogonadism (4)
- **COMPLICATIONS**
  - **Hypogonadism**: (5)
  - Metabolic syndrome: Anemia, increased fasting blood sugar, increased triglycerides, increased cholesterol, increased body fat
  - Appetite changes (increased or decreased)
  - Balance problems
  - Body hair loss
  - Dry eyes
  - Edema or leg pain
  - Fatigue
  - GI and/or respiratory disturbances
  - Dry mouth
  - Hot flashes/flashes/sweats
  - Loss of libido/impotence
  - Muscle weakness/wasting
  - Osteoporosis
  - Psychologic: Depression, memory difficulties, emotional lability
  - Testicular atrophy
  - Weight gain/increased body fat
  - There are no alternative therapies that will cure hypogonadism
  - No data to support the use of over the counter or direct to consumer “natural” T supplements.

### Ongoing Care
- Radiation therapy to restore T levels to the normal range by adjusting dosage of medication and improve symptoms of hypogonadism (4)

### Complications
- **Hypogonadism**: (5)
  - Metabolic syndrome: Anemia, increased fasting blood sugar, increased triglycerides, increased cholesterol, increased body fat
  - Appetite changes (increased or decreased)
  - Balance problems
  - Body hair loss
  - Dry eyes
  - Edema or leg pain
  - Fatigue
  - GI and/or respiratory disturbances
  - Dry mouth
  - Hot flashes/flashes/sweats
  - Loss of libido/impotence
  - Muscle weakness/wasting
  - Osteoporosis
  - Psychologic: Depression, memory difficulties, emotional lability
  - Testicular atrophy
  - Weight gain/increased body fat

### Prognosis
- Excise ability to restore T levels to the normal range by adjusting dosage of medication and improve symptoms of hypogonadism (4)

### Prognosis
- Excise ability to restore T levels to the normal range by adjusting dosage of medication and improve symptoms of hypogonadism (4)
TESTOSTERONE, DECREASED (HYPOGONADISM)

- T replacement:
  - Fluid retention
  - Gynecomastia
  - Hepatotoxicity
  - Sleep apnea
  - Theoretical risk of progression of prostate cancer: Unsubstantiated in recent studies

FOLLOW-UP

Patient Monitoring
- Every 3 mo (CBC, PSA, DRE) after starting treatment annually for response and adverse effects
- In men with known osteopenia or osteoporosis, bone mineral density should be verified after 6, 12, or 24 mo of TRT
- Monitoring lipid and glycemia is not routinely required for safety but should be done as part of general health maintenance

Patient Resources
- Urology Care Foundation AUA. www.urologyhealth.org/urology/index.cfm?article=132

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Hyperprolactinemia
- Hypogonadism, Society Definitions
- Infertility
- Kallmann Syndrome
- Klinefelter Syndrome
- Laurence–Moon–Bardet–Biedl Syndrome
- Prader–Willi Syndrome
- Testosterone (Free and Total) Lab Testing
- Testosterone Replacement Therapy, General Principles
- Testosterone, Decreased (Hypogonadism) Algorithm

CODES
- ICD9 257.2 Other testicular hypofunction
- 792.2 Nonspecific abnormal findings in semen
- 799.81 Decreased libido

ICD10
- E29.1 Testicular hypofunction
- R68.82 Decreased libido
- R86.9 Unsp abnormal finding in specimens from male genital organs

CLINICAL/SURGICAL PEARLS
- Early morning serum total T below 300 ng/dL on at least 2 occasions in a symptomatic man usually confirms hypogonadism.
- Gonadotropins (LH and FSH) distinguish between a primary and a secondary cause.
- When caused by pituitary adenoma, patients can have additional symptoms due to mass effects, such as headaches or peripheral visual disturbance. There may also be signs and symptoms of other pituitary hormone deficiencies.
- Low T might be transient suppression (critical, acute/subacute illness, short-term use of certain medications; transient malnutrition; or excessive and chronic strenuous endurance exercise).
TORSION, TESTIS OR TESTICULAR/EPIDIDYMAL APPENDAGES
Julia S. Barthold, MD, FACS

BASICS

DESCRIPTION
- Torsion of the testicle or testicular appendages results in vascular compromise to the testicle or 1 of the appendages.
- Impaired perfusion of the testis, appendix testis, or appendix epididymis is caused by spermatic cord (intravaginal) torsion or appendix torsion.
- Presents as acute scrotal and/or inguinal pain with or without scrotal erythema and swelling.
- Occurs primarily in children.

EPIDEMIOLOGY
Incidence
- Most scrotal pain occurs at age 12–18
- Bimodal age distribution
- Puberty: Peak incidence of intravaginal testicular torsion, but can occur at any age

Prevalence
14,000 males <25 yo

RISK FACTORS
- Usually none
- Cryptorchidism
- History of contralateral torsion

GENETICS
- Rectal torsion reported in 10% of family members, may be autosomal or X-linked recessive
- No specific genetic defects identified

PATHOPHYSIOLOGY
- Testicular torsion can be either intravaginal or extravaginal
- Intravaginal testicular torsion
- Twisting of the spermatic cord within the tunica vaginalis
- Due to congenital incomplete fixation of testis within the tunica vaginalis (bell-clapper deformity, see images)
- Intermittent or sustained
- Impaired venous outflow, impaired arterial inflow, ischemia, potential testicular necrosis
- May progress to compartment syndrome
- Torsion: Usually painless and asymptomatic
- Appendiceal torsion
- Usually more gradual but may be acute
- Pain may be mild or severe
- Nausea/vomiting uncommon
- No prior episodes
- Impaired or abdominal pain may be associated or may be only site of pain in younger boys
- Inflamed epididymis reported as “epididymitis”

HISTORY
- Intravaginal testicular torsion
- Usually severe pain, sudden onset
- Nausea/vomiting more common
- May be recurrent usually same side
- Extravaginal testicular torsion
- Usually painless and asymptomatic
- Appendiceal torsion
- Usually more gradual but may be acute
- Pain may be mild or severe
- Nausea/vomiting uncommon
- No prior episodes
- Impaired or abdominal pain may be associated or may be only site of pain in younger boys
- Inflamed epididymis reported as “epididymitis”

PHYSICAL EXAM
- Note: Phren sign (elevation of scrotum relieves pain in epididymitis but in torsion it is no longer considered reliable)
- Intravaginal testicular torsion
- These are possible findings but these may be highly variable
- Early
  - Generalized testicular tenderness
  - Loss of spermatic cord Doppler
  - Elevated gonadotropin levels (see the appendix for this in intermittent testicular torsion cases)
- Appendiceal torsion
  - Late
  - Any of the above, increasing scrotal swelling and erythema
  - Loss of scrotal rugation ± hydrocele
  - Inability to distinguish epididymal landmarks
- Extravaginal testicular torsion
  - Firm to hard nontender testes
  - Scrotal discoloration
- Appendix torsion
  - Localized tenderness superior to testis
  - Supernumerary appendix
  - Preserved spermatic cord Doppler
  - Normal testicular position and orientation
- Blue dot sign: Rare, more likely in prepuberal/early pubertal boys; tender nodule with blue discoloration on the upper pole of the testis and more easily seen in light-skinned individuals
  - Lab
  - Any of the above
  - Generalized tenderness
  - Increasing scrotal swelling and erythema
  - Hydrocele

DIAGNOSIS

HISTORY
- Intravaginal testicular torsion
- Usually severe pain, sudden onset
- Nausea/vomiting more common
- May be recurrent usually same side
- Extravaginal testicular torsion
- Usually painless and asymptomatic
- Appendiceal torsion
- Usually more gradual but may be acute
- Pain may be mild or severe
- Nausea/vomiting uncommon
- No prior episodes
- Impaired or abdominal pain may be associated or may be only site of pain in younger boys
- Inflamed epididymis reported as “epididymitis”

PHYSICAL EXAM
- Note: Phren sign (elevation of scrotum relieves pain in epididymitis but in torsion it is no longer considered reliable)
- Intravaginal testicular torsion
- These are possible findings but these may be highly variable
- Early
  - Generalized testicular tenderness
  - Loss of spermatic cord Doppler
  - Elevated gonadotropin levels (see the appendix for this in intermittent testicular torsion cases)
- Appendiceal torsion
  - Late
  - Any of the above, increasing scrotal swelling and erythema
  - Loss of scrotal rugation ± hydrocele
  - Inability to distinguish epididymal landmarks
- Extravaginal testicular torsion
  - Firm to hard nontender testes
  - Scrotal discoloration
- Appendix torsion
  - Localized tenderness superior to testis
  - Supernumerary appendix
  - Preserved spermatic cord Doppler
  - Normal testicular position and orientation
- Blue dot sign: Rare, more likely in prepuberal/early pubertal boys; tender nodule with blue discoloration on the upper pole of the testis and more easily seen in light-skinned individuals
  - Lab
  - Any of the above
  - Generalized tenderness
  - Increasing scrotal swelling and erythema
  - Hydrocele

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis
  - If pyuria suspect epididymitis/UTI
  - If hematuria consider renal or ureteral source of pain (e.g., stone)
- Urine culture if indicated
  - Additional labs not needed

Imaging
- Social US with Doppler
  - Need to identify waveforms that originate in the central parenchyma
  - Intravaginal testicular torsion findings:
    - Usually shows decreased or absent arterial flow but may be normal
    - Increased flow possible in intermittent testicular torsion
    - Increased or mixed echogenicity suggests torsion: Compare both sides
    - Hydrocele and/or enlarged epididymis may be present
    - Visible twist of cord: Requires expertise but highly specific if present
    - Additional US findings:
      - Heterogeneous appearance typical
      - Doppler flow may be hard to demonstrate in neonatal testes
      - Calcification may be present
- Appendix torsion findings:
  - Normal exam must precede
  - Supernumerary complex mass w/o vascular flow may be present
  - Enlarged epididymis reported as “epididymitis” often present
  - Doppler flow normal or increased
  - Doppler flow normal
  - Thickened scrotal skin and hydrocele are nonspecific findings in acute scrotum cases
  - Nuclear scan: Rarely performed
Diagnostic Procedures/Surgery

Exploration for diagnosis if equivocal findings on exam and/or US; suspicion of testicular rupture, or tumor

Pathologic Findings

- Testicular necrosis (intravaginal) or subclinical loss of tubules with eddy current (extravaginal) testicular torsion
- Severity of injury depends on age, duration of testicular torsion, number of twists/thickness of spermatic cord
- In cases of appendicular torsion the necrotic tissue is reabsorbed usually without any sequelae

Differential Diagnosis

- Acute testicular pain
  - Appendicitis most common in prepubertal boys
  - Testicular torsion most common in peri-pubescent boys but can occur at any age; less common than epididymitis
  - Appendicitis due to LUTI or STD: Rare in pediatric age group
- Communicating hydrocele
- Incarcerated inguinal hernia
- Trauma and possible testicular rupture
- Noma testicularis present
- Orchitis (eg, mumps)
- Henoch–Schönlein purpura
- Rapidly usually present
- Fournier gangrene (rare in children)
- Delayed pain from orchidopexy or intra-abdominal process such as appendicitis
- Orchialgia; consider voiding dysfunction

Treatment

General Measures

- Testicular torsion: Consider manual detorsion in ER
  - Not effective; 1/3 of cases may rotate further
- Does not preclude need for immediate surgery
- Emergency surgery is indicated for all cases of testicular torsion

Medication

First Line

- Ibuprofen to reduce inflammation in appendix
  - Appendix torsion: Rest until pain resolves

Second Line

- None

Surgery/Other Procedures

- Emergent exploration indicated if evaluation suggests intraabdominal testicular torsion or diagnosis is equivocal
- Detorsion, observation for reperfusion, and bilateral orchidopexy via scrotal approach with fixation of tests extravaginally
- Consider capsulotomy if flow improves with placement of tunica vaginalis patch

- Urgent exploration, bilateral fixation for extravaginal testicular torsion to avoid asynchronous contralateral torsion
- Avoid imaging delays if findings are classic
- Elective surgery for resolved intermittent testicular torsion
- Consider delay in intraabdominal extraperitoneal testicular torsion if or testis appears nonviable after detorsion or circumscription
- Consider delayed prosthesis placement for mumps orchitis
- Appendix torsion
  - Prolonged pain not responsive to conservative measures
  - Recurrent episode (rare) or diagnostic uncertainty

Additional Treatment

- Radiation Therapy

Additional Therapies

- Experimental agents such as nitric oxide (NOS) inhibitors to reduce reperfusion injury in testicular torsion not used clinically

Complementary & Alternative Therapies

- N/A

Ongoing Care

Prognosis

- Intravaginal testicular torsion
  - Risk of postoperative atrophy increases with duration of torsion
  - Risk of contralateral torsion in the neonatal period
  - Risk of postoperative atrophy increases with duration of torsion
  - Risk of postoperative atrophy increases with duration of torsion
  - Risk of postoperative atrophy increases with duration of torsion
  - Risk of postoperative atrophy increases with duration of torsion

Complications

- Recurrent testicular torsion: Rare, occurs with failure of absorbable or nonabsorbable suture fixation of a testis that remains within an intact tunica vaginalis
- Testicular atrophy

Follow-Up

- Patient Monitoring
  - Follow for at least 6 mo to determine risk of atrophy
  - Monitor for recurrent testicular pain
  - Social protection in contact sports

- Education of healthy adolescent populations about the signs/symptoms of testicular torsion and the benefits of early evaluation and treatment
- Specific educational focus on family members of affected individuals

Patient Resources


References


Additional Reading

- Mellick LB. Torsion of the testicle: It is time to stop tossing the dice. Pediatr Emerg Care 2012;28:80–86.

See Also (Topic, Algorithm, Media)

- Appendix Testis and Appendix Epididymis
- Torsion, Tumor and Mass, Pediatric, General
- Torsion, Testis or Testicular/Epididymal Appendages

Icd9

- 608.20 Torsion of testis, unspecified
- 608.23 Torsion of appendix testis
- 608.24 Torsion of appendix epididymis

Icd10

- N44.00 Torsion of testis, unspecified
- N44.03 Torsion of appendix testis
- N44.04 Torsion of appendix epididymis

Clinical/Surgical Pearls

- Diagnosis of spermatic cord torsion requires a high index of suspicion, particularly in patients with intermittent testicular pain
- Emergent surgery is indicated for all cases of suspected spermatic cord torsion
- The risk of testicular loss increases after 4–6 hr of untreated spermatic cord torsion

519
ASSOCIATED CONDITIONS

Common causes include end-stage renal disease, diabetes, hypertension, glomerulonephritis, cystic renal disease.

GENERAL PREVENTION

- Avoid incompatible donors for kidney transplant recipients. Avoid transplants across a positive crossmatch or with preformed DSAs.
- Induction immunosuppression with lymphocyte-depleting agents, especially for high immunologic-risk recipients.
- Compliance with immunosuppressant medications.
- Monitor renal function and maintain therapeutic immunosuppressant drug levels.
- Minimize sensitizing events (eg, blood transfusions and pregnancies).

DIAGNOSIS

HISTORY

- Medication noncompliance or tapering off immunosuppression for a failed allograft.
- Often asymptomatic with plasma creatinine elevation as sole abnormality.
- Severe rejection may result in decreased urine output and pain over kidney transplant.
- Fluid retention/weight gain

PHYSICAL EXAM

- May be normal
- Increased blood pressure
- Volume overload
- May have tenderness over kidney transplant

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Rising BUN/plasma creatinine
- Rule out pyelonephritis.
- Otherwise unexplained plasma creatinine rise >20% over baseline is suggestive of rejection.
- Urinalysis and urine culture
- Rule out pyelonephritis.
- Determine drug levels (bacteriuria or cyclosporine)
- 12-24 hr trough level (usually before morning dose)
- Suspect calcineurin inhibitor (CNI: tacrolimus or cyclosporine) toxicity if abnormally high levels
- Target levels vary by patient and assay
- If antibody-mediated rejection (AMR) is suspected, test for donor-specific antibodies (DSAs)

Imaging

- Renal ultrasound
  - Rule out obstructive uropathy or stone.
  - Assess for diminished renal blood flow.
- Color flow Doppler evaluates vascular status
- Detect graft swelling (with acute rejection; graft may be small with chronic rejection).
- Nuclear medicine renal scan:
  - Rejection: Decreased renal blood flow/glomerular filtration rate
  - Arterial or venous thrombosis: Decreased or absent perfusion.
- Complete obstruction, a reniform photopenic area can be seen
- Acute rejection/tube/tubular necrosis: Marked parenchymal retraction with normal or mildly reduced perfusion. Rejection cell show progressive decrease in function over time.

Diagnostic Procedures/Surgery

- Needle biopsy of transplant kidney (continuation of rejection)
  - Usually under ultrasound guidance.
  - Automated biopsy gun device, needle sizes 14–18 gauge
  - Adequate sample
  - <2 cores of cortex, ≥2 glomeruli, and ≥2 arteries required

Pathologic Findings

- Acute cellular rejection
  - Interstitial mononuclear cell infiltrate
  - Tubules
  - Vascularis (in more-severe cases)
- Acute antibody-mediated rejection
  - Pathology variable
  - Acute tubular necrosis (ATN)
  - Glomerulitis
  - Peritubular capillaritis
  - Pyelonephritis
  - C3 glomerular (C6) is a complement split product that covalently binds to tissue indicating antibody-mediated complement activation
- Chronic rejection
  - Interstitial fibrosis
  - Tubular atrophy

DIFFERENTIAL DIAGNOSIS

- Prerenal: volume depletion or hypertension
- CNI (calcineurin inhibitor) toxicity (bacteriuria or cyclosporine)
- Pyelonephritis
- ATN
- Technical complications
  - Arterial or venous thrombus
  - Arterial stenosis
  - Urinary obstruction or urine leak (early posttransplant)
- Obstructive urology
- Recurrence of original renal disease
TREATMENT

GENERAL MEASURES
• Attempt to reverse rejection with medical therapy
• Graft removal may be necessary in severe rejection eg, hyperacute rejection.

MEDICATION
First Line
• Acute cellular rejection: High-dose glucocorticoids
  – Methylprednisolone 1–2 g IV bolus, 5 mg/kg/d for 3–5 days followed by taper to maintenance dosing
• Antibody-mediated rejection: Plasmapheresis and rituximab in attempt to remove, neutralize, or prevent the production of DSAs, respectively
• Chronic rejection: No effective therapy.
• Hyperacute rejection: Remove transplanted kidney (ZEA)
  – Can result in DIC if not removed promptly

Second Line
• Acute cellular rejection: Lymphocyte-depleting agents such as antithymocyte globulin (ATG) or alemtuzumab may be given for severe rejection or rejection refractory to high-dose glucocorticoid therapy (3A).
• Significant reactions possible with 1st doses (eg, hyperacute rejection).
• Monitor for recurrence of native kidney disease
• Continue maintenance immunosuppression

SURGERY/OTHER PROCEDURES
• Allograft nephrectomy
  – Remove a symptomatic, irreversibly rejected allograft
  – Remove an asymptomatic, chronically rejected kidney to withdraw immunosuppression and prevent further development of anti-HLA antibodies

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
• Severe rejection and graft failure may require acute dialysis

Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
• Repeated episodes of acute rejection reduce allograft survival
• Relative risk of graft failure is 1.8 for patients who have had 1 episode of rejection compared to none (4)

COMPLICATIONS
• DIC can accompany hyperacute rejection
• Graft loss can result from untreated or unrecognized rejection episode
• Cyclosporin toxicity can resemble mild acute rejection
• Need to resume dialysis

FOLLOW-UP

Patient Monitoring (3)
• Compliance with anti rejection critical
• Therapeutic drug levels: Including monitoring of CNI toxicity
• Plasma creatinine
  – Monitor for recurrence of native kidney disease (eg, diabetes, hypertension, etc.)
• Protocol transplant biopsies (optional)

Patient Resources

REFERENCES

ADDITIONAL READING
• Danovich R. Handbook of Renal Transplantation. 5th ed. Lippincott Williams & Wilkins; 2009.

See Also (Topic, Algorithm, Media)
• Acute Kidney Injury, Adult (Renal Failure, Acute)
• Acute Kidney Injury, Pediatric (Renal Failure, Acute)
• Chronic Kidney Disease, Adult (Renal Failure, Chronic)
• Chronic Kidney Disease, Pediatric (Renal Failure, Chronic)
• Pyelonephritis, Adult

CODES

ICD9
596.81 Complications of transplanted kidney
T86.12 Kidney transplant failure
T86.11 Kidney transplant rejection

ICD10
T86.1 Kidney transplant rejection
T86.12 Kidney transplant failure

CLINICAL/SURGICAL PEARLS
• Don’t confuse kidney transplant rejection with pyelonephritis
• Cyclosporin toxicity can resemble mild acute rejection.

521
**TRASURETHRAL RESECTION (TUR) SYNDROME**

**Raju Thomas, MD, MHA, FACS**

**Philip J. Dorsey, Jr., MD, MPH**

**DESCRIPTION**

- Transurethral resection (TUR) syndrome is classically associated with TUR of the prostate (TURP) and is characterized by confusion, hypotension (HTN), bradycardia, and visual disturbances.
- Symptoms are caused by hyponatremia, dilutional hyponatremia, and solute effects from irrigation absorption during resection.
- While traditionally associated with prostate resection, it can also be seen in TUR of bladder tumor (TURBT) and has also been described for procedures such as cystoscopy.
- Use of bipolar TURP and laser TURP techniques with normal saline irrigant has led to decreased incidence of TUR syndromes.
- Syncytial TURP syndrome

**EPIDEMIOLOGY**

**Prevalence**
- N/A

**Risk Factors**
- Resection time > 60 min
- Gland size > 45 g
- Intravesical pressures > 30 mm Hg
- Operative technique (open venous sinuses, capsular perforations increase risk)
- Sympathetic blockade associated with spinal anesthesia may contribute to late hypotension.

**Genetics**
- N/A

**PATHOPHYSIOLOGY**

- Irrigants used are osmotically active.
- Osmolarity of TUR irrigation solutions:
  - Normal saline: 280–310 mOsm/L
  - 5% mannitol: 275 mOsm/L
  - 2.5% sodium/0.5% mannitol: 178 mOsm/L
  - 3% dextrose: 165 mOsm/L
- Irrigant is absorbed by venous sinuses opened during resection or by slow absorption from the periurethral and perivesical spaces in case of capsular perforation.
- As osmotically active solute enters the intravascular space, the plasma sodium concentration drops, leading to hypo-osmolality.

**Volume effects:**
- Increase in intravascular volume initially leads to hypervolemia, HTN, and renal failure. As gland size increases, the left ventricle may also lead to PE and respiratory failure.

**ALERT**

After 35–50 min of resection, flow from the intravesical space to peripheral tissues increases and can cause hyponatremia and hypotension (2).

- Hypotension:
  - Caused by loading the intravesical space with nonelectrolyte solution.
  - Contributes to CNS disturbances.
- If severe enough, negative intraperitoneal pressures may initiate hypotension.

**DIAGNOSTIC TESTS & INTERPRETATION**

**PHYSICAL EXAM**

- Nonspecific physical findings: Although skin may be clammy, patient may complain of any of the following:
  - Headache
  - Lethargy
  - Confusion
  - Chest pain
  - Nausea and vomiting
  - Syncope of breath

**ASSOCIATED CONDITIONS**

- BPH
- Bladder tumors

**GENERAL PREVENTION**

- Using irrigants such as glycine, sorbitol, and mannitol solutions reduces the hemolytic effects associated with sterile water irrigation.
- Glycine is no longer recommended as an irrigation fluid.
- Intravesical pressure can be reduced by using continuous flow equipment, shunting the bladder with a suprapubic tube, or lowering the fluid height to ~60 cm.
- If a significant extraperitoneal perforation occurs during the TURP, or TURBT, it is best to abandon the procedure after achieving hemostasis to prevent excessive fluid absorption.
- Appropriate selection of patients for TURP is based on gland size:
  - Limited resection time to <60–90 min.
  - Consider open prostatectomy, or other appropriate options, for adenoma >100 g measured by imaging studies.
  - Judicious use of IV diuretics.
- Use of bipolar resectoscopes to perform TURP allows for saline irrigation.
- Reduces the hypo-osmotic effect of the absorbed fluid.
- Use of laser energy sources for TUR management also decreases occurrence of TUR syndrome.

**DIAGNOSIS**

A patient who is slow to awaken from anesthesia or complains of visual disturbances should be considered to have the TUR syndrome following TURP.

**HISTORY**

- During TURP procedure: HTN and bradycardia may be a prodrome to rapid reduction in BP.
- Postoperatively: No classic presentation, but patient may complain of any of the following:
  - Chest pain
  - Confusion
  - Headache
  - Lethargy
  - Nausea and vomiting
  - Syncope of breath

**PHYSICAL EXAM**

- Nonspecific physical findings: Although skin may be clammy

**LAB**

- Serum sodium < 125 mEq/L
- Serum ammonium and glycine may be elevated if glycine solution is used.
Hemodynamic and cardiopulmonary support should be provided as needed. Patients with normal renal function need no further intervention, except to be monitored for rapid correction of hyponatremia. Monitoring of serum sodium is essential. Prompt diagnosis, evaluation, and management are essential to prevent adverse events.

If a significant extraperitoneal perforation occurs, if therapy is delayed and hyponatremia is severe, risk of significant morbidity and mortality.

COMPLICATIONS
- Cardiopulmonary collapse
- Cerebral edema and brainstem herniation
- Seizures
- Transient blindness

FOLLOW-UP
- Patient Monitoring: Hemodynamic monitoring and close attention to serum electrolytes, especially sodium, is essential during and after procedure.
- Serial neurologic exams/mental status exams should be performed until symptoms improve.

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Blender Suture Distraction (BSD)
- Hyponatremia, Urologic Considerations
- Prostate, Benign Hyperplasia/Hyper trophy (BPH)

CODES
- ICD9: 276.1 Hyponatremia and/or hyponatremia
- 276.99 Other fluid overload
- 195.9 Urological complications, not elsewhere classified
- ICD10: E87.3 Hypo-osmolality and hyponatremia
- E87.7 Fluid overload, unspecified
- N99.89 Oth postprocedural complications and disorders of fluid volume

CLINICAL/SURGICAL PEARLS
- Diagnosis of the TUR syndrome requires high clinical suspicion.
- Prompt diagnosis, evaluation, and management are essential to prevent adverse events.
- If a significant extraperitoneal perforation occurs during the TUR, consider abandoning procedure after achieving hemostasis to prevent excessive fluid absorption.
- Limit resection time to 60–90 min.
- Consider open prostatectomy, or other appropriate options (e.g., laser-assisted techniques), for adenoma >100 g.
- Use of bipolar resectoscopes to perform TUR permits use of saline irrigation reducing risk of TUR syndrome.
TROCAR INJURY DURING LAPAROSCOPY

Costas D. Lallas, MD, FACS
Leonard G. Gomella, MD, FACS

ASSOCIATED CONDITIONS
- For urologic laparoscopy: the underlying indication for the laparoscopy: (H)Nephrectomy (kidney, prostate, testicular, uterine, bladder)
- Observation: Ureteropelvic junction obstruction
- Invasion: Adenocarcinoma, retroperitoneal
- Others: Lymphoma, hemia

GENERAL PREVENTION
- Reason technique: (brusk down OR "open trocar placement") for initial access; allows direct visualization of peritoneum.
- Use of visual obturator trocar for primary port placement.
- Use of a nonbladed port for all ports.
- Utilization of confirmatory testing to ensure proper placement of initial Veress needle before full insufflation (4):
  - Modified Palmer test: Inject 10 mL of saline into the needle and attempt to aspirate. Inability to aspirate the fluid suggests that the fluid has dispersed into the abdomen and the needle is in correct position.
  - Initial pressure reading <8 mm Hg. The insufflator is turned on with no flow to obtain a pressure reading.
  - A decrease in pressure with elevation of the abdominal wall.
  - If perforation of a viscus occurs, the needle should be removed and discarded. A new needle may then be inserted at another location or the surgeon may choose to obtain open access using the Hasson technique. The injury should be observed laparoscopically or through open intervention if there is any concern over the degree of injury.
- Utilizing a LUS insertion site (Palmers point, located 3 cm above the middle of the left costal margin, for primary port)
- Increase pneumoperitoneum to 20–25 mm Hg during port placement to increase tension of abdominal wall and decrease posterior displacement during trocar insertion
- Ensure adequate skin incision for trocar size to avoid excess insertion pressure
- Subdiaphragm abdominal wall when inserting trocar
- Describe vision of secondary port placement and transfundulation of abdominal wall to avoid more superficial vessels
- Bladder catheter placement
- Nasogastric tube placement
- Surgeons should completely familiarize themselves with a new trocar device or design before 1st use
- Visualization of port removal can help identify unrecognized anterior abdominal wall vascular injury.

DIAGNOSTIC TESTS & INTERPRETATION
- Lab: Sudden unexplained drop in blood pressure at the beginning of the case consistent with unrecognized major vascular injury
- Need to differentiate from insufflation causing compromised blood pressure

DIAGNOSTIC PROCEDURES/SURGERY
- Primary site of injury
- Pathologic Findings
- Differential Diagnosis

PHYSICAL EXAM
- Intraoperative findings that suggest trocar injury:
  - Blood in the port after initial placement
  - Retroperitoneal hemorrhage on initial abdominal inspection
  - Air in the bladder catheter bag after initial trocar placement
- Visualization of port removal can help identify unrecognized anterior abdominal wall vascular injury
- Drop pneumoperitoneum to 5 mm Hg at the end of the case to uncover possible significant small vessel or venous bleeding.

DIFFERENTIAL DIAGNOSIS
- Sudden loss in vision without mydriasis
**TREATMENT**

**GENERAL MEASURES**
- In general Veress needle injuries often heal with conservative management whereas trocar injuries or gross spillage of bowel contents require formal repair
- Direct injury may be observed laparoscopically or during conversion laparotomy
- Abdominal wall/gastric vessel bleeding may be recognized after ports are removed under direct visualization
- If a port is placed into a major vessel, do not remove but keep in place during laparotomy
- During an emergent open conversion, use anteriorly deflected port or laparoscope to cut down into abdomen (unless in major vessel)

**MEDICATION**

**First Line**
N/A

**Second Line**
N/A

**SURGERY/OTHER PROCEDURES**

- **Laparoscopic or open repair of injury**
  - Always have open tray available for each case
  - If the Veress needle aspiration returns frank blood or other fluid (T)
    - Consider leaving the needle in place to help tamponade and identify the injury site
    - If the patient is unstable, consider an alternate access site and laparoscopically evaluate the site.
  - For abdominal wall bleeding:
    - Clips or electrocautery
    - Advancement of a central venous line into the right heart with subsequent attempts to aspirate gas may sometimes be helpful.
  - For gas embolism (4):
    - Immediate cessation of insufflation and prompt deflation of the peritoneal cavity
    - Advancement of a central venous line into the right heart with subsequent attempts to aspirate gas may sometimes be helpful.
  - **Bladder injury**:
    - Veress needle injury can usually be managed by bladder catheter for 7–10 days
    - More significant injury requires 2-layer closure with absorbable suture and catheter drainage
  - **Bowel injury**:
    - Requires further inspection and repair either laparoscopically or via laparotomy.

**ADDITIONAL TREATMENT**

**Radiation Therapy**
N/A

**Additional Therapies**

**Complementary & Alternative Therapies**
N/A

**ONGOING CARE**

**PROGNOSIS**
- Excellent if injury is recognized and managed quickly.
- Delayed or unrecognized visceral injury can lead to significant morbidity or mortality.
- Many bowel injuries are not recognized initially and typically present with peritonitis.

**COMPLICATIONS**
- Unrecognized injury can lead to ongoing hemorrhage, infection.

**FOLLOW-UP**
- Dependent on injury and management.

**Patient Resources**

**REFERENCES**


**CODES**

**ICD9**
- 902.9 Injury to unspecified blood vessel of abdomen and pelvis
- 998.3 Accidental puncture or laceration during a procedure, not elsewhere classified

**ICD10**
- S35.91XA Laceration of unspecified blood vessel during laparoscopy
- S35.91XA Laceration of unspecified blood vessel of abdomen, lower back and pelvis level, initial encounter
- S36.90XA Unspecified injury of unspecified abdominal organs, with open wound into cavity
- K91.72 Acc pnctr & lac of a dgstv sys org during oth procedure
- S33.91XA Laceration of unspecified blood vessel at abdomen, lower back and pelvis level, initial encounter
- 998.3 Accidental puncture or laceration during a procedure, not elsewhere classified

**CLINICAL/SURGICAL PEARLS**
- **Bladder injury**:
  - Veress needle injury can usually be managed by bladder catheter for 7–10 days
  - More significant injury requires 2-layer closure with absorbable suture and catheter drainage
  - Bowel injury:
    - Requires further inspection and repair either laparoscopically or via laparotomy.

**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)
- Hypercarbia During Laparoscopy
- Rectal Injury During Radical Prostatectomy or Radical Cystectomy
- **Trocar Injury During Laparoscopy** Image Of
**RISK FACTORS**

- Immunocompromised states (e.g., AIDS)
- Malnutrition
- Poor living conditions/poverty/drug use
- Malnutrition
- Chronic TB infection
- Chronic cystitis unresponsive to therapy
- Dysuria from seeding of the bladder with TB
- Men commonly present with epididymitis.
- Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common.
- Common presentation with epididymitis.
- Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
- Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
- Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
- Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

**BASICS**

- **DESCRIPTION**
  - Genitourinary tuberculosis (TB) refers to urinary and GU infection with Mycobacterium tuberculosis. Common GU sites include the kidney, urinary bladder, prostate, and testicles/epididymis.
  - GU tract is 2nd most common site after lungs for tuberculosis infection. Unreported TB represents 27% of extrapulmonary cases (1).
  - Tuberculosis found in 7–29% of urine in patients with extrapulmonary TB.
  - In 1882, the bacillus causing TB, M. tuberculosis, was first identified and described by Robert Koch.
  - 10% of TB is extrapulmonary with GU locations accounting for 33% of these sites and these rates double in developing countries.
  - TB is 2nd only to HIV/AIDS as the greatest killer of women aged 15–44.
  - 10% of TB is extrapulmonary with GU locations accounting for 33% of these sites and these rates double in developing countries.
  - TB is 2nd only to HIV/AIDS as the greatest killer of women aged 15–44.
  - 10% of TB is extrapulmonary with GU locations accounting for 33% of these sites and these rates double in developing countries.

- **ASSOCIATED CONDITIONS**
  - Chronic TB infection
  - Immunocompromised states (e.g., AIDS)
  - Malnutrition
  - Poor living conditions/poverty/drug use
  - Malnutrition
  - Chronic cystitis unresponsive to therapy
  - Dysuria from seeding of the bladder with TB
  - Men commonly present with epididymitis.
  - Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common.
  - Common presentation with epididymitis.
  - Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
  - Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
  - Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
  - Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

**HISTORY**

- Initial symptoms may be minimal, even in presence of extensive disease. No classical clinical picture, most symptoms are of bladder/urinary origin.
- History or exposure to TB; determine past PPD testing results; latency can be >20 after primary TB.
- Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common.
- Common presentation with epididymitis.
- Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
- Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
- Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
- Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

**PATHOPHYSIOLOGY**

- Hematogenous spread to kidneys from pulmonary disease proved by Medlar, et al. in 1949.
- 2–12 wk; often ensue before mycobacterial numbers are sufficient to mount a clinically detectable cellular immune response.
- M. tuberculosis infections acquired by inhalation of aerosolized droplet nuclei (1–5 μm), which reach pulmonary alveoli.
- Invasion of GU organs by ascept (prostate to bladder) or decendent (kidney to bladder, prostate to epididymis).
- Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
- Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
- Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
- Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

**DIAGNOSIS**

- **PHYSICAL EXAM**
  - Physical exam is often of limited value in the diagnostic process, because physical signs develop late in the disease. The most common physical finding is an abdominal scirrhold mass in about half the patients.
  - Suspected when disease is extensive
  - Painful scissel tests
  - Chronic draining scrotal sinuses should be considered TB until proven otherwise.
  - Nodular, indurated prostate and thickened seminal vesicles on rectal exam mitotic neoplasms.
  - Upper abdominal bruit may be indication of advanced renal disease.
  - Up to 25% of patients will present only with sterile pyuria and 13% might have gross or microscopic hematuria as their only presentation.

- **TUBERCULOsis, Genitourinary, General Considerations**

  - **DESCRIPTION**
    - Genitourinary tuberculosis (TB) refers to urinary and GU infection with Mycobacterium tuberculosis. Common GU sites include the kidney, urinary bladder, prostate, and testicles/epididymis.
    - GU tract is 2nd most common site after lungs for tuberculosis infection. Unreported TB represents 27% of extrapulmonary cases (1).
    - Tuberculosis found in 7–29% of urine in patients with extrapulmonary TB.
    - In 1882, the bacillus causing TB, M. tuberculosis, was first identified and described by Robert Koch.
    - 10% of TB is extrapulmonary with GU locations accounting for 33% of these sites and these rates double in developing countries.
    - TB is 2nd only to HIV/AIDS as the greatest killer of women aged 15–44.
    - 10% of TB is extrapulmonary with GU locations accounting for 33% of these sites and these rates double in developing countries.

  - **ASSOCIATED CONDITIONS**
    - Chronic TB infection
    - Immunocompromised states (e.g., AIDS)
    - Malnutrition
    - Poor living conditions/poverty/drug use
    - Malnutrition
    - Chronic cystitis unresponsive to therapy
    - Dysuria from seeding of the bladder with TB
    - Men commonly present with epididymitis.
    - Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common.
    - Common presentation with epididymitis.
    - Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
    - Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
    - Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
    - Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

  - **HISTORY**
    - Initial symptoms may be minimal, even in presence of extensive disease. No classical clinical picture, most symptoms are of bladder/urinary origin.
    - History or exposure to TB; determine past PPD testing results; latency can be >20 after primary TB.
    - Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common.
    - Common presentation with epididymitis.
    - Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
    - Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
    - Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
    - Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

  - **PATHOPHYSIOLOGY**
    - Hematogenous spread to kidneys from pulmonary disease proved by Medlar, et al. in 1949.
    - 2–12 wk; often ensue before mycobacterial numbers are sufficient to mount a clinically detectable cellular immune response.
    - M. tuberculosis infections acquired by inhalation of aerosolized droplet nuclei (1–5 μm), which reach pulmonary alveoli.
    - Invasion of GU organs by ascept (prostate to bladder) or decendent (kidney to bladder, prostate to epididymis).
    - Kidney and epididymis are primary sites of TB infection in the GU tract in men, and tubular tubules in women.
    - Tuberculosis develops in glomerular capillaries as a result of hematogenous seeding from lungs.
    - Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
    - Adrenal TB is seen in <6% of active TB cases (up to 56% of patients with adrenal TB will have a subnormal cortisol response to corticotrophin stimulation).

  - **DIAGNOSIS**
    - **PHYSICAL EXAM**
      - Physical exam is often of limited value in the diagnostic process, because physical signs develop late in the disease. The most common physical finding is an abdominal scirrhold mass in about half the patients.
      - Suspected when disease is extensive
      - Painful scissel tests
      - Chronic draining scrotal sinuses should be considered TB until proven otherwise.
      - Nodular, indurated prostate and thickened seminal vesicles on rectal exam mitotic neoplasms.
      - Upper abdominal bruit may be indication of advanced renal disease.
      - Up to 25% of patients will present only with sterile pyuria and 13% might have gross or microscopic hematuria as their only presentation.
Medication

**DIFFERENTIAL DIAGNOSIS**

- **Aminic cystitis**
- **BCG urologic/Cystitis**
- **Chronic nonspecific cystitis or pyelonephritis**
- **Disseminated coagulopathies**
- **Granulomatous prostatitis, prostatic cancer**
- **Mediastinal sponge kidney**
- **Necrotizing papillitis**
- **Nonspecific-epididymitis**
- **Renal stones or nephrocalcinosis**
- **Urinary lithiasis (chrocomiasis)**

**TREATMENT**

**GENERAL MEASURES**

- **Quarantine until appropriate medications**
- **Screen close contacts**

**MEDICATION**

**First Line (2)**

- **Antituberculous drugs**: isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin.
- **Patient with uncomplicated TB infection**: isoniazid (300 mg/d), rifampin (550–600 mg/d), and pyrazinamide (25 mg/kg) once a day in the morning, 3 times a week, for 2–4 mo, followed by isoniazid and rifampin once a day, 3 times a week, for an additional 2–4 mo. (Add 1 g of vitamin C, 3 times a week, for 4 mo with above regimen).

**Second Line**

- **Patient with complicated TB infection**: Add streptomycin to the above for severe infection or severe bladder symptoms.
- **Drug resistance**: increasing and necessitates tight therapy control. Expand antibiotic regimen of 4 of the following: ethambutol, pyrazinamide, quinolones, thiamphenicol, ciprofloxacin, kanamycin, ciprofloxacin, capreomycin, thiocarbazone, and para-amoxycycline.
- **Steroids**: No role in initial therapy but can be used for acute TB cystitis or structure at distal ureter (maintenance 20 mg PO TID).

**SURGERY/OTHER PROCEDURES**

- **Nephrectomy**: for symptomatic or severe renal or clinical renal cell carcinoma.
- **Peritoneal nephrectomy**: for severe renal or clinical renal cell carcinoma.
- **Pericystectomy**: indicated for caseating abscess. Perform 4–6 wk after onset of antituberculous drugs.
- **Epididymectomy**: Indicated for chronic draining scrotal sinus. Perform 4–6 wk after start of antituberculous drugs.
- **Bladder augmentation**: Small capacity, fibrotic bladder. Surgery not necessary for TB abscesses; Treat medically.

**ONGOING CARE**

**PROGNOSIS**

- **Awareness of renal TB is urgently needed by physicians to suspect this disease in patients with unexplained urinary tract abnormalities, mainly in those with any immunosuppression and those coming from TB-endemic areas**.
- **No specific statistics, but overall patients can do well with appropriate, early antituberculosis medications and surgical interventions**.

**COMPLICATIONS**

- **Urinary TB**: formation of hematomas, hydronephrosis, scarring, and renal destruction
- **Complete nonfunctioning of an affected kidney (“autonephrectomy”)**
- **Renal TB**: Obliteration of the renal and psoas shadow on plain radiographs, perinephric abscess may cause an enlarging mass in the flank.
- **Genital TB**: Stenosis as a consequence
- **Bladder TB**: Stenosis of ureterovesical junction, fibrosis, and contracture of bladder
- **Nephrotoxicity induced by antimicrobial agents (especially rifampin)**

**FOLLOW-UP**

- **Completion of TB regimen long term is essential.**
- **Structures can evolve after organism is eradicated.**
- **Follow regularly after completion of therapy as stricturing can continue**.
- **Need long-term imaging follow-up of calcifications**.

**REFERENCES**


**ADDITIONAL READING**


**See Also (Topic, Algorithm, Media)**

- **Bacteremia and Pylaria**
- **BCG urologic/Cystitis**
- **Prostatitis, Granulomatous**
- **Prostatitis, Tuberculous**
- **Tuberculosis, Bladder, and Urethra**
- **Tuberculosis, Genitourinary, General Considerations**
- **Tuberculosis, Kidney, and Ureter**
- **Tuberculosis, Male External Genitalia**

**CODES**

- **ICD9**: 016.90 Genitourinary tuberculosis, unspecified
- **ICD10**: A18.11 Tuberculosis of genitourinary system, unspecified

**CLINICAL/SURGICAL PEARLS**

- **Chronic draining vesical ulcers should be considered TB until proven otherwise.**
- **Sterile pus is the classic finding, typically >20 WBC/HF.**
- **Renal involvement by TB infection is underdiagnosed in most health care centers.**
- **Posttreatment follow-up is essential as strictures can evolve after organism is eradicated.**

- **ICD9**: 016.00 Tuberculosis of kidney, unspecified
- **ICD10**: A18.10 Tuberculosis of bladder, unspecified
- **ICD9**: 016.90 Tuberculosis, genitourinary unspecified

- **ICD10**: A18.12 Tuberculosis of kidney and ureter
- A18.12 Tuberculosis of bladder
TUBERCULOSIS, KIDNEY AND URETER

Mohamed S. Ismail, MBChB, MRCS, PhD
Jayram Krishnan, DO, MBA

ASSOCIATED CONDITIONS
- Chronic TB infection
- Immunocompromised states (HIV/AIDS)
- Malnutrition
- Poor living conditions/notify

GENERAL PREVENTION
- Diagnose and treat patients with TB before development of active disease
- Take careful precautions with patients hospitalized with TB
- Test annually with the purified protein derivative (PPD) skin test if at high risk for exposure

DIAGNOSIS

HISTORY
- Often mimics a wide range of nonspecific urologic symptoms and are often renal flare with extensive disease
- History or exposure to TB; determine last PPD test results; latency can be > 20 yr after primary TB
- Vague, intermittent, nonspecific complaints such as malaise, lethargy, weight loss, and low-grade fevers common
- Men commonly present with epididymitis
- Bacterial cystitis may be superimposed on bladder with TB

PHYSICAL EXAM
- Significant physical signs develop late with extensive disease
- Storage symptoms are the most common overall presentation (55.4%)(11)
- Hematuria (35.6%)(11)
- Lumbar pain (44.4%)(11)
- Most common physical finding in men is an abnormal urinalysis (49.8%)(11)
- Scolial lumps, epididymal hardening, or draining abnormal scrotal exam (49.8%)(11)
- Upper abdominal bruits may indicate advanced renal disease

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis and culture:
  - Clue finding: sterile pyuria (>20 white blood cells/high power field)
  - 20% of patients will also have bacterial cystitis or urinary tract infection with E. coli
  - 13% of patients will present with gross or microscopic hematuria (10)
- GOLD STANDARD: Specific staining of urine for acid-fast bacteria and mycobacterial culture
- Nontuberculous mycobacteria can also stain positive, so culture more useful
- Ziehl-Neelsen or Kinyoun acid-fast stain; more rapid if fluorescent microscopy
- 1st morning urine specimen has highest yield of tubercle bacilli

- Minimum 3 and up to 6 early-morning urine specimens are recommended, as TB organisms shed into urine intermittently.
- 64.2% of patients had M. tuberculosis in their urine (11)
- High index of suspicion for persistent pyuria without bacteria on repeated cultures (stain with methylene blue)
- Polynuclear chain reaction (PCR) assay may identify organisms
- Complete blood count and electrolytes
- Renal failure is present in 7.4% of cases (creatinine > 1.5)(11)
- Functional loss of the affected kidney can be present in up to 25% of cases (11)
- Erythrocyte sedimentation rate (ESR)
- Measure monthly as indicator of response to therapy
- Proteinuria may suggest secondary involvement of the kidney with amyloidosis

Imaging
- Chest radiograph: Abnormal in 75%
- Abdominal radiograph:
  - Enlargement of 1 kidney
  - Renal stones in 10%
  - Focal punctate calcifications occur within the caudate lesions in renal parenchyma
  - Obliteration of psoas shadow due to perinephric abscess
- Characteristic diffuse, uniform, extensive parenchymal calcifications are present with lobar cast of the kidney (auto nephrectomy)
- Scarring pattern:
  - Nodular or linear appearance in atrophied calyces (4E)
  - Obliteration of upper tract secondary to ureteral stricture (4F)
  - Obliteration of calyces
  - Loss of kidney function due to complete occlusion or renal destruction
- Computed tomographic (CT)
  - Most common finding: Renal parenchymal sarcoidosis (75%)
  - Hydronephrosis, hydropnephrosis, or hydronephrosis due to stricture (67%) (11)
  - Thick walls of the renal pelvis, ureters, and bladder (67%)

Diagnostic Procedures/Surgery
- Tuberculin skin test (PPD):
  - 98% patients have positive skin tests
  - 5 mm or more of induration is considered positive in persons with the highest likelihood of developing active disease
  - HIV, immunosuppression, organ transplants
  - 15 mm or more of induration is considered positive in those who are at high risk for TB
- Drug abuse, health care workers, family members
  - 15 mm or more of induration is considered positive in any patient
- Positive reaction indicates exposure, not necessarily active disease
**MEDICATION**

**GENERAL MEASURES**

- Early diagnosis of active disease is imperative and requires prompt initiation of adequate drug regimens.
- Surgical treatment is reserved for advanced cases and with the goal of renal preservation.
- Correct the obstructive effects of fibrosis and scarring rather than removal of infected tissues.
- Drainage of abscesses
- Balanced approach is required between medications and surgery to preserve function and eradicate mycobacteria.
- A surgical approach is required if medications and surgery do not achieve adequate disease response.
- Compliance to treatment regimen is essential for adequate disease response.

**COMPLICATIONS**

- Loss of renal function
- Hydronephrosis
- Hyponatremia
- Perinephric abscess may cause an enlarging flank mass
- Autonephrectomy: Complete nonfunctioning of an affected kidney
- Resistant to at least isoniazid and rifampin, and possibly additional agents
- Extensively drug-resistant TB (XDR-TB)
- Resistant to at least isoniazid and rifampin, and additionally resistant to fluoroquinolones and other antimicrobials or both

**SURGERY/OTHER PROCEDURES**

- 55% of patients with GU TB will require surgical intervention
- Ureteral obstruction
- Early stent or nephrostomy may decrease loss of renal function and increase opportunity for later reconstruction (2JE)
- Some strictures may resolve after medical therapy
- Nephrectomy
- Steroids
- Prednisone 20 mg 3 times daily orally
- Some strictures may resolve after medical therapy
- Enteric or nephrostomy tubes
- Nephrostomy
- Drainage of abscesses
- Percutaneous renal drainage
- Percutaneous or ureteral stent
- Ureteral stricture
- Early stent or nephrostomy may decrease loss of renal function
- Not recommended for routine use
- Some strictures may resolve after medical therapy
- Late strictures are refractory to medical therapy and require surgical intervention
- Stents
- Used for treatment of TB-induced ureteral strictures or cysts
- Prednisone 20 mg 3 times daily orally
- Not recommended for routine use
- Late strictures are refractory to medical therapy and require surgical intervention
- BCG Sepsis/BCGosis
- Prostatitis, Granulomatous
- Tuberculosis, Bladder and Urethra
- Tuberculosis, Genitourinary, General Considerations
- Tuberculosis, Kidney and Ureter
- Tuberculosis, Male External Genitalia

**Ongoing Care**

- Prognosis is good in patients who are compliant in therapy
- Better prognosis with early diagnosis of disease

**Follow-up**

- All TB patients should be screened for HIV/AIDS
- Structures can evolve after mycobacteria is eradicated
- Imaging (excretory urography/contrast computed tomography) and urine culture every 3 mos for 1st yr then annual abdominal radiographs
- Continue long-term imaging if calcifications present

**ADDITIONAL READING**

- Also See (Topic, Algorithm, Media)
  - BCG Sepsis/BCGosis
  - Prostatitis, Granulomatous
  - Tuberculosis, Bladder and Urethra
  - Tuberculosis, Genitourinary, General Considerations
  - Tuberculosis, Kidney and Ureter
  - Tuberculosis, Male External Genitalia

**ICD9**

- 016.20 Tuberculosis of ureter, unspecified
- 016.20 Tuberculosis of kidney, unspecified

**ICD10**

- A16.11 Tuberculosis of kidney and ureter

**CLINICAL/SURGICAL PEARLS**

Compliance to treatment regimen is essential for adequate disease response.
TUNICA ALBUGINEA/PARATESTICULAR TUMORS AND CYSTS
John L. Phillips, MD, FACS
Vladimir A. Valera, MD, PhD

PATHOPHYSIOLOGY

- Arise from epithelial, mesothelial, or mesenchymal tissues
  - Epithelium
  - Adenomatoid tumor
  - Cystadenoma (1/3 occur in VHL)
  - Spermatic cord
  - Sarcoma (arise from undifferentiated mesoderm)
  - Adenoma (found incidentally during hernia repair)
  - Lipoma/leiomyoma/liposarcoma, etc.
  - Tunica vaginalis (TV)
  - MM

ASSOCIATED CONDITIONS

- Germline conditions
  - Von Hippel–Lindau disease
  - Li–Fraumeni syndrome
  - Nevoid basal cell carcinoma syndrome
  - Li–Fraumeni syndrome

- Somatic (acquired) conditions
  - Inflammatory/infectious scrotal conditions
  - Morphologic changes (and asbestos exposure in MM of the TV)

- Solid masses require exploration
  - Cystic structures such as tunica albuginea cyst may be monitored serially
  - CT scan of the chest, abdomen, and pelvis required when malignancy suspected and to rule out metastasis in cases of known malignancy

DIAGNOSTIC PROCEDURES/SURGERY

- Fine needle aspiration may lead to false negatives or positives
- Solid lesions require inguinal approach
- Germ lesions
  - Observation
  - Testis-sparing surgery
- Malignant or suspicious lesions
  - Radical orchiectomy, inguinal approach
  - High dissection to internal ring
  - Early vascular control
- Removal of adenohypophysis
- Skin
  - Fascia
  - Muscle

Pathologic Findings

- Benign lesions usually need low power H&E
- Adenomatoid tumor
  - Well circumscribed
  - May involve tunica albuginea
- Benign appearing cords and cystic tubules lined by eosinophilic cells with small nuclei
- Focal cystadenoma
  - Well circumscribed
  - Brown fronds within cystic space
  - May have clear cells that resemble renal cell carcinoma commonly associated with VHL
- Malignant lesions may need electron microscopy
  - Stalk
  - Rhabdoid, multiphasic within hydrocele
  - Epithelioid, papillary, tubulovillous pattern
  - Fibrovascular core
  - Rhabdomyosarcoma (RMS)
  - Embryonal in 90%
  - Alveolar
  - Mixed pleomorphic

DIAGNOSIS

HISTORY

- Slowly growing inguinal or scrotal mass
- Often painless
- Found in workup for herna
- Found in evaluation of scrotal trauma or inflammation/infectious scrotal conditions

PHYSICAL EXAM

- Inguinal or scrotal mass
- Tenderness or discoloration and normal
- Adenomatous tumors may occur more inferiorty on the testis
- Superior pole tumors may mimic a spermaticcele (SC)
- Evaluate for herna, hydrocele, SC, and varicocele

ALERT

- Fixation to inguinal canal or testis suggests malignancy. Prepare for and rule out sarcoma.
- Fixation or involvement of testis and not the cord suggests primary testicular or MM
- Rule out germ cell tumor or MM
- Large size > 5 cm suggests RMS

ALERT

- Transformation does not rule out tumor
- Rule out secondary or, more so, primary lymphoma.
Therapies
Additional Therapies
malignant PT sarcomas
Reserved for local adjuvant or salvage control of
Radiation Therapy
ADDITIONAL TREATMENT
N/A

DIFFERENTIAL DIAGNOSIS
Epidermoid tumors (rare)
—Adenocarcinoma
—Cystadenoma
—Proliferative papillitis
—Resemble nodular fascitis
—Incidental at hemiorrhaphy
—Hematoma, direct or indirect
—Hydrocele
—Lymphadenopathy
—Secondary resection
—Vasitis nodosa
—Tunica albuginea cyst
—Vasitis nodosa

TREATMENT
GENERAL MEASURES
—Cephalic PT structures are treated with observation or rarely post-vasectomy.
—Secondary hernia
—Pain
—Hematoma
—Infection
—Secondary resection

MEDICATION
First Line
—Malignant rhabdomyosarcoma (RMS)
—Vincristine
—Dactinomycin
—Muscle biopsy
—METHA for bladder protection

Second Line
IFL

ADDITIONAL TREATMENT
Radiation Therapy
Reserved for local adjuvant or salvage control of malignant PT sarcomas

Additional Therapies
Secondary resection
—Local recurrence of benign lesions
—Local recurrence of malignant lesions if localized, no evidence of metastatic disease, and radiation not given

Complementary & Alternative Therapies
N/A

ONGOING CARE
PROGNOSIS
Benign lesions
—Resolution is usually curative
—Fertility can be maintained
—Malignant lesions
—RMS
—Favorable prognosis in children
—Stage I in 60–80%
—Unfavorable prognosis in adults and children
—>10 yr
—DRT unfavorable prognosis with nodal and pulmonary metastasis
—Malignant: Aggressive; similar to peritoneal mesothelioma
—Lipo-/leiomyosarcoma
—Excellent prognosis but may recur locally and require retreatment
—Metastases exceedingly rare, reportable

COMPLICATIONS
—General as seen for inguinal surgery
—Secondary hernia
—Infection
—Hematoma
—Pain
—Loss of tests after testicular sparing surgery (TSS) (rare)
—Infertility (eg, after excision of bilateral cystadenoma or epididymal masses in VHL)

FOLLOW-UP
Patient Monitoring
—Benign lesions
—Physical exam semiannual and self-exam yearly
—Malignant lesions
—Liposarcoma rarely metastasize but can recur locally
—RMS
—Immunosuppressive oncologic team (O)
—Serial imaging
—40% metastases to retroperitoneum
—Role of RPLND in RMS controversial

Patient Resources
National Cancer Institute
—Childhood Rhabdomyosarcoma Treatment: www.cancer.gov/cancertopics/pdq/treatment/chidrhabdomyosarcoma/patient
textbook/Self/Exam
—www.nih.gov/podmed-podpdx/ency/article/003909.htm
—Local Schnitzer Sarcoma Initiative—sarcomahelp.org (Accessed August 22, 2014)

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
—Epitheloid, Mass (Epitheloid Tumor and Cyst)
—Paratesticular Tumors
—Rhabdomyosarcoma, Pediatric (Sarcoma Botryoides)

CODING
ICD9
—214.8 lipoma of other specified sites
—295.3 Neoplasm of unspecified nature of other genitourinary organs
—808.89 Other specified disorders of male genital organs

ICD10
—D49.5 Neoplasm of unspecified behavior of other genitourinary organs
—R44.1 Cyst of tunica albuginea testis
—R50.8 Other specified disorders of male genital organs

CANCER PORTAL
—Cancer.org
textbook/Self/Exam
—www.cancer.gov/cancertopics/pdq/treatment/chidrhabdomyosarcoma/patient

CLINICAL/SURGICAL PEARS
—Most common benign adult paratesticular tumor: Lipoma
—Most common adult malignant paratesticular tumor: Liposarcoma
—Most common pediatric PT tumor is malignant RMS (Rhabdomyosarcoma)
— Cure rate of RMS with multimodality therapy: 90%
UMBILICAL ABNORMALITIES, UROLOGIC CONSIDERATIONS

Evalynn Vasquez, MD, MBA
Derek Matoka, MD

BASICS

DESCRIPTION

- Umbilical abnormalities result from failure of umbilical cord to close or persistence of umbilical structures.
- Abnormalities can be classified as:
  - Uss: Umbilical sinus
  - Infection: Umbilical granuloma
  - Persistent drainage: Umbilical fistula
- Most likely to present during the neonatal period or early infancy

EPIDEMIOLOGY

Incidence
- Most common mass at the umbilicus in an infant is umbilical hernia with a prevalence of 1/1000 live births

Prevalence
- N/A

PATHOPHYSIOLOGY (1)

- The primitive umbilical cord develops with the anterior abdominal wall during weeks 2–3 of gestation.
  - Early in gestation, the umbilical cord contains the vitelline duct, allantois, two arteries, and one vein.
  - The vitelline duct is a connection between the midgut and yolk sac. It involutes to the ligamentum teres of the liver.
  - The ligament attaches to the inferior portion of the umbilicus. The urachus involutes to a fibrous cord leaving only an umbilical ring.
- Urachal remnants are common but often asymptomatic (1% of adult autopsy specimens).
- Failure of normal development or failure of development results in umbilical abnormalities:
  - Omphalitis: Tender, erythematous, bleeding, and infective process of the umbilicus.
  - Umbilical hernia: 10–20% of all infants
  - Umbilical sinus: Umbilical granuloma
  - Urachal remnants are common but often asymptomatic (1% of adult autopsy specimens)
- Patent urachus occurs in 1/8000 live births
- Urachal carcinoma: 1 in 5 million cases annually

ASSOCIATED CONDITIONS

- Vitelline umbilical fistula: Found in newborn period with the appearance of an umbilical stoma with pink, circular, intestinal remnant.
- Medial diverticulum: Asymptomatic unless bowel obstruction from intussusception occurs or GI bleed due to mucosal ulceration from acid secretion.
- Meckel diverticulum: May present with urinary tract infections.
- Vitelline umbilical fistula: Found in newborn period with the appearance of an umbilical stoma with pink, circular, intestinal remnant.
- Medial diverticulum: Asymptomatic unless bowel obstruction from intussusception occurs or GI bleed due to mucosal ulceration from acid secretion.
- Meckel diverticulum: May present with urinary tract infections.

HISTORY

- Most umbilical disorders are found antenatally or at birth and can be diagnosed prenatally.
- Urachal carcinoma may be positive in cases of umbilical carcinoma.

DIAGNOSIS

HISTORY

- Most umbilical disorders are found antenatally or at birth and can be diagnosed prenatally.
- Urachal carcinoma may be positive in cases of umbilical carcinoma.

PHYSICAL EXAM

- Ultrasound: Evaluates anterior abdominal wall.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Assess the fluid level and determine if it could be a patent urachus.
- Meckel scan: Specific for gastric mucosal cells and evaluates for bladders/small bowel communication.
- VCUG: Assess for a urachal remnant and can rule out associated bladder outlet obstruction.

Lab

- Urinalysis: Evaluate hematuria or infection.
- Check creatinine of draining umbilical fluid to determine if it could be a patent urachus.
- Urine cytology may be positive in cases of urachal carcinoma.

Imaging

- Ultrasound: Best tool for initial assessment. It accurately determines anatomy of umbilical structures and evaluates for bladder/small bowel communication.
- VCUG: Assess for a urachal remnant and can rule out associated bladder outlet obstruction.
- Radiography/Sonography: Catheterization of tract and injection of contrast may be difficult and unreliable.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
-eline, calcified, partially obstructed with local extension is concerning for but not diagnostic of urachal carcinoma.

Diagnostic Procedures/Surgery

- Cesarean: For delivery of babies with umbilical abnormalities.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Ultrasound: Best tool for initial assessment. It accurately determines anatomy of umbilical structures and evaluates for bladder/small bowel communication.
- VCUG: Assess for a urachal remnant and can rule out associated bladder outlet obstruction.
- Radiography/Sonography: Catheterization of tract and injection of contrast may be difficult and unreliable.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.

Assessment

- Ultrasound: Best tool for initial assessment. It accurately determines anatomy of umbilical structures and evaluates for bladder/small bowel communication.
- VCUG: Assess for a urachal remnant and can rule out associated bladder outlet obstruction.
- Radiography/Sonography: Catheterization of tract and injection of contrast may be difficult and unreliable.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.

- Ultrasound: Best tool for initial assessment. It accurately determines anatomy of umbilical structures and evaluates for bladder/small bowel communication.
- VCUG: Assess for a urachal remnant and can rule out associated bladder outlet obstruction.
- Radiography/Sonography: Catheterization of tract and injection of contrast may be difficult and unreliable.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
- CT or MRI of abdomen and pelvis with IV and PO contrast: Gold standard for diagnosis and staging particularly for cancer.
Pathologic findings

- Urachal polyp: Persistence of urachal remnant
- Urachal adenocarcinoma: Malignant tumor
- Urachal sinus: Fistula connecting the bladder to the umbilicus
- Urachal abscess
- Umbilical polyp: Granuloma
- Umbilical hernia: Defect in the abdominal wall
- Umbilical cancer: Malignant tumor

Identify the abnormality and manage accordingly.

GENERAL MEASURES

Pathologic Findings

- Patent urachus: Resect entire duct via infra-umbilical incision.
- Omphalitis (infants): Broad spectrum antibiotics.
- Granuloma and umbilical polyp (infants): Very difficult to differentiate clinically.

DIFFERENTIAL DIAGNOSIS

- Umbilical hernia: All ages
- Urachal neoplasm: Adults
- Bezold (very rare): Adenomas, fibromas, endometriosis, hydatid cysts
- Malignant (very rare, less than 0.5% of all bladder cancers): Most adenocarcinoma
- Sister Mary Joseph nodules (adults): Umbilical metastases of primary tumors (if primary is known, usually from genital or GI tract)
- Others: Dermoid cyst, sebum cyst, spontaneous umbilical fistula from Crohn disease/Meckel's diverticulum, umbilicus, posterior rectus sheath, and skin cancers such as basal-cell and squamous-cell carcinoma
- Infection
- Omphalitis
- Infected urachal cyst
- Drainage
- Urachal remnant
- Patent urachus (50%)
- Blind urachus (30%)
- Urachal sinus (15%)
- Vesicourethral fistula (9%)
- Vesicovaginal fistula (9%)
- Vesicovaginal fistula (9%)

TREATMENT

GENERAL MEASURES

- Identify the abnormality and manage accordingly.

SURGERY/OFFICE PROCEDURES (2,3)

- Granuloma and umbilical polyp (infants): Very difficult to differentiate clinically. Treat with silver nitrate. If there is no response after two or three attempts, surgical excision may be necessary.

- Umbilical hernia: Up to 20% of infants, the majority will resolve by 3 yr of life.

- Umbilical polyp: Excision of urachal remnant.

- Urachal remnant: Surgical exploration with excision.
- If urachal cyst is infected, it may be treated initially with broad spectrum antibiotics and drainage.
- Complete excision can be performed once infection has subsided. Risk of malignant degeneration has been reported in the literature.
- Patent urachal duct: Urachal remnant fistula (enteric contents per umbilicus). Surgical exploration with excision needs prompt laparotomy and duct excision to avoid intra-abdominal infection.
- Medial diverticulum: Surgical exploration with excision.
- Urachal carcinoma:
  - Radical cystectomy or partial cystectomy with wide surgical margins and en-bloc resection of urachal remnant extending from bladder to umbilicus, posterior rectus sheath, and all tissue between medial umbilical ligaments is recommended for lower stage, resectable disease.
  - Partial cystectomy may offer a comparable oncologic outcome and less morbidity to radical cystectomy if tumor is completely resected (IC)
  - Failure to resect the umbilicus and positive surgical margins are associated with a worse outcome (IB).
- Bilateral pelvic lymph node dissection
  - Should follow the standard template for bladder cancer.
  - May be useful for staging but does not provide any survival advantage.
  - Surgical resection is particularly well-suited to a laparoscopic or robotic approach with comparable short-term outcomes.

ADDITIONAL TREATMENT

Radiation Therapy

Limited role for unresectable urachal carcinoma

Additional Therapies

- None

COMPLEMENTARY & ALTERNATIVE THERAPIES

- N/A

ONCONEUROLOGY

PROGNOSIS

- Minimal long-term sequelae when managed appropriately.
- Urachal carcinoma:
  - 5-yr overall survival: 27–80%, about 50% for locally advanced disease
  - Less than 20% for metastatic disease
  - 93% for disease confined to the urachus and bladder after surgical resection with bladder preservation
  - 69% for extravesical and perivesical disease after surgical resection with bladder preservation

COMPILATIONS

- Mortality related to the abdominolocalin and the specific treatment modality that is utilized.

Patient Resources

Urology Care Foundation: Urachal Abnormalities http://www.urologyhealth.org/urology/index.cfm?article=41

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Bladder Cancer, Adenocarcinoma
- Urachal Abnormalities
- Urachal Carcinoma

CODES

ICD-9

- 753.1 Urachal hernia without mention of obstruction or gangrene
- 759.89 Other specified congenital anomalies
- 772.3 Urachal hemorrhage after birth

ICD-10

- K42.9 Urachal hernia without obstruction or gangrene
- P51.9 Urachal hemorrhage of newborn, unspecified
- O89.8 Other specified congenital malformations

CLINICAL/SURGICAL PEARLS

- In the newborn, a granuloma is the most common cause of persistent drainage.
- Ultrasound is an accurate, minimally invasive imaging modality.
- Umbilical hernias may be seen in up to 20% of infants, but the majority will resolve by 3 yr of life.
- If surgical excision of a urachal remnant is performed, a bladder cuff should be taken if there is involvement of the dome of the bladder.
UNDERACTIVE BLADDER (DETRUSOR UNDERACTIVITY)
Michael J. Amirian, MD
Leonard G. Gomella, MD, FACS

**BASICS**

**DESCRIPTION**
- Detrusor underactivity (DU) often referred to as underactive bladder is a bladder contraction of reduced strength and/or duration.
- Results in prolonged bladder emptying.
- Failure to complete bladder emptying within a normal time span.
- Observed in many neurologic conditions and myogenic failure.
- DU is a common cause of lower urinary tract symptoms (LUTS) in both men and women.
- A wide range of terminology is currently applied in the literature.
- The only formal definition was from the International Continence Society (ICS) in 2002.

**EPIDEMIOLOGY**

**Incidence**
- Present in 9–48% of men and 12–45% of older women undergoing urodynamic evaluation for non-neurogenic LUTS (1).

**Prevalence**
- N/A

**RISK FACTORS**
- Overactive bladder (OAB) may lead to underactive bladder (UAB).
- Diabetes mellitus.
- Aging.
- Acute cerebrovascular accident (CVA).
- Multiple sclerosis (MS).
- Parkinson disease.
- Injury to spinal cord, cauda equina, and pelvic plexus.
- Pelvic surgery.
- Pelvic and sacral fractures.
- Herniated disc.
- Lesions of pudendal nerve.

**PATHOPHYSIOLOGY**
- Diabetic mellitus leading to diabetic cystopathy.
  - Metabolic derangement of Schwann cells.
  - Altered metabolism of glucose.
  - Ischemia.
  - Superoxide-induced, free-radical formation.
  - Impaired axonal transport.
- Alteration in physiology of detrusor smooth muscle cell.
- Aging.
  - Reduction in acetylcholinesterase-positive nerve.
- Reduced parasympathetic innervation.
- CVA.
- Cerebellar defect leading to detrusor areflexia.

**ASSOCIATED CONDITIONS**
- OAB syndrome.

**GENERAL PREVENTION**
- Diabetic patients.
  - Control blood glucose levels.
- Hypertension and hyperlipidemia control.
- Smoking cessation.

**DIAGNOSIS**

**HISTORY**
- History of neurologic injury or medical disorder.
- Recurrent episodes of urinary retention.
- Lower urinary tract symptoms.
  - Straining to urinate.
  - Sensation of incomplete bladder emptying.
  - Diminished and interrupted urinary stream.
  - Urinary urgency.
  - Rely on abdominal straining to urinate.
- Impotence.
  - Overflow, urge, or stress.
- Recurrent urinary tract infections.

**PHYSICAL EXAM**
- May reveal a distended bladder.
- Suspected or known neurologic injury due to pelvic or sacral injury.
- Testing of anal dermatomes.
  - Assessing perianal sensation.
  - Anal sphincter tone.
  - Bulbocavernosus reflex.
- Neurologic testing.
  - Deep tendon reflexes in the lower extremities.
  - Clonus.
  - Plantar responses.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Beyond routine urinalysis and culture, none specific.

**Imaging**
- Upper tract screening if obstruction suspected.

**Diagnostic Procedures/Surgery**
- Urodynamic evaluation (basis of current ICS definition of UAB).
  - Cystometry.
  - Long-curve with lack of sensation.
  - Low detrusor pressure.
  - Electromyography.
  - Usually normal.
  - May show sphincter denervation and uninhibited sphincter relaxation.
- Uroflowmetry.
  - Low peak flow.
  - Prolonged duration of flow.
  - Increased residual urine.

**Pathologic Findings**
- N/A

**DIFFERENTIAL DIAGNOSIS**
- Bladder outlet obstruction.
- Detrusor overactivity.
UNDERACTIVE BLADDER (DETRUSOR UNDERACTIVITY)

**TREATMENT**

**GENERAL MEASURES**
- Limited management available (3)
  - No validated, effective oral drugs, no FDA approved medications. All used off label.
  - Double void or straining to void
  - Avoidance of bladder overdistention
    - Indwelling urinary catheter
    - Intermittent catheterization (preferred)

**MEDICATION**

**First Line**
- α-Adrenergic blockers
  - Alfuzosin
  - Doxazosin
  - Terazosin
- Muscarinic receptor agonists
  - Bethanechol, carbachol
- Choline esterase inhibitors
  - Distigmine (Approved outside of US)

**Second Line**
- Potential therapy
  - Prostaglandin E2
    ◦ Increase detrusor contraction
    ◦ Relax the urethra

**SURGERY/OTHER PROCEDURES**
- Sacral nerve stimulation and intravesical electrical stimulation
  - Potentially beneficial in select patients
- Invasive surgical reconstruction
  - Latissimus dorsi muscle transposition to restore bladder function

**ADDITIONAL TREATMENT**

**Radiation Therapy**

**Additional Therapies**
- Experimental therapeutics:
  - Stem cell therapy
    ◦ Allow weak detrusor to improve contractility
  - Targeted gene therapy

**COMPLEMENTARY & ALTERNATIVE THERAPIES**

**ONGOING CARE**

**PROGNOSIS**
- Good prognosis with appropriate bladder management

**COMPLICATIONS**
- Urinary retention
- Urinary tract infections
- Damage to upper urinary tract

**FOLLOW-UP**

**Patient Monitoring**
- Post-void residual
- Uroflowmetry
- Urinalysis and urine culture

**Patient Resources**
- Underactive Bladder Foundation
  - www.underactivebladder.org

**REFERENCES**


**ADDITIONAL READING**


**CODES**

**ICD9**
- 596.59 Other functional disorder of bladder
- 789.21 Incomplete bladder emptying
- 789.99 Other symptoms involving urinary system

**ICD10**
- N31.8 Other neuromuscular dysfunction of bladder
- R33.8 Other retention of urine
- R39.19 Other difficulties with micturition

**CLINICAL/SURGICAL PEARLS**

The term DU remains surrounded by ambiguity and confusion with a lack of accepted terminology, definition, and diagnostic methods and criteria.

**U**
UNTENDED TESTES (CRYPTORCHIDISM)
Julia S. Barthold, MD, FACS

BASES
DESCRIPTION
• Cryptorchidism, or undescended testes (UDT), is failure of one or both testes to descend or remain descended in a dependent scrotal position.
• Position — Intra-abdominal (10–20%)
• Gubernaculum: Within inguinal canal
• Distal to external ring, including prepubic, pretesticular/gubernaculum, superficial inguinal pouch — True ectopic: Perineal most common
• Subclassifications — Congenital: Testis extrascrotal at birth
— Acquired: Testis extrascrotal at birth but found in an extrascrotal position at a subsequent time (T)
— Delayed diagnosis of primary UDT
— After inguinal surgery
— After spontaneous postnatal descent (recurrent cryptorchidism)
— Vanishing: Blind-ending spermatic vessels and vas deferens in a boy initially diagnosed with UDT

EPIDEMIOLOGY
Incidence
• 2–4% of full-term boys
• Up to 30% of premature boys (<37 weeks gestational age)
• Up to half descend spontaneously in the first 3–6 months of life but some will reascend
• Tectes of premature boys are more likely to descend and may take a year or longer

Prevalence
• 1% of boys at 1 year of age
• Up to 4% of boys undergo orchidopexy for UDT during childhood, presumably related to risk of acquired UDT
• Up to half of boys present with acquired UDT

RISK FACTORS
• Increased incidence in families (2)
— Fathers, brothers, identical twins, monozygotic twins
— Low birth weight: Prematurity or SGA
— Maternal environment
— Retardate testes is a risk factor for acquired UDT in some individuals
— Unilateral — bilateral
— Risk of ascent 7–32% (3)
— Normal testes frequently retractile >6 mo up to puberty, peak at 4–7 y
— Environmental exposure — endocrine and estrogenic compounds in animal models but weak evidence for etiology in human population

Genetics
• Rare variants of INSL3 (or its receptor RXFP2)
• Possible association with AR or ESR1 variants
• Likely polygene/multifactorial

PATHOPHYSIOLOGY
• Failure of complete testicular descent
• Requires normal development and function of the gubernaculum
• Arises from intermediate mesoderm: 1st trimester, enlarges 2nd trimester, regresses and then regresses 3rd trimester—birth
• Requires stimulation by testicular androgens and INSL3

Acquired UDTs are frequently located in the superficial inguinal pouch and in most cases represent primary undescended testes not clinically identifiable until a later age

ASSOCIATED CONDITIONS
• Intra- or extrascrotal persistent vesicovaginal sinus
— 50–90%, increased incidence in younger boys
— Rarely clinically apparent
• Epididymal anomalies
— Long-looping most common
— Detachment of caput
— Atresia rete
— Association with patent processus vaginalis
— Clinical misdiagnosis
• Hypoplasia
• Abdominal wall defects
— Prune Belly (Blind) syndrome; omphalocele; gastrochisis
• Neurologic and musculoskeletal diseases
— Myelomeningocele, cerebral palsy
• Component of over 30 syndromes
• Abnormal Leydig cell function
— Subtle reduction in testosterone (T) and/or increased LH
— Low incidence in non-syndromic UDT
• Disorders of sex differentiation (DSD)
— Usually associated with abnormal urethral and/or penile development
— 46XX congenital adrenal hyperplasia (CAH) with complete penile development; very rare; bilateral non-palpable testes; urgent diagnosis in newborn due to risk of salt wasting

GENERAL PREVENTION
Uncommon

DIAGNOSIS
HISTORY
• Family history of UDT
• History of inguinal hernia and/or surgery
• Maternal exposures or illness during pregnancy
• Birth history: Gestational age and birth weight
• Physical exam:
— Assess scrotal development: May be hypoplastic
— Assess penile development
— Hypoplasia
— Microopenis (<2 SD below mean for age)
— Ambiguous genitalia (DSD)
— Continual periodic exams to assess for spontaneous testicular descent for at least 6 mo
— Assess maintenance of scrotal position
— After spontaneous descent
— Older boys with retractile testes
— Yearly exam, warm room, warm hands, relaxed child if possible
— Upright cross-legged position or supine with legs abducted
— Evidence that a nonpalpable testis is absent
• Intrascrotal “nubbin” = vanishing testis
• Congenital testicular hypoplasia (length ≤1.8 cm) (4)

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• Bilateral nonpalpable testes: No testing
• Bilateral nonpalpable testes
— Rule out CAH in newborns: Karyotype, electrolytes, 17-OH progesterone
— Hormone levels: T and gonadotropin levels during postnatal surge at 1–3 mo
— Low anti-Müllerian hormone (AMH)
— Abnormal NGS stimulation test

Imaging
• Imaging rarely indicated (5)
— US inaccurate to determine position
— MRI/US more accurate but rarely used
— Potentially useful in selected cases after referral to specialist
— Observe boys with a history of palpable testes
— Rule out to identify spermatic vessels after laparoscopy or abdominal exploration

Diagnostic Procedures/Surgery
• Laparoscopy
— Procedure of choice for localization and determination of status of nonpalpable testes
— Open internal ring: Distal testes likely
— Closed internal ring: No vessels; look for high abdnominal or inguinal testes (image); onamalatic vessels suggests distal “vanishing” testes
— Retroperitoneal exploration to kidney may be required

Pathologic Findings
• Testicular biopsy
— Not standard practice at orchidopexy
• Reduced spermoprosis numbers in UDT
• Reduced sperm (suck dark) spermoprosis most predictive of spermatogenic function
• Leydig cell hyperplasia and/or Sertol cell degeneration—limited data

DIFFERENTIAL DIAGNOSIS
• Nonobstructive UDT
• Vanishing testis: Confirmation of blind-ending spermatic vessels; atretic testis, torsion, or vascular accident
• True agenesis
• Rare; bilateral failure of Wolfian duct development and Müllerian duct regression

TREATMENT
GENERAL MEASURES
• Observe for spontaneous postnatal descent
• Identify clinical hernia or torsion
• Reduce permanent, stable scrotal position by 6 mo of age, then yearly observation
• Observe longer for descent if premature
• Plan surgery at 6–18 mo of age if testis fails to descend to improve testicular growth (6)
• Plan surgery at diagnosis in boys with acquired UDT

MEDICATION
• Hormonal treatment not efficacious (7)
• NGS injections or LHRH nasal spray (not available in the United States)
• Slight benefit over placebo; efficacy 15–20%
• Possible adverse effects: Pigmentation, transient pubic hair, behavior changes, adverse testicular effects
• Inadequate follow-up to rule out recurrence
Surgery/Other Procedures

Alert
In cases of nonpalpable tests, the surgeon must identify the spermatic vessels and confirm that they are blind-ending or associated with an intact testis.

- Surgery vs treatment of choice (3)
- Approach depends on testis palpability
  - Inguinal orchidopexy
    - Standard approach for palpable testis
    - Mobilize testes via inguinal incision
    - High ligation of hemiasac if present
    - Transection of lateral retroperitoneal fascial bands to provide additional length
    - Mobilization performed proximal to spermatic vessels (Penrose nonwoven) rarely needed
    - Higher abdominal counterincision possible if further mobilization needed
  - Placement of testis in sub-Dartos pouch without tension
  - Success rate = 95%
  - Complications: Testicular retraction, testis, cord or nerve injury, bleeding, infection, recurrent hernia (all rare)
  - Primary scrotal orchidopexy (Bland)
    - Increasingly reported as preferred approach for testes distal to external inguinal ring
    - Mobilization of testes and cremasteric muscle/vasa from cord via scrotal incision
    - Standard fixation in subdartos pouch
    - Best for low tests without associated patent processus vaginalis
    - Repair of hernia through scrotal approach along long-term failure rate uncertain and may be higher (18)
  - Similar success and complication rates as compared to inguinal orchidopexy
  - Laparoscopic orchidopexy
    - Procedure of choice for abdominopelvic or high canicular testes near internal ring
    - Laparoscopy for testis localization with two additional lower quadrant ports
    - Mobilization of lateral and medial peritesticular attachments to cord
    - Transection of peritoneum over cord
    - Transection of mobilized testis through existing or neo-inferior and standard fixation in subdartos pouch
    - Success rate = 72–91%
    - Open abdominal orchidopexy
      - High inguinal incision: Potentially more limited access to proximal cord
      - Mobilization similar to laparoscopic approach
      - Success rate = 77–86%
  - Fowler-Stephens orchidopexy
    - One or two-stage procedure via open or laparoscopic approach
    - Required for high tests and/or short spermatic vessels
    - Maintain vascular supply between vas and spermatic vessels
    - Transection of spermatic vessels
    - Success rates 80–94%
  - Orchidectomy of unilateral UDT
    - Consider in high abdominopelvic tests; short vas deferens, hydropsplastic testes, adolescent/young patient
  - Special considerations
    - Testicular biopsy in dysmorphic testis; consider in high abdominal testis, short vas deferens, hypoplastic testes, adolescent/young patient
    - Testicular atrophy; increased risk for abdominal hernia
    - Malignancy: Overall relative risk 2.9–6.5
    - Pregnancy
      - Conception success essentially normal in unilateral, 90%; reduced in bilateral, 30–50%
    - Malgnancy
      - Overall relative risk 2.9–6.5
      - Palpation
        - Femal prolapse/thrombosis; risk may be decreased by prophylactic orchidopexy
      - Testis position may influence histology
      - Abdominal: Seminoma more common
      - Scrotal: Nonseminomatous germ cell tumor more common
  - Complications
    - Testicular atrophy; increased risk for abdominal hernia
    - Torsion risk
      - 10
    - Paternity
      - Testicular position may influence histology
      - Conception success essentially normal in unilateral, 90%; reduced in bilateral, 30–50%
      - Abnormal semen analysis: Highly variable in undescended testes
      - Scrotal: Nonseminomatous germ cell tumor more common

Additional Treatment

Additional Therapies
Adjuvant hormonal therapy may improve germ cell number and/or maturation; long-term efficacy uncertain

Ongoing Care

Prognosis
- Testicular biopsy in dysmorphic testis; consider in high abdominal testis, short vas deferens, hypoplastic testes, adolescent/young patient
- Transection of spermatic vessels
- Required for high testis and/or short spermatic vessels
- High inguinal incision; Potentially more limited access to proximal cord
- Success rates 72–91%
- Similar success and complication rates as compared to inguinal orchidopexy
- Laparoscopy for testis(es) localization with two additional lower quadrant ports
- Mobilization performed proximal to spermatic vessels (Penrose nonwoven) rarely needed
- Higher abdominal counterincision possible if further mobilization needed
- Repair of hernia through scrotal approach along long-term failure rate uncertain and may be higher (18)
- Similar success and complication rates as compared to inguinal orchidopexy

Follow-Up

Patient Monitoring
- Testicular development and position during peripubertal period
- Counseling regarding potential subfertility
- Testicular self-exam
- Counseling regarding potential subfertility
- Microvascular autotransplant requires specific expertise; solitary tests in low risk patients
- Subcutaneous tests placed as last resort to maintain endocrine function

Additional Reading
- Throup J, Cortes D. Surgical treatment and follow up on undescended tests. Pediatr Endocrinol Rev. 2009;7:38
- See Also (Topic, Algorithm, Media)
  - Disorders of Sex Development (DSD)
  - Genitourinal Mass, Male, and Female
  - Groin Hernia, Pediatric
  - Groin/inguinal Mass, Male, and Female
  - Disorders of Sex Development (DSD)
- Undescended Testes (Cryptorchidism) Algorithm
  - Undescended Testes (Cryptorchidism) Images
- Codes
  - ICD-9
    - 752.31 Undescended testes
    - 752.32 Retractile testes
    - 752.89 Other specified anomalies of genital organs
  - ICD-10
    - O37.9 Undescended testes, unspecified
    - O37.11 Abdominal testis, unilateral
    - O55.22 Retractile testes

Clinical/Surgical Pearls
- Spontaneous testicular descent is common in the first 6 mos of life but tests may re-ascend.
- Surgery is the standard treatment.
- Tests that appear to be scrotal at birth can be later diagnosed as cryptorchid with potentially increased risk in retroperitoneal tests.
- Routine tests exams with well-child visits are indicated.

References
URACHAL CARCINOMA
Michael O. Koch, MD, FACS
Andrew D. Strine, MD

DIAGNOSIS

HISTORY
- Increasing incidental detection due to routine use of imaging.
- Often asymptomatic until more advanced.
- Presenting signs and symptoms:
  - Hematuria (most common) or mucosuria
  - Abdominal pain
  - Voiding symptoms or urinary tract infection (UTI)
  - Uterine drainage
  - Urethral mass

PHYSICAL EXAM
- Palpable urachal mass
- Large, fixed mass or concurrent ascites
- Cystoscopy with transurethral biopsy or resection

DIAGNOSTIC TESTS & INTERPRETATION
- Urothelial carcinoma markers:
  - CA-125 and CA 19-9
  - Urine cytology to evaluate for a urothelial malignancy
  - Urinalysis and urine culture to evaluate for infection and metastatic disease.

DIAGNOSTIC EUS & IMAGING
- Abdominal ultrasound:
  - Often obtained during the initial evaluation and in follow-up
- CT or MRI of the abdomen and pelvis with IV and PO contrast:
  - May be elevated in 40–60% of patients
- Bone scan if advanced disease, bony symptoms, or metastasis
- Chest x-ray or CT of chest for staging
- Hematologic and chemistry panels
- Pathologic findings:
  - Favorable (well-differentiated) histology may have a better prognosis than unfavorable (poorly differentiated) histology
  - Absence of urothelial dysplasia or carcinoma
  - Presence of urachal remnant in tumor
  - Presence of urachal remnants in tumor

DIFFERENTIAL DIAGNOSIS
- Vesicourachal diverticulum
- Urachal neoplasms: Adults
  - Benign (very rare): Adenomas, fibromas
  - Malignant: adenocarcinoma
- Vesicourachal fistula from Crohn disease
- Other malignancies:
  - Bladder cancer
  - Kidney cancer
  - Colon cancer
  - Prostate cancer

DIFFERENTIAL DIAGNOSIS
- Urachal remnants, including patent urachus, urachal sinus, cyst, and diverticulum

GENERAL PREVENTION
- None

DESCRIPTION
- Urachal carcinoma is a rare non-urothelial malignancy (almost always adenocarcinoma) usually involving the dome of the bladder due to direct extension from the urachal ligament, the structure from which this tumor arises.
- Rare malignancy
- Less than 1% of all bladder cancers
- Almost exclusively occurs in adults and most commonly in the 4th to 5th decades.
- Adenocarcinoma is the most common histologic subtype.
- Staging is distinct from bladder cancer but not standardized.
- Urachal neoplasms: Adults
  - Urachal remnants
  - Urachal cyst
  - Patent urachus
  - Vesicourachal diverticulum
  - Urachal neoplasm: Adults
    - Benign (very rare): Adenomas, fibromas, fibroadenomas, fibromyxomas, hamartomas
    - Malignant (very rare): less than 0.5% of all bladder cancers

RISK FACTORS
- Nature
- Unknown due to its rarity and often asymptomatic nature
- Prevalence
- 1 in 5 million cases annually
- Incidence
- EPIDEMIOLOGY
- URACHAL CARCINOMA
- Originates from the urachus.
- Serves as a communication between the developing bladder and allantois but becomes a fibrous band by 12 weeks of gestation and is recognized as the median umbilical ligament in adults.
- Composed of urothelium-lined lumen of epithelial origin as well as submucosa and smooth muscle of mesenchymal origin.
- Any layer may undergo a malignant transformation.
- Locally invades into muscularis propria and perivesical fat with demarcation from urothelium.
- Metastasizes to pelvic lymph nodes, lungs, liver, and bone.

ASSOCIATED CONDITIONS
- Urachal remnants, including patent urachus, urachal sinus, cyst, and diverticulum

GENERAL PREVENTION
- None

DIAGNOSTIC PROCEDURES/SURGERY
- Cystoscopy with transurethral biopsy or resection:
  - Evaluate for intravesical invasion, drop metastases, or metastatic disease.
  - Any tumor arising from the dome of bladder should be considered urachal in origin until proven otherwise.
- Percutaneous biopsy may be performed but raises a theoretical concern for seeding the biopsy tract.

PATHOLOGIC FINDINGS
- A majority (50–60%) is adenocarcinoma with glandular features and prostatic mucin.
- Similar immunohistochemistry to colorectal adenocarcinoma (1):
  - Strong reactivity for CDX2 and lack of diffuse nuclear reactivity for α1-antichymotrypsin is more suggestive of urachal origin.
  - No immunohistochemical markers to differentiate adenocarcinoma originating from the urachus and bladder
- Other subtypes:
  - Sarcoma
  - Squamous-cell carcinoma
  - Urothelial carcinoma

PATHOLOGY
- Definitive:
  - Tumor located in the dome of bladder or along midline
  - Demarcation between tumor and urothelium
  - Presence of urachal remnant in tumor
  - Enteric-type pathology
  - Absence of urothelial dysplasia or carcinoma
  - Absence of cystic glandularis and pylorus
  - Favorable (well-differentiated) histology may have a better prognosis than unfavorable (poorly differentiated) historical tumors

DIFFERENTIAL DIAGNOSIS
- Vesicourachal diverticulum
- Urachal neoplasm: Adults
**TREATMENT**

**GENERAL MEASURES**
- Typically manifests as locally advanced or metastatic disease.
- About 20% of patients present with stage 1 (no invasion) or 2 (invasion confined to urachus) disease based on ICD staging system in most series.
- Management is controversial but typically involves surgical resection.
- Chemotherapy and radiation therapy are generally thought to be less effective and reserved for higher stage disease.

**MEDICATION**
- Chemotherapy is typically reserved for unresectable or metastatic disease.
- No standard regimen established.
- Regimens using 5-fluorouracil, cisplatin, and either uracil or gemcitabine and docetaxel are superior to others.
- Median overall survival of 20 months reported in patients with at least a partial response to established disease (48).
- No definitive role for neoadjuvant chemotherapy.

**SECOND LINE**
- No definitive role but often used as an adjuvant therapy for margin- and node-positive disease as well as recurrences.

**SURGERY/OTHER PROCEDURES**
- Radical cystectomy or partial cystectomy with wide surgical margins and en bloc resection of urachal remnant extending from bladder to umbilicus, posterior rectus sheath, and all tissue between medial umbilical ligaments is recommended for lower stage, resectable disease.
- Partial cystectomy may offer a comparable oncologic outcome and less morbidity to radical cystectomy if tumor is completely resected on clinical examination.
- In case of positive surgical margins, additional neoadjuvant chemotherapy and radiation therapy may be beneficial.
- For patients initially staged as locally advanced disease, surgical resection is not recommended, and patients should be considered for neoadjuvant therapy with chemotherapy and radiation therapy, respectively (1).

**ADDITIONAL TREATMENT**
- Radiation Therapy
  - Limited evidence.
  - Occasional use for unresectable or metastatic disease (with chemotherapy) or as an adjuvant therapy for margin- and node-positive disease as well as recurrences.
- Median overall survival of 19.5 mo and 21 mo reported after radiation therapy alone and radiation therapy with chemotherapy, respectively (38).

**ADDENDUM**
- Complementary & Alternative Therapies
  - None

**ONGOING CARE**

**PROGNOSIS**
- Clinical and pathologic staging is the most important predictor of survival (1-3).
- Two staging systems: Chahed and Ashley (6) (See Section II: Urachal Carcinoma Staging Systems).
- 5-yr overall survival rate ranges from 27 to 80%, depending on the series.
- About 50% for locally advanced disease (1-3) (9% for disease confined to the urachus and bladder after surgical resection with bladder resection (5)).
- 89% for extravesical and peri-urachal disease after surgical resection with bladder preservation (10).

**COMPLICATIONS**
- Bleeding
- Infection
- Injury to surrounding organs
- Urinary tract
- Lymphocele
- Postoperative cardiopulmonary complications, including myocardial infarction, deep vein thrombosis, and pulmonary embolism
- Development of recurrent or progressive disease

**FOLLOW-UP**

**Patient Monitoring**
- No standard schedule for oncologic surveillance established.
- Adaptation from bladder cancer
  - Radical cystectomy
  - History and physical examination, electrolytes, serum creatinine, and urine cytology every 3–6 mo for 2 yr and then as clinically indicated
  - Imaging of the chest, abdomen, and pelvis every 6 mo for 2 yr and then as clinically indicated
  - Partial cystectomy
  - Same as above
  - Cystoscopy every 3–6 mo for 2 yr and then at increasing intervals as clinically indicated

**Patient Resources**
- Bladder Cancer, National Cancer Institute, National Institutes of Health
  - www.cancer.gov/cancertopics/types/bladder
- Urachal cancer, Office of Rare Diseases Research, National Institutes of Health
  - rarediseases.info.nih.gov/guidelines/7886/urachal-cancer-resourcekit
- Urachal Anomalies, Urinary Tract Foundation, American Urologic Association
  - www.urologyhealth.org/urology/index. cfm?index=41

**REFERENCES**

**ADDITIONAL READING**

**CLINICAL/SURGICAL PEARLS**
- It is difficult to differentiate between an infection and urachal carcinoma for symptomatic urachal lesions.
- There should be a high clinical suspicion for urachal carcinoma in any adult with an urachal lesion.
- Any tumor arising from the dome of bladder should be considered urachal carcinoma until proven otherwise.
- Surgical management of urachal carcinoma should involve a complete resection of the urachus and umbilicus with wide surgical margins.
URETER AND RENAL PELVIC TUMORS, GENERAL CONSIDERATIONS

Julie M. Riley, MD
Timothy D. Averch, MD, FACS

DESCRIPTION
- Tumors of the ureter and renal pelvis are relatively rare.
- Tumors are most often malignant and account for 5% of all urothelial tumors; most commonly TCC (transitional cell carcinoma), also called urothelial cell carcinoma (UCC).

Epidemiology
- Incidence
  - 1 in 113,333 or ~2400 cases/yr.
  - 7% of all kidney tumors.
- Uterine TCC account for 1 in every 25 upper tract tumors.
- More common in Caucasian population; Asians more often have high-grade tumors.

Prevalence
- Rare.
- Prevalence rate: 6th-7th decade.

Risk Factors
- Smoking: Risk from 2.6-4.0.
- Increases with higher dose and duration.
- History of bladder cancer: 2–25% of patients with bladder cancer develop upper tract TCC.
- Occupational exposure: Similar to bladder cancer; increases with higher dose and duration.
- History of bladder cancer: 2–25% of patients with bladder cancer develop upper tract TCC.
- Smoking: Risk from 4.0 to 5.5.
- Rare benign tumors include inverted papilloma and papilloma.
- Rare malignant tumors include sarcoma, SCC, adenocarcinoma, and carcinocarcinoma.
- Lynch syndrome.
- Black Foot disease: Vasculopathy in Taiwan; arsenic contamination of water.
- Balkan nephropathy: Endemic to Bulgaria, Greece, and Romania.
- Cyclophosphamide: Hemorrhagic cystitis and carcinoma; 9 times increased risk of carcinoma after a dose of 10–15 g over 10 yr; tend to be women.
- Analgesic abuse: All components implicated;
  - Coffee: Minor contribution, relative risk of 1.3.
  - Red meat: Risk from 2.6–4.0.
- Asymmetric azoic urea (color dye, fabrics).
- Naphthalenes, arsine (arsenic) in coal, cigarette smoke.
- High-risk jobs: Autoworkers, leather workers, dry cleaners, dental technicians, beauticians, and painters.
- Coffee: Minor contribution, relative risk of 1.3.
- Analgesic abuse: All components implicated; higher risk with phenacetin abuse.
- Latency of 25 yr.
- Most have no family history of disease.
- Familial clustering exists; difficult to determine if related to environmental factors.
- Low-grade superficial TCC: p16 and p16 loss (chromosome 9p).
- High-grade TCC: p53 loss (chromosome 17p).
- Amplification and overexpression of genes that code for growth factors or their receptors
  - EGFR (chromeosome 7); loss of tumor suppressor gene p16.
- Smoking cessation.
- Avoid or limit chronic analgesia use.
- Avoid exposure to implicated toxins.

PHYSICAL EXAM
- Usually normal.
- Pain or abdominal mass with advanced disease.

DIAGNOSTIC TESTS & INTERPRETATION

Imaging
- Intravenous urogram (IVP): 50–75%.
- Radiolucent filling defect, irregular and continuous with the wall.
- 10–30% show obstruction or non-visualization of the collecting system, which indicates more invasive disease.
- Ascites contralateral kidney for lesion and function.
- Retrograde pyelography (RGP): Better visualization than IVP (>75% accuracy).
- Arteriography, CT angiography.
- Used only if not possible to visualize collecting system via retrograde approach utilizing a percutaneous nephrostomy tube.

Pathologic Findings
- Unilateral or abdominal mass with advanced disease.

Histology
- Urothelial carcinoma of the bladder
- Urothelial carcinoma: Papillary (exophytic).
- Selective cytology barbotage (repeated injection and aspiration of saline): Localize tumor.
- Retrograde pyelography: Better visualization than IVP (>75% accuracy).
- Papillary and squamous cell carcinoma.
- Bucchial glosses.
- High-grade relative risk of bleeding and perforation.
- Selective chemotherapy (image).

Intravenous pyelogram (IVP):
- Used in all cases for staging TCCs due to difficulty in determining the depth of invasion, particularly renal pelvic TCC.
- 10–30% show obstruction or non-visualization of the collecting system.
- Accuracy increases with increasing grade of tumor.

Magnetic resonance imaging (MRI):
- Primary imaging study used for diagnosis and staging of tumors.
- CT urography: Usually normal.

Urine analysis: Hematuria (gross or microscopic).
- Complete blood count: Erythropoietin (EPO) levels.
- Bone marrow biopsy: Metastatic disease.
- Urinary cytology: False negatives.
- Voided specimen: Low sensitivity for upper-tract tumors.

Computed Tomography Urogram (CTU): Primary imaging study used for diagnosis and staging of tumors.
- Magnetic resonance imaging (MRI): Staging.

Antegrade pyelography:
- Used only if not possible to visualize collecting system via retrograde approach utilizing a percutaneous nephrostomy tube.
- Retrograde pyelography: Better visualization than IVP (>75% accuracy).
- Arteriography, CT angiography.
- Used only if not possible to visualize collecting system via retrograde approach utilizing a percutaneous nephrostomy tube.

Intravenous urogram (IVP):
- Used in all cases for staging TCCs due to difficulty in determining the depth of invasion, particularly renal pelvic TCC.
- Radiolucent filling defect, irregular and continuous with the wall.
- 10–30% show obstruction or non-visualization of the collecting system.
URETER AND RENAL PELVIC TUMORS, GENERAL CONSIDERATIONS

DIFFERENTIAL DIAGNOSIS
- Malignant filling defect of the ureter and renal pelvis:
  - TCC, ureteral or renal pelvic: Urothelial carcinoma
  - Adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  - Renal cell carcinoma (RCC)
- Benign filling defect of the ureter and renal pelvis:
  - Air, gas-forming, infectious, or due to fistula
  - Blood clot
  - Pseudoaneurysm
  - Hemangiomata
  - Inflammatory lesions: Granuloma, miliary peliosis, tuberculous
  - Inverted papilloma
  - Radiolucent calculus
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Renal or sloughed papilla
  - Diffuse or focal patterns
  - Protein matrix
  - Mucus: Urinary diversion patients
  - Renal or sloughed papilla
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Ureteritis or pyelitis cystica
  - Mucus: Urinary diversion patients
  - Renal or sloughed papilla
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Ureteritis or pyelitis cystica
  - Mucus: Urinary diversion patients
  - Renal or sloughed papilla
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Ureteritis or pyelitis cystica
  - Mucus: Urinary diversion patients
  - Renal or sloughed papilla

TREATMENT

GENERAL MEASURES
- If positive pathology is the only sign of upper tract TCC, close follow-up is required.
- Standard treatment is surgical for most benign and malignant lesions.

MEDICATION

First Line
- Hikth

Second Line
- Immobilization therapy with BCG or mitomycin not proven to increase survival
- Appears to be safe
- May be used in multiple superficial tumors or bilateral disease
- Difficult to deliver the agent in adequate doses and dwell-time

SURGERY/OTHER PROCEDURES
- Standard treatment is nephroureterectomy (NU) or laparoscopic or open
- Renal sparing surgery indicated: Solitary kidney, bilateral disease, poor function of contralateral kidney, or low grade and stage
- Survival related to stage and grade of tumor rather than to treatment modality
- Radical NU and excision of bladder cuff: 60-90% 5 yr survival (low grade and stage)
- Radical lymphadenectomy not shown to improve survival
- Endoscopic approach to bladder cuff resection has slightly higher rate of bladder recurrence (1)
- Endoscopic treatment (uroscopy (URS) or percutaneous:
  - Indications: solitary kidney, poor renal function, bilateral disease, moderate tumor burden, low-grade, poor surgery candidate
  - Risk of perforation is higher than that in bladder (overall complication rate: 7%)
  - Requires close follow-up due to high recurrence rate (recurrence-free survival ~ 20% at 10 yr (2)
  - Laser ablation in low-grade or multiple tumors
  - Seeding of perinephric space is low (0.03%) (3)
- Segmental ureteral resection: Solitary low-grade upper and mid-ureteral lesions
- Recurrence rate of 6%, higher if multifocal
- Distal ureterectomy and ureteroneocystostomy: Distal, solitary ureteral lesion
- Benign tumors such as fibroepithelial polyp or inverted papilloma: Endoscopic management

ADDITIONAL TREATMENT

Radiation Therapy
Can be used for advanced tumors not amenable to surgery, with decreased efficacy

Additional Therapies
- Neoadjuvant/adjuvant chemotherapy has not been established as in bladder cancer (3)
- Capital therapies have been successful

Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS
- Recurrence site related with more aggressive resection: tumor:
  - 40% recurrence with nephrectomy
  - 32% with nephrectomy plus partial ureterectomy
  - 24% with nephrectomy plus subtotal ureterectomy
  - 12% with NU
  - Prognosis largely unchanged in locally advanced disease
  - Better survival for tumors in renal pelvis than ureteral in T3 or higher disease

COMPLICATIONS
- Obstruction of urinary tract
- Development of metastatic disease

FOLLOW-UP

Patient Monitoring
- Uroscopy with cystoscopy every 3–6 mo for 2–3 yr, then yearly
- 6-mo CT urogram + chest x-ray, then annually
- URS is more sensitive than radiologic techniques for follow-up of upper tract TCC

Patient Resources
- Urology Care Foundation http://www.urolgyhealth.org/urology/index.cfm?artid=39

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Reference Tables: TTM: Renal Pelvis and Ureter Cancer
- Reference Tables: TTM: Renal Pelvis and Ureter Cancer
- Reference Tables: TTM: Renal Pelvis and Ureter Cancer

CODES

ICD9
- 188.1 Malignant neoplasm of renal pelvis
- 188.2 Malignant neoplasm of ureter

ICD10
- C44.9 Malignant neoplasm of unspecified renal pelvis
- C44.9 Malignant neoplasm of unspecified ureter

CLINICAL/SURGICAL PEARLS
- Universal and renal pelvic tumors are rare
- Management remains surgical with NU being the gold standard
- Endoscopic management is becoming more accepted but the risk of under staging and under grading remains
- Close follow-up is warranted and uroscopy remains the most sensitive surveillance test.
ASSOCIATED CONDITIONS
Pathophysiology
- Chronic inflammation
- Struvite stones
- Xanthogranulomatous pyelonephritis
- Paraneoplastic syndrome
- Chronic infection
- Hypercalcemia

BASICS
DESCRIPTION
- Squamous-cell carcinoma (SCC) of the renal pelvis and ureter is a rare but aggressive tumor characterized by nests of squamous cells with hyperchromatic nuclei and prominent keratin production.
- Most common non-urothelial tumor of the upper urinary tract.

PREVALENCE
- Prevalence unknown due to rarity of tumor.
- 6-15% of all upper tract urothelial cancers
- 0.5-0.8% of all malignant renal tumors
- Most common non-urothelial tumor of the upper urinary tract.

RISK FACTORS
- Prior percutaneous nephrolithotomy
- Analgesic abuse
- Parasitic infection
- Chronic pyelonephritis or pyonephrosis
- Struvite stones
- Genitourinary tuberculosis
- Presumed that chronic irritation of urothelium to be associated with chronic infection and inflammation

DIAGNOSIS
HISTORY
- History of chronic renal infections or stones
- Vague abdominal or flank pain
- Gross hematuria
- Lab:
  - Hematuria
  - Pyuria
  - Serum creatinine may be elevated due to tumor infiltration, obstruction, chronic infection, or scarring
  - Paraneoplastic syndrome which may resolve following resection includes:
    - Hypercalcemia
    - Thrombocytosis
    - Keratin pearls and intercellular bridges may not be apparent in advanced cases

DIAGNOSTIC TESTS & INTERPRETATION
- Imaging:
  - Diagnosis suggested (but not definitive) with radiologic imaging
  - Excretory imaging useful (including intravenous pyelogram, CT urogram) and may demonstrate:
    - Filling defect
    - Solid mass w/ or w/o calcifications
    - Hydronephrosis
  - Oncologic pathology confirmed, CT or MRI/MRA necessary for surgical planning
  - Vascular anatomy
  - Presence of metastases
  - Evaluation of contralateral renal unit
  - Size and extent of tumor

Pathologic Findings
- Most moderately or poorly differentiated
- Gross (180):
  - Nonspecific symptoms:
    - Local symptoms more common than those with TCC
  - Nonspecific symptoms:
    - Anorexia
    - Lethargy
    - Weight loss
  - Physical exam:
    - Flank or abdominal mass may be present with advanced disease
    - May have calcifications
    - Definitive diagnosis confirmed following nephroureterectomy (see TREATMENT)

DIFFERENTIAL DIAGNOSIS
- Primary renal neoplasms
  - Renal cell carcinoma
  - Urothelial cancer
  - Wilms tumor

- Secondary renal neoplasms
  - Metastasis to kidney
  - Metastasis to kidney (breast, lung, and others)

- Benign renal masses
  - Xanthogranulomatous pyelonephritis
  - Rare form of chronic pyelonephritis
  - Angiomyolipoma
URETER AND RENAL PELVIS, SQUAMOUS CELL CARCINOMA

TREATMENT

GENERAL MEASURES
Surgery (nephroureterectomy) is mainstay of treatment (3)[C]

MEDICATION
First Line
Medical therapy not effective although some patients require broad-spectrum antibiotics in the setting of concurrent infection

Second Line
N/A

SURGERY/OTHER PROCEDURES
Referent standard treatment is surgical excision (radical nephroureterectomy with excision of bladder cuff) (3)[C]
Role of retroperitoneal lymph node dissection controversial
For those patients with infection, pre- and post-operative antibiotics may be required

ADDITIONAL TREATMENT
Radiation Therapy
Occasionally used for adjuvant treatment following surgery; however shown to have little benefit (1)[C]

ADDITIONAL TREATMENT
Complementary & Alternative Therapies
No complementary therapies have shown benefit

ONGOING CARE

PROGNOSIS
• Generally poor if found at advanced stage
  – Median survival of 7–14 mo postoperatively (2–4)[C]
  – Median 5-yr survival: 7.7% (3)[C]
• Tumor stage at diagnosis most important for prognosis (3)[C]
• Grade has been found to add little value (3)[C]

COMPLICATIONS
• Renal insufficiency or failure
  • Metastatic disease (3)[C]
  • Regional lymph nodes
  • Liver
  • Bone

FOLLOW-UP
Patient Monitoring
• Limited data for patient monitoring
• Similar to TCC of upper tract
  – Urine cytology and cystoscopy every 3–4 mo for first 2 yr
  – Value of cystoscopy questionable due to low number of concurrent bladder cancers
  – Metastatic workup every 6–12 mo, depending on stage
    – Chest imaging
    – CT abdomen/pelvis
  – Monitor renal function periodically

ADDITIONAL READING

CLINICAL/SURGICAL PEARLS
• SCC of upper tract is the most common non-urothelial cancer of the renal pelvis and ureter
• A few symptoms manifest, but once hematuria and pain present, often advanced stage.
• Usually presents as advanced disease and has poor prognosis at this stage.
• Nephroureterectomy is standard of care with chemotherapy and radiation of limited benefit.

ICD-9
189.1 Malignant neoplasm of renal pelvis
189.2 Malignant neoplasm of ureter

ICD-10
C65.1 Malignant neoplasm of right renal pelvis
C65.9 Malignant neoplasm of unspecified renal pelvis
C66.9 Malignant neoplasm of unspecified ureter
URETER AND RENAL PELVIS, UROTHELIAL CARCINOMA

Emma F.P. Jacobs, MD
Michael O. Koch, MD, FACS

DESCRIPTION
Urothelial carcinoma (formerly known as transitional cell carcinoma or TCC) is an epithelial neoplasm of the urinary, renal pelvic, and calyces.

Epidemiology
Incidence
- 5–10% of renal tumors are renal pelvis TCC
- 2–5% of urothelial tumors occur in the upper urinary tract (UUT)
- Peak incidence of 10 per 100,000 yr in 75–79 age group
- Male age at presentation is 65, seldom appear before age 40 yr.
- Incidence is increasing.

Prevalence
Poor data available given rarity of condition.

Prevalence
Incidence
EPIDEMIOLOGY

DESCRIPTION
Urothelial carcinoma (formerly known as transitional cell carcinoma or TCC) is an epithelial neoplasm of the urinary, renal pelvic, and calyces.

Clinical Features
- Male
- White
- Typically bilateral, multifocal, low-grade
- Renal pelvic TCC
- Sites: Ureter (50–80% present with hematuria)
- Diagnosis
- General measures
- Smoking
- Cyclophosphamide
- Radiographic imaging
- Voided urine cytology: Low sensitivity for low-grade

RECOMMENDATIONS
- Pap screening of UUT TCC is difficult due to the limited size of biopsy specimens.
- Staging is predicted by biopsy grade.
- Tumor grade may be a more important prognostic factor than pathologic stage in UUT.
- Sending all biopsies for cytopathologic exam can improve the diagnostic yield (full block).

DIAGNOSTIC TESTS & INTERPRETATION
- Vein analysis: Gross or microscopic hematuria
- Electrolytes, LFTs: normal in absence of urinary obstruction, or metastatic disease
- Voided urine cytology: Low sensitivity for low-grade TCC, better for high-grade, CIS

DIAGNOSTIC PROCEDURES/SURGERY
- IVP:—traditional diagnostic study largely replaced by CT Urograms
- Retrograde pyeloureterography
- Computerized tomographic urography (CTU):—3D reconstruction image quality is equivalent to CT Urograms
- Intravenous urogram (IVU) or intravenous pyelogram

TREATMENT

GENERAL MEASURES
- Topical therapy—BCG, mitomycin, thiotepa
- Fungal infection
- Intravesical urothelial neoplasms
- General measures

BASICS
Urothelial carcinoma (formerly known as transitional cell carcinoma or TCC) is an epithelial neoplasm of the upper urinary tract (UUT). Urothelial carcinoma, also known as urothelial cancer, bladder cancer, or transitional cell carcinoma (TCC), is the most common type of urinary tract cancer in adults. It is characterized by the presence of abnormal cells lining the urinary tract, typically in the bladder or ureter. The condition can be associated with various risk factors, including smoking, cyclophosphamide use, and occupational exposure to certain chemicals. The incidence of urothelial carcinoma is increasing, and it is more common in men than in women. Diagnostic procedures such as cystoscopy, retrograde pyelography, and computerized tomographic urography (CTU) are used to identify and stage the disease. Treatment options include surgery, chemotherapy, and immunotherapy, with the goal of preserving renal function and improving quality of life.
URETER AND RENAL PELVIS, UROTHELIAL CARCINOMA

SURGERY/OTHER PROCEDURES
- Open radical nephroureterectomy (RNU) with en-bloc excision of peri-ureteric and peri-bladder cuff:
  - Traditional treatment
  - Provides adequate surgical margins, local control, removes need for bilateral ureteroscopy
- Role of lymphadenectomy is unclear
- Laparoscopic RNU:
  - Equivalent disease-specific and overall survival compared to open RNU
- Skin incision positioned to allow for distal ureteral reimplantation
- Nephron-sparing surgery—For locally contained low-grade disease or high-grade disease with overwhelming concern for loss of renal function
- Segmental ureterectomy:
  - Used for noninvasive low-grade TCC of proximal or mid ureter too large for endoscopic ablation
  - Distal ureterectomy with reimplantation
- Used for distal ureteral TCC too large for endoscopic ablation or high-grade TCC
  - Endoscopic treatment:
    - Indications include solitary kidney, bilateral disease, poor renal function, moderate tumor burden, low-grade disease, high-risk surgical candidates
    - Retrograde or percutaneous antegrade approach
    - Tumor biopsy with cold-cup or basket
    - Treatment techniques include electrocautery, fulguration, laser ablation
    - Recurrence rate: 33% for unilateral TCC, 31% for renal pelvis TCC

ADDITIONAL TREATMENT
Radiation Therapy
Possible role for adjuvant radiation after complete excision. Studies have been small and collectively inconclusive.

Additional Therapies
- Consider systemic chemotherapy for high-stage or node-positive disease in patient with adequate renal function
  - Standard chemotherapy agents used for bladder cancer
  - Methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC)
  - Gemcitabine and cisplatin

Complementary & Alternative Therapies
- No accepted therapy

ONGOING CARE
PROGNOSIS
- Overall 5-yr survival based on grade:
  - Grade 1–2: 40–87%
  - Grade 3–4: 0–33%
- 5-yr survival based on stage:
  - Stage T1: 75–85%
  - Stage T2: 43–75%
  - Stage T3: 16–33%
  - Stage T4: 0–5%

COMPLICATIONS
- Local obstruction, metastatic dissemination

FOLLOW-UP
Patient Monitoring
- If RNU is performed:
  - Cystoscopy and cytology every 3 mo for 2 yr, then every 6 mo for 2 yr, then yearly thereafter (VP or CTU) yearly
- If nephron-sparing surgery is performed:
  - Ureteroscopy, surveillance, and cytology every 3 mo until tumor-free, then every 6 mo thereafter (VP or CTU) yearly

Patient Resources
Urology Care Foundation http://www.urologyhealth.org/urologyvideo/ch/7articleid=9

REFERENCES

ADDITIONAL READING

CODES
ICD9
- 189.1 Malignant neoplasm of renal pelvis
- 189.2 Malignant neoplasm of ureter

ICD10
- C65.9 Malignant neoplasm of unspecified renal pelvis
- C66.9 Malignant neoplasm of unspecified ureter

CLINICAL/SURGICAL PEARLS
Due to the high distal recurrence rate (33–55%), it is prudent to ensure that the entire ureteral stump is removed at the time of radical nephroureterectomy (RNU).
URETER, INTRAOPERATIVE INJURY

John M. Barry, MD, FACS
Daniel D. Dugi III, MD

DESCRIPTION

• Intraoperative injury to the ureter can occur during open, laparoscopic, or endoscopic surgery
• May be direct laceration, suture ligation, crush injury, thermal injury, or devascularization
• Lower 1/3 of ureter (within the pelvis) is most commonly injured
• Injury may cause obstruction of kidney if ureter is ligated or urinary extravasation if lacerated
• Due to the proximity to the vagina, some injuries may result in ureter-vaginal fistula

ASSOCIATED CONDITIONS

• Radiation therapy, cancer, prior pelvic surgery
• Ureteral stones

RISK FACTORS

• Women with leakage of urine per vagina
• Symptoms of urinary tract infection

EPIDEMIOLOGY

Incidence

• Most series report 1–5% of pelvic surgeries; highest rates among radical hysterectomy cases (18)
• 1–5% of ureteroscopic surgeries (19)
• Approximately half of iatrogenic injuries occur during gynecologic surgery (20)

Prevalence

N/A

HISTORY

Most ureteral injuries are not recognized preoperatively (16). Postoperative recognition is essential to prevent or recognize an intraoperative injury.

PHYSICAL EXAM

• Intravenous or intravesical administration of an indigo carmine or methylene blue dye helps identify ureteral injury if dye is seen in the operative field after intravenous or intravesical administration.
• Contrast studies are critical for postoperative diagnosis. CT scan with IV contrast and excretory phase imaging may show urine extravasation or a urinoma.

DIAGNOSTIC PROCEDURES/SURGERY

Indigo carmine or methylene blue may help identify ureteral injury if dye is seen in the operative field after intravenous or intravesical administration.

Diagnostic Procedures/Surgery

• Indigo carmine or methylene blue dye is administered prior to placement of a ureteral stent. The dye should be administered to both ureters if bilateral ureteral stenting is needed.
• Injuries above the true pelvis (proximal ureter) may be repaired with direct anastomosis if proximal and distal mobilization allows tension-free repair.
• Injuries within the pelvis are usually best repaired by direct reimplantation into bladder, with psoas hitch, if necessary (15).
• Partial-thickness, clean lacerations may be closed by direct reapproximation.
• Ligation injuries: Remove suture and inspect for surrounding tissue has not be devascularized.
• Injuries above the true pelvis (proximal ureter) may be repaired with direct anastomosis if proximal and distal mobilization allows tension-free repair of healthy, well-vascularized edges.
• More complex repairs, such as flap, trans-ureteral-reimplantation, or ureteral patch should be undertaken cautiously in the acute setting.
• In unstable patients, the ureter may be left ligated and a percutaneous nephrostomy tube placed postoperatively to drain the kidney.
• It is best to leave an indwelling ureteral stent postoperatively.

DIAGNOSIS

History

• Indigo carmine or methylene blue dye may help identify ureteral injury if dye is seen in the operative field after intravenous or intravesical administration.
• Partial-thickness, clean lacerations may be closed by direct reapproximation.
• Injuries above the true pelvis (proximal ureter) may be repaired with direct anastomosis if proximal and distal mobilization allows tension-free repair of healthy, well-vascularized edges.
• More complex repairs, such as flap, trans-ureteral-reimplantation, or ureteral patch should be undertaken cautiously in the acute setting.
• In unstable patients, the ureter may be left ligated and a percutaneous nephrostomy tube placed postoperatively to drain the kidney.
• It is best to leave an indwelling ureteral stent postoperatively.

Medication

First Line

Indigo carmine or methylene blue may help identify ureteral injury if dye is seen in the operative field after intravenous or intravesical administration.

Second Line

SUTURES

SURGERY/OTHER PROCEDURES

• Indigo carmine or methylene blue dye may help identify ureteral injury if dye is seen in the operative field after intravenous or intravesical administration.
• Partial-thickness, clean lacerations may be closed by direct reapproximation.
• Injuries above the true pelvis (proximal ureter) may be repaired with direct anastomosis if proximal and distal mobilization allows tension-free repair of healthy, well-vascularized edges.
• More complex repairs, such as flap, trans-ureteral-reimplantation, or ureteral patch should be undertaken cautiously in the acute setting.
• In unstable patients, the ureter may be left ligated and a percutaneous nephrostomy tube placed postoperatively to drain the kidney.
• It is best to leave an indwelling ureteral stent postoperatively.
Injuries recognized postoperatively:
- If recognized in the first few days to 1 week after initial injury, operative repair is recommended
- If recognized later, reoperation after resolution of surgical inflammation 6 weeks or more postoperatively is recommended (2)
  - Retrograde ureteropyelography is helpful in diagnosing ureteral injury and allows for attempt at ureteral stent placement in low-grade injuries (2)
  - Small lacerations or partial ligations may heal after a period of ureteral stenting
- Peritoneal nephrostomy drainage is recommended if ureteral stenting is not possible. This also allows attempt at antegrade ureteral stent placement
  - Optimal duration of ureteral stenting is not known, but 6 wk is reasonable
  - Percutaneous drainage of urinoma is necessary if the urinoma is infected, symptomatic, or does not decrease in size after successful renal drainage is established

Additional Treatment
Radiation Therapy
N/A
Additional Therapies
N/A
Complementary & Alternative Therapies
N/A

Ongoing Care

Prognosis
- Intraoperative recognition and repair usually prevents complication of urine extravasation or renal obstruction
- Ureteroneocystostomy for distal ureteral injuries has an excellent prognosis. Proximal ureteral repair have a higher risk of long-term complications because of compromised blood supply
- Patients who have delayed recognition of injuries have higher rates of complications and more procedures needed to resolve injury than those with injuries recognized intraoperatively (2)

Complications
- Urine leakage from a ureteral injury may lead to urine extravasation and renal obstruction
- Extravasated urine may cause irritation of the intestines and peritoneum and result in pain and/or ileus
- Urinary stricture and renal obstruction may cause loss of renal function
- Ureterovaginal fistula
- Complications of ureteral injury and repair may result in nephrectomy

Follow-Up
Patient Monitoring
- Perform follow-up imaging of the kidney to assure no obstruction from ureteral stricture. Renal ultrasound can evaluate for hydronephrosis and urinoma and has no radiation
- Intravenous imaging (i.e., ExU, CT urography, retrograde ureterography with hydrodynamic washout) may be indicated in complex circumstances or when hydronephrosis is found by ultrasound.

Patient Resources
N/A

References

Additional Reading

See also (Topic, Algorithm, Media)
- Ureter, Stricture
- Ureter, Trauma

ICD9
- 867.2 Injury to ureter, without mention of open wound into cavity
- 997.5 Urinary complications, not elsewhere classified
- 998.2 Accidental puncture or laceration during a procedure, not elsewhere classified

ICD10
- N99.71 Acc pnctr & lac of a GU sys org during a GU sys procedure
- N99.81 Other intraoperative complications of genitourinary system
- S37.10XA Unspecified injury of ureter, initial encounter

Clinical/Surgical Pearls
- During mobilization of the ureter, avoid "skeletonization" and include periureteral tissue to better preserve blood supply
- Repair ureteral injuries and avoid nephrectomy unless the repair will place the patient at risk
- A cystostomy allows easy access to the ureteral orifice to aid in stent placement during open surgery.
URETER, OBSTRUCTION

Jennifer E. Heckman, MD, MPH
Stephen Y. Nakada, MD, FACS

BASICS

DESCRIPTION
- Ureteral obstruction can be anatomic or functional blockage of the ureter and further classified as:
  - Congenital or acquired
  - Acute or chronic
  - Benign or malignant
  - Intrinsic or extrinsic
  - Unilateral or bilateral
- Impact of obstruction dependent on:
  - Degree and duration of obstruction
  - Baseline renal function
  - Potential for reversibility
- Associated definitions:
  - Hydronephrosis
  - Dilation of renal pelvis and calyces
  - Can occur with or without obstruction (obstruction may be anywhere in urinary tract, from urethral meatus to calyces)
  - Hydroaureterohydronephrosis
  - Dilation of renal pelvis, calyces, and ureter
  - Obstructive uropathy
  - Impedance to urinary flow anywhere in urinary tract
  - Obstructive nephropathy
  - Renal parenchymal damage from urinary tract obstruction
- Urinary tract infection and sepsis may be superimposed

EPIDEMIOLOGY

Incidence
- No data available in unselected populations
- Etiology-dependent

Prevalence
- Can occur during fetal development, childhood, or adulthood
- Occurrence increases with increasing age
- Unilateral > bilateral
- Hydronephrosis may be surrogate marker for obstruction
- Overall prevalence in autopsy series: 3.1% (1)

RISK FACTORS
- Renal or ureteral calculus
- Malignancy
- Hematopoietic
- Infection
- Trauma
- Radiation

Genetics
- No specific associated familial or hereditary disorder, but cause may be congenital
- 10–50% of children with end-stage renal disease have obstructive uropathy associated with congenital anomalies

PATHOPHYSIOLOGY
- Ureteral obstruction results in elevated intravesical pressure
- With increased pressures in proximal tubule and Bowman capsule, glomerular filtration rate (GFR) decreases
- Persistent obstruction leads to decreased renal blood flow and subsequent ischemia and nephron loss
- Three major points of anatomic ureteral narrowing:
  - Ureteropelvic junction (UPJ)
  - Where ureter crosses iliac vessels
  - Ureterovesical junction (UVJ)

ASSOCIATED CONDITIONS
- Congenital
  - Vescoureteral reflux
  - Megacephaly
  - UPJ obstruction
- Structural
- Inflammatory
  - Abscess
  - Amyloidosis
  - Tuberculosis
- Malnutrition
- Malignancy
  - Urinary cancer
  - Bladder cancer
  - Metastatic disease
- Vascular
  - Anastomoses
  - Abnormal vessels
- Other
  - Urolithiasis
  - Pregnancy
  - Trauma
- Reconstructive/urologic disease
  - Ureteral obstruction

GENERAL PREVENTION
Dependent on underlying etiology

DIAGNOSIS

HISTORY
- Presentation reflects underlying etiology
- May be asymptomatic
- Acute obstruction may cause significant pain
  - Upper tract:
    - Flank pain (renal colic)
    - Pain radiating to abdominopelvic region (renal obstruction)
  - Lower tract:
    - Distal obstruction:
      - Pain, hematuria, pyuria, or crystals
    - Ureterovesical obstruction:
      - Urinary straining
    - Abdominal tenderness
  - Hypertension possible
  - Pyrexia if associated with infection

DIAGNOSTIC TESTS & INTERPRETATION

Imaging
- Renal ultrasound
  - Screening test of choice (inexpensive, no radiation or contrast required)
  - Can identify parenchymal thickness, urinary tract dilation
- Intravenous pyelogram (IVP)
  - Delineate collecting system anatomy
  - Requires contrast (limit use in renal insufficiency)
  - Low false-positive rate
- Retrograde pyelogram
  - Define collecting system anatomy
  - Requires contrast (limit use in renal insufficiency)
- Urography
  - Provides anatomic and functional information
  - Low false-positive rate
  - Requires contrast (limit use in renal insufficiency)
  - Requires contrast (limit use in renal insufficiency)

Lab
- Serum studies:
  - Creatinine
  - Often elevated, though may be normal in setting of normal contralateral kidney
  - Electrolytes
  - Urine studies:
    - Uretal culture:
      - May see hematuria, pyuria, or crystals
    - May see elevated pH secondary to nephron destruction in affected kidney
    - Urine electrolytes

PHYSICAL EXAM
- Renal ultrasound
  - Screening test of choice (inexpensive, no radiation or contrast required)
  - Can identify parenchymal thickness, urinary tract dilation
  - Intravenous pyelography (IVP)
  - Delineate collecting system anatomy
  - Requires contrast (limit use in renal insufficiency)
  - Low false-positive rate
  - Requires contrast (limit use in renal insufficiency)
  - Requires contrast (limit use in renal insufficiency)

Diagnosis Procedures/Surgery
Perform Whitaker test (pressure flow test) in equivocal cases

Pathologic Findings
- Gross
  - Renal papillemal dilatation
  - Papillary infarct
- Histological
  - Cortical and medullary atrophy
  - Parietal edema
  - Enlarged, edematous proximal tubular obstruction
- Microscopic
  - Urinary tract obstruction
    - Collecting duct, tubule, and lymphatic dilatation
  - Intestinal edema and fibrosis
  - Tubular basement membrane thickening

548
URETER, OBSTRUCTION

Differential Diagnosis
- Intrinsic:
  - Urolithiasis
  - Striated papilla
  - Malignancy
- Extrinsic:
  - Adenomyopic tumors
  - Retroperitoneal fibrosis
  - Pregnancy
  - Vascular anomalies
  - Aneurysm of ureter (aortic, caval)
- Systemic disease (congenital or acquired)
- Inflammatory disorder
- Neuromuscular dysfunction
- In children:
  - Potter (ureteral valves [nuke])
  - UPI obstruction
  - UO obstruction
  - Ectopic ureter
  - Megaureter
  - Ureterolysis

TREATMENT
Urinary obstruction, if high-grade, bilateral, or associated with renal failure or infection warrants urgent decompression

GENERAL MEASURES
- Early recognition important in preventing irreversible renal functional impairment
- Management of acute obstruction directed at establishing drainage
- After initial stabilization and drainage, determine location and cause of obstruction
- Unilateral obstruction does not always require intervention
- May observe (e.g., terminally ill patient with normal contralateral kidney, normal serum Cr, and electrolytes)
- Supportive care (pain control, correction of electrolyte abnormalities)

MEDICATION
First Line
- Part management (oral or parenteral)
  - 1st line: Non-steroidal, anti-inflammatory medications
  - 2nd line: Narcotic medications

Second Line
- NSAIDs

SURGERY/OTHER PROCEDURES
- Renal drainage:
  - Nephrostomy
  - Retrograde ureteral stent placement
  - Placement of an indwelling ureteral stent in ureteral obstruction
  - Techniques depend on clinical scenario (e.g., stent preferred if uncorrectable coagulopathy, stent not as effective for extrinsic ureteral obstruction)
- After management of acute obstruction, definitive management directed by cause, renal function, and patient condition
- Urolithiasis:
  - Ureteroscopy with laser lithotripsy
  - Extracorporeal shockwave lithotripsy
  - Calculus extraction, percutaneous nephrolithotomy (location and calculus dependent)
- UPI obstruction
  - Open or laparoscopic pylonephrotomy
  - Vascular lesions (e.g., aortic aneurysm)
  - May require urgent operative intervention
- May consider nephrectomy if affected kidney contributes <10% to global renal function

ADDITIONAL TREATMENT
Radiation Therapy
- None

Additional Therapies
- None

Ongoing Care
Prognosis
- Progressive renal damage may occur
- Poor if untreated bilateral obstruction

Complications
- Acute renal failure
- Postobstructive diuresis in setting of bilateral ureteral obstruction

Follow-Up
Patient Monitoring
- Serum osmolality
- Serum electrolytes
- Renal ultrasound
- Nuclear renal scan

Patient Resources
NIDDK: Unilateral hydronephrosis

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Bladder, Renal and Genitourinary, General Considerations
- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)

ICD9
- 593.3 Obstructive defects of renal pelvis and ureter
- 753.20 Unspecified obstructive defect of renal pelvis and ureter

ICD10
- N13.3 Hydronephrosis
- N13.3 Stenosis or narrowing of ureter
- N13.3:20 Unspecified obstructive defect of renal pelvis and ureter

ICD11
- N13.3 Hydronephrosis: Renal pelvis and ureter
- N13.3:20 Unspecified obstructive defect of renal pelvis and ureter

Clinical/Surgical Pearls
- Hydronephrosis is an anatomic, not functional, diagnosis.
- Renal scan best study if renal function adequate
- Bilateral ureteral obstruction, unilateral obstruction in a solitary kidney, and ureteral obstruction associated with renal failure or infection warrant immediate renal drainage.
## URETER, TRAUMA

Brad Figler, MD
Hunter Wessells, MD, FACS

### BASICS

**DESCRIPTION**
- Due to its mobility, narrow diameter, and protected location, ureteral injury from external trauma is rare.
- 75% of ureteral injuries are iatrogenic; 18% from blunt trauma and only 7% from penetrating trauma (1).
- Iatrogenic injury is discussed in detail elsewhere (see Section II: “Ureter, Intraoperative Injury”).

**EPIDEMIOLOGY**

**Incidence**
- Ureteral injuries represent < 1% of all genitourinary injuries caused by violent trauma.
- Typically result from gunshot wounds.
- Blunt trauma and stab wounds responsible for ~ 20% of ureteral injuries.
- Typically occurs concomitant with other injuries (chest, retroperitoneal, pelvic).

**Prevalence**
- Unknown

**RISK FACTORS**
- Penetrating injury to the abdomen and low chest.
- Flank or lower abdominal tenderness.
- Gross hematuria.
- Abdominal distention.
- Flank pain.
- Nausea/vomiting.
- Fever.

**Genetics**
- Unknown

**PATHOPHYSIOLOGY**
- Direct injury from penetrating object.
- Stretching of ureter as a result of hyperextension of the body.
- Compression against transverse process as a result of rapid deceleration.
- American Association for the Surgery of Trauma (AAST) Injury Scoring Scale for ureteral trauma (2).

**DIFFERENTIAL DIAGNOSIS**
- Other urinary tract trauma.
- Kidney.
- Bladder.
- Nephrostomy tube.
- Ureteral stenting or autotransplantation.

**Associated Conditions**
- Small bowel injury.
- Colon injury.
- Point injury.
- Bladder injury.

**GENERAL PREVENTION**
- Avoid high-risk activity.
- Seatbelt use.

### DIAGNOSIS

**HISTORY**
- Requires a high index of suspicion.
- History of urologic condition or surgery.
- Mechanism of injury:
  - Hyperextension
  - Deviation
  - Fall from height
  - Primary location of impact
- Presence of hematuria
  - Uirit
  - Duration
- Flank pain
- Fever
- Nausea/vomiting

**PHYSICAL EXAM**
- Enlargement wounds.
- Gross hematuria.
- Flank or lower abdominal tenderness.
- Flank bulge.
- Abdominal distention.

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- Hematuria is unreliable; absent in 26% of cases (3).
- Creatinine may (rarely) be elevated due to extravasation and reabsorption of urine or obstruction.

**Imaging**
- Demonstration of extravasation of contrast is the gold standard for the diagnosis of ureteral trauma.
- Retrograde pyelography is most reliable for diagnosing ureteral injury, often impractical in trauma patient.
- CT with IV contrast and delayed images is an acceptable alternative. Most trauma patients have C T scans before being taken to the OR emergently.
- On table “one-shot” IVP is sometimes performed in the operating room.
- Administration of 2 ml/kg IV contrast with on table x-ray plain film after 10 min.

**Pathologic Findings**
- Microvascular injury from high-velocity missiles or thermal injury can extend up to 2 cm beyond evidence of gross injury.

**TREATMENT**

**GENERAL MEASURES**
- Initial management of the trauma patient employs primary survey, resuscitation stabilization, and primary survey, resuscitation stabilization, and trauma patient.
- Nondistended or - Nephrostomy tube.
- Some common options for complete ureteral injury:
  - Upper third: Uretero-ureterostomy or Blandy cystoplasty.
  - Middle third: Uretero-ureterostomy or Blandy flap.
  - Lower third: Direct reimplantation or psoas hitch.
- Complete ureteral loss: Neobladder or ileal interposition as a delayed procedure.

**ALER**
- Delay in diagnosis of ureteral injury is a major contributing factor to morbidity in a trauma patient.

### Associated Conditions

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Perirenal Only</td>
</tr>
<tr>
<td>2</td>
<td>Laceration ~ 50% of circumference</td>
</tr>
<tr>
<td>3</td>
<td>Complete tear ~ 2 cm of devascularization</td>
</tr>
<tr>
<td>4</td>
<td>Complete tear &gt; 2 cm of devascularization</td>
</tr>
</tbody>
</table>

**Medial extravasation of contrast at the level of the UPJ, suggestive of UPJ or renal pelvis injury.**

- Ureters should opacify to the level of the bladder on delayed imaging to be diagnostic.
- Access for foreign bodies, fluid collection, and hydrothorax.
- Ultrasound is generally not useful, except in demonstrating a urinoma or hydrothorax.
- MRI not used acutely in the trauma setting.

**Diagnosis Procedures/Surgery**
- Retrograde pyelogram: Useful to verify presence or absence of suspected injury.
- Ureteral exploration is highly sensitive.
- Probe wounds to establish trajectory.
- Bladder
- Nephrostomy tube.
- Ureteral stenting or autotransplantation as a delayed procedure.

**Alert**
- Absence of hematuria does not exclude ureteral injury. Clinical suspicion should guide investigation.

- Duration.
- Onset.
- Primary location of impact.
- Fall from height.
- Deceleration.
- Hyperextension.
**MEDICATION**

**First Line**
- Methylene blue and indigo carmine may help identify the site of a ureteral perforation or transection (see Section I: “Ureter, Intraoperative Injury”).

**Second Line**
- Furosemide (20–40 mg IV) can be administered to speed indigo carmine excretion.

**SURGERY/OTHER PROCEDURES**

- Principles of ureteral repair include:
  - Careful mobilization
  - Preserve adventitia
  - Avoid electrocautery
  - Debridement of nonviable tissue to bleeding
  - Sphincterotomy
  - Tension-free
  - Watertight
  - Mucosa to mucosa
  - Spatulated
  - Debridement of nonviable tissue to bleeding

- Advanced techniques typically not appropriate in the unstable patient.
  - Bowel interposition
  - S37.19XA Other injury of ureter, initial encounter
  - S37.10XA Unspecified injury of ureter, initial encounter
  - N99.81 Other intraoperative complications of open wound
  - 997.5 Urinary complications, not elsewhere classified
  - 867.3 Injury to ureter, with open wound into cavity

**PROGNOSIS**

- Long-term outcomes not reported in this population, but long-term results of ureteral surgery are excellent (4).

**COMPLICATIONS**

- Delayed complications include:
  - Retained ureteral stent
  - Ureteral stricture
  - Prolonged leakage

- Hydronephrosis

**FOLLOW-UP**

**Patient Monitoring**
- Check if stone in at least 2 days after abdominal injury. If consistent with stone, consider removing.
- Stent removal 4–6 wk
- Renal scintigraphy with Lasix 2–4 wk after stent removal to document function/drainage

**Patient Resources**
- Ureter Trauma Image
- Ureter, Intraoperative Injury
- Renal Trauma, Adult
- Bladder Injury, Intraoperative
- Ureter, Stricture
- Ureter Trauma Image

**REFERENCES**


**ADDITIONAL READING**


** Hình ảnh**

- Ureter, Intraoperative Injury
- Renal Trauma, Adult
- Bladder Injury, Intraoperative
- Ureter, Stricture
- Ureter Trauma Image

**CODES**

- ICD9: 551.9 Other injury of ureter, without mention of open wound into cavity
- ICD-10: S37.5 Other intraoperative complications of peritoneal system
- S37.59 Other intraoperative complications of genitourinary system
- S37.10XA Unspecified injury of ureter, initial encounter
- S37.19XA Other injury of ureter, initial encounter

**CLINICAL/SURGICAL PEARLS**

- Diagnosis of ureteral injury requires a high index of suspicion.
- Absence of hematuria does not exclude ureteral injury. Hematuria absent in 25–45% of ureteral trauma.
- Ureteral injury is indicated by extravasation of contrast.
- Primary anastomosis and reimplant with psoas hitch are effective methods for repairing ureteral injuries.
- More complicated injuries can be managed in a delayed fashion.
- Unstable patients can be managed with temporary drainage followed by delayed management.
URETEROCELE
Ross M. Decter, MD, FRCS
Paul H. Smith III, MD

BASICS
DESCRIPTION
Ureterocele is a cystic dilation of the terminal/intravesical ureter. May be classified based on anatomic location:
– Intravesical: Contained entirely within the bladder above the bladder neck; seen frequently in single system ureteroceles.
– Extravesical (Ectopic): Some portion of ureterocele permanently located at the level of the bladder neck or urethra; seen frequently in duplex system ureteroceles.

Descriptive classification:
– Cecoureterocele: Ureterocele extends into urethra, but orifice within the bladder
– Sphincteric
– Stenotic
– Sphinctero-stenotic
– Blind
– Nonobstructive

Most ureteroceles are associated with the upper pole of a duplex collecting system and are usually ectopic

Today many ureteroceles are detected during routine prenatal screening ultrasounds

When discovered in adults they are rarely of clinical consequence.

EPIDEMIOLOGY
Incidence
1 in 500 to 1 in 4,000
Prevalence
As high as 1 in 500 (autopsy study)

RISK FACTORS
– More common in girls (5–7:1)
– More common in whites
– Bilateral in 10–15% of cases
– Extravesical ureteroceles associated with upper pole of duplex system often diagnosed in infancy or childhood

Genetics
 Likely multifactorial inheritance

PATHOPHYSIOLOGY
Several hypotheses:
– During embryogenesis, the mesonephric duct and the distal ureteral bud incorporate into the anterior cloaca/urogenital sinus. Chawalla membrane breaks down allowing the incorporation of the distal ureter into the developing bladder. Incomplete breakdown of Chawalla membrane is thought to be one cause of the ureterocele.
– Delay in canalization of ureter-urethral bud is another theory.

ASSOCIATED CONDITIONS
– Duplicated collecting system: 60%
– Single system: 20%
– Most common type in boys, but uncommon in girls (5%)
– Vesicoureteral reflux (VUR) – Ureteral lower pole in duplex system: 50–70% – Contralateral kidney: 10–30%

GENERAL PREVENTION
Antibiotic prophylaxis in patients at risk for upper-tract infection (VUR or obstruction)

DIAGNOSIS
HISTORY
– Prenatal hydronephrosis
– UTI/sepsis/failure to thrive
– Hematuria
– Bladder outlet obstruction
– Bladder outlet obstruction is most common cause of bladder outlet obstruction in newborn girls
– Intravesical mass (ectopic ureterocele)

PHYSICAL EXAM
– Abdominal mass (hydronephrosis)
– Intralabial prolapsing cystic mass
– Smooth, broad- based filling defect near trigone

IMAGING
– Renal/bladder US:
– Prenatal hydronephrosis
– Thin-walled intravesical cystic structure or septations in the bladder
– Hydronephrosis
– Duplex collecting system with dilated upper pole
– Voiding cystourethrogram (VCUG):
– Smooth, broad- based filling defect near trigone
– Critical to image during early filling

DIAGNOSTIC TESTS & INTERPRETATION
Lab
– Serum creatinine
– Urinalysis
– Urine culture

Imaging
– Renal/bladder US:
– Prenatal hydronephrosis
– Thin-walled intravesical cystic structure or septations in the bladder
– Hydronephrosis
– Duplex collecting system with dilated upper pole
– Voiding cystourethrogram (VCUG):
– Smooth, broad- based filling defect near trigone
– Critical to image during early filling

– May efface as bladder fills

DIFFERENTIAL DIAGNOSIS
– Bladder polyp
– Ectopic ureter
– Edema
– Mesonephric duct cyst
– Tumor
– Urethral prolapse

TREATMENT
GENERAL MEASURES
Surgical treatment is needed in most cases

MEDICATION
First Line
– Culture-directed antibiotics for treatment of UTI
– Antimicrobial prophylaxis until reflux or obstruction repaired in children
– Amoxicillin: 5–7 mg/kg as neonate
– Trimethoprim-sulfamethoxazole: 2 mg/kg/d OR nitrofurantoin 1–2 mg/kg/d beyond 2 mo of age

Second Line
Endoscopic incision if acutely septic
URETEROCELE

Surgery/Other Procedures

- Endoscopic transurethral incision:
  - Usually effective in relieving obstruction
  - Risk of developing reflux in that system
  - Outpatient procedure
  - Effective for intravesical and single-system ureteroceles, less so for extravesical ureteroceles (CUB)
  - Can be a temporizing measure until definitive repair (CUB)
- Formal surgical repair:
  - Definitive treatment but higher morbidity
  - Goals of surgery: Preserve functional renal parenchyma, relieve obstruction, correct reflux
  - Upper-pole heminephrectomy if dilated, non-functioning upper pole
  - Ureteroureterostomy if upper pole is functional and no lower pole reflux
  - Ureterocele excision and common sheath reimplantation if reflux is present (CUB)

Additional Treatment

Radiation Therapy
No

Additional Therapies

Observation if asymptomatic; no or mild reflux or obstruction

Complementary & Alternative Therapies
No

Ongoing Care

Prognosis

Depends on extent of obstruction, infections, and presence or absence of renal dysplasia

Complications

- The major complication in adults and children is ureteral obstruction (4)
- Sepsis, loss of renal function
- Incontinence (primary or secondary)
- Persistent dilution of ureteral stump
- Persistent VUR

Follow-Up

- Patient Monitoring:
  - Renal and bladder US
  - VCUG to diagnose/follow-up VUR
  - Monitor renal function if bilateral
  - Treat UTI

Patient Resources


References


Additional Reading


See Also (Topic, Algorithm, Media)

- Bladder Mass
- Collecting System, Complete Duplication
- Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Prenatal
- Ureterocele Image
- Vesicoureteral Reflux, Pediatric

Additional Treatment

Radiation Therapy
No

Additional Therapies

Observation if asymptomatic; no or mild reflux or obstruction

Complementary & Alternative Therapies
No

Ongoing Care

Prognosis

Depends on extent of obstruction, infections, and presence or absence of renal dysplasia

Complications

- The major complication in adults and children is ureteral obstruction (4)
- Sepsis, loss of renal function
- Incontinence (primary or secondary)
- Persistent dilution of ureteral stump
- Persistent VUR

Follow-Up

- Patient Monitoring:
  - Renal and bladder US
  - VCUG to diagnose/follow-up VUR
  - Monitor renal function if bilateral
  - Treat UTI

Patient Resources


References


Additional Reading


See Also (Topic, Algorithm, Media)

- Bladder Mass
- Collecting System, Complete Duplication
- Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Prenatal
- Ureterocele Image
- Vesicoureteral Reflux, Pediatric

Codes

ICD9
- 583.70 Vesicoureteral reflux unspecified or without reflux nephropathy
- 583.89 Other specified disorders of kidney and ureter
- 753.23 Congenital ureterocele

ICD10
- N13.30 Vesicoureteral reflux, unspecified
- N28.89 Other specified disorders of kidney and ureter
- Q62.31 Congenital ureterocele, orthotopic

Clinical/Surgical Pearls

- Early filling x-rays during VCUG mandatory to enhance detection of ureterocele.
- Choice of treatment driven by acuity of illness, degree of obstruction, VUR, and degree of renal dysplasia.
- Definitive endoscopic treatment most successful for single-system ureteroceles.
URETEROENTERIC ANASTOMOTIC STRicture

David F. Penson, MD, MPH
Chad R. Ritch, MD, MBA

DESCRIPTION
Ureteroenteric anastomotic stricture (UE) is typically a benign obstruction of the ureter at the level of the ileal urinary diversion.

- Typically benign process that develops 7–18 mo postoperatively (1)
- Most often performed in setting of radical cystectomy and urinary diversion; therefore, recurrent malignancy must be ruled out (malignant stricture)

PHYSICAL EXAM
- Full acute pain on palpation of flank
- May be sharp if associated with infection

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Complain of flank pain or fever and UTI suggestive of pyelonephritis
- Typically presents 6–18 mo after surgery or chronic as opposed to acute process

IMAGING
- If kidney appears atrophic consider renal scan to assess function
- Ultrasound cost-effective and highly sensitive for obstructive process
- CT imaging with pre- and post-IV contrast dye can provide further anatomic and functional information
- More costly than US and risk of radiation exposure and contrast-dye allergy in susceptible patients
- Patients may have compromised renal function that precludes the use of IV contrast
- Some patients may have compromised renal function if feasible contrast dye allergy in susceptible patients
- Nephrostogram can be therapeutic by providing instant drainage via nephrostomy as well as access to locate and cannulate ureteral orifice during loop enterostomy

DIFFERENTIAL DIAGNOSIS
- Ureteral stone
- Extrinsic compression
- Urinary infection
- Recurrent malignancy
- Pyelonephritis
- Differential can be explored with CT or MR imaging which will provide anatomical detail

TREATMENT
- Consider pain relief if obstruction causing hydronephrosis and flank pain
- Rule out and treat UTI if suspected
- Ureteral stent may prevent urine leak
- Nephrostomy tube and systemic antibiotics
- If patient comfortable and no evidence of infection, then consider elective repair

DIAGNOSIS
- Complain of flank pain or fever and UTI suggestive of pyelonephritis
- Typically presents 6–18 mo after surgery
- Chronic as opposed to acute process

GENERAL MEASURES
- Consider pain relief if obstruction causing hydronephrosis and flank pain
- Rule out and treat UTI if suspected
- Ureteral stent may prevent urine leak
- Nephrostomy tube and systemic antibiotics
- If patient comfortable and no evidence of infection, then consider elective repair

Epidemiology
- Various series report range of 3–10% (1,2)
- More common on left (1,2)

Prevalence
N/A

RISK FACTORS
- Surgical technique is the main risk factor
- Aggressive handling of the ureter leads to stricture formation
- Excessive tension on the ureter
- A non-refluxing anastomosis may be more prone to stricture formation than a refluxing anastomosis
- Suture-line gaps lead to urine leak and predispose to stricture

Genetics
N/A

PATHOPHYSIOLOGY
- Aggressive handling, suboptimal technique devascularizes tissue causing poor blood flow and ischemia
- Ectasia interferes with healing of ureteral tissue and causes stricture formation
- Ureteral stricture formation or leakage causes inflammation around anastomotic site
- Lack of mucosa to mucosa apposition impairs healing

ASSOCIATED CONDITIONS
- Any condition where surgical or injury occurs may result in stricture formation
- Urinary tract infection
- Bladder carcinoma
- Neurogenic bladder
- Gynecologic malignancies
- Pelvic exenteration for malignancy

GENERAL PREVENTION
- Good surgical technique essential
- No grasping of ureter with instruments, may crush and devascularize tissue
- Maintain good blood supply—Avoid skeletonization
- Minimize stretching and tension
- Ensure mucosa to mucosa apposition
- Balance wright Anastomosis with excessively devascularized tissue
- Urinary stent may prevent urine leak

Lab
- CT imaging with pre- and post-IV contrast dye can provide further anatomic and functional information
- More costly than US and risk of radiation exposure and contrast-dye allergy in susceptible patients
- Patients may have compromised renal function that precludes the use of IV contrast
- Some patients may have compromised renal function if feasible contrast dye allergy in susceptible patients
- Nephrostogram can be therapeutic by providing instant drainage via nephrostomy as well as access to locate and cannulate ureteral orifice during loop enterostomy

DIFFERENTIAL DIAGNOSIS
- Ureteral stone
- Extrusive compression
- Urinary infection
- Recurrent malignancy
- Pyelonephritis
- Ureteral kinking
- Recurrent malignancy
- Differential can be explored with CT or MR imaging which will provide anatomical detail
URETEROENTERIC ANASTOMOTIC STRicture

MEDICATION
First Line
- No therapeutic medications
- Consider narcotics and anti-inflammatories for temporary relief of pain
- If infection noted and patient clinically stable, mildly symptomatic, treat with fluoroquinolone or culture specific antibiotics for 7–14 days
- Asymptomatic infection can be treated prior to elective repair

Second Line
- SAH

SURGERY/OThER PROCEDURES
- Nephroureteral or antegrade ureteral stent placement for temporary relief of obstruction or in the setting of palliative care
- Definitive therapy. Open versus endoscopic repair – Decision is based on surgeon experience, prior attempts at repair (primary vs secondary) and length/complexity of stricture
- Retrospective series suggest higher success rates with open repair (see below)
- Indwelling stent for 2–3 wk after repair
- Open surgical repair – Recommended for strictures >1 cm and failed endoscopic repairs
- Success rates of up to 71.4–100% reported for primary open revision (2,3)
- Difficult procedure with mean reported operative time of 240+ (145–450) min, EBL 300+ (150–500) cc (2,4)
- Endoscopic repair – Recommended for stricture <1 cm and primary repairs
- Typically performed antegrade with Ho:Yag laser or Accucise device (2,5). Balloon dilation less commonly used and may be less efficacious
- Success rates of 36–50% reported for primary repair (3–5)
- Secondary or redo endoscopic repair has low success rate (50%) (5)
- Left side strictures and those >1 cm in length appear more prone to failure after repair (2,5)

ADDITIONAL TREATMENT
Radiation Therapy
- N/A

Additional Therapies
- If external stricture very long, ureter deaucesalvored or insufficient length and renal unit still functional consider bowel interposition (tailed ileum)
- If renal scan demonstrates poorly functioning kidney (<15%) consider nephrectomy

Complementary & Alternative Therapies
- N/A

Ongoing care

PROGNOSIS
- Mean time to failure after open and endoscopic repair are 12 and 5 mo, respectively (3)
- Left sided and redo repairs are at higher risk for failure

COMPLICATIONS
- Uretero enteric stricture – Stone formation
- Hydroureter
- Renal insufficiency
- Pyelonephritis
- Open repair: complication rate of up to 40% (2,4)
- Complications include vascular injury, contralateral ureteral injury, urine leak, damage to diversion bowel segment, bowel injury (2,4)
- Endoscopic repair:
  - Complications are rare, most common is infection (UTI)success rate (2,3-5)

FOLLOW-UP
Patient Monitoring
- Consider renal US at 6 weeks following repair
- If hydroureter present consider waiting 2 wk potential post-op anastomotic edema and perform repeat imaging with contrast based study to rule out obstruction/failure
- Reflux may occur following repair so should also rule out as possible cause of hydroureter

Patient Resources
- N/A

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Hydroureter/hydroureteronephrosis, (bladder Ureteral Reflux Disease), Adult
- Ureter, Obstruction

CODES
ICD9
- 593.3 Stricture or kinking of ureter
- 667.2 Injury to ureter, without mention of open wound into cavity
- 997.5 Urinary complications, not elsewhere classified

ICD10
- N13.5 Crossing vessel and stricture of ureter into hypogastric
- N69.89 Other postprocedural complications and disorders of GI sys
- S37.10XA Unspecified injury of ureter, initial encounter

CLINICAL/SURGICAL PEARLS
- Avoid aggressive handling of the ureter to prevent deaucesalvored or ischemia during urinary diversion operation
- If hydronephrosis, fever, and UTI in a patient with a urinary diversion requires emergent treatment with percutaneous drainage
- Open primary repair of UE stricture has higher success rate than endoscopic repair
- Open repair is complex procedure best performed in experienced hands
URETEROPELVIC JUNCTION OBSTRUCTION
Christopher E. Keel, DO
Raju Thomas, MD, MHA, FACS

BASICS
DESCRIPTION
- Ureteropelvic junction obstruction (UPJO) is a restriction of urine flow from the renal pelvis to the ureter.
- Most common cause of significant dilation of collecting system in fetal kidney

EPIDEMIOLOGY
Incidence
- 1: 500–1000 newborns
- 25% diagnosed by 1 yr, 50% by 5 yr
- Adult presentation usually in 10th–40th decade

Prevalence
- Left > right side (6:1)
- Male > female (2:1:1)

RISK FACTORS
- Familial disposition
- Congenital renal anomalies:
  - Contralateral UPJO: 10–40% risk
  - Vescoureteral reflux (VUR): 0.5–5% risk
- Familial disposition
- Male
- Left
- Adult presentation usually in 3rd–4th decade

ASSOCIATED CONDITIONS
- 50% associated with another congenital anomaly:
  - Contralateral renal agenesis or multicystic dysplastic kidney (MCDK)
  - Contralateral UPJO
- Most common:
  - Horsehoe kidney: 15% risk
  - Ectopic kidney: 15% risk

PATHOPHYSIOLOGY
- Congenital (most common etiology):
  - Adynamic ureteral segment due to ureteral smooth muscle maldevelopment: the most common cause of pediatric UPJO
  - Trabeculation: due to inadequate ureteral recanalization during fetal development
  - Persistent valvular mucosal folds
  - Ectopic ureter:
  - Crossing accessory lower pole vessel: most common cause of adult UPJO
  - High ureteral insertion into renal pelvis
  - Horsehoe kidney, ectopic, or malpositioned kidney causing kinking at ureteropelvic junction (UPJ)

- Acquired:
  - Severe VUR can cause ureteral tortuosity and kinking at UPJ
  - Inflammation and scarring from trauma, ureterolithiasis, instrumentation, infected urine, or perirenal fibrosis

ASSOCIATED CONDITIONS
- 50% associated with another congenital anomaly:
  - Contralateral renal agenesis or multicystic dysplastic kidney (MCDK)
  - Contralateral UPJO
- Most common:
  - Horsehoe kidney: 15% risk
  - Ectopic kidney: 15% risk
- Incomplete renal duplication
- Unilateral renal agenesis
- VACTERL/VACTERL syndrome
- VUR

GENERAL PREVENTION
None

DIAGNOSIS
HISTORY
- Prenatal/infant presentation:
  - Hydronephrosis seen on antenatal US
  - Typically asymptomatic but occasionally sees feeding difficulties, failure to thrive, sepsis
- Childhood presentation:
  - Episodic abdominal complaints or bilateral colicky flank pain
  - Cyclical nausea and vomiting
  - Gross hematuria, classically after minor abdominal or flank trauma
- Adult presentation:
  - Episodic (isolated) colicky flank pain, classically after dextrin or alcohol intake (aka Diet crisis)
  - Cyclical nausea and vomiting
  - UTI or pyelonephritis

PHYSICAL EXAM
- Prenatal/infant presentation:
  - Painless abdominal mass
  - Fever (in neonates)
- Childhood presentation:
  - Costovertebral (CVA) tenderness
  - Palpable abdominal mass
  - Feeding difficulties, failure to thrive
- Adult presentation:
  - CVA tenderness
  - Hypertension (HTN) due to acute pain or activation of renin–angiotensin–aldosterone system

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Serum BUN and creatinine
- Urine analysis:
  - Microscopic hematuria, rarely gross
  - Trace proteinuria
  - Pyuria and bacteriuria
- Urine culture

Imaging
- Renal US:
  - Most often used as initial screening study in pediatric population
  - Useful to distinguish renal masses and ureteropelvic junction obstruction from UPJO
- Delay until 2nd or 3rd day of life to avoid false-negative result secondary to physiologic oliguria
- Renal ultrasound
  - Cystoscopy with retrograde pyelography:
  - Allows visualization of collecting system and renal vasculature (crossing vessels)
  - Peritoneal catheter with pressure transducer
    - Defined as > 20 cm/H2O
    - Allows for placement of temporary ureteral stent to relieve ureteral obstruction
  - Magnetic resonance urography (MRU)
    - Allows for recanalization during fetal development
  - Intravenous pyelogram (IVP)
    - Most often used as initial screening study in pediatric population

DIFFERENTIAL DIAGNOSIS
- Obstructive dilation:
  - Fecal balls
  - Impacted ureteral calculus
  - Intrarenal-bowel or malignant neoplasm
  - Sloughed papilla
- Nonobstructive dilation:
  - Perinephric and periureteral fluid:
  - VUR
  - Megacyste

TREATMENT
GENERAL MEASURES
- Prevent further deterioration in renal function
- Relieve symptoms of obstruction

MEDICATION
First Line
- Neointestinal stent placement:
  - Prophylactic antibiotics to maintain sterile urine
  - UPI prophylaxis: amoxicillin 25 mg/kg/d as neonates THEN
  - Trimethoprin-sulfamethoxazole 2 mg/kg/d OR nitrofurantoin 1–2 mg/kg/d beyond 2 mo of age
  - Repeat imaging—to monitor for resolution or deterioration of function (1)
- Childhood and adult presentation:
  - No medical therapy appropriate except to treat active infection

Diagnostic Procedures/Surgery
- Cystoscopy with retrograde pyelography:
  - Allows visualization of collecting system and renal vasculature (crossing vessels)
- Magnetic resonance imaging (MRI): 3D reconstruction:
  - Allows visualization of collecting system and renal vasculature (crossing vessels)
- Helical CT scan with 3D reconstruction:
  - Allows visualization of collecting system and renal vasculature (crossing vessels)
- Peritoneal catheter with pressure transducer
  - Defined as > 20 cm/H2O
- Bilateral UPJ obstruction
  - Residual urine: 22 cm/H2O
  - Obstructed: > 20 cm/H2O
URETEROPELVIC JUNCTION OBSTRUCTION

SUGERY/OHER PROCEDURES

- **Purpose:** Restore renal function
- **Definitive operative treatment:**
  - Expectant management in the neonate:
  - Treat pyonephrosis if present:
- **Purpose:** Restore renal function

- **Laparoscopic pyeloplasty:** Success rate ~ 95%; appropriate for adults with stricture < 2 cm, UPJO associated with renal calculus, children with secondary UPJO
- **Robotic assisted laparoscopic pyeloplasty:**
  - Employ dismembered or Y-V plasty technique;
  - Offers decreased morbidity, better cosmesis, and ease in surgical dissection and suturing
  - Gaining more acceptance and is now becoming the standard approach, even in the pediatric population, with increasing access to robotic surgical technology (3).
- **Ureterocalycostomy:**
- **Spiral or vertical flap:** Appropriate for large narrowed ureter
- **Foley Y-V plasty:** Appropriate for high ureteral involvement; excise anatomic and functional abnormal segments
- **Open pyeloplasty:** Procedure of choice in pediatric patients
- **Dismembered (Anderson-Hynes) pyeloplasty:**
  - Most common open technique; success rate ~ 95%
  - Indicated for high insertion, accessory vessels, massive dilatation, long-segment involvement; excise anatomic and functionally abnormal segments
- **Pediatric Y-V plasty:** Preferred for high insertion
- **Ureteric flap technique:** Appropriate for large extrarenal pelvis and long segment of narrowed ureter
- **Ureteroureterostomy:** Appropriate for rotational anomalies or reoperation after failed pyeloplasty; partial lower pole nephrectomy is required to prevent anastomotic stenosis
- **Simple nephrectomy:** May be appropriate for unilateral poor renal function and normal contralateral renal function, especially if differential renal function < 10–15%, extensive stone disease, chronic infection, multiple failed repairs

- **Endoscopic procedures:**
  - **Minimal invasive alternative to open procedures:** in adults (5)
  - Antegrade cold-knife incision endopyelotomy: Success rate ~ 90%; requires percutaneous access, nephrostomy tube left indwelling 24–48 hr; ureteral stent left indwelling 4–6 wk; appropriate for adult patients with stricture < 2 cm, UPJO associated with renal calculus, children with secondary UPJO
  - Retrograde ureteroscopic beam incision: Success rate 90–95%, allows direct visualization of incision; required specialized ureteroscopic equipment and endourologic expertise
  - Ureteroceles: reserved for patients who are not candidates for definitive operative treatment

ONGOING CARE

- **Frequent visits**
- **Bilateral nephrectomy:** May be appropriate for the management of patients who have undergone failed pyeloplasty
- **Ureteroureterostomy:**
- **Urinary tract infection:**
- **Rarely nephrectomy**

FOLLOW-UP

- **Patient Monitoring:**
  - **Urine analysis:**
  - **Renal US or MAG3 6–12 wk postop**
  - **Antegrade cold-knife endopyelotomy:**
  - **Retrograde ureteroscopic beam incision:**
  - **Endoscopic procedures:**

COMPLICATIONS

- **Renal structure:**
  - **Ureteroureterostomy:**
  - **Ureteroneocystostomy:**
  - **Renal infection:**
- **Rarely nephrectomy**

PEARLS

- **RECOMMENDATION:**
  - **Ureterocalycostomy:**
  - **Open pyeloplasty:**
  - **Laparoscopic pyeloplasty:**
  - **Robotic assisted laparoscopic pyeloplasty:**

REFERENCES


ADDITIONAL READING

- **See Also (Topic, Algorithm, Media):**
  - Hydro nephrosis/hydronephrosis, (Dilated Ureter/renal Pelvis), Adult
  - Hydro nephrosis/hydronephrosis, (Dilated Ureter/renal Pelvis), Pediatric
  - Hydronephrosis/hydronephrosis, (Dilated Ureter/renal Pelvis), Neonatal
  - Magruder, Congenital
  - Ureter, Obstruction
  - Ureteropelvic junction Obstruction Image at

CODES

- **ICD9:**
  - **592.1** Calculus of ureter
  - **593.4** Other ureteric obstruction
  - **757.2** Congenital obstruction of ureteropelvic junction

- **ICD10:**
  - N13.3 Hydro nephrosis in ureteral structure, NEC
  - N13.5 Cross vessel and stricture of ureter with hydronephrosis
  - N13.69 Other obstructive defects of renal pelvis and ureter

CLINICAL/SURGICAL PEARLS

- **Purpose:** To relieve obstruction and preserve kidney function
- **Open or laparoscopic surgical repair remains the best option for treatment.**
URETHRA, ABSCESS (PERIURETHRAL ABSCESS)

H. Henry Lai, MD, FACS
Gerald L. Andriole, MD, FACS

ASSOCIATED CONDITIONS (2)
- Diabetes mellitus
- Immunosuppression (eg, HIV)
- Sexually transmitted disease
- Urinary tract infection

GENERAL PREVENTION
- Excise and prevent sexually transmitted disease
- Sterilize the urine and defer instrumentation if the urine is infected
- Division of urine away from the urethra
- Adequate management of urethral stricture: – Dilatation
- – Interventional urotherapy
- – Urethroplasty and reconstruction
- – Perineal urotherapy

DIAGNOSIS

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Evaluate for septic shock
- Look for extravasation, stricture, fistula
- Not recommended during acute phase

DIAGNOSTIC PROCEDURES/SURGERY
- – Look for extravasation, stricture, fistula
- – Transrectal ultrasound imaging of prostate: not recommended during acute phase

PATHOPHYSIOLOGY
- Perineal extravasation of infected urine
- Ureteral extravasation may be caused by:
- High-pressure voiding behind a stricture
- Difficult dilatation of a stricture, false passage
- Traumatic urethral instrumentation
- Often localized to the bulbar urethra or spongiosum
- Once eroded through Buck’s fascia, may cause extensive necrosis of the fascia and adjacent tissues, leading to Fournier gangrene.
- Three potential sources of Fournier gangrene: – Perineal
- – Perirectal
- – Subcutaneous
- Fistula may develop in delayed cases following spontaneous abscesses rupture
- Common organisms: – Aerobic gram negative
- – Anaerobic gram negative
- – Enterococci
- – Anaerobes

HISTORY
- Symptoms may include urethral discharge, dysuria, pain, swelling of penis or scrotum, foul-smelling urine, fever, chills, weak urine stream, incomplete emptying, urinary frequency, urgency
- History of urethral stricture and treatment
- Recent history of urethral instrumentation, dilatation, catheterization, bulking agent, sling, or other surgery
- History of sexually transmitted disease, pelvic radiation, trauma (risk factors of stricture)
- History of recurrent UTI
- Diabetes, including glomerular control
- Immunosuppression (eg, HIV)
- Prior periurethral abscesses and treatment
- Maintain an index of suspicion for neoplasm for recurrent periurethral abscesses and stricture

DIAGNOSIS

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM
- Evaluate for septic shock
- Look for extravasation, stricture, fistula
- Not recommended during acute phase

DIAGNOSTIC PROCEDURES/SURGERY
- – Look for extravasation, stricture, fistula
- – Transrectal ultrasound imaging of prostate: not recommended during acute phase

PATHOPHYSIOLOGY
- Perineal extravasation of infected urine
- Ureteral extravasation may be caused by:
- High-pressure voiding behind a stricture
- Difficult dilatation of a stricture, false passage
- Traumatic urethral instrumentation
- Often localized to the bulbar urethra or spongiosum
- Once eroded through Buck’s fascia, may cause extensive necrosis of the fascia and adjacent tissues, leading to Fournier gangrene.
- Three potential sources of Fournier gangrene: – Perineal
- – Perirectal
- – Subcutaneous
- Fistula may develop in delayed cases following spontaneous abscesses rupture
- Common organisms: – Aerobic gram negative
- – Anaerobic gram negative
- – Enterococci
- – Anaerobes
TREATMENT

GENERAL MEASURES
Supportive treatment of other medical issues (diabetes, hypotension, septic shock, or organ failures).

MEDICATION

First Line
- Broad-spectrum antibiotics coverage
  - Ceftriaxone 2g IV q24 + gentamicin 1.5–2 mg/kg loading dose, followed by 5–7 mg/kg IV q24
  - Consider vancomycin (15–20 mg/kg IV q12)

Second Line
- Antibiotics are adjusted based on culture sensitivity

SURGERY/OTHER PROCEDURES
- Incision and drainage of abscess with debridement and excision of necrotic tissue
- May require repeated exploration and debridement as the margin between necrotic tissue and viable tissue becomes more apparent
- Needle aspiration or endoscopic transurethral incision may be considered in selected cases
- Wet to dry dressing change twice a day
- Exposed testicle may be placed in the scrotum or thigh pouch
- Wound vac placement after debridement if the wound is clean and if wound location permits
- Needle aspiration or endoscopic transurethral incision may be considered in selected cases
- Incision and drainage of abscess with debridement and excision of necrotic tissue
- Board spectrum antibiotics coverage
- Supportive treatment of other medical issues:
  - General measures
  - Testing for sexually transmitted disease
  - Periodic evaluation of urine for infection
  - Monitoring for recurrent stricture (eg, uroflow)
  - Frequent wound check until healed

FOLLOW-UP

Patient Monitoring
- Frequent wound check until healed
- Monitoring for recurrent stricture (eg, uroflow)
- Periodic evaluation of urine for infection
- Testing for sexually transmitted disease

Patient Resources
- Urology Care Foundation: Benign urethral lesions Patient Monitoring
- Urology Care Foundation: Urinary incontinence
- Urology Care Foundation: Benign prostatic hypertrophy
- Urology Care Foundation: Urinary tract infection
- Urology Care Foundation: Urethral diverticulum

URINARY DIVERSTION
- Urinary diversion with suprapubic tube are important in the treatment of urethral abscess
- Urinary diversion with suprapubic tube are important in the treatment of urethral abscess
- Urinary diversion with suprapubic tube are important in the treatment of urethral abscess
- Urinary diversion with suprapubic tube are important in the treatment of urethral abscess

ADDITIONAL READING


CLINICAL/SURGICAL PEARLS

- In men, urethral abscess is associated with urinary infection, urethral stricture, diabetes, and immunosuppression. In women, it is associated with urethral diverticulum.
- Incision and drainage of abscesses may include exploration and debridement of necrotic tissues.
- Board spectrum antibiotics coverage and supportive care.
- Urinary diversion with suprapubic tube are important in the treatment of urethral abscess.
- Early recognition and treatment is key to prevent progression to life-threatening Fournier gangrene and septic shock.
URETHRAL CARCINOMA, GENERAL CONSIDERATIONS

Michael A. Poch, MD
Philippe E. Spiess, MD

BASICS

DESCRIPTION
• Urethral carcinoma is a tumor arising from the lining of the male or female urethra
• Considered a rare cancer (<1 of all malignancies)
• Urethral carcinoma is most common histologic type followed by squamous cell carcinoma and adenocarcinoma.

EPIDEMIOLOGY (1)

Incidence
• Incidence (male): 1.6 per 1,000,000
• Incidence (female): 0.6 per 1,000,000

RISK FACTORS (1)

- Incidence increases steadily with age, more steeply in men as compared to women peaks at age 75:
- 7,811,000,000

Prevalence

N/A

DIAGNOSIS

HISTORY
• Urethral bleeding
• Perineal discomfort
• Decrease force of stream
• Urinary frequency
• Urinary urgency
• Dysuria
• Urinary fistula
• Urinary tract infection

PHYSICAL EXAM
• Perineal exam
  - Identifies palpable mass in proximal urethra
  - Pelvic exam
    - Identifies visual or palpable mass associated with female urethra
    - Examination under anesthesia with bimanual exam
    - Inguinal exam to evaluate palpable inguinal adenopathy

Diagnostic Procedures/Surgery

Cylcoplasty with brachytherapy/external beam

Pathologic Findings (2)

- Urethral carcinoma 30-40%
- Squamous cell carcinoma 16-25%
- Adenocarcinoma 10-16%
- More common in women, traditionally considered more prevalent

ASSOCIATED CONDITIONS

- HPV, condyloma
- External beam or seed implant
- CT thorax and abdomen in patients with invasive disease (rule out metastasis)
- CT scan of pelvis
- C7 scan of pelvis
- CT those and abdomen in patients with invasive disease (rule out metastasis)

Lab

- Urinalysis
- Urine culture
- Urine cytology
  - Sensitivity 55-59%

Imaging

- Urography—Arduous in the diagnosis of diverticula and/or stricture disease
  - Water-soluble contrast (WSS) or IVU
  - Retrograde urethrogram
  - Cross sectional imaging identifies local extension
    - MRI or CT
  - Preferred imaging modality for urethral carcinoma
- C7 scan of pelvis
- CT those and abdomen in patients with invasive disease (rule out metastasis)

- Indwelling catheter
- Urethroplasty
- Interstitial therapy
- External beam or seed implant

Primary tumor staging based on TNM classification
- T—Primary tumor
  - T0—Primary tumor cannot be assessed
  - T1—Primary tumor (less than or equal to T1a)
  - T2—Primary tumor extends to surrounding structures
  - T3—Primary tumor extends to surrounding structures beyond prostate capsule
  - T4—Primary tumor invades the pelvic cavity

- N—Regional lymph nodes
  - N0—No regional lymph node metastases
  - N1—Metastasis in a single lymph node 2 cm or less
  - N2—Metastasis in a single lymph node > 2 cm or multiple nodes

- M—Distant metastasis
  - M0—No distant metastasis
  - M1—Distant metastasis

- Primary tumor in prostatic urethra
  - Ta—Non-invasive papillary carcinoma
  - T1—Carcinoma in situ
  - T2—Carcinoma in situ invading the prostatic ducts
  - T3—Carcinoma in situ invading the prostatic capsule
  - T4—Carcinoma in situ invading beyond the prostatic capsule

- Adequate lymphadenectomy
- Neoadjuvant therapy
- Radical or partial urethral resection

- Adjuvant therapy
- Radiation therapy
- Hormonal therapy
- Surgical salvage

PREVENTION

- Prevention of traumatic injury leading to stricture disease
  - Indwelling catheter
  - Urethroplasty

- Indwelling catheter
- Urinary fistulae
- Dysuria
- Urinary urgency
- Perineal discomfort
- Urethral bleeding

- History of sexually transmitted infection (STI/STD)
- Chronic inflammation
- Adenocarcinoma of bulbar urethra
- Prior radiation

- Urethral stricture disease
- Urethritis
- History of sexually transmitted infection (STI/STD)
- Chronic inflammation

- Adenocarcinoma: Occurs in urethra diverticula
- Squamous-cell carcinoma: Occurs at distal 2/3 of the urethra
- Adenocarcinoma: Occurs in the proximal 1/3 of the urethra
URETHRAL CARCINOMA, GENERAL CONSIDERATIONS

DIFFERENTIAL DIAGNOSIS
- Adenocarcinoma
- Squamous papilloma
- Transitional cell papilloma
- Lymphoma
- Naphrogenic adenoma
- Ameloblastoma
- Urethral cancer
- Leukoplakia
- Vesical ulcer
- Skin gland, inflammation/adenitis
- Urethral diverticulum
- Urethral fistula
- Urethral stricture
- Malignant neoplasms
  - Adenocarcinoma
  - Melanoma
  - Metastatic disease
  - Skene (paraurethral gland) adenocarcinoma
  - Squamous cell carcinoma
  - Urethral carcinoma

TREATMENT
GENERAL MEASURES (1,3)
Based on pathology, stage, location of tumor

MEDICATION
First Line
- No medical therapy as first-line treatment
- Preoperative cisplatin-based systemic chemotherapy followed by surgery for locally advanced urothelial cancer has demonstrated a survival advantage
- Preoperative chemoradiation followed by surgery for locally advanced squamous cell carcinoma has demonstrated a survival advantage

Second Line
- Adjusted systemic chemotherapy based on underlying tumor histopathology

SURGERY/OTHER PROCEDURES
- Male
  - Perineal urethra
    - Transurethral resection (TUR)
  - Proximal penile urethra—total penectomy
  - Prostatic urethra
  - TUR + BCG for Ta or Tis
  - Higher stage radical cystoprostatectomy
  - Bulking materials
  - TUR
  - Primary excision with primary anastomosis
  - Cystoprostatectomy with urethroctomy and total penectomy, with possible pelvic lymph node dissection
  - Locally advanced disease. Excision of pubic rami
- Female
  - Distal
  - Partial urethrectomy or TUR
  - Prostate—often presents at higher stage
  - Anterior pelvic exenteration
  - Pelvic lymph node dissection

ADDITIONAL TREATMENT
Radiation Therapy
- Used as primary therapy for low-stage distal urethral carcinoma in females
- Primary brachytherapy or external beam
- Used as adjuvant therapy for advanced cancer

Additional Therapies
- Neoadjuvant chemotherapy only recommended for palpable disease or for high-risk disease in the distal urethra

Complementary & Alternative Therapies
- None

ONGOING CARE
PROGNOSIS (4)
- Male
  - 5-yr survival: Depends on location, stage, and pathology
- Female
  - 5-yr survival: Depends on location, stage, and pathology
- Complications
  - Associated surgical complications
  - Abcess
  - Cystitis
  - Incontinence
  - Stricture
  - Fistula

FOLLOW-UP
Patient Monitoring
- O3–4 mo cystoscopy and urine cytology
- Cross-sectional imaging to evaluate for local recurrence
- Recurrences often occur early (1–2 yr)

Patient Resources

REFERENCES

ADDITIONAL READING

CODES
- ICD9
  - 189.3 Malignant neoplasm of urethra
  - 597.80 Urethritis, unspecified
  - 599.0 Urethral stricture, unspecified

- ICD10
  - C68.0 Malignant neoplasm of urethra
  - N35.9 Urethral stricture, unspecified
  - N34.2 Other urethritis
  - N35.9 Urethral stricture, unspecified

CLINICAL/SURGICAL PEARLS
- Urethral cancers appear to be associated with infection with human papillomavirus (HPV), particularly HPV16, a strain of HPV known to be causative for cervical cancer.
- Most urethral cancers are managed surgically.
- Low-grade female distal urethral cancer can be managed with radiotherapy.
- Most locally advanced urethral tumors are best approached by neoadjuvant systemic chemotherapy (i.e., radiotherapy) followed by consolidative surgical resection.
- Outcome strongly correlates with stage.
URETHRAL CARUNCLE
Margarita M. Aponte, MD
Victor W. Nitti, MD, FACS

BASICS
DESCRIPTION
Urethral caruncle is a benign tumor consisting of friable mucosa at the posterior edge of the urethral meatus in females.
• Most are asymptomatic.
• Most common in postmenopausal females.

EPIDEMIOLOGY
Incidence
• Most common benign tumor of the female urethra.
• Occurs more frequently in postmenopausal women.
• Uncommon in childbearing years.
• Extremely rare in children.

Prevalence
Common in postmenopausal elderly women.

RISK FACTORS
• Postmenopausal vaginal atrophy
• Chronic irritation to the urethral meatus

Genetics
No known genetic association

PATHOPHYSIOLOGY
• Mucosal ectropion of posterior urethral wall secondary to retraction of an atrophic vagina due to decreased estrogens
• Appears unrelated to any viral etiology
• Some cases may be related to the autoimmune phenomena of IgG4-associated disease

ASSOCIATED CONDITIONS
Vaginal atrophy

GENERAL PREVENTION
Prevention of vaginal atrophy

DIAGNOSIS
HISTORY
• Determine menopausal status, as more common in postmenopausal females
• Incidental finding on pelvic exam in asymptomatic women
• Light bleeding or spotting on underwear
• Micropapillary hematuria
• Vaginal irritation
• Occasional dyspareunia
• Voiding or obstructive symptoms infrequent
• Tenderness is infrequent

PHYSICAL EXAM
• Erythematous, soft, friable mass seen protruding from a segment of the urethral meatus and palpated on vaginal inspection
• Usually reddish, occasionally may appear blue or black
• Usually located at the ventral (posterior) urethral meatus
• May be tender to palpation
• Usually < 1–2 cm

DIAGNOSTIC TESTS & INTERPRETATION
Lab
• There are no diagnostic lab tests
• Urine analysis may show RBCs or epithelial cells
• Urine cytology may identify malignancy but it is unrelated to the urethral caruncle

Imaging
• Urethroscopy: May help delineate extent of lesion and may be performed in the work up of microscopic hematuria
• Biopsy: Excisional or incisional
– Not usually required for diagnosis, but indicated if mass is suspicious for malignancy, it increases in size or fails to respond to topical estrogen cream.

Pathologic Findings
• Papillomatous, granulomatous, and angiomatous varieties
• Histologic:
– Connective tissue containing many inflammatory cells and blood vessels and covered by an epithelial layer
– Evidence of neovascularization, inflammation, and hemorrhage may be present.
• Transitional or stratified squamous epithelium
• 2% of caruncles have associated malignancy
• Case reports of intestinal heterotopia (1)

DIFFERENTIAL DIAGNOSIS
• Urethral prolapse:
– Eversion of urethral mucosa
– Typically circumferential
– Seen in women of all ages (pubertal through postmenopausal), caruncle is almost exclusively seen in post-menopausal females
• Malignancy:
– Urethral carcinoma:
– Uncommon
– Peak incidence 5th–7th decade
– Usually a firm, nontender, indurated mass
– Irritative and obstructive voiding symptoms may be associated
– Bleeding from urethra or on toilet tissue is more typical.
– Four subtypes of urethral carcinoma: Squamous cell, transitional cell, adenocarcinoma, melanoma (2B).
– Lymphoma
– Intestinal metaplasia
– Periurethral glands abscesses
• Urethral polyp: Pediatric equivalent of urethral caruncle
• Urethral syndrome
• Urethral condyloma
• Urethral varicosities
• Thrombosis of urethral vein:
– Bluish, swollen, very tender lesion in similar location to caruncle
• Other causes of postmenopausal bleeding: Cervical, ovarian, uterine pathology

TREATMENT
GENERAL MEASURES
• Most urethral caruncles are asymptomatic and do not require definitive treatment.
• Conservative management with sitz baths, topical estrogen creams, topical anti-inflammatory agents should be used in the majority of patients.
• Excessive or persistent bleeding of obstructive voiding symptoms may prompt treatment.
• If there is any doubt concerning the diagnosis, biopsy should be performed.
URETHRAL CARUNCLE

MEDICATION
First Line
- Topical estrogen: Apply cream 0.3 mg daily for 2 weeks, then decrease to twice a week for maintenance.
  - Due to minimal absorption, progesterone is not usually needed.
- Anti-inflammatory medications for mild discomfort, PO, or topical.

Second Line
Systemic estrogen replacement

SURGERY/OTHER PROCEDURES
- Excision:
  - Outpatient procedure performed under local anesthesia with or without sedation
  - Remove the entire caruncle and approximate the ventral urethral meatal mucosa to the vaginal epithelium
- Ligation (3)
  - Outpatient procedure performed under local anesthesia
- Cryoablation
- Laser fulguration

ADDITIONAL TREATMENT
- Radiation Therapy
  - Applicable only for certain distal urethral malignancies
  - Not for urethral caruncle
- Additional Therapies
  - Sitz baths may alleviate discomfort.
- Complementary & Alternative Therapies
  - None

ONGOING CARE
- Excellent

COMPLICATIONS
- Urethral stricture or meatal stenosis with surgical excision

FOLLOW-UP
- Patient Monitoring
  - None specific
  - Routine gynecologic follow-up as this is a benign lesion

Patient Resources

PROGNOSIS
- Excellent

ADDITIONAL READING

REFERENCES

CODES
- ICD9
  - 599.3 Urethral caruncle
  - 627.3 Postmenopausal atrophic vaginitis
  - V49.81 Asymptomatic postmenopausal status (age-related) (natural)
- ICD10
  - N36.2 Urethral caruncle
  - N95.2 Postmenopausal atrophic vaginitis
  - Z78.0 Asymptomatic menopausal state

CLINICAL/SURGICAL PEARLS
- Urethral caruncles occur most frequently in postmenopausal women.
- Most are asymptomatic and do not need treatment.
- Biopsy is indicated if there is a suspicion for malignancy.
- Topical estrogen is the first-line treatment.
- Surgical intervention should be reserved for patients with large symptomatic lesions or who fail conservative therapy.
URETHRAL DISCHARGE
Ryan Cleary, MD
Leonard G. Gomella, MD, FACS

ASSOCIATED CONDITIONS
With STI infection common (e.g., gonorrhea and chlamydia)

GENERAL PREVENTION
- Abstinence
- Female and male condoms
- Education and awareness of risky behavior

DIAGNOSIS
History
- Age, sex, and duration
- Roles are more likely to have discharge from a venereal cause
- STIs are most common in the 15–24-yr-old age group
- Venereal or traumatic cause is more likely to have acute onset while chronic inflammation or tumor is usually insidious

- Obtain thorough sexual history to discover risk of STI/STD
- See with men, women, or both
- Oral, vaginal, or anorectal intercourse
- History of STI/STD
- Condyloma
- Ask the time since onset, any inciting events, quality or character, quantity, prior treatments, associated symptoms
- History of irritative or obstructive voiding symptoms
- Hematuria, dysuria, frequency, urgency, incontinence, pollakiuria, dribbling, straining, incomplete emptying
- Hematuria noted at beginning, middle or total voiding course to urethra, bladder or upper tracts, or prostate
- Frequency and urgency can indicate an acute inflammatory response
- Incontinence can indicate a diverticula source
- Straining and incomplete emptying indicate obstructive cause
- History of penile, scrotal, or perineal pain
- Assist in localizing source of discharge
- Any vaginal symptoms
- Vaginal, vulvar, or anorectal symptoms

Lab
- Positive leukocyte esterase on first voided urine is diagnostic of urethritis.

Imaging
- If the cause of the discharge is unclear additional imaging
- Men
- Scrotal ultrasound
- Renal/bladder ultrasound
- CT abdomen and/or pelvis
- MRI pelvis
- Women
- Pelvic ultrasound (transabdominal or transvaginal)
- Renal/bladder ultrasound
- CT abdomen and/or pelvis
- MRI pelvis

PHYSICAL EXAM
- Men
- Request the patient avoid urination before being examined.
- Genital skin exam to evaluate for evidence of trauma, ulcers, rashes, abrasions, or masses
- If no discharge is seen, the urethra should be gently massaged from the ventral part of the penis toward the meatus.
- Examination of testicles and spermatic cord, scrotum, and inguinal lymph nodes
- Women
- Genital skin exam to evaluate for evidence of trauma, ulcers, rashes, abrasions, masses, or masses
- External genitaiia inspection
- Palpation of urethra for mass, fluctuance, or discharge
- Bimanual exam to evaluate for tenderness, mobility, and masses
Diagnostic Procedures/Surgery
- Cystourethroscopy
- Generally needed for more apical presentations and if discharge persists in spite of adequate medical therapy
- Evaluate for mass, erythema, false passage, stricture, or diverticulum of urethra
- Inspect prostate for friability, vascularity, hypertrophy, narrowing, and areas of visual fluctuation

Pathologic Findings
N/A

DIFFERENTIAL DIAGNOSIS
- Inflammatory causes
- Gonococcal urethritis
- Non-gonococcal urethritis
- Chlamydial urethritis
- Mycobacterial genitourinary tract
- Trichomonal vaginitis
- Ureaplasma urealyticum
- Urethral diverticulum
- Urethral tuberculosis
- Trichomoniasis
- TB
- Periurethral abscess
- Reactive arthritis (Previously called Reiter syndrome)
- Masses
- Urethral tumor
- Urethral caruncle
- Urethral hemangioma
- Urethral condyloma
- Urethral caruncle
- Urethral tumor
- Urinary tract system
- Local invasion or metastasis of malignant lesion
- Systemic infection
- Abscess formation in urethra, prostate, epididymis, or testicle
- Local spread to other genitourinary organs – cystitis, prostatitis, epididymitis, orchitis
- Abscess formation in urethra, prostate, epididymis, or testicle
- Systemic infection
- Local invasion or metastasis of malignant lesion
- Recurrent pain

TREATMENT
GENERAL MEASURES
Cause of discharge dictates treatment

MEDICATION
First Line
- Gonococcal and non-gonococcal urethritis
  - Azithromycin 1 g PO x 1 or doxycycline 100 mg PO BID x 7 days plus ceftriaxone 125 mg IM x 1 or cefixime 400 mg PO x 1 as first-line empiric therapy
- Trichomonal
  - Metronidazole 2 g PO x 1 or 250 mg TID x 7 days
- Reactive arthritis
  - N / A
  - Ibuprofen, naproxen, cyclosporine, and sometimes corticosteroids
- BPH
  - See 5α-reductase inhibitors can be used for refractory prostatic bleeding

Second Line
- See 5α-reductase inhibitors can be used for refractory prostatic bleeding

ADDITIONAL READING
- See also (Topic, Algorithm, Media)
  - Gonorrhea Microscopic Image &
  - Urethra, Bleeding (Blood at Meatus)
  - Urethral Carcinoma, General Considerations
  - Urethral Condyloma
  - Urethral Diverticulum
  - Urethral Hemangioma
  - Urethritis, Gonococcal and Non-gonococcal

REFERENCES
URETHRAL DIVERTICULA, FEMALE
Alana M. Murphy, MD

BASICS

DESCRIPTION
- A urethral diverticulum is an out-pouching off the urethra between the submucosal layer and the periurethral fascia
- Often contains a collection of urine and/or pus
- Usually connects to the urethra through a neck or ostium
- Classic symptoms are dysuria, dyspareunia, and post void dribbling

EPIDEMIOLOGY

Incidence (1)
- Diagnosis depends on history with which it is sought
- Mean age at surgery: 48 yr

Prevalence
- Difficult to determine true prevalence
- 1-3% asymptomatic women

ASSOCIATED CONDITIONS

Genetics
- No known genetic risk factors

PATOPHYSIOLOGY

- Congenital female urethral diverticula are uncommon
- Most common theory regarding adult female diverticula (2)
  - Infection or obstruction of periurethral glands
  - Obstruction or abscess formation leads to cyst-like cavity
- Diverticulum is contained within periurethral fascia

ASSOCIATED CONDITIONS

- Urinary incontinence
- Dyspareunia
- Dysuria
- Storage or voiding symptoms
  - Occasional urinary retention

GENERAL PREVENTION

No known method of prevention

DIAGNOSIS

HISTORY
- Classic: 3 D's (see table for all to be present):
  - Dysuria: Pain during voiding
  - Urinary (in)convenience: Typically due to urine leaking from the diverticulum, patient may also have concurrent stress and/or urgency incontinence
  - Dyspareunia: Pain with intercourse
- Non-specific complaints are common:
  - Frequency/urgency
  - Hematuria
  - Palpable or visible vaginal lump/lump
  - Perineal pain
  - Recurrent UTIs
  - Voiding symptoms or urinary retention
- May be an incidental finding

PHYSICAL EXAM
- Inspect the anterior vaginal wall:
  - Some diverticula are visible as a suburethral mass
  - Assess bladder neck mobility
  - Observe for stress incontinence
  - Assess for point tenderness suburethraly, which may be the only sign of a vesical diverticulum.
- If a suburethral mass is noted:
  - Classic sign: Compressing the mass expresses urine or pus from urethral meatus.
  - If the mass does not compress:
    - Vaginal wall cyst
    - Obstructed (noncommunicating) diverticulum
    - Induration suggests stone or cancer
  - Evaluate for other pelvic pathology

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Urine analysis, urine culture
- Preoperative tests appropriate to patient’s age and medical condition

Imaging
- Magnetic resonance imaging (MRI)
  - Diverticulum has high signal intensity on T2-weighted imaging
  - Most accurate diagnostic test
  - Does not require the patient to void
  - Helpful in decision-making
  - Not mandatory in straightforward cases
  - Main value: Rule out other pathology
  - Shows size, extent, location, and presence of filling defects
  - Voiding cystourethrogram (VCUG): (3)
    - Advantage: Less anatomic detail
    - Less sensitive for diagnosis
    - Patient must be able to void
  - Fluoroscopic UDS: Combines VCUG with urodynamic assessment of other causes of voiding symptoms
    - Useful if the patient has incontinence or voiding difficulty
    - Not mandatory in straightforward cases
    - Useful if the patient has recurrence or voiding difficulty

DIFFERENTIAL DIAGNOSIS

Benign neoplasms:
- Primary urethral carcinoma; more common in females:
  - Squamous cell (80%)
  - Transitional cell (15%)
  - Adenocarcinoma (4%)
  - Melanoma (1%)
  - Rarely and adenocarcinoma can arise as a urethral diverticulum or in Skene gland

TREATMENT

GENERAL MEASURES
- No treatment is necessary if the patient is asymptomatic
- Patient must understand the small risk that the diverticulum may harbor neoplastic cells
- Little is known about the natural history of untreated diverticula
- Antibiotics and analgesics may control symptoms
- With significant symptomatology, surgical excision is recommended

MEDICATION

First Line
- Antibiotics (eg, trimethoprim/sulfamethoxazole)
- Analgesics (eg, ibuprofen), and antispasmodics (eg, oxybutynin) may control mild symptoms

Second Line
- If first-line medications do not alleviate symptoms, then surgical excision is appropriate

Pathologic Findings

- Histology of epithelium may be:
  - Transitional
  - Stratified squamous
  - Cuboidal
  - Simple (i.e., flat epithelium)
  - May have carcinoma (4)
- Adenocarcinoma more common than transitional or squamous cell
- Diverticulum may contain stones

566
URETHRAL DIVERTICULA, FEMALE

SURGERY/OTHER PROCEDURES
- Transvaginal excision and reconstruction is the most common operation.
- Key principles of excision include:
  - Well-vascularized anterior vaginal wall flap
  - Preserve periurethral fascia
  - Excise diverticulum completely
  - Watertight, tension-free urethral closure
  - Avoid overlapping suture lines
  - Close dead space
  - Multiple layer closure (consider Martius flap)
  - Avoid overlapping suture lines
  - Close dead space
  - Multiple layer closure (consider Martius flap)
  - Adequate bladder drainage with a urethral catheter ± suprapubic catheter
  - Antimuscarinics can be used to prevent bladder spasms

Perform simultaneous anti-incontinence procedure (fascial sling) for stress urinary incontinence (SUI) if:
- Stress incontinence is present before surgery
- Patient desires concomitant treatment

ADDITIONAL TREATMENT
Radiation Therapy
- N/A
Additional Therapies
- N/A
Complementary & Alternative Therapies
- N/A

ONGOING CARE
PROGNOSIS
- If untreated, natural history is not well known
- Reported surgical success rates 70–99%

COMPLICATIONS
- Related to the diverticulum:
  - Stones
  - Carcinoma: Adenocarcinoma, transitional cell, squamous cell
  - Renal UTIs
  - Dysuria
  - Dyspareunia
  - Urinary incontinence
  - Storage or voiding symptoms
- Related to the surgery:
  - Infection
  - Bleeding
  - Urinary incontinence
  - Recurrent diverticulum
  - Urethrovaginal fistula
  - Urinary tract or necrosis
  - Bladder or urethral injury
  - Vaginal scarring or narrowing

FOLLOW-UP
Patient Monitoring
- VCUG after surgery at the time of catheter removal
- History and genitourinary exam on follow-up visits
- Additional studies if indicated based on history and exam findings

Patient Resources
http://www.urolgyhealth.org/urology/index.cfm?article=110

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Dribbling, Post-Void
- Dyspareunia
- Markers Flap
- Müllerian Duct Remnants and Syndrome
- Skene (paraurethral) gland, adenocarcinoma
- Skene (paraurethral) gland, inflammation/adenitis
- Urethra, Abscess (Periurethral Abscess)
- Urethra, Carcinoma
- Urethra, Caruncle
- Urethra, Diverticula Carcinoma
- Urethra, Leiomyoma
- Urethra, Mass
- Urethra, Nephrogenic Metaplasia (Adenoma)
- Urethra, Prolapse (Female)
- Urethral Diverticula Image
- Urinary tract infection (UTI), Adult female
- Vaginal Discharge, Urologic Considerations

CODES
ICD9
- 599.2 Urethral diverticulum
- 625.0 Dyspareunia
- 788.1 Dysuria
ICD10
- N96.1 Urethral diverticulum
- N98.1 Dyspareunia
- R30.0 Dysuria

CLINICAL/SURGICAL PEARLS
- Classic symptoms include dysuria, dyspareunia, and post-void dribbling
- Definitive management requires transvaginal excision with a multilayer closure.
URETHRAL MASS

Bic N. Cung, MD
Jack H. Mydlo, MD

DESCRIPTION
- Urethral masses may be palpable; they are often visualized on cystoscopy or other imaging modalities.
- In females the most common differentials include: urachal cyst, periurethral/biunary duct cyst, prostatic urethral stenosis, periurethral abscess, and malignancy.
- In men inflammatory lesions such as: lichen sclerosus (LS) or balanitis xerothema obliterans (BXO), periurethral abscess and malignancy can be commonly seen.

EPIDEMIOLOGY
Incidence
- Incidence of urethral mass unknown.
- With respect to urethral malignancy:
  - African Americans twice as likely of developing primary urethral cancer as whites.
  - Primary urethral cancer at least twice as common in males as in females (1).
- Most common from 1st to 7th decades of life.

Prevalence
N/A

RISK FACTORS
- Malignancy:
  - Chronic UTIs may suggest anatomic problem such as diverticuli.
  - HPV-16 infection has been linked to urethral malignancy.
  - History of bladder cancer may suggest urethral malignancy.
- Inflammatory:
  - Most common from 5th to 7th decades of life.
  - African Americans twice as likely of developing primary urethral cancer as whites.
- Congenital:
  - Benign fibroepithelial polyp
  - Retention cysts of Cowper gland ducts
  - Urethral diverticulum
  - Pelvic MRI or CT often considered imaging study of choice for urethral neoplasms.

ASSOCIATED CONDITIONS
None

GENERAL PREVENTION
Self sexual practices can prevent STDs and decrease risk of inflammatory/infectious conditions.

DIAGNOSIS

HISTORY
- Age and sex of patient
- Malignancy: more common >50
- Prior history of bladder cancer may suggest urethral recurrence, particularly in men
- Sexual history
- General facts, gonorrhea may predispose to malignancy.
- Lower urinary tract symptoms:
  - Frequency, urgency, hematuria, or dysuria may be associated with stricture or malignancy.
  - Obstructive voiding symptoms such as weak stream, straining, and dribbling
- History of UTI
  - May be associated with urethral diverticulum

PHYSICAL EXAM
- General exam:
  - Assess for lower extremity edema.
- Lymph node assessment:
  - May be associated with urethral diverticulum
  - May be associated with urethral malignancy

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urate analysis
- Urine culture
- Urethral cytology
- Urethral secretions: Culture for gonorrhea, Chlamydia, and TB

Imaging
- Ultrasound to evaluate urethral stricture, diverticulum, and foreign body
- VUCs can help diagnose urethral diverticulum.
- Retrograde urethrogram (RUG) to assess for location and length of urethral stricture.
- Pelvic MRI or CT to assess for urethral diverticulum, metastasis to the pelvis and inguinal LNs, evidence of corporal invasion by carcinoma.
- Pelvic MRI often considered imaging study of choice for urethral neoplasms.

Differential Diagnosis
- Depends on clinical presentation and age of patient:
  - Children are more likely to have congenital disease
  - Young adults are more likely due to trauma or STIs/STDs
  - Older adults are at greater risk for primary or metastatic malignancy
- Congenital conditions:
  - Benign fibroepithelial polyp
  - Retention cysts of Cowper gland ducts
  - Urethral diverticulum
  - The 3 Ds: diverticulum, dysuria, dyspareunia, dribbling

Inflammatory
- Stricture disease secondary to gonoctocal urothitis
- Perirectal abscess
- Accessory gland cysts/abscesses
- Condyloma acuminata
- TB
- Lichen sclerosus (LS) or balanitis xerothema obliterans (BXO)
- Most common cause of mental stress in adults
- Traumatic:
  - Stricture disease secondary to injury: hematoma, foreign body
- Benign neoplasms:
  - Hyperplasia
  - Adenomatous polyps
  - Squamous papilloma
  - Transitional cell papilloma
  - Lichen plan
  - Inverted papilloma
  - Benign fibroepithelial polyp
  - Type 1 (benign), type 2 higher malignant potential and requires follow-up.
- Foreign body
  - Most common seen in patients with chronic catheter use.
  - Neoplastic:
  - Adenocarcinoma
  - Amyloidosis
  - Syncytial (parasquamous) gland, inflammation/ adenomalacation
  - Urethral carcinoma
  - More common in postmenopausal women
URETHRAL MASS

TREATMENT

GENERAL MEASURES
- Management is directed by the pathologic findings.
- Cystoscopic exam with biopsy is usually provided to diagnose.
- Imaging and bimanual exam will provide staging information in the case of malignancy.
- In cases with locally advanced disease, multimodality therapy using chemotherapy is sometimes used.
- Condyloma of the urethra: Intravesical 5-FU cream, anti-inflammatory cream.
- Biopsy with fulguration/laser ablation.
- Radiation is sometimes used.

Malignant neoplasms:
- Excision, fulguration, laser ablation.
- Biopsy for diagnosis.
- Excision, fulguration, laser ablation.

ADDITIONAL TREATMENT

Radiation Therapy
- May be indicated in some cases of urethral cancer to decrease local recurrence.
- In women, radiation therapy using biatriality and external beam radiation combination is a suitable alternative.

Complementary & Alternative Therapies
Combination of chemotherapy, radiation therapy, and surgery is recommended for advanced female urethral cancer.

ONGOING CARE

PROGNOSIS
- Depends on etiology of mass.
- Neoplasms:
  - Male: survival dependent on grade and stage of tumor.
  - Female: survival dependent on grade and stage of tumor.
- Urethral carcinoma in females of low stage has 70–90% cure rates with surgery.
- In females, this includes an anterior exenteration (urethrectomy, cystectomy with pelvic lymphadenectomy, hysterectomy with salpingectomy, and anterior vaginal wall).

COMPLICATIONS
- Depends on pathology and treatment.
- Urethral stricture: Complications secondary to instrumentation and treatment of urethral mass.

FOLLOW-UP

Patient Monitoring
- Cystoscopy and urethrocystogram every 6 mo for urethral carcinoma.
- Biopsy and surveillance for disease eradication.

MEDICATION

See Also (Topic, Algorithm, Media)
- Urethral Carcinoma, General Considerations
- Urethra, Caruncle
- Urethra, Carcinoma, General Considerations
- Urethra, Diverticulum, Female
- Urethra, Squamous Cell Carcinoma

CODES

International Classification of Diseases (ICD-10)
- D30.4 Benign neoplasm of urethra
- C68.0 Malignant neoplasm of urethra
- 599.84 Other specified disorders of urethra

ICD-9
- 189.3 Malignant neoplasm of urethra
- 223.81 Benign neoplasm of urethra
- 198.84 Other specified disorders of urethra
- 680.4 Malignant neoplasm of urethra
- 198.8 Other specified disorders of urethra

REFERENCES


ADDITIONAL READING


Patient Resources
- Urology Care Foundation: Urethral cancer.
- Urology: Urethral cancer.

Urology Care Foundation: Urethral cancer.
- http://www.urologyfoundation.org/urology/index.cfm?
- Urology: Urethral cancer.
- Urology: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.

Urology: Urethral cancer.
- Urology Care Foundation: Urethral cancer.
URETHRAL SQUAMOUS-CELL CARCINOMA

Zachary L. Smith, MD
S. Bruce Malkowicz, MD, FACS

BASICS

DESCRIPTION

Squamous-cell carcinoma (SCC) of the urethra is a malignancy arising from the native squamous lining of the male and female urethra.

EPIDEMIOLOGY

Incidence

• Prevalence is higher in African American patients as compared to their white counterparts.
  – White males: 0.58 per 1,000,000
  – African American males: 2.3 per 1,000,000
  – White females: 0.43 per 1,000,000
  – African American females: 0.69 per 1,000,000

• Incidence increases steadily with age, more steeply in men as compared to women (1).

Prevalence

NR

RISK FACTORS

• Male urethral SCC:
  – Chronic irritation after prior intermittent catheterization (ICC)
  – History of sexually transmitted infection (STI): Nearly 25% of patients with urethral carcinoma will give history of STI.

• Urethral stricture disease (≥ 50% of patients).

• HPV

• History of external beam radiation therapy

• Female urethral SCC:
  – Leukoplakia
  – Chronic irritation
  – Porfus
  – Human papilloma virus
  – Visceral infections
  – Recurrent urinary tract infections
  – Possibly urethral diverticula: 4% of female urethral carcinoma is found within the diverticulum.

GENETICS

• Possibly linked to alterations in chromosomes Y, 2, 3, 4, 6, 7, 8, 11, and 20 (2).

• Notably, there have been no abnormalities described in chromosomes 9 and 17: those largely responsible for the development of urethral carcinoma.

PATHOPHYSIOLOGY

• Male urethral SCC:
  – Occurs in the male membranous urethra (80% SCC), bulbar urethra (80% SCC), and penile urethra (90% SCC).

• Female urethral SCC:
  – Occurs in the distal 2/3 of the female urethra.
  – Both male and female urethral carcinoma spread via direct local extension and via lymphatics:
    – Anterior urethra drains to superficial and deep inguinal nodes.
    – Posterior urethra drains to pelvic lymph nodes.

ASSOCIATED CONDITIONS

• Condyloma acuminatum
• History of STIs
• Presence of indwelling catheter
• Urethral diverticula
• Urethral stricture disease

GENERAL PREVENTION

Prevention of STIs with the use of barrier protection such as condoms

DIAGNOSIS

HISTORY

• Particular attention must be made to risk factors and associated GI conditions.

• Male urethral SCC:
  – Urethral bleeding
  – Perineal discomfort
  – Decreased force of stream

• Female urethral SCC:
  – Urethral bleeding
  – Palpable urethral mass
  – Urethral urgency or frequency
  – Induration of urethra or anterior vaginal wall

PHYSICAL EXAM

• Particular attention must be made to risk factors and associated GU conditions.

DIAGNOSTIC TESTS & INTERPRETATION

• Cytology of initial voided urine
• Urine culture
• Urine polymerase chain reaction for Neisseria gonorrhoeae and Chlamydia trachomatis
• Cystoscopy with biopsy or transurethral resection:

IMAGING

• Retrograde urethography/voiding cystourethrograph (RUG/VCGU):
  – Evaluates entire urethra
  – Aids in assessment for stricture disease, urinary fistula, or urethral diverticula

• Cross-sectional imaging (CT or MRI):
  – Aids in the determination of local involvement, spread to regional lymphatics, or invasion of contiguous structures

• MRI particularly helpful for assessment of corporal involvement

• CT-urography provides evaluation of upper urinary tract drainage and presence or absence of upper urinary tract neoplasia (more critical in patients with urethral urothelial carcinoma).

Diagnostic Procedures/Surgery

• Cystoscopy with biopsy or transurethral resection:
  – Gold standard in histologic diagnosis of urethral carcinoma
  – Cystoscopic appearance of fungating growth extending into urethral lumen

• Surgical specimen/excisional biopsy for concern for involvement of GI tract based upon physical exam or imaging

• Particularly important in cases of urethral adenocarcinoma to rule out a GI primary source

Pathologic Findings

Fungating tumor with varied cytologic differentiation ranging from well-differentiated lesions producing keratinized epithelium to anaplastic giant-cell tumors

DIFFERENTIAL DIAGNOSIS

• Condyloma acuminatum
• Benign neoplasms:
  – Hemangioma
  – Adenomatous polyps
  – Squamous papilloma
  – Urethral cell papilloma
  – Leukoplakia
  – Urethral caruncle (more common in postmenopausal women)

• Skene (periurethral) gland inflammation:
  – Sigmoidoscopy/colonoscopy if concern for malignancy

• Leukoplakia
• Neourethral abscess
• Skin infections:
  – Staphylococcus aureus
  – Enteric organisms
• Urethral fistula
• Urethral stricture
• Malignant neoplasms:
  – Primary urethral carcinoma:
    – Squamous cell
    – Adenocarcinoma
  – Carcinoma in situ
  – Squamous cell carcinoma
  – Adenocarcinoma

Alert

The clinician must have a very high index of suspicion when considering urethral carcinoma, considering the often insidious and nonspecific nature of the patient’s complaints.

570
URETHRAL SQUAMOUS-CELL CARCINOMA

TREATMENT

GENERAL MEASURES
- Treatment decisions based on sex, stage, and location of tumor.
- TNM staging (See Reference tables: TNM: Urethra Cancer)

MEDICATION

GENERAL MEASURES
- Male penile urethral SCC (3):
- Male bulbomembranous urethral SCC (3):

Localized disease:
- Preoperative chemotherapy or chemoradiotherapy has been shown to be of benefit over surgical resection alone.
- Cisplatin-based polychemotherapeutic regimens should be used.

Second Line
N/A

SURGERY/OTHER PROCEDURES
- Male suburethral urethral SCC (3):
- Early lesions have been treated successfully with transurethral resection or local excision with end-to-end urethral anastomosis.
- Radical excision offers best chance at cure, with radical cystoprostatectomy, total penectomy, bilateral pelvic lymphadenectomy recommended.
- With locally advanced disease, consider en-bloc excision to include the pubic rami and urogenital diaphragm.
- Male penile urethral SCC (3):
- Transurethral resection, fulguration, or local excision may be employed for superficial low-grade tumors.
- For tumors involving the corpus spongiosum, partial penectomy with a 2-cm margin is treatment of choice if localized to the distal half of the penis.
- With involvement of the proximal penile urethra, total penectomy is required to obtain an adequate margin of excision.
- Biopsies of urethral margin are indicated in prius of palpable disease, as there has been no documented benefit of prophylactic lymphadenectomy.
- Distal female urethral carcinoma (5):
- Tumors of the distal urethra tend to be low-stage with cure rates of 70%-80% with local excision alone.
- External beam radiation therapy is also therapeutic option for distal female urethral carcinoma.
- Proximal female urethral SCC (3):
- For more likely to extend into the anterior vaginal wall and bladder.
- Requires anterior exenteration with wide resection of the vagina; pelvic lymph node dissection is often required to achieve negative surgical margins.

ADDITIONAL TREATMENT

Radiation Therapy
- Localized disease.
  - Male urethral SCC:
    - Preoperative radiation therapy for patients with early-stage lesions of the anterior urethra who refuse surgery.
    - Possible role in radiation for occasional advanced use with extensive resection.
  - Female urethral SCC:
    - Local pelvic disease:
      - Low-stage disease can be treated with external beam radiation or brachytherapy combined with 5-yr survival rates approaching 75%.
      - Although there appears to be some role to adjuvant external beam or brachytherapy in the treatment of locally advanced female proximal urethral urethral carcinoma, the possible role of radiation therapy remains unclear.
    - Advanced disease:
      - While surgical resection remains standard of care, preoperative radiation therapy combined with cisplatin-based chemotherapeutic regimens have been shown to give remarkable results in comparison to surgical resection alone.

Additional Therapies
N/A

Compensation & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS
- Male urethral carcinoma (4):
  - 5-yr overall survival (OS): 42.3%.
  - 5-yr OS (superficial disease): 83.3%.
  - 5-yr OS (invasive disease): 35.7%.
  - 5-yr OS (anterior urethra): 69.1%.
  - 5-yr OS (bulbar urethra): 44.4%.
- Female urethral carcinoma (5):
  - 5-yr OS: 32%.
  - 5-yr OS (low-stage): 78%.
  - 5-yr OS (high-stage): 31%.
  - 5-yr OS (anterior urethra): 54%.
  - 5-yr OS (posterior urethra): 25%.

COMPLICATIONS
- Abscess
- Cystitis
- Incontinence
- Urethral stricture
- Urinary fistula

FOLLOW-UP

Patient Monitoring
- Most majority of recurrences occur within 1-2 yr following definitive therapy.
- Surveillance is not well established, but routine cystoscopy and urinary cytology for 1-2 yr, with increasing intervals between surveillance cystoscopy in the absence of recurrence seems reasonable.

Patient Resources

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
  - Prostate Cancer, Urethral
  - Reference Tables: TNM: Urethra Cancer
  - Skene (Paraurethral) Gland, Adenocarcinoma
  - Urethra Diverticula
  - Urethral Mass
  - Urethra, General Considerations
  - Urethral Stricture/Stricture, Female

CODES
ICD9
- 189.3 Malignant neoplasm of urethra
- 199.9 Urethral stricture, unspecified
- 571.09 Personal history of other infectious and parasitic diseases

ICD10
- C89.3 Malignant neoplasm of urethra
- N39.9 Urethral stricture, unspecified
- Z91.19 Personal history of other infectious and parasitic diseases

CLINICAL/SURGICAL PEARLS
- Primary urethral SCC is a rare entity.
- Surgical excision is the mainstay of treatment.
- Distal tumors tend to be less advanced and more amenable to localized treatment.
- Proximal tumors tend to have a worse prognosis and require more aggressive treatment.
- Preoperative chemoradiotherapy may be used in advanced disease.
URETHRAL STRICTURE, MALE
Hunter Wessells, MD, FACS

ASSOCIATED CONDITIONS
- Trauma
- STD/STI
- Urethral instrumentation
- BPH
- Prostate cancer
- Lichen sclerosis/BXO

GENERIC PREVENTION
- Limited urethral instrumentation
- Appropriately sized instruments for transurethral procedures
- STD/STI prevention and early treatment (gonorrhea most common)

DIAGNOSIS
HISTORY
- Voiding symptoms
  - Hematuria
  - Reduction in stream
  - Post void dribbling
  - Urethral discharge
  - Hesitancy
  - Retention
- Prior surgery
- Transurethral surgery or manipulation
- Prostatitis
- Lichen sclerosis/BXO
- Urinary retention

PHYSICAL EXAM
- Palpable bladder with retention
- Lichen sclerosis/BXO
- Hypertrophy, meatal stenosis
- Thickened foreskin with glandular adhesions
- Evidence of discharge

DIAGNOSTIC TESTS & INTERPRETATION
- Urethroscopy with flexible cystoscope or hysteroscope
- Diagnostic Procedures/Surgery
- Proper size for transurethral procedures
- Injection of local anesthetic
- Dilatation and direct vision internal urethrotomy
- Abnormalities noted
- Residual urine
- Voiding symptoms
- Urethroscopy

TREATMENT

FIRST LINE
- No role for primary medical management of urethral stricture disease
- Medication
- General measures
- Imaging
- SURGERY/OTHER PROCEDURES
- Dilation and direct vision internal urethrotomy
- Dilation, cold DVIU, laser DVIU equivalent results
- Effective for short (<1 cm), large caliber (>15 Fr) strictures in which dilation or DVIU have not been previously attempted
- Use spanning in long, narrow or refractory strictures
- TECHNIQUES
  - Stabaler, balloon, sounds, filters, and followers
  - DVIU: Instil at 12:00 to limit bleeding
  - For balloon and DVIU, use helpful
  - 18 French Foley catheter for 48–72 h

Genetics
No known associations

PATHOPHYSIOLOGY
- Anterior urethral strictures
  - Compromised viability of corpus spongiosum secondary to trauma, inflammation or ischemia
  - Posterior urethral strictures
  - Pelvic fracture-associated urethral injury and related distraction defects
  - Scarring following TURP or radical prostatectomy

EPIDEMIOLOGY

DESCRIPTION
- A urethral stricture is a narrowing of the caliber of the anterior or posterior urethra. Progressive scarring can cause voiding symptoms possibly urethral obstruction
- True stricture of the female urethra is very rare.

RISK FACTORS
- Posterior urethral strictures
- Anterior urethral strictures
- Hypospadias, with or without prior repair
- Lichen sclerosis/balanitis xerotica obliterans (BXO)
- Trauma (straddle injury or pelvic fracture)
- Catheterization (usually prolonged)
- Previous TURP or radical prostatectomy
- Recurrent infection
- STD/STI associated with urethral stricture
- Urethral instrumentation
- Male urethral strictures in VA: 274/100k men
- Urethral strictures in Medicare: 4.5k/100k men
- Some data from Medicare suggests black Americans may have higher stricture rates

Prevalence
- Unknown

FACTORS
- Sexually transmitted infections (STIs) (sexually transmitted diseases [STDs]), particularly gonorrhea
- Posterior urethral injury in 6% of pelvic fractures and 15% of severe pelvic fractures
- Urethral strictures in VA: 274/100k men
- Urethral strictures in Medicare: 4.5k/100k men
- True stricture of the female urethra is very rare.
PROGNOSIS

Ongoing Care

Additional Reading

Urethroplasty: Anterior
- Short strictures (≤2 cm) amenable to excision and primary anastomosis
- Long strictures (>2 cm) require substitution with flap or graft
- Long strictures with narrow segment may need combination of resection and substitution (augmented anastomosis)
- Long strictures that are diffusely narrow may need staged urethroplasty with substitution (split-harvest urethroplasty)

- Urethroplasty: Posterior
  - Typically, excision and skin grafting required
  - Techniques used to bridge defect:
    - Urethral mobilization
    - Corporal separation
    - Inferior pubectomy
  - Suprapubic urethrostomy

- Grafts
  - Buccal mucosa widely used, favorable outcomes
  - No difference in success rates with ventral/dorsal graft position
  - Lichen sclerosus urethral reconstruction
  - One-stage or staged repairs using oral mucosa grafts are the most recommended

ADDITIONAL TREATMENT

Radiation Therapy

Additional Therapies
- Intermittent catheterization for 3–6 mo in select cases may improve patency rates
- Suprapubic placement is selected cases with inability to pass catheter or postoperatively following open repair
- Urolume™ stent approved for short bulbar urethral strictures; no longer manufactured
- Memokath™ stent may be useful after dilation or internal urethrotomy for recurrent bulbar strictures

ADDITIONAL READING

See Also (Topic, Algorithm, Media)

References

Codes

ICD9

ICD10

CLINICAL/SURGICAL PEARLS

COMPLICATIONS

- Immediate
  - UTI
  - Bleeding
  - Urinary leak and/or fistula
  - Lower extremity compartment syndrome
  - Delayed
    - Postoperative erectile dysfunction may occur, but recovers by 3–6 mo.
    - Stress incontinence is rare, but can occur if internal and external sphincters are damaged—either prior to or at time of urethroplasty
    - Post-void dribbling
    - Bleeding
    - Urethrostomal fistula
    - Perineal cureuture

FOLLOW-UP

Patient Monitoring

- Recurrence most likely within 1 yr
- Uroflowmetry, PVR, and AUA-SS sufficient to monitor for recurrence; cystoscopy optional

Patient Resources


COMMENTS


ADDITIONAL READING

URETHRAL TRAUMA (ANTERIOR AND POSTERIOR)

Lee C. Zhao, MD, MS
Allen F. Morey, MD, FACS

ASSOCIATED CONDITIONS
- Pelvic fracture
- Pelvic hematoma
- Bladder injury
- Vaginal injury

GENERAL PREVENTION
- Seat belts
- Cautious instrumentation of the urethra to prevent iatrogenic injury

ALERT
- The amount of urethral bleeding does not correlate with the degree of injury.
- Pain with urination or inability to void is highly suggestive of urethral disruption in the trauma patient.

DIAGNOSIS

HISTORY
- Description of trauma and mechanism of injury
- Voiding history
- Retention
- Hematuria

PHYSICAL EXAM
- Classic clinical triad:
  - Blood at meatus:
  - Hematuria
  - Retention
- Grade V: complete or partial disruption of the bladder neck, rectum or vagina
- Grade IV: complete disruption
- Grade III: partial disruption
- Grade II: contusion
- Grade I: stretch injury

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- CBC, electrolytes, BUN, creatinine
- Urinalysis

Imaging
- Retrograde urography
- 30-degree oblique position with bottom leg flexed at knee and top leg straight.
- Place Foley catheter into Tossa navicularis, inflate balloon with 2–3 mL
- Injection of ~25 mL of contrast into urethra
- Extravasation of contrast indicates the location of the tear
- Complete injury usually has no contrast flow into the bladder
- CT is inadequate to evaluate urethral trauma
- Generally obtained for staging of associated injuries

TREATMENT

GENERAL MEASURES
- Perform retrograde urethrography (RUG) prior to placement of Foley catheter, avoid urethral instrumentation until urethral imaging if the patient is stable.
- If catheter has already been placed, do not remove it. Perform percutaneous RUG with pediatric feeding tube or angiocatheter.
- Establish prompt urinary drainage in patients with pelvic fracture associated urethral injury as typically unable to void and undergo aggressive resuscitation.
- Urethral injury confirmed be:
  - Extravasation on RUG or VCUG
  - Cystoscopy
- Classification of urethral injury can guide treatment decisions
  - EAU Classification of blunt urethral injury (1CE):
    - Grade I: stretch injury
    - Grade II: contusion
    - Grade III: partial disruption
    - Grade IV: complete disruption
    - Grade V: complete or partial disruption of posterior urethra with associated tear of the bladder neck, rectum or vagina

RISK FACTORS
- Pelvic fracture
- Penile/urethral instrumentation
- Perineal straddle injury
- Pelvic fracture

PATHOPHYSIOLOGY
- Anterior urethra injuries
  - Less common due to mobility of anterior urethra and protection of the pubovesical ligament
  - Penile fracture (often intercourse related) can cause anterior urethral injury
  - Penile constriction bands
  - Penile fracture (often intercourse related) can cause anterior urethral injury
- Posterior urethra
  - More common due to fixed location of urethra
  - Penetrating trauma (gunshot, stabbing)
  - Straddle injuries
  - Pelvic fracture
- More common due to fixed location of urethra
- Urethral instrumentation
  - Transurethral surgery using oversized resectoscopes
  - Chronic indwelling catheters
  - Catheter placement in patient with urethral stricture
  - False passage: instrument or catheter
  - Urethral injury: contusion, complete, partial
- Violation of Buck fascia, hematoma confined by Colles fascia
- Greater than 75% of patients with anterior urethral (AU) injury
- Place Foley catheter into fossa navicularis, inflate balloon with 2–3 mL
- 30-degree oblique position with bottom leg flexed at knee and top leg straight.
- Place Foley catheter into Tossa navicularis, inflate balloon with 2–3 mL
- Injection of ~25 mL of contrast into urethra
- Extravasation of contrast indicates the location of the tear
- Complete injury usually has no contrast flow into the bladder
- CT is inadequate to evaluate urethral trauma
- Generally obtained for staging of associated injuries

DIFFERENTIAL DIAGNOSIS
- Urethral injury: collision, complete, partial
- Injury to bladder neck, urethra
- Pelvic or vaginal injury

BASICS

DESCRIPTION
- Injury that disrupts the watertight integrity of the urethra, typically in male patients.
- Injury to the urethra in women is less common.

PREVALENCE
- Estimate 10–20% of anterior urethral stricture from injury (1).
- Occurs in 10% of pelvic fractures

INCIDENCE
- Joint has the highest risk of urethral injury
- Straddle fractures with diastasis of the sacroiliac joint has the highest risk of urethral injury

DIAGNOSTIC PROCEDURES/SURGERY
- Flexible cystoscopy
- Cystoscopy
- Retrograde urethrography
- VCUG
- Ultrasonography

ARTICLE 574
In an unstable trauma patient, a cautious attempt should be made to pass a urethral catheter. If there is any difficulty a suprapubic catheter can be placed and a retrograde urethrogram performed later [4].

In women, primary open repair is recommended for disruption of the urethra with associated tear of bladder neck and vagina (IIIc) due to risk of incontinence and vesicovaginal fistula.

Penetrating trauma:
- Immediate reconstruction is highly successful.
- High velocity projectiles create blast effect, making immediate reconstruction less reliable.
- Intracorporeal urethral injury: Place indwelling Foley for 7 days, followed by voiding cystourethrogram.

**ADDITIONAL TREATMENT**

**Radiation Therapy**

Additional Therapies:
- Repeat endoscopic treatment of traumatic urethral strictures may lead to longer strictures (IVB).
- In an unstable trauma patient, a cautious attempt can be made to pass a urethral catheter.
- If there is any difficulty a suprapubic catheter can be placed and a retrograde urethrogram performed later [4].

**MEDICATION**

First Line
- Antibiotics
- Second Line
- N/A

**SURGERY/OTHER PROCEDURES**
- Pelvic fracture and posterior urethral injury: Place large bore suprapubic catheter (16 Fr Foley) using percutaneous peel-away sheath.
- We advise against using small pigtail suprapubic catheters.
- For complex injuries with associated bladder trauma, open suprapubic tube placement with bladder inspection is suggested. Place suprapubic tube (SPT) in patients undergoing ORIF for pelvic fractures (24 Fr; high on bladder and tunneled through skin away from hardware).
- Open surgical realignment should be avoided due to high risk of urethral stricture formation.
  - Primary endoscopic realignment may be attempted but has a success rate of 25% (IIIR), but may delay the ultimate curative therapy for this condition. In our experience, traumatic strictures tend to be short and dense, and refractory to endoscopic treatment. Success rates for open anastomotic urethroplasty are greater than 90%.
- In women, primary open repair is recommended for disruption of the urethra with associated tear of bladder neck and vagina (IIIc) due to risk of incontinence and vesicovaginal fistula.

**COMPLICATIONS**
- Urethral stricture
- Erectile dysfunction

**FOLLOW-UP**

**Patient Monitoring**
- Recovery often complicated by other orthopedic and neurologic injuries.
- Anterior urethral injury: Good prognosis after primary repair.

**COMPLICATIONS**
- Urethral stricture
- Erectile dysfunction
- Follow-up
  - Perform reconstructive procedures at 4–6 mo
  - If endoscopic alignment has been performed, the suprapubic tube should be kept in place for at least one week after removal of urethral Foley. Most endoscopic alignment will fail at 1 wk.
  - Perform reconstructive procedures at 4–6 mo.

**Patient Resources**

Urology Care Foundation: Urethral trauma.
https://urology.org/index.cfm?article=44

**REFERENCES**


**ADDITIONAL READING**


See Also (Topic, Algorithm, Media)
- Bladder Trauma
- Perine. Trauma
- Urethra, Strictures, Male
- Urethra, Trauma (Anterior and Posterior) / Images

**ADDITIONAL READING**

- Retrograde urethrography is considered the gold standard for evaluating urethral injury.
- Most pelvic fracture associated injuries occur in the posterior urethra.
- Penetrating urethral injury should be managed with suprapubic catheter and delayed definitive repair.
- When placing a suprapubic catheter, should use a large bore Foley catheter placed via a peel away sheath.
- Urethral injury in women associated with bladder neck or vaginal injury should be repaired primarily.
- Anastomotic repair of traumatic strictures has a high success rate.
URETHRITIS, GONOCOCCAL AND NONGONOCOCCAL

Daniel C. Parker, MD
Jack H. Mydlo, MD

ASSOCIATED CONDITIONS
- Other STDs/STIs
- Pendulous urethral stricture
- Epididymitis/orchitis

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urine analysis
  - Obtain 1–4 h after voiding
  - ≥ 15 PMN leukocytes per HPF of spun sediment in the first-void urine specimen
- Positive leukocyte esterase on urine dip in the absence of UTI suggests urethritis
  - Up to 30% of patients with urethritis will not have WBC in the urine
- Urethral smear for gram-stain and culture
  - Calcium alginate swab inserted 1–2 cm into urethra best to obtain 1–2 hours after voiding
  - Culture plated on Thayer-Martin media for GU
- Sensitivity of DNA targeted assays is improving
  - NAAT available for: C trachomatis and N gonorrhoeae. Labs can also test for Mycoplasma, Ureaplasma, and Trichomonas vaginalis but these assays are no commonly performed since they are very costly and may not alter the recommended antibiotic regimen

Pathologic Findings

DIFFERENTIAL DIAGNOSIS
- GU
  - Nongonococcal urethritis
    - Chlamydia trachomatis
    - Mycoplasma genitalium
    - Trichomonas vaginalis
  - Ureaplasma urealyticum
  - Uncommon infectious causes: TB, adenovirus, uropathogenic Escherichia coli (unprotected anal intercourse), herpes simplex, cytomegalovirus

- Urethral diverticulum
- Reiter’s arthritis
- Reactive urethritis (formerly Reiter syndrome) associated with conjunctivitis, arthritis, and tenosynovitis
- No growth on culture
- Minimal number of leukocytes in urethral smear or urine
- Mikulicz’s: Urethral irritation from detergents, soap bubble, lather, spermicides, contraceptives, manipulation, and/or foreign body insertion.

DIFFERENTIAL DIAGNOSIS
- GU
  - Nongonococcal urethritis
    - Chlamydia trachomatis
    - Mycoplasma genitalium
    - Trichomonas vaginalis
    - Ureaplasma urealyticum
  - Uncommon infectious causes: TB, adenovirus, uropathogenic Escherichia coli (unprotected anal intercourse), herpes simplex, cytomegalovirus
  - Urethral diverticulum
  - Reiter’s arthritis
  - Reactive urethritis (formerly Reiter syndrome) associated with conjunctivitis, arthritis, and tenosynovitis
  - No growth on culture
  - Minimal number of leukocytes in urethral smear or urine
  - Mikulicz’s: Urethral irritation from detergents, soap bubble, lather, spermicides, contraceptives, manipulation, and/or foreign body insertion.

DIFFERENTIAL DIAGNOSIS
- GU
  - Nongonococcal urethritis
    - Chlamydia trachomatis
    - Mycoplasma genitalium
    - Trichomonas vaginalis
    - Ureaplasma urealyticum
  - Uncommon infectious causes: TB, adenovirus, uropathogenic Escherichia coli (unprotected anal intercourse), herpes simplex, cytomegalovirus
  - Urethral diverticulum
  - Reiter’s arthritis
  - Reactive urethritis (formerly Reiter syndrome) associated with conjunctivitis, arthritis, and tenosynovitis
  - No growth on culture
  - Minimal number of leukocytes in urethral smear or urine
  - Mikulicz’s: Urethral irritation from detergents, soap bubble, lather, spermicides, contraceptives, manipulation, and/or foreign body insertion.

DIFFERENTIAL DIAGNOSIS
- GU
  - Nongonococcal urethritis
    - Chlamydia trachomatis
    - Mycoplasma genitalium
    - Trichomonas vaginalis
    - Ureaplasma urealyticum
  - Uncommon infectious causes: TB, adenovirus, uropathogenic Escherichia coli (unprotected anal intercourse), herpes simplex, cytomegalovirus
  - Urethral diverticulum
  - Reiter’s arthritis
  - Reactive urethritis (formerly Reiter syndrome) associated with conjunctivitis, arthritis, and tenosynovitis
  - No growth on culture
  - Minimal number of leukocytes in urethral smear or urine
  - Mikulicz’s: Urethral irritation from detergents, soap bubble, lather, spermicides, contraceptives, manipulation, and/or foreign body insertion.
TREATMENT

GENERAL MEASURES
- Cases are reportable to health department.
- Sexual intercourse should be avoided until cure.
- Sexual partners within 60 days of diagnosis or symptoms should be evaluated and treated.
- Dual treatment for both N. gonorrhoeae and C. trachomatis is recommended.

ALERT
The CDC now recommends against the use of quinolones and oral cephalosporins for treatment of gonococcal urethritis in the US due to widespread bacterial resistance (31A).

MEDICATION

First Line
- GU:
  - CDC recommends dual therapy for GU and NGU
    - Ceftriaxone 250 mg IM once
    - Erythromycin 500 mg PO q.i.d. for 7 days
    - Azithromycin 1 g PO once, or doxycycline 100 mg PO b.i.d. for 10-14 days
- NGU:
  - Azithromycin 1 g PO once, or doxycycline 100 mg PO b.i.d. for 10-14 days

Second Line
- GU:
  - Cefixime 400 mg PO once
  - Doxycycline 300 mg PO b.i.d. for 10-14 days
- NGU:
  - Ceftriaxone 250 mg IM once
  - Doxycycline 100 mg PO b.i.d. for 10-14 days

SURGERY/OTHER PROCEDURES
- Surgery typically not indicated

ADDITIONAL TREATMENT
- Radiation Therapy: N/A
- Additional Therapies
  - Patient education
  - Proper use of condoms and safe sexual practice
  - Reduce number of sexual partners
  - Evaluation and treatment of sexual partners at risk (31A)
- Complementary & Alternative Therapies: N/A

ONGOING CARE

PROGNOSIS
- Generally good prognosis with treatment for both GU and NGU
- Systemic manifestations of gonococcal dissemination are rare today:
  - Arthritis
  - Dermatitis
  - Meningitis
  - Endocarditis

COMPLICATIONS
- GU:
  - Pelvic inflammatory disease
  - May lead to abscess
  - Urethral stricture
  - Epididymitis/orchitis
  - May lead to testicular atrophy or infertility
  - Prostatitis
  - May lead to abscess
  - NGU:
    - Emotional sequelae are common
    - Fear of loss of sexual function or guilt may produce depression
    - Epididymitis and/or nonspecific prostatitis
    - Usually does not cause severe physical complications in men

FOLLOW-UP
- Patient Monitoring
  - GU and NGU:
    - Post therapy culture and urethral smear to confirm response to therapy
- Patient Resources
  - CDC: STD fact sheets: http://www.cdc.gov/std

REFERENCES

ADDITIONAL READING
- Centers for Disease Control and Prevention. Sexually Transmitted Disease Treatment Guidelines, 2010. MMWR. 2010;59 (No. RR-12).
- www.cdc.gov/gonorrhea/STDFact-gonorrhea.html

See Also (Topic, Algorithm, Media)
- Gonorrhea
- Gonorrhea Microscopic Image
- Sexually Transmitted Diseases (STD), General
- Urethra, Stricture, Male
- Urethral Discharge
- Urethra Discharge Algorithm

CODES
- ICD9: 098.0 Gonococcal infection (acute) of lower genitourinary tract
  - 099.40 Unspecified other nongonococcal urethritis (NGU)
  - 131.02 Trichomonal urethritis
- ICD10: A51.01 Gonococcal cystitis and urethritis, unspecified
  - A59.03 Trichomonal cystitis and urethritis
  - A72.1 Non-specific urethritis

CLINICAL/SURGICAL PEARLS
- GU is caused by the gram-positive diplococci Neisseria gonorrhoeae.
  - NGU is most commonly caused by Chlamydia trachomatis.
- Up to 35% of cases of GU are coinfected with NGU.
- The CDC recommends simultaneous treatment for both GU and NGU in patients presenting with urethritis.
- Sexual partners within 60 days of diagnosis or symptom onset should be evaluated and treated.
URGENCY, URINARY (FREQUENCY & URGENCY)
Jessica M. DeLong, MD
Kurt A. McCammon, MD, FACS

BASICS

DESCRIPTION
- Urge is the complaint of a sudden compelling desire to void that is difficult to defer while frequency is the complaint by a patient that he or she voids too often.
- Urgency: – Urge is the most common symptom of overactive bladder (OAB).
- Urge incontinence is involuntary leakage of urine precipitated by the above symptom (1).
- Frequency: – There is no minimum number of voids.
- Nocturia is the complaint of waking at night to void one or more times.
- These are classified as storage symptoms.

RISK FACTORS
- Genetics
- Pathophysiology
  - Inflammation
  - Narrowing (IC/PBS)
  - Diverticulosis
  - Polyuria

ASSOCIATED CONDITIONS
- Bladder outlet obstruction
- Diverticulosis
- Dysfunctional voiding
- Interstitial cystitis (IC/PBS)
- OAB
- Urinary tract infection (UTI)
- Vaginitis

GENERAL PREVENTION
- Treat any underlying condition (eg, UTI)
- Maintain good voiding habits and regular bowel pattern

DIAGNOSIS

HISTORY
- Use validated questionnaires when possible
  - International prostate symptom score (IPSS), (IPSS-GQ)
  - Urgency sensation scale
- Initial voiding symptoms:
  - Urgency, frequency, urge incontinence, nocturia
- Obstructive voiding symptoms:
  - Hematuria, slow stream, post-void dribbling, retention
- Consider causes of bladder outlet obstruction
- Other medical history
  - Stone disease
  - Bladder malignancy
- Symptoms of infection
  - Polymerase chain reaction (PCR) – Tissue
- Episodes of gross hematuria
- Bowel habits
- Sexual function
- Current medications
  - Diuretics, alpha blockers
  - Tobacco use
  - Family history
  - Pregnancy
  - Urinary incontinence

PHYSICAL EXAM

- Urine analysis (UA) – Exclude other pathology
  - Specific gravity
  - Protein
  - Microhematuria necessitates further work up
  - Cystoscopy, triphasic CT
  - Glucose: Assess for diabetes
  - Proteins: Assess for medical renal disease
  - Obtain culture if UA suggestive of infection
  - Urinary cytology to rule out urothelial carcinoma

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urine analysis (UA) – Exclude other pathology
  - Specific gravity
  - Protein
  - Microhematuria necessitates further work up
  - Cystoscopy, triphasic CT
  - Glucose: Assess for diabetes
  - Proteins: Assess for medical renal disease
  - Urinary cytology to rule out urothelial carcinoma

Imaging
- Radiologic imaging – If bladder outlet obstruction (BOO) suspected
  - If hematuria or persistence symptoms
  - If conservative therapy fails
  - If stones suspected, non-contrast CT

Alert
- If UA suggests infection or hematuria, appropriate evaluation is key.

Diagnostic Procedures/Surgery
- Check post void residual (PVR)
- Cystoscopy
- If hematuria or persistent problems
- May direct bladder pathology tumor, calculus, BOO
- Urodynamics (UDS)
  - If conservative therapy fails
  - Can help define treatment options and evaluate for neurogenic component

Pathologic Findings
- Dependent upon etiology

DIFFERENTIAL DIAGNOSIS

- Inflammation: UTI, urethritis
- Radiation cystitis
- IC/PBS
- Trauma—local or neurologic
- Foreign body
- Neurologic condition (ie, spina bifida, spinal cord injury, neuropathy)
- Neoplasm—urologic or neurologic by local extension
- Urothelial carcinoma, especially CIS
- Other causes of urinary frequency
- Urolithiasis
- Polyuria
- Drugs—diuretics, irritants
- Gynecologic/vaginitis, pregnancy
TREATMENT

GENERAL MEASURES
- Based on underlying etiology
  - Treat UTI with appropriate antibiotics
  - Initiate appropriate workup and management of hematuria
- In general, treatment is divided into:
  - Conservative (behavioral)
  - Pharmacotherapy
  - Surgery

MEDICATION

First Line
- Choice based on etiology
- Antimuscarinics are used to inhibit detrusor contraction by competitively inhibiting muscarinic cholinergic receptors. Common side effects: dry mouth and constipation. maximal effect after 3 mos
  - Oxybutynin
    - 5 mg PO TID; XL, 15 mg daily BID
    - Transdermal patch 3.9 mg/24 h: may be good option to avoid cognitive side effects
  - Tolterodine 1–2 mg PO BID
  - Darifenacin 7.5–15 mg PO daily
  - Solifenacin 5–10 mg PO daily
  - Tamsulosin 0.4 mg PO qhs

- P-3 adrenergic receptor antagonists: A newer drug, induces detrusor relaxation
  - Mipolargon 25–50 mg PO daily
  - α-blockers are used to decrease outflow obstruction due to prostatic hyperplasia. Common side effects: dizziness, retrograde ejaculation
    - Tamsulosin 0.4 mg PO qhs
    - Alfuzosin 10 mg PO daily
  - Dutasteride 0.5 mg PO daily
  - Tamsulosin 0.4 mg PO qhs

- 5α-reductase inhibitors are used to lower DHT in men with prostatomegalia
  - Finasteride 5 mg PO daily
  - Dutasteride 0.5 mg PO daily

Second Line
- PES/UTIs
  - Documented efficacy for men with lower urinary tract symptoms (LUTS)/OAB
  - FDA approved for signs and symptoms of BPH
  - With or without erectile dysfunction
  - Imiquimod
    - No good quality RCTs
  - Estrogens (vaginal superior to systemic)

In general, treatment is divided into:
- Conservative (behavioral)
- Pharmacotherapy
- Surgery

BASED ON UNDERLYING ETAIOLOGY
- Generally a long-term problem; dependent on etiology
- Prognosis
- Generally a long-term problem; dependent on etiology
- Follow-up
- Depends upon etiology, treatment, response
- Often periodic visit with voiding diary, uroflow, PVR

PATIENT MONITORING
- Depends upon etiology, treatment, response
- Often periodic visit with voiding diary, uroflow, PVR

PATIENT RESOURCES
- MedHelpDoc frequent or urgent urination.

REFERENCES

ADDITIONAL TREATMENT

Radiation Therapy

- Additional Therapies
  - Behavioral therapy is first-line
    - Bladder training may include biofeedback and pelvic floor physical therapy
    - Timed voiding
    - Kegel exercises may be of benefit

Complementary & Alternative Therapies

ON GOING CARE

URGENCY, URINARY (FREQUENCY & URGENCY)

ICD9
- 596.51 Hypertonicity of bladder
- 788.41 Urinary frequency
- 788.63 Urgency of urination

ICD10
- N02.81 Overactive bladder
- R35.0 Frequency of micturition
- R35.15 Urgency of urination

CLINICAL/SURGICAL PEARLS

- Hematuria warrants appropriate workup. May be a presentation of genitourinary malignancy.
- Anticholinergics are contraindicated in patients with untreated narrow-angle glaucoma.
- Combination of antimuscarinics plus α-blockers may be better than either alone for men with LUTS/OAB.
- Use anticholinergics with caution in elderly patients, as cognitive effects may be pronounced.
- Use of intravesical estrogen for postmenopausal women may worsen incontinence.
URINARY RETENTION AFTER STRESS URINARY INCONTINENCE SURGERY IN FEMALES
Bradley C. Gill, MD, MS
Sandip P. Vasavada, MD, FACS

DIAGNOSIS

HISTORY
Details of retention
- Timing of symptom onset with regard to surgery
- Duration of symptoms and consistency with voiding
- Associated with discomfort, distention, or incontinence

Rheologic conditions
- Detrusor hypocontractility or urodynamics studies
- Episodes of cystolithiasis
- Recurrent urinary tract infections
- Cystocele
- Rheologic interventions
- Intact detrusor botulinum toxin injections
- Previous midurethral sling or retropubic urethropexy
- Other interventions
- Abdominopelvic surgery, radiation, or injury
- Spleen surgery or injury
- Current medications
- Antimuscarinics or anticholinergics
- Alpha adrenergic agonists
- Diabetes mellitus

PHYSICAL EXAM
- Visual inspection of the abdomen and suprapubic area
- Abdominal palpation with attention to the suprapubic area
- Visual inspection of the external genitalia for discharge or bleeding
- Speculum examination
- Swelling or bulging anterior vaginal wall
- Incisional discharge or bleeding
- Cystocele
- Pus from external genitalia, vaginal wall, or pelvic floor muscles
- Urethral or anterior vaginal wall bulging or tension
- Tension and mobility of surgically placed sling or sutures
- Pelvic floor muscle tension, spasm, or tenderness

TREATMENT
GENERAL MEASURES (2,3)
- Catheterization and observation of iatrogenic obstruction
- Trial of intermittent catheterization to observe for resolution
- Considerative intervention if no resolution within 3 mo

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Serum electrolytes
- Blood counts

Imaging
- Bladder ultrasound
- Abdominopelvic surgery, radiation, or injury

DIFFERENTIAL DIAGNOSIS
- Bladder diverticulum
- Detrusor hypocontractility
- Occult urinary retention or incomplete emptying
- Spleen surgery or injury
- Cystocele
- Medication
- Diabetes mellitus

BASICS

DESCRIPTION
- Inability to void spontaneously following surgery for stress urinary incontinence
- Voiding with Valsalva or straining following surgery for stress urinary incontinence
- Procedure performed may be either midurethral sling or retropubic urethropexy

EPIEDEMOLOGY
- Incidence
  - Estimated 3–11% for midurethral sling
  - Estimated 3–7% for retropubic urethropexy
- Prevalence
  - More common with retropubic or transvaginal slings than transobturator slings
  - Likely more common with synthetic than biologic sling materials
- Episodes are generally transient and last days to weeks but resolution up to 3 mo can occur

RISK FACTORS (1)
- Weak detrusor contraction or incomplete voiding preoperatively
- Procedure done with “tension” rather than “tension-free” placement
- Inability to urinate or elevated post-void residual postoperatively

PATHOPHYSIOLOGY
- Iatrogenic obstruction by extrinsic compression
- Retropubic suspension can cause urethral “kinking”
- Incisional discharge or bleeding
- Cystocele
- Pus from external genitalia, vaginal wall, or pelvic floor muscles
- Urethral or anterior vaginal wall bulging or tension
- Tension and mobility of surgically placed sling or sutures
- Pelvic floor muscle tension, spasm, or tenderness

ASSOCIATED CONDITIONS
- Bladder diverticulum
- Cystocele
- Cystolithiasis
- Detrusor hypocontractility
- Recurrent urinary tract infections
- Urethral stricture
URINARY RETENTION AFTER STRESS URINARY INCONTINENCE SURGERY IN FEMALES

• Emergent bladder drainage for an impassable urethra
  – Operative sling revision pending anticipated delay for arranging surgery
  – Suprapubic aspiration and drainage at bedside
  – Percutaneous nephrostomy tubes if no other options are possible
• Careful urethral dilation may be considered soon after surgery
• Evacuation of hematoma if suspected as etiology of urethral compression

MEDICATION

First Line
N/A
Second Line
N/A

SURGERY/OTHER PROCEDURES

• Elective bladder diverticulectomy as indicated
• Transvaginal retropubic urethrolysis if more conservative measures fail

ADDITIONAL TREATMENT

Radiation Therapy
N/A
Additional Therapies
N/A
Complementary & Alternative Therapies
N/A

ONGOING CARE

PROGNOSIS

• Excellent considering multiple options
• Major risk is incontinence recurrence
  – 15–20% recurrence of stress urinary incontinence symptoms

COMPICATIONS

• Infection
• Urinary/bladder injury
• Recurrent incontinence

FOLLOW-UP

Patient Monitoring

• Office follow-up every 7–14 days for trials of voiding
  if an indwelling catheter placed
• Standard postoperative follow-up if a surgical intervention is pursued

Patient Resources
N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

• Urethral Sling, Indications, and Anatomic Positions
• Urethral Sling, Materials
• Urethra, Obstruction
• Urinary Retention, Adult Female

CODES

ICD9

599.60 Urinary obstruction, unspecified
788.29 Other specified retention of urine
997.5 Urinary complications, not elsewhere classified

ICD10

N36.8 Other specified disorders of urethra
N99.89 Oth postprocedural complications and disorders of GU sys
R33.8 Other retention of urine

CLINICAL/SURGICAL PEARLS

• Think about how sling vectors impact function.
• Many cases will resolve themselves with time.
• If consistently occurring change the technique.
URINARY RETENTION, ADULT FEMALE
Mary K. Powers, MD
Raju Thomas, MD, MHA, FACS

DIAGNOSIS

HISTORY
• Complaints of frequency, decreased force of stream, urgency or urge incontinence, or UI are indicative of bladder outlet obstruction (BOO)
• Feeling of vaginal urge
• History of stroke, diabetes, MS, Parkinson’s disease, "back problems," neurologic conditions, depression
• Chronic narcotic medication use
• Chronic constipation
• Use of psychotropic medication

PHYSICAL EXAM
• Examine bladder distension
• Examine abdomen to evaluate any prior surgeries
• Motor/sensory tone to rule out neurologic disorder
• History of stroke, diabetes, MS, Parkinson’s disease, feeling of vaginal bulge, complaints of frequency, decreased force of stream, urgency or urge incontinence, or UTI are indicative of bladder outlet obstruction (BOO)
• Tension-free vaginal tape has lowest range of reoperation
• Retropubic suspension can cause urethral "kinking"
• 2–8% of women require reintervention. Retropubic suspension can cause urethral "kinking"
• Anticholinergics (26%)—most commonly following anti-incontinence surgery
• Retention is frequently self-limited and will resolve within 6–12 wk following anti-incontinence surgery
• Manage with catheterization or clean intermittent catheterization

• Anatomic:
  - Urethral stricture (13%)
  - Ectopic ureterocele
  - Urethral diverticulum (3%)
  - Urethral malignancy
  - Bladder neck obstruction
  - Pelvic organ prolapse (24%)
  - Dysfunctional Voiding (5%)
  - Pseudodystonia—severe spasticity of sphincter without nerve stimulation (rare)

  • Fowler syndrome—young women without neurologic disease. Highly responsive to neuromodulation.
  • Higher incidence of depression and polycystic ovarian syndrome

• Neurologic
  - Detrusor sphincter dyssynergia (5%)
  - Pharmacologic:
    - Anticholinergic, opioid, and other narcotic medications
    - Anticholinergics: Atropine, belladonna, benztropine, mecamylamine
    - Cyclic antidepressants, phenothiazines, ipratropium bromide
  - Antispasmodics
    - Tricyclic antidepressants
    - Anticholinergic: Atropine, belladonna, benztropine, mecamylamine, cyclic antidepressants, phenothiazines, ipratropium bromide
  - Antispasmodics
  - Trospium, oxybutynin, solifenacin, hyoscyamine
  - Anticholinergic: Atropine, belladonna, benztropine, mecamylamine
  - Cyclic antidepressants, phenothiazines, ipratropium bromide

  • Antihistamines
  • Tamsulosin (alpha-1 Agonists: Cold preparations, ephedrine derivatives, antihistamines

  • Narcotics
  • Detrusor muscle relaxants: Tolterodine, trospium, indanylth, solifenacin, hyoscyamine, NSAIDs

  • Psychogenic
  • Myogenic (eg, detrusor acontractility)
URINARY RETENTION, ADULT FEMALE

TREATMENT

GENERAL MEASURES (2)
- Treatment based on underlying cause
- Stop medications predisposing to retention
- Evaluation and management of chronic constipation/bowel dysfunction
- Foley catheterization vs. clean intermittent catheterization (preferred) to manage acute retention

MEDICATION

First Line
- Alpha-adrenergic blockade can be useful in patients with dysfunctional voiding
  - Tamsulosin: 0.4 mg daily
  - Doxazosin: 1–4 mg daily
  - Terazosin: 1–5 mg daily
  - Prazosin: 1–5 mg daily

Second Line
- Baclofen for patients with neurologic causes of dysfunctional voiding
  - 5 mg TID, increase 15 mg q3 days, max. 80 mg divided TID/QID

SURGERY/OTHER PROCEDURES
- For iatrogenic causes, intervention should be postponed for a period of 12 wk to allow for stabilization of symptoms
  - Urethral dilation for urethral strictures. Caution not to cut too deep and develop fistulas
  - Refractory strictures can undergo reconstruction with vaginal flap

ADDITIONAL TREATMENT

Radiation Therapy
NA

Additional Therapies
- Urethral dilation for urethral strictures. Caution because this can lead to fibrosis and is falling out of favor
- Clean intermittent catheterization may be best choice for patients with intractable bladder outlet obstruction
- Constipation management
  - Colace 100 mg 1 tab by mouth BID
  - Magnesium citrate 250 mL PO

Complementary & Alternative Therapies
Concurrent evaluation and management by gastroenterology

ONGOING CARE

PROGNOSIS
- Depends on the etiology
  - Iatrogenic retention following slings has a good success rate with urethral dilation up to 90%
  - A blockage shows 50% improvement in PVR, symptoms, and flow rate

COMPLICATIONS
- Urethral stricture can lead to development of stress incontinence
- Bladder neck incision can lead to incontinence, vesicovaginal fistula, or need for repeat procedures
- Urethral dilation can cause recurrent stricture and fibrosis

FOLLOW-UP

Patient Monitoring
- Repeat urodynamic studies are recommended if problem persists
- Videourodynamics should be done if concern for bladder neck obstruction
- Neurologic evaluation if new diagnosis of MS, Parkinson’s disease

Patient Resources

REFERENCES

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Bladder Outlet Obstruction (BOD)
- Multiple Sclerosis, Urologic Considerations
- Pelvic Organ Prolapse (Cystocele and Enterocoele)
- Urinary Retention after Stress Urinary Incontinence Surgery in females
- Urinary Retention, Adult Male
- Urinary Retention, Adult Male Algorithm

URINARY RETENTION, POSTOPERATIVE
- Refractory strictures can undergo reconstruction with vaginal flap

URINARY RETENTION, ADULT MALE
- Recurrence or development of stress incontinence high as 30%
- Urinary Retention, Pediatric

URINARY RETENTION, ADULT MALE ALGORITHM

URINARY RETENTION AFTER STRESS URINARY INCONTINENCE SURGERY IN FEMALES

URINARY RETENTION, ADULT MALE
- Pelvic Organ Prolapse (Cystocele and Enterocoele)

MULTIPLE SCIENCES, UROLOGIC CONSIDERATIONS

URINARY RETENTION, POSTOPERATIVE

CLINICAL/SURGICAL PEARLS
- There are multiple causes of urinary retention in females; urodynamics can help distinguish causes.
- In young females with new onset voiding complaints must rule out diabetes or neurologic diagnosis such as MS.
- Pelvic organ prolapse is a major cause of retention.

ICD9
- 583.8 Urinary stricture, unspecified
- 788.19 Other specified retention of urine

ICD10
- R15.9 Urinary stricture, unspecified
- R33.8 Other retention of urine
- R33.9 Retention of urine, unspecified

CODES

URINARY INCONTINENCE, ADULT MALE

583
URINARY RETENTION, ADULT MALE
Akhil Das, MD, FACS
Amar J. Raval, MD

BASICS

DESCRIPTION
Urinary retention is the inability to properly empty the urinary bladder. It can be further classified as acute and chronic.

- Acute retention of urine is defined by the International Continence Society (ICS) as a painful, palpable, or percussionable bladder, when the patient is unable to pass any urine.
- Chronic retention of urine is defined by the ICS as a non-palpable bladder, which remains palpable or percussionable after the patient has passed urine. Such patients may be incontinent.

EPIDEMIOLOGY
Incidence
Incidence increases with age in males (~10% in men aged 70 yr).

Prevalence
Exact prevalence is difficult to estimate.

RISK FACTORS
- General disease, herpes zoster, drugs, psychogenic, neurologic disease, bladder calculus, recent surgery (especially with epidural or spinal anesthesia), groin surgery such as hernia repair, prostate brachytherapy, stroke, pelvic trauma.
- Elderly: BPH, prostate cancer, history of retention, urologic procedures or instrumentation, medications, prostatitis, urethral carcinoma (rare cause).
- Recent inguinal/pelvic surgery (ie, hernia).

HISTORY
- Acute retention: sudden onset of inability to void more than small volumes of urine
- Associated with an uncomfortable sensation and a distended bladder.

Chronic retention: longstanding inability to completely void, with occasionally large PVRs, but not usually associated with discomfort.

Retention may suggest infection or BPH:
- Prostate:
  - Recent blood loss, may indicate prostatitis, recent prostate surgery, etc.
  - Hematuria suggestive of infection, tumor, or calculus
  - PSA usually not checked acutely due to false positive

DIAGNOSIS

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM

- Painful, palpable, or percussionable bladder
- Urinary leakage

Lab
- Chemistry: BUN and creatinine may be abnormal in patients after surgery, due to bandaging of the perineum, or after regional anaesthesia such as an epidural anesthetic.
- Urologic:
  - Ultrasound: Can delineate bladder calculi, prostate size, hydronephrosis, bladder wall thickening
  - CT of abdomen/pelvis: CT of abdomen/pelvis is useful for diagnosis of acute and chronic urinary retention
  - Renal/bladder US: Can be obtained if diagnosis uncertain
  - DRE: Boggy, tender prostate suggests prostatitis
  - Nodularity suggests cancer
  - Symmetrically enlarged prostate suggests BPH
  - Assess for severe urgency and/or pain on palpation

DIAGNOSTIC PROCEDURES/SURGERY

- Radial abdominal mass: Assess for severe urgency and/or pain on palpation
- DRE
- Prostatic biopsy
- Bladder washout
- Transurethral resection of prostate
- Cystoscopy
- Nephrostomy
- Urethral dilatation
- Retrograde urethrogram
- ICS as a non-palpable bladder
- Release of bladder neck obstruction or with a known history of neurologic voiding dysfunction
- Infection, bleeding, or over distension is the usual precipitating event
- Damage to bladder results in prompt symptomatic relief.

Although acute retention is usually thought of as painful, in certain circumstances pain may not be a presenting feature.

- When due to prostatic intra-urethral disc, post partum, or after regional anesthesia such as an epidural anesthetic.
- The retention volume should be significantly greater than the expected normal bladder capacity.

In patients after surgery, due to bandaging of the lower abdomen or abdominal wall pain, it may be difficult to detect a painful, palpable, or percussionable bladder.

ASSOCIATED CONDITIONS

- Diabetes
  - Disease of prostate
  - BPH
  - Prostate cancer
  - Prostatitis
- Neurologic conditions
  - Neurogenic bladder
- Multiple sclerosis
- Cerebrovascular accident
- Parkinson disease
- Spinal cord injury
- Demyelinating disorders
- UUI
- Recent hemia or other surgery

PATOPHYSIOLOGY

Most commonly occurs in patients with preceding bladder outlet obstruction or with a known history of neurologic voiding dysfunction.

Infection, bleeding, or over distension is the usual precipitating event.

Bladder outlet obstruction results in prompt symptomatic relief.

- Pain: Bone pain and weight loss suggest prostate cancer
- Spinal cord injury or pelvic trauma
- Recent surgery, especially in those with spinal or epidural anesthetics
- Diabetes mellitus
DIFFERENTIAL DIAGNOSIS
- Generally either bladder outlet obstruction or bladder dysfunction:
  - Anatomic:
    - Peri: Phimosis, paraphimias, meatal stenosis, foreign-body constriction
    - Prostatic: BPH, prostate cancer, bladder neck contracture, prostatitis, prostatic infection
  - Trauma:
    - Urinary disruption
  - Neurologic:
    - Motor paralytic: Spinal shock, spinal cord injuries, spina bifida or meningomyelocele
    - Sensory paralytic: Tabels dorsalis, diabetes, multiple sclerosis, and peri-ocular amnesia
    - Syringomyelia, myelopathy, subluxation
    - Hepeza zoster, poliomyelitis
  - Hematologic:
  - Drugs: see *Risk Factors*

TREATMENT
GENERAL MEASURES
- Acute urinary: Catheterization for decompression
- In men with BPH: consider immediate urological therapy to improve likelihood of successful catheter removal
- Some consider suprapubic tube (SPT) superior in the management of short-term retention
- Chronic retention: Clean intermittent catheterization preferred over long-term indwelling catheter
- Definitive management may involve medications, surgical intervention, or chronic catheterization strategies
- Unindicated studies may be required to establish diagnosis
- Treatment should be directed toward cause, with goal of preventing future episodes
- Antibiotics as indicated for infection
- Decrease or stop medications that can contribute to voiding dysfunction

MEDICATION
First Line
- Most medications are used for BPH: may also help with transient postoperative retention (2).
  - α1-Adrenergic blockers: Relax proximal bladder neck smooth muscle tone, most useful for acute retention
    - Alphazosin (10 mg)
    - Doxazosin start 1 mg/d to max. 10 mg
    - Silodosin (8 mg)
    - Terazosin start 0.4 mg/d to max. 0.8 mg
  - α2-Agonists: Lower urinary tract symptoms (LUTS)
  - α5-Reductase inhibitors: Reduce prostatic volume, longer-term effects
    - Finasteride or dutasteride
    - Side effects: Decreased libido and sexual dysfunction
  - Reduce PSA by ~50% and ambition should be used when evaluating risk for cancer
  - Combination therapy (α-adrenergic blocker + 5α-Reductase Inhibitor)
  - Tailor 2.5–5 mg/5 mg/5 mg/day to treat both lower urinary tract symptoms (LUTS) and erectile dysfunction (ED)

Second Line
- Behandol (10–50 mg PO tid-qid)
  - Direct cholinergic stimulant; increases detrusor tone
  - Indicated for the treatment of acute postoperative and postpartum obstructive (Functional)
  - Urinary retention and for neurogenic atony of the urinary bladder with retention
- Side effects: Dizziness, nausea, bronchoospasm, hyper tension, tachycardia, seizure

SURGERY/OTHER PROCEDURES
- If catheter placement fails, bedside or inoperative cystoscopy can be performed:
  - Cystoscopy is usually diagnostic and can delineate urethral stricture, false passage, bladder neck contracture, and obstructing prostate tissue.
  - Once bladder is entered under direct vision, a wire can be placed and dilations sequentially performed. The wire can then be used to allow passage of a Council tip catheter.
- If cystoscopy is unsuccessful, consider SPT placement
  - Open SPT preferable in patients with history of multiple abdominal surgeries
  - If no prior surgery, place SPT via percutaneous approach

ADDITIONAL TREATMENT
Radiation Therapy

Additional Therapies

COMPLEMENTARY & ALTERNATIVE THERAPIES

ONGOING CARE

PROGNOSIS
- ~85% of patients with an episode of urinary retention will recur if untreated
- Prevention of recurrence underscores management decisions

COMPLICATIONS
- Bladder rupture in acute urinary retention; usually associated with trauma
- Relief of chronic prolonged obstruction may result in post-obstructive diuresis or major hemorrage secondary to bladder mucosal disruption or tearing of bladder vessels, hematuria may require evacuation of clots
- Significant hypotension may occur secondary to vaso-vagal response
- Longstanding, untreated urinary retention can lead to reflux nephropathy and permanent vesicoureteral dysfunction

FOLLOW-UP
- Monitoring of electrolyte imbalance and fluid resuscitation in post-obstructive diuresis (>200 mL/h)
- Patient with signs of infection or impaired renal function should be admitted and observed

Patient Resources
URINARY RETENTION, PEDIATRIC

Dana A. Weiss, MD
Douglas A. Canning, MD, FACS

BASICS
DESCRIPTION
Urinary retention is the inability to properly empty the urinary bladder. Can be acute or chronic partial or complete.
- Acute
  - Uncommon in children
  - Acute onset of inability to void for over 12 h
  - Associated with uncomfortable often painful sensation and distended bladder.
- Chronic
  - Inability to void over long period of time
  - Usually asymptomatic

EPIDEMIOLOGY
Incidence
Not reported
Prevalence
2:1 boys:girls

RISK FACTORS
- Acute onset
  - Surgery, narcotic use, immobility, urinary tract infection (bacterial or viral), local inflammation (balanitis, meatal stenosis, labial adhesions, cellulitis), constipation, incarcerated inguinal hernia, acute neurologic inflammatory processes, invasive mass, drug related
- Chronic
  - Dysfunctional voiding, Hinman syndrome (non-neurogenic neurogenic bladder), lazy bladder syndrome, spina bifida, reduced mental status, benign obstructing mass, locally invasive mass, posterior urethral valves, prune belly syndrome

GENETICS
Genes related to underlying etiology

PATHOPHYSIOLOGY
- Obstipation
  - Surgery, narcotic use, immobility, urinary tract infection (bacterial or viral), local inflammation (balanitis, meatal stenosis, labial adhesions, cellulitis), constipation, incarcerated inguinal hernia, acute neurologic inflammatory processes, invasive mass, drug related
- Neurogenic bladder
- Inflammation/infection
  - Effect on brain/meninges (encephalitis, meningitis, Guillain–Barre syndrome, encephalitis
  - Neurologic inflammatory disorders: Transverse myelitis, Guillain–Barre syndrome, encephalitis
  - Neurologic neoplasms: neuroblastoma, ependymoma, Ewing sarcoma
  - Benign neurologic abnormalities: Tethered cord

ASSOCIATED CONDITIONS
- Dysfunctional elimination syndrome
- Neurogenic bladder
- Inflammation/infection
  - Effect on brain/meninges (encephalitis, meningitis, Guillain–Barre syndrome, encephalitis
  - Neurologic inflammatory disorders: Transverse myelitis, Guillain–Barre syndrome, encephalitis

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Urinalysis
- Urine culture
- Bacterial infection
- Cytomegalovirus (CMV)
- Epstein Barr Virus (EBV)
- Isosporic cysts
- Prostatitis
- Adverse drug effect
- Neurogenic dysreflexia
- Neurogenic bladder
- Cystitis (bacterial or viral) (2)
- Bacterial
  - Gram positive
  - Gram negative
- Viral
  - Neoplastic virus (HSV)
  - Varicella Zoster virus (VZV)
  - Cytomegalovirus (CMV)
  - Epstein Barr Virus (EBV)

DIFFERENTIAL DIAGNOSIS
- Tumor
- Adverse drug effect
- Neurogenic dysreflexia
- Neurogenic bladder
- Myelodysplasia
- Sacrococcygeal teratoma
- Prune belly syndrome
- Tethered spinal cord
- Detrusor sphincter dyssynergia
- Other
  - Constipation
  - Adverse drug effect
  - Trauma
  - Electrolyte abnormalities (hypermagnesemia) (1)
TREATMENT

GENERAL MEASURES
- Empty bladder with catheter
- Initiate clean intermittent catheterization until resolution.
- Complete workup based upon findings on history and physical exam.
- For chronic retention, after complete workup to rule out pathologic cause, begin behavioral modification (increase water intake, increasing voiding attempts to every 3 h, treat constipation)

MEDICATION
First Line
- Polyethylene Glycol 3350 for constipation/dysfunctional elimination syndrome – 0.5–1.5 g/kg daily, max. dose 17 g/d.
  - Use only in children older than 6 mo

Second Line
- α-Blockers (3,4)
  - Smooth muscle relaxation and decreased bladder outlet resistance:
    - Doxazosin <6 yr 0.5 mg daily
    - Doxazosin >6 yr 1 mg daily
- Steroids for inflammatory processes (2)
  - Very seldom used. Stress dose steroids.

SURGERY/OTHER PROCEDURES
- In acute setting, place urethral catheter
- If unable to place catheter, place suprapubic cystostomy tube.
- For posterior urethral valves, perform cystoscopy, transurethral incision of valves.
- For urethral stones, cystoscopy and laser lithotripsy or basket extraction (may require antegrade and retrograde approach).
- For obstructing fibroepithelial polyp, transurethral resection possible, vs. open cystotomy and excision.
- For obstructing prolapsing ureterocele, incision of ureterocele may leave obstructing tissue. May require resection of ureteroureterostomy or bladder neck reconstruction.
- Urthral stricture—based on length
- For significant detrusor sphincter dyssynergia, may benefit from bladder wash injection into urethral sphincter vs. urethral dilatation

ADDITIONAL TREATMENT
Radiation Therapy
N/A

Additional Therapies
- Behavioral modification
  - Timed voiding
  - Increased water intake
  - Pelvic floor relaxation

Complementary & Alternative Therapies
Biofeedback program for dysfunctional elimination syndrome

ONGOING CARE

PROGNOSIS
Based upon etiology.

COMPLICATIONS
- Bladder rupture in acute urinary retention; usually associated with trauma
- Postobstructive diuresis after relief of acute retention
- Urinary tract infection from stasis of chronic retention
- Chronic retention with high detrusor pressure can lead to renal impairment
- Misdiagnosis of malignant cause of urinary retention

FOLLOW-UP
Patient Monitoring
- Monitor for post-obstructive diuresis after drainage.
- May require fluid replacement in neonates

Patient Resources

REFERENCES

ADDITIONAL READING
N/A

See Also (Topic, Algorithm, Media)
- Posterior Urethral Valves
- Prune Belly Syndrome
- Sacral agenesis, urologic considerations
- Ureteroscopy
- Urinary Retention, Female
- Urinary Retention, Adult Female
- Urinary Retention, Adult Male
- Urinary Retention, Adult Male Algorithm
- Urinary Tract Infection, Complicated Pediatric

CODES
ICD9
- 596.0 Bladder neck obstruction
- 999.0 Urinary tract infection, site not specified
- 798.20 Retention of urine, unspecified

ICD10
- N32.0 Bladder-neck obstruction
- N39.0 Urinary tract infection, site not specified
- R33.9 Retention of urine, unspecified

CLINICAL/SURGICAL PEARLS
- Urinary retention in a newborn must be closely evaluated with RBUS and VCUG to rule out posterior urethral valves, ureteroceles, and urethral strictures.
- Young boys presenting with acute urinary retention should undergo DRE to rule out prostatic or bladder neck obstruction.
**URINARY TRACT INFECTION (UTI), ADULT FEMALE**
Duane R. Hickling, MD
Victor W. Nitti, MD, FACS

### BASICS

**DESCRIPTION**
- Urinary tract infection (UTI) in a female is defined as a symptomatic urothelial inflammation secondary to bacterial adhesion and internalization within the urinary tract.
- Most common human bacterial infection.
- Tremendous economic impact.
- $3.5 Billion annually in the United States.
- Possibility of progression to urosepsis.

**Prevalence**
- 58,067 cases per 100,000 adult women (1)
- 44% have at least 1 rUTI in 12 mo
- 13,320 cases per 100,000 adult women/yr (1)
- Complicated: Structural or functional abnormality, or anatomical: Lower (confined to bladder and/or urethra) vs. upper (involving the ureters and/or kidneys).

### EPIDEMOLOGY

#### Incidence
- 13,320 cases per 100,000 adult women (1)
- 44% have at least 1 UTI in 12 mo
- 5% more than 3 UTIs in 12 mo

#### Bacteriology of female UTI (1):
- Antibiotic: Escherichia coli (74.2%), Klebsiella pneumonia (6.2%), Enterococcus sp (5.3%), Streptococcus pyogenes (3.9%), Proteus mirabilis (2.0%), and Staphylococcus saprophyticus (1.4%).
- Nosocomial: E. coli (65.5%), Enterococcus species (8.6%), K. pneumonia (8.0%), E. aeruginosa (8.3%), P. mirabilis (2.2%), Pseudomonas aeruginosa (1.8%).
- Nursing home: E. coli (86%), Enterococcus species (11.1%), Proteus mirabilis (10.1%), K. pneumonia (9.7%), Pseudomonas aeruginosa (3.2%).

#### Prevalence
- 53,067 cases per 100,000 adult women (1)

### RISK FACTORS

#### Behavioral factors
- Sexual intercourse, spermicide use, barrier contraceptive, recent antibiotic use, dysfunctional voiding

#### Anatomic variations
- Perineal and urogenital anatomy is thought to be important only in absence of other risk factors
- Urinary tract obstruction: Medullary sponge kidney, calyceal diverticula, ureteral obstruction, ureterocele; junction obstruction, vesicoureteral reflux, primary bladder neck, urethral stricture, or benign prostatic hyperplasia

#### Physiologic factors
- Diabetes mellitus
- Obstetric history
- Pregnancy
- Anatomic or functional abnormalities of the urinary tract

### GENERAL PREVENTION

- Avoidance of spermicides and barrier contraceptives
- Although hygiene, pericoital voiding, hydration has not been shown to be uniformly effective in UTI prevention women are encouraged to clean perineum wiping from back to front and should empty bladder before, and after intercourse.

### DIAGNOSIS

#### HISTORY
- UTI signs/symptoms: General malaise, frequency, urgency, urge incontinence, dysuria, suprapubic pain, pelvic pain, cloudy urine, foul smelling urine, hematuria
- Pyelonephritis: Fever, chills, flank pain
- Nephrogenic: Vascular, renal failure
- Neurologic: Dizziness, confusion
- Gastrointestinal: Nausea, vomiting, diarrhea
- Dermatologic: Pruritus, rash
- Obstetric: Abnormal vaginal discharge, pelvic pain, vaginal discharge
- Immunocompromised: Widened differential diagnosis

#### PHYSICAL EXAM
- Vital signs: Hemodynamic instability can be associated with pyelonephritis/urosepsis
- Gynecologic: Menstrual cycle, birth control, menopausal status, STI/STD’s, pelvic organ prolapse
- Neurologic: Dizziness, confusion
- Dermatologic: Pruritus, rash
- Obstetric: Abnormal vaginal discharge, pelvic pain, vaginal discharge
- Immunocompromised: Widened differential diagnosis

#### DIAGNOSTIC TESTS & INTERPRETATION

#### Lab
- Urinalysis: Leukocyte esterase, Sensitivity 68–99%
- Specificity 98–96%
- Positive predictive value 19–86%
- Negative predictive value 91–97%
- Nitrite: Sensitivity 19–45%
- Specificity 95–98%
- Positive predictive value 50–78%
- Negative predictive value 62–89%
- Diabetes mellitus
- Unilateral or symmetric abnormalities of the urinary tract

#### Associated conditions
- Pregnancy
- Diabetic mellitus
- Unilateral or symmetric abnormalities of the urinary tract

#### TREATMENT
- Empiric antibiotics: Ciprofloxacin, nitrofurantoin, trimethoprim-sulfamethoxazole
- Empiric antibiotic selection based on local resistance patterns
- Discontinue empirical antibiotics if negative urine cultures
- Complete UTI treatment:
  - Most severe infections: Hospitalization, antibiotics, Foley catheter
  - Not severe infections: Oral antibiotics
- Discontinue antibiotic prophylaxis if symptomatic freedom is achieved

#### ASSOCIATED CONDITIONS

- Pregnancy
- Diabetic mellitus
- Unilateral or symmetric abnormalities of the urinary tract
URINARY TRACT INFECTION (UTI), ADULT FEMALE

- Leukocyte esterase and nitrite
  - Sensitivity 35–46%
  - Specificity 98–100%
  - Positive predictive value 89%
  - Negative predictive value 98%
- Microscopy
  - Urinalysis: 3–5 million cells/mL
  - 100 red blood cells/mL
- Bacterial culture
  - Sensitivity 80–90%
  - Culture organisms: 105 cfu/mL
- Antimicrobial susceptibility testing
- Leukocyte esterase
- Nitrite
- C-reactive protein
- Ultrasound
- Imaging
- Generally unnecessary; obtain if suspect pyelonephritis
- Indications: persistent fever (72 h after initiation of treatment), suspected urolithiasis (urine pH <6.0, history of calculus, very severe flank pain), unexplained persistent hematuria, bacterial persistence, acute/chronic urinary tract infection with fever
- First-line: renal ultrasound
- CT: if pyelonephritis; further evaluation or other imaging

DIAGNOSTIC PROCEDURES/SURGERY
- Cystoscopy: generalized erythema and edema of bladder
- Imaging: generally unnecessary; obtain if suspect complicated UTI
- Indications: persistent fever (72 h after initiation of treatment), suspected urolithiasis (urine pH <6.0, history of calculus, very severe flank pain), unexplained persistent hematuria, bacterial persistence, acute/chronic urinary tract infection with fever
- First-line: renal ultrasound
- CT: if pyelonephritis; further evaluation or other imaging

SURGERY/OTHER PROCEDURES
- Rarely indicated unless the following present:
  - Obstruction and uropathies: Stent or percutaneous nephrostomy tube (PNT)
  - Renal access drainage: Percutaneous drainage
  - Urethral diverticulum
  - Emphysematous pyelonephritis

ADDITIONAL TREATMENT
- Radiation Therapy
  - N/A

ADDITIONAL THERAPIES
- Complementary & Alternative Therapies
  - Cranberry extract: Hydrolyzed to ammonia and emphysematous pyelonephritis: Drainage or nephrostomy

CLINICAL/SURGICAL PEARLS
- Always consider urolithiasis with UTI when flank pain is severe.

REFERENCES

ADDITIONAL READING
**URINARY TRACT INFECTION (UTI), ADULT MALE**

Patricia Lewandoski, MD  
Akhil Das, MD, FACS

**BASICS**

- **DESCRIPTION**
  - A urinary tract infection (UTI) is a male is an inflammatory response of urothelium to bacterial invasion with associated bacteriuria and pyuria (1).
  - Defined by source of infection:
    - Cystic: Infection of bladder; dysuria, frequency, urgency, suprapubic pain, hematuria.
    - Isolated cysts in men rare, usually associated with prostatitis or pyelonephritis.
    - Pyelonephritis: Infection of kidney, chills, fever, flank pain is symptoms of cystitis.
    - Prostatitis infection or inflammation of prostate; acute or chronic; either bacterial or nonbacterial based on NIH Classification (see Section I: “Prostatitis, General”).
  - Urethritis: Infection of urethra
  - Defined as uncomplicated or complicated
    - Uncomplicated: Isolated infection or reinfecion in a healthy young male with normal urinary tract; urethral or prostatic.
    - Complicated: Infection associated with:
      - Structurally abnormal urinary tract (eg, bladder outlet obstruction/PROLIF), or
      - Functionally abnormal urinary tract (eg, neurogenic bladder)
      - Injured/host defense (eg, immunosuppression/diabetes)
      - Increased bacterial virulence
    - Most UTIs in men are complicated.
  - Defined based on chronicity:
    - Recurrent: UTI that has not responded to antimicrobial treatment.
    - Recurrent: UTI that occurs after complete resolution (proven by negative culture after complete antimicrobial course) of previous UTI.
  - Risk factors of UTI:
    - History of childhood UTI
    - History of adolescence UTI
    - Recent antimicrobial use
    - Previous UTI
    - Male gender
    - Diseases: Diabetes mellitus; recent UTI, urinary tract obstruction (eg, BPH, urethral stricture disease); urinary stasis
    - Immunosuppressive disease or diseases requiring immunosuppressive therapy
  - **EPIDEMIOLOGY**
    - **Prevalence**
    - Incidence 12.8/100 person years if prostatitis included as UTI (1)
    - Infections may increase with age to > 10% in men aged 85 yrs.
    - Asymptomatic bacteriuria in elderly men approaches 80%. (2)
  - **RISK FACTORS**
    - Risk factors for complicated UTI:
      - Male gender
      - Diabetes: Diabetes mellitus; recent UTI
      - Immunosuppressive disease or diseases requiring immunosuppressive therapy such as steroids
      - Recent antimicrobial use
      - Involuntary urinary catheter
      - Recent urologic intervention or hospitalization
      - Urethral tract obstruction (eg, BPH, urethral stricture disease); urinary stasis
        - Urinary calculi
        - Hematuria
        - Porous cirrhotic prostate
        - History of childhood UTI
  - **GENETICS**
    - Certain individuals (including those with HLA-A3) more prone to recurrent UTIs have increased epithelial cell receptivity for uropathogenic Escherichia coli.
  - **PATHOPHYSIOLOGY**
    - UTI occurs via 1 of 3 routes (1):
      - Ascending:Via inoculation of urethra/urethral catheter with bowel flora
      - Bladder: Host recognition of bacteria, with innate host defense mechanisms and bacterial virulence:
        - Inherent host defense mechanisms
          - Urinary flora helps denature extracellular infection; conversely, residual urine/bacterial density increases risk of infection
        - Virulence: Urine, pH, organic acids help prevent growth; glucuronic acid provides environment conducive for bacterial growth and increases risk of infection
      - Hemorrhages: Host recognition of bacteria, with innate immune response against infection; exfoliation of infected urothelial cells
      - Infection of urinary tract involves attachment of bacterium to host’s epithelium
        - Adherence of bacteria to urothelial cells necessary for infection; some virulent bacteria have type 1 pili (mediating attachment to cells); pyelonephritis bacteria contain F pilus
      - Common community acquired uropathogens: E. coli (most common), Proteus, Klebsiella pneumoniae, Providencia rettgeri, Staphylococcus epidermidis
      - Common nosocomial uropathogens: E. coli, Klebsiella, Enterobacter, Citrobacter, Proteus, Providencia, S. epidermidis
      - Associated conditions:
        - “Risk Factors”
      - **DIAGNOSIS**
        - **Lab**
          - **Urinalysis:** Qualitative tests of specimen already assessed by presence (p30) or absence (p30) of squamous cells.
          - **Microscopic analysis:** Bacteria: False positive from foreskin contamination if poor-quality specimen; false negative 10^7–10^9 bacteria/mL (too few to be seen under slide).
          - **Urethral swab:** WBC must be present for infection but false negative if 10^7–10^9 bacteria/mL (too few to be seen under slide).
          - **Urinary tract infection (UTI):**
            - **WBC:** Bacterial reduction of nitrate in urine
            - **Nitrite:** Presence of WBC
            - **Leukocyte esterase:** Presence of WBC
            - **Low-grade bacterial infection:** Positivity varies greatly; does not replace microscopic analysis for bacteria.
          - **Culture:** Minimum clean catch. Reduce bacterial contamination of culture in uncircumcised men by retracting foreskin and cleansing.
          - **Sensitivity:** Uptake of 10^7–10^9 bacteria/mL.
          - **Specificity:** Sensitivity of nitrite and leukocyte esterase positivity varies greatly; does not replace microscopic analysis for bacteria.
        - **Imaging**
          - Recommended in most men to rule out complicated infection, if not responding to therapy, in patients with rapid recurrent infection and found to have bacteria susceptible to antimicrobial used (i.e., resistant), when obstruction suspected.
          - **CT urogram or MRI:** Provide excellent detail, evidence of urinary tract abnormalities, stones, or foreign bodies, among others.
        - **Diagnosis Procedure/Surgery**
          - **Cystoscopy:** Same indications as stated under “Imaging,” allows direct visualization of bladder to assess for foreign body, ectopic ureters, diverticula, stones, or other abnormalities.
          - **IVU:** Should be considered in men with BPH, voiding dysfunction, high residual with stasis increases risk of infection.
        - **Localization studies:** Selective drainage from each infected site.
          - **Selective cultures from each infected site:**
          - **Localization studies:** Selective drainage from each infected site.
          - **Selective cultures from each infected site:**
          - **Localization studies:** Selective drainage from each infected site.
  - **PHYSICAL EXAM**
    - Assess for any of risk factors listed above.
    - Workup of recurrent UTI, inquire about risk factors and obtain a complete and thorough culture history of involved bacteria, treatment course, and documented evidence of clearance of bacteria.
  - **DIAGNOSTIC TESTS & INTERPRETATION**
    - **Culture:** Minimum clean catch. Reduce bacterial contamination of culture in uncircumcised men by retracting foreskin and cleansing.
    - **Sensitivity:** Uptake of 10^7–10^9 bacteria/mL.
    - **Specificity:** Sensitivity of nitrite and leukocyte esterase positivity varies greatly; does not replace microscopic analysis for bacteria.
    - **Culture:** Minimum clean catch. Reduce bacterial contamination of culture in uncircumcised men by retracting foreskin and cleansing.

**GENERAL PREVENTION**

Maintenance of low residual urine, cleaning any foreign bodies (catheters, stones).

---

**REFERENCES**

DIFFERENTIAL DIAGNOSIS

- Urinary, frequency, dribbling, and dysuria can be symptoms of prostatitis.
- Prostatitis:
  - NH Class I: Acute bacterial prostatitis, sudden onset.
  - NH Class II: Chronic bacterial prostatitis, insidious onset, relapsing, recurrent UTI
- For cystitis: Interstitial cystitis vs. urethritis
- For pyelonephritis: Papillitis vs. appendicitis vs. diverticulitis vs. acute focal/multifocal nephritis

TREATMENT

GENERAL MEASURES

- Maintain adequate hydration and hygiene.
- Remove urinary catheters as soon as possible to prevent catheter-associated UTI

MEDICATION

First Line

- Antimicrobial therapy for UTI in men is extrapolated from data for treatment of women. (see Section II: "Prostatitis, General")
- If fever or infection is present, CT should be obtained to rule out obstructive pyelonephritis; if found, decompression is critical.
- Common oral antimicrobials (1):
  - Trimethoprim-sulfamethoxazole: Inexpensive, covers staphylococci, streptococci, and most gram-negatives except Pseudomonas
  - Fluoroquinolones: More expensive (levofloxacin > ofloxacin), cover staphylococci and most gram-negatives (including Pseudomonas)
- Common parenteral antimicrobials:
  - Ampicillin: Covers streptococci, enterococci, E. coli. Probenecid addition of p-lactamase inhibitor covers Klebsiella and haemophilus; no pseudomonal coverage; good 1st-line antibiotic.

For cystitis (1)

- Trimethoprim-sulfamethoxazole: Ineffective, covers staphylococci, streptococci, and most gram-negatives except Pseudomonas
- Fluoroquinolones: More expensive (levofloxacin > ofloxacin), cover staphylococci and most gram-negatives (including Pseudomonas)
- Common parenteral antimicrobials:
  - Gentamicin: Staphylococci, most gram-negatives; good 1st-line IV drug coverage in pyelonephritis
- Ampicillin: Covers streptococci, enterococci, E. coli. Probenecid addition of p-lactamase inhibitor covers Klebsiella and haemophilus; no pseudomonal coverage; good 1st-line antibiotic.

For prostatitis (1)

- Take into account local resistances
- No controlled trials; antimicrobials based on local resistances, previous culture
- Further tailored to culture sensitivities
- Duration: For most men with complicated infections, treat for at least 10 days
  - In complicated UTI, obtain culture during therapy and 1–2 wk after therapy is complete to document clearance.
- For uncomplicated UTI, longer duration treatment (>7 days) has no association with a reduced risk for early or late recurrence compared to shorter treatment (≤7 days)

- Trimethoprim-sulfamethoxazole (14 days)
- Fluoroquinolones (14 days)
- For men, pyelonephritis is a complicated UTI and outpatient therapy is initiated only after treatment of complicating factors is initiated.

For pyelonephritis (1)

- For men, pyelonephritis is a complicated UTI and outpatient therapy is initiated only after treatment of complicating factors is initiated.
- Renal/pelvi-perineal abscess: Suspected if renal/intrarenal fever >72 h and/or persistently positive urine culture despite therapy, CT when suspect, if small abscess antimicrobial treatment; if large (>3 cm) abscess or pyelonephritis abscess, percutaneous drainage

- Outpatient therapy:
  - Fluoroquinolones (7 days) is more effective than trimethoprim-sulfamethoxazole (14 days)
  - Tailor antimicrobial to culture sensitivities
  - If no improvement, use IV therapy

- Initial therapy:
  - IV fluoroquinolone or ampicillin + gentamicin or 3rd generation cephalosporin
  - Duration without bacteremia: 2–3 days IV then 10–14 days PO antimicrobial
  - Duration with bacteremia: 7 days IV then 10–14 days appropriate PO antimicrobial

- Repeat cultures on therapy and 10–14 days after completion of course should be negative; if positive, continue a 14 day specific regimen

SECOND LINE

- Abscesses in the upper urinary tract or prostate often require percutaneous drainage.

SURGERY/OTHER PROCEDURES

- As needed for cause of recurrent UTI, such as stone, foreign body, or enlarged prostate.
- Transurethral resection (TUR) (unroofing procedure) or percutaneous drain may be required for prostatic abscess.

ADDITIONAL TREATMENT

Radiation Therapy

- N/A

Additional Therapies

- N/A

Complementary & Alternative Therapies

- Cranberry juice: No male evidence (4)

ONGOING CARE

PROGNOSIS

When appropriate antimicrobial therapy is chosen, complicating factors are identified and treated, and close follow-up is achieved with documentation of clearance of infection, a good prognosis is expected.

COMPLICATIONS

- Sepsis
  - Upper urinary tract infections with abscess formation can cause loss of renal function.

FOLLOW-UP

Patient Monitoring

- Follow-up culture, post void residual urine (PVR) and decompression.

Patient Resources


REFERENCES


ADDITIONAL READING

- See Also (Topic, Algorithm, Media)
  - Prostatitis, Acute, Bacterial (NH 1)
  - Prostatitis, Chronic, Nonbacterial, Noninflammatory (NH CPP/CPPS III B)
  - Prostatitis, Chronic, Bacterial, (NH II)
  - Prostatitis, Chronic, Nonbacterial, Inflammatory (NH CPP/CPPS III A)
  - Prostatitis, General
  - Pyelonephritis
  - Urethritis, Acute Male
  - Urinary Tract Infection (UTI), Complicated, Adult
  - Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

- 595.80 Pyelonephritis, unspecified
- 595.9 Cystitis, unspecified
- 596.5 Urinary tract infection, site not specified

ICD10

- N39.0 Urinary tract infection, site not specified
- N30.90 Cystitis, unspecified without hematuria
- N29.0 Urinary tract infection, site not specified

CLINICAL/SURGICAL PEARLS

- Most UTIs in men are considered complicated and require a longer course of antibiotics.
- UTI-related prostatitis requires a minimal of 7 days of treatment.
URINARY TRACT INFECTION (UTI), CATHETER-ASSOCIATED (CAUTI, CA-UTI)

Jeremy N. Reese, MD, MPH
Timothy D. Averch, MD, FACS

BASICS

DESCRIPTION
- Catheter-associated urinary tract infection (CAUTI) (CA-UTI) is defined as an infection occurring in a person whose urinary tract is currently catheterized or has been catheterized within the previous 48 h.
- May refer to indwelling urethral or suprapubic catheters as well as routine intermittent catheter use.
- Catheter-associated asymptomatic bacteriuria (CA-ASB) is the presence of bacteria in the urinary tract without signs or symptoms of infection.
- CA-UTI and CA-ASB are often not distinguished from each other in reported cases of catheter associated bacteriuria and may result in inappropriate antibiotic use contributing to antimicrobial resistance and adverse event reporting to governmental agencies.
- UTIs are the most common type of healthcare-associated infection reported to the National Healthcare Safety Network (NHSN).

EPIDEMOLOGY

Incidence
- CA-UTI is the most common nosocomial infection in the United States, accounting for 40% of hospital-acquired infections and over 80% of the 900,000 cases of bacteriuria annually.
- 15–25% of hospitalized patients have a urethral catheter inserted during their stay.
- Incidence of CA-bacteriuria is thought to be 3–8% per catheter-day, with 3–7.4 CA-UTIs per 1000 urinary catheter days reported in US intensive care units.
- Cost: $1006 per episode of CA-UTI

Prevalence
- 5–10% of long-term care facility patients are managed with indwelling or intermittent catheterization, accounting for >100,000 patients in the United States at any given time.

RISK FACTORS

Duration of catheter use, placement outside operating room, open drainage system, female sex, diabetes mellitus, renal insufficiency, and inappropriate use (discussed below)

Genetics
- N/A

PATHOPHYSIOLOGY

- Urinary catheterization is most important predisposing factor for nosocomial UTI
- Disrupted mucosa exposes new binding sites for bacteria allowing for growth of less virulent organisms
- Indwelling catheter may introduce bacteria at time of insertion, allowing ascension of uropathogens into bladder at time of insertion and then via intra- and extra-luminal spread
- 2/3 of identified pathogens are extrinsically acquired vs. 1/3 intrinsically acquired

- Bacterial adhesions and production of exopolysaccharides allow for replication on the catheter surface and formation of biofilms
- Short-term catheter use tends to be associated with a single organism, whereas longer catheter use is associated with polymicrobial growth
- Biofilms protect bacteria from antimicrobials and host immune response, facilitating spread of antimicrobial resistance genes
- Enterococci is most common isolate, as well as Klebsiella, Enterococcus, Enterobacter, Proteus, Pseudomonas, Streptococcus, and Enterococcus
- Providencia, Morganella, and Proteus species are more commonly isolated from long-term catheters

ASSOCIATED CONDITIONS

Spinal cord injury, neurogenic bladder, urinary incontinence, scar or perineal wounds, prolonged immobilization

GENERAL PREVENTION

- Limiting use of urinary catheters, aseptic insertion, early discontinuation of catheter use, use of pre-sealed closed drainage systems, maintaining drainage bag below level of bladder (1A)
- Absolute indications include urinary retention, accurate measurement of urine output in critically ill patients, prolonged general or spinal anesthetic, following selected urologic or gynecologic procedures, comfort care
- Application of institutional reminders such as nurse or electronic-based reminders, automatic stop-orders, use of reminder stickers or dated collection bags, requirement of physician order to place and maintain catheters
- No trials support use of: antimicrobial or chemical prophylaxis, routine catheter irrigation, antimicrobial use in drainage bag, antibiotic use at time of routine catheter exchange or removal
- Routine screening for CA-ASB should be avoided (1A)
- Alternatives to indwelling urethral catheters
- Condom catheters provide alternative to short-term catheter use in men with low-post void residuals
- Urethral and suprapubic catheters have similar rates of CA-UTI, although suprapubic catheters are often more comfortable, spare urethral catheterization, and are easier to exchange
- Intermittent catheterization significantly reduces rates of CA-ASB and is associated with higher patient satisfaction

- Healthcare providers should clean their hands with soap and water or use an alcohol-based hand rub before and after touching catheters.
- Avoid disconnecting the catheter and drain tube.
- The catheter is secured to the leg to prevent pulling on the catheter.
- Keep the bag lower than the bladder to prevent urine from backflowing to the bladder.
- Empty the bag regularly, the drainage spout should not touch anything while emptying the bag.

DIAGNOSIS

HISTORY
- CA-UTI: Patients with signs and symptoms of UTI with current or recent (<48 h) indwelling urinary catheter or routine intermittent catheter use
- Symptoms may include dysuria, urgency, altered mental status, malaise, flank pain, and pelvic discomfort
- Patients with a recently removed catheter may report dysuria, urinary urgency and/or frequency
- Spinal cord injury patients may report increased spasticity, autonomic dysreflexia and/or sense of uneasiness

PHYSICAL EXAM
- A few physical exam findings are reliable to diagnose CA-UTI but may include suprapubic and/or costovertebral angle tenderness, hematuria, or fever
- Foul-smelling and/or cloudy urine have not been shown to be significant clinical predictors of CA-UTI
- Encourage hydration if no other clinical indicators of infection and reassess thereafter

DIAGNOSTIC TESTS & INTERPRETATION

- CA-UTI: Patients with signs and symptoms of UTI with current or recent (<48 h) indwelling urinary catheter or routine intermittent catheter use with cultures growing >103 cfu/mL (1A)
- CA-ASB is defined as cultures growing >105 cfu/mL (1A)
- Urine specimens should be sent for culture prior to initiation of antimicrobials (1A)
- Catheters should be replaced, if still indicated, and a culture should be obtained from newly placed catheter (1A)
- If catheter can be discontinued, a midstream voided specimen should be used for culture (1A)
- Pyuria on urinalysis is not sufficient to diagnose CA-UTI or CA-ASB, but its absence can exclude infection (1A)

Imaging
- Not routinely indicated
- May be necessary in cases of suspected complicated UTI such as concern for urinithiasis, foreign body, abscess, emphysematous infection, or vesicoureteral reflux

Diagnostic Procedures/Surgery
- Not routinely indicated
- Unidiagnostic studies may be useful to determine necessity of routine catheterization, particularly in spinal cord injury (SCI) population
- For patients with long-term catheter use (eg, SCI, neurogenic bladder population), routine cystoscopy has been suggested for cancer detection due to increased risk of both transitional cell and squamous-cell carcinomas
- Lifetime bladder malignancy incidence ranges from 0.39% to 2.24% in published retrospective reviews of SCI patients

Pathologic Findings
- Pathology is not routinely performed
Differential Diagnosis

- In patients presenting with fever, chills, altered mental status, and other non-specific symptoms, all other sources of infection must be ruled out as CA-ASB is diagnosed in >95% of patients with long-term catheter use
- Bladder tumor: Hematuria must be worked up, given increased risk of malignancy from long-term catheter use
- Bladder calculus: Associated with chronic urinary stasis
- Local inflammation: Vaginitis, urethritis, interstitial cystitis

Treatment

General Measures

- Prevention through early removal of urinary catheters is best preventative treatment
- Routine screening for and treatment of CA-ASB should be avoided
- Optimal duration of therapy is unknown, but typically ranges from 3 to 21 days depending on severity of symptoms (e.g., cystitis, pylephritis, associated abscess, or bacteremia)

- Most literature suggests 7–14 days of therapy for CA-UTI
- 3-day regimen suggested in younger women (< 65 y) in whom a catheter was recently removed
- Catheters placed > 2 wk prior should be exchanged at time of diagnosis (prior to cultures being sent) to improve antimicrobial penetration and reduce bacterial sensitivity
- When possible, antibiotic therapy should be culture driven to avoid exposure to additional antimicrobial agents

Medication

First Line (2,3)

- Given incidence of polymicrobial colonization as well as involvement of both gram-positive and -negative organisms, no 1st-line agent can be recommended
- Serious infections must be covered with broad-spectrum antibiotics and narrowed based on bacterial sensitivities
- Treatment of minor infections should be delayed until culture sensitivities are available to guide antimicrobial selection

Second Line

- N/A

Surgery/Other Procedures

- Filled indicated, but may be necessary in cases of encrusted catheters, emphysematous or abscess forming infections (see Section I. UTI, complex, adult)

Additional Treatment

Radiation Therapy

- N/A

Additional Therapies

- Complementary & Alternative Therapies
- Antimicrobial coated catheters may delay detection of CA-ASB in short-term catheter use (<1 wk)
- Mercurineux salts may reduce CA-ASB and CA-UTI in short-term catheter use (<1 wk)
- Cranberry products have not been shown to be effective in the prevention or treatment of infection in CA-UTI population

Ongoing Care

Prognosis

- Generally good
- Patient hospitalization lengths and costs are elevated when diagnosed with CA-ASB or CA-UTI
- Mortality rate among hospitalized patients with bacteremic UTI is < 1%, however, > 1% of CA-ASB results in bacteremia

Complications

- Patients with indwelling catheter experience increased rates of bacteremia, upper tract infection, catheter obstruction, urinary stone formation, fistula formation, urethral erosion, incontinence, and bladder cancer

Follow-Up

- Patient Monitoring
- Institutional education on indications for catheter use and reminder systems for early catheter removal such as nursing protocols, electronic reminders, chart and collection bag stickers
- Attention to staff education to urologically essential care

- Patient Resources
- Medline Plus: Catheter Related UTI
- Website: http://www.nlm.nih.gov/medlineplus/ency/article/000483.htm

References


Additional Reading


See Also (Topic, Algorithm, Media)

- Cytotox, General Considerations
- Pyelonephritis
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Complicated, Adult
- Urinary Tract Infection (UTI), Pediatric

Codes

ICD-10

- G44.49 Other and unspecified Escherichia coli
- G98.0 Urinary tract infection, site not specified
- J09.64 Infection and inflammatory reaction due to indwelling urinary catheter

ICD10

- B96.20 Urinary catheter as the cause of disease, closed drainage
- N09.0 Urinary tract infection, site not specified
- T85.53XA Infective/Inflammatory reaction due to indwelling urinary catheter, intr

Clinical/Surgical Pearls

- Advise against routine screening for CA-ASB due to increasing antimicrobial resistance and inappropriate use
- Most important prevention is adherence to indications for catheter use and prompt removal when no longer indicated
- When catheter use is unavoidable, it should be aseptically inserted, maintained with closed drainage system and removed as early as possible
- When infection is suspected, culture specimen should be sent from a newly placed catheter or midstream voided specimen
- Treatment should be driven by culture sensitivities and typically last 7–14 days.
URINARY TRACT INFECTION (UTI), COMPLICATED, ADULT

Steve Dong, MD
Leonard G. Gomella, MD, FACS

PATHOPHYSIOLOGY

Primary UTI occurs via 1 of 3 routes (1):
- Ascending by inoculation of urethra/vesical catheter with bowel flora. Most common
- Hematogenous seeding of kidney
- Lymphatic spread
- Structural, functional, or metabolic abnormalities allow infection of more uncommon pathogens, and increase the rate of therapy failure
- E. coli, accounts for only approximately half of infections with complicated UTI, compared to uncomplicated (15–95%)
- A broader range of organisms can seen in complicated (ET), include Pneumococci, Klebsiella pneumoniae as well as Pseudomonas, Staphylococci, enterococci, staphylococci, and fungi (3)

ASSOCIATED CONDITIONS
- Diabetes mellitus (10%)
- Renal failure
- Multiple sclerosis
- Spinal cord injury

GENERAL PREVENTION

Proper infection control practice in health care facilities to avoid contact transfer of resistant organisms between patients.
- Patients with multiple sclerosis may present with fatigue or worsening neurologic function.
- Patients with spinal cord injuries can present with fever, pain, or placing a Foley catheter for urethral stricture.
- Patients with spinal cord injury, maintain a low bladder pressure to prevent reflux, ascending infections, and progression to renal failure.
- Monitoring of bladder pressure and function can be done with urodynamics testing.
- Prevention of complicated UTI with long-term prophylaxis in at-risk adult population is not recommended due to the emergence of resistant organisms (4)

DIAGNOSIS

HISTORY

Assess for any of risk factors listed above.
- Clinical presentation may or may not be associated with clinical symptoms (eg, dysuria, urgency, flank pain, fever)
- Clinical presentation may vary from severe obstructive polynephritis with imminent urosepsis to catheter associated UTI, which disappears once the catheter is removed.
- Patients with spinal cord injuries can present with bladder, leg spasms, or autonomic dysreflexia.
- Patients with multiple sclerosis may present with fatigue or worsening neurologic function.
- Fever without localized findings is a common presentation of UTI in patients with chronic indwelling catheters.

PHYSICAL EXAM

- Check vital signs to assess severity of infection, presence of systemic disease.
- Assess for suprapubic pain, flank pain, urethral discharge, renal exam for tenderness.
- Evaluate for anatomical abnormalities, such as the presence of a nephrostomy tube, or an renal conduit.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urinalysis
- Pyuria is almost always present
- Unless the collecting system is obstructed
- White cell casts suggest a renal origin
- Urine culture is positive for a UTI with the following:
  - ≥10^5 cfu/mL in mid-stream sample
  - ≥10^3 cfu/mL in a straight catheter urine sample

Imaging
- Is recommended in patients suspected of complicated infection, especially in those not responding to therapy for 48–72 h. In patients with rapid recurrent infection and found to have bacteria susceptible to antimicrobial used (eg, persistence), when obstruction suspected, as well as history of kidney stones or signs of renal colic.
- For patients who could not be exposed to radiation
- Cheaper and readily available
- Best to evaluate for hydronephrosis
- Lack details and sensitivities of other imaging modalities
- Computed tomography (CT) urogram
  - Most sensitive in detecting abnormalities and able to delineate extent of disease. Has 3 phases:
    - No contrast—evaluate for renal or ureteral calculi, gas-forming infections, hemorrhage
    - Contrast—detect areas lacking perfusion due to infection induced ischemia
    - Delayed phase—detect for any filling defects such as fungus ball
- Magnetic resonance imaging (MRI)
  - No advantage over CT except in patients who wants to avoid contrast and radiation (3)

Diagnostic Procedures/Surgery
- Urologic evaluation is often necessary in the setting of complex UTI
- Urinary obstruction associated with UTI must be relieved emergently, eg, placing a ureteral stent or nephrostomy tube for a obstructing ureteral calculus, or placing a Foley catheter for urethral stricture.
- Cystoscopy allows direct visualization of bladder to assess for foreign body, ectopic ureters, diverticula, stones, or other abnormalities that could be a nidus for infection.
TREATMENT

GENERAL MEASURES
If severe infection or toxicity is present, CT should be considered to rule out obstructive pyelonephritis; if found, decompression is critical.

DIFFERENTIAL DIAGNOSIS

• For cystitis: interstitial cystitis vs. urethritis.
• For pyelonephritis:
  – Pyelonephritis vs. appendicitis vs. diverticulitis vs. acute focal/multifocal interstitial nephritis – Urolithiasis

Medication

First Line

• Common oral antimicrobials:
  – Fluoroquinolones: More expensive (levoﬂoxacin > ciproﬂoxacin), cover staphylococci and most gram-negatives including Pseudomonas
  – Trimethoprim-sulfamethoxazole: Resistance is often seen, therefore not recommended for empiric therapy (3)
• Commonly parenteral antimicrobials:
  – For those who have hematologic instability, or cannot tolerate oral therapy, or for patients with suspected resistant organisms:
  – Gentamicin: Can cause Staphylococci, most gram-negatives including Pseudomonas
  – Augmentin for coverage in pyelonephritis – Cephalexin
  – Carbenicillin – Aminopenicillin PLUS a β-lactamase inhibitor: Amoxicillin by itself (eq, ampicillin) is not recommended for empiric therapy (3)
• For complicated pyelonephritis (1, 3)
  – Renal/renal pelvis abscess is suspected if indwelling catheter fever >37.8° and/or persistently positive culture despite antimicrobial treatment; CT when suspect; if small renal abscess, then antimicrobial treatment; if large (>3 cm) renal abscess or perinephric abscess, then percutaneous drainage
  – Inpatient therapy is recommended
• For cystitis: interstitial cystitis vs. urethritis.
 – Pseudomonas gram-negatives including Pseudomonas
  – Tigecycline: Has activity against ESBL bacteria, but is unstable in urinary tract.

SURGERY/OTHER PROCEDURES

As needed for cause of complicated UTI, such as stone, foreign body, or enlarged prostate.

ADDITIONAL TREATMENT

Radiation Therapy
N/A

Additional Therapies
N/A

Complementary & Alternative Therapies

Cranberry juice and products have not been shown to reduce the risk of complicated UTI.

ONGOING CARE

PROGNOSIS

When appropriate antimicrobial therapy is chosen, complicating factors are identified and treated, and close follow-up is achieved with documentation of clearance of infection, a good prognosis is expected.

COMPLICATIONS

• More likely to occur in patients with comorbidities
• Acute complicated pyelonephritis can progress to emphysematous pyelonephritis, renal abscess, perinephric abscess, or papillary necrosis.
• Infections can spread to cause bone and joint infection, or endocarditis.
• Renal failure in patients with spinal cord injury with recurrent sepsis

FOLLOW-UP

Patient Monitoring
Repeat urine cultures must be obtained because patients with complicated UTI are more at risk for recurrent infection.

REFERENCES


See Also (Topic, Algorithm, Media)

• Pyelonephritis
• Urethritis
• Acute Male
• Urinary Tract Infection (UTI), Adult Female
• Urinary Tract Infection (UTI), Adult Male
• Urinary Tract Infection (UTI), Complicated, Adult Image
• Urinary Tract Infection (UTI), Complicated, Pediatric

URINARY TRACT INFECTION (UTI), COMPLICATED, ADULT

ICD9
599.0 Urinary tract infection, site not specified
600.01 Hypertrophy (benign) of prostate with urinary obstruction and other lower urinary tract symptoms (LUTS)

ICD10
N29.0 Calculus of kidney
N40.1 Enlarged prostate with lower urinary tract symptoms (LUTS)
N59.0 Urinary tract infection, site not specified
N60.1 Enlarged prostate with lower urinary tract symptoms

CLINICAL/SURGICAL PEARLS

• Complicated UTI can have a wide range of atypical presentations, eg, MS patients with neurologic decompensation, spinal cord injury patients with symptoms of autonomic dysreflexia, or nursing home patient who has indwelling Foley with fever should be suspected of UTI.
• CT should be considered the imaging of choice, and with a low threshold with any history of stone, flank pain, or pyelonephritis not improving or persistent positive culture.
• Presence of obstruction on imaging requires urgent decompression.
URINARY TRACT INFECTION (UTI) COMPLICATED, PEDIATRIC

Christopher J. Long, MD
Douglas A. Canning, MD, FACS

PATHOPHYSIOLOGY
- Acute swelling of the pelvis allows ascending infection of the GU tract
- Bladder formation on stents or catheters
- Increased bladder pressure
  - Decreased bladder capacity
- Compromised Foley catheter drainage
- Dysfunctional voiding
- Bacteriology of E. coli increase affinity for GU tract: P fimbriae and MRHA (mannose-resistant hemagglutinin)

ASSOCIATED CONDITIONS
- Urinary stasis increases risk of UTI
- Stents or catheters located within the GU tract act as a nidus for bacterial colonization
- Surgically correctable conditions of the GU tract

GENERAL PREVENTION
- Antibiotic prophylaxis
  - Low-dose daily antibiotic
  - Healthy children have no proven benefit
- Consider circumcision in boys < 12 mo of age with GU tract anomalies
- Consider correction of vesicoureteral reflux (VUR) in females approaching puberty for increased risk of pyelonephritis during pregnancy
- Treatment of constipation and dysfunctional voiding

DIAGNOSIS
- History
  - Vague in infants and nonverbal children: Fever, irritability, poor feeding, vomiting, diarrhea
  - Older children: Dysuria, incontinence, voiding dysfunction, lower abdominal pain, enuresis
- Physical exam
  - Single-use, sterile catheters show no benefit
- Urinary stream, voiding history
- Presence and severity of fever
- Previous UTIs and how documented (urine analysis, culture, how culture was obtained)
- Previous GU/GI surgery
- Family history of infections and/or GU anomalies
- Prerenal history including ultrasound

ASSOCIATED CONDITIONS
- Family history of infections and/or GU anomalies
- Urinary stream, voiding history
- Presence and severity of fever
- Previous UTIs and how documented (urine analysis, culture, how culture was obtained)
- Previous GU/GI surgery
- Family history of infections and/or GU anomalies
- Prerenal history including ultrasound

LAB
- Blood work: CBC, BMP, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin
- Procalcitonin, CRP: ESR correlate with systemic illness and suggest pyelonephritis/sepsis
- Diagnosis: 2 or more symptoms, > 100,000 CFU/mL of a single organism, and > 10 WBC/HFP on urine microscopy
- Urinalysis (UA)
  - leukocyte esterase, nitrite
  - Microscopic: WBC, bacteria
- Urine culture: obtained with UA
  - Consider lower threshold (> 50,000 CFUs per mL)
  - PLUS yeasts: bacteria in some cases

IMAGING
- Renal and bladder ultrasound: Assess hydronephrosis or incomplete bladder emptying
- Voiding cystourethrogram if not already performed
- Consider Gallium scan for complicated cases
- Renal cortical scan: Rule out scarring or pyelonephritis
- Consider test of cure prior to study
- Renal cortical scan: Rule out scarring or pyelonephritis
- Renal cortical scan: Rule out scarring or pyelonephritis

DIAGNOSTIC PROCEDURES/SURGERY
- Catheterized or midstream specimen is preferred depending upon patient age
- Suprapubic aspiration has highest accuracy but increases morbidity for patients
- Bagged specimen not recommended
- Cystoscopy is rarely indicated
- Urine culture: obtained with UA

SPECIFIC INTERVENTION FOR GU ANOMALIES
- Consider treatment if reflux once therapy is completed

PATHOLOGIC FINDINGS
- Ziehl-Neelsen and/or Warthin-Starry stain
- Bacteria in the lower urinary tract
- Blood group antigen phenotype has been shown to increase risk of pyelonephritis

RISK FACTORS

TRIGGERS

GENETICS
- Polymorphisms of the interleukin-8 (IL-8) cytokine and decreased receptor expression increase risk for developing pyelonephritis
- Blood group antigen phenotype has been shown to play a role in UTI resistance

HISTORY
- Acute swelling of the pelvis allows ascending infection of the GU tract
- Bladder formation on stents or catheters
- Increased bladder pressure
  - Decreased bladder capacity
- Compromised Foley catheter drainage
- Dysfunctional voiding
- Bacteriology of E. coli increase affinity for GU tract: P fimbriae and MRHA (mannose-resistant hemagglutinin)

ASSOCIATED CONDITIONS
- Urinary stasis increases risk of UTI
- Stents or catheters located within the GU tract act as a nidus for bacterial colonization
- Surgically correctable conditions of the GU tract

GENERAL PREVENTION
- Antibiotic prophylaxis
  - Low-dose daily antibiotic
  - Healthy children have no proven benefit
- Consider circumcision in boys < 12 mo of age with GU tract anomalies
- Consider correction of vesicoureteral reflux (VUR) in females approaching puberty for increased risk of pyelonephritis during pregnancy
- Treatment of constipation and dysfunctional voiding

DIAGNOSIS
- History
  - Vague in infants and nonverbal children: Fever, irritability, poor feeding, vomiting, diarrhea
  - Older children: Dysuria, incontinence, voiding dysfunction, lower abdominal pain, enuresis
- Physical exam
  - Single-use, sterile catheters show no benefit
- Urinary stream, voiding history
- Presence and severity of fever
- Previous UTIs and how documented (urine analysis, culture, how culture was obtained)
- Previous GU/GI surgery
- Family history of infections and/or GU anomalies
- Prerenal history including ultrasound

ASSOCIATED CONDITIONS
- Family history of infections and/or GU anomalies
- Urinary stream, voiding history
- Presence and severity of fever
- Previous UTIs and how documented (urine analysis, culture, how culture was obtained)
- Previous GU/GI surgery
- Family history of infections and/or GU anomalies
- Prerenal history including ultrasound

LAB
- Blood work: CBC, BMP, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin
- Procalcitonin, CRP: ESR correlate with systemic illness and suggest pyelonephritis/sepsis
- Diagnosis: 2 or more symptoms, > 100,000 CFU/mL of a single organism, and > 10 WBC/HFP on urine microscopy
- Urinalysis (UA)
  - leukocyte esterase, nitrite
  - Microscopic: WBC, bacteria
- Urine culture: obtained with UA
  - Consider lower threshold (> 50,000 CFUs per mL)
  - PLUS yeasts: bacteria in some cases

IMAGING
- Renal and bladder ultrasound: Assess hydronephrosis or incomplete bladder emptying
- Voiding cystourethrogram if not already performed
- Consider Gallium scan for complicated cases
- Renal cortical scan: Rule out scarring or pyelonephritis
  - Consider Gallium scan for complicated cases

DIAGNOSTIC PROCEDURES/SURGERY
- Catheterized or midstream specimen is preferred depending upon patient age
  - Suprapubic aspiration has highest accuracy but increases morbidity for patients
- Bagged specimen not recommended
- Cystoscopy is rarely indicated
- Urine culture: obtained with UA

SPECIFIC INTERVENTION FOR GU ANOMALIES
- Consider treatment if reflux once therapy is completed

PATHOLOGIC FINDINGS
- Ziehl-Neelsen and/or Warthin-Starry stain
- Bacteria in the lower urinary tract
- Blood group antigen phenotype has been shown to increase risk for developing pyelonephritis

TRIGGERS

GENETICS
- Polymorphisms of the interleukin-8 (IL-8) cytokine and decreased receptor expression increase risk for developing pyelonephritis
- Blood group antigen phenotype has been shown to play a role in UTI resistance

HISTORY
- Acute swelling of the pelvis allows ascending infection of the GU tract
- Bladder formation on stents or catheters
- Increased bladder pressure
  - Decreased bladder capacity
- Compromised Foley catheter drainage
- Dysfunctional voiding
- Bacteriology of E. coli increase affinity for GU tract: P fimbriae and MRHA (mannose-resistant hemagglutinin)
Differential Diagnosis

- Younger children (<24 mo) presenting with fever, otitis media, gastroenteritis, upper respiratory tract infection
- Stone disease
- Urerovaginitis
- Dysfunction voiding/diuresis syndrome
- Pregnancy
- Appendicitis
- Bladder outlet obstruction
- Epipidymitis
- Abuse

Treatment

General Measures (2,3)

- Antibiotic therapy after urine culture obtained
- Oral antibiotic therapy vs. IV antibiotics dependent upon severity of infection
- Strive for absence of fever, concern for sepsis, elevated WBC, etc.
- Duration of therapy 7–14 days
- Increased rate of resistant organisms

Medication

First Line

- 3rd generation cephalosporin + aminoglycoside
  - Ceftriaxone: 100–150 mg/kg (q8–12h)
  - Ceftazidime: 100–150 mg/kg (q6–8h)
  - Aminoglycoside (gentamicin, tobramycin): 2.5 mg/kg (q8h)
- Combination therapy:
  - Aminoglycoside (gentamicin, tobramycin): 2.5 mg/kg (q8h)
  - Ceftazidime: 100–150 mg/kg (q6–8h)

Second Line

- Fluoroquinolones
  - Ciprofloxacin 40–90 mg/kg (q12–24h)
  - Levofloxacin 50–75 mg/kg (q24h)
  - Norfloxacin 90–150 mg/kg (q12h)

- 3rd- or 4th-generation cephalosporin

Surgery/Other Procedures

- Circumcision
- VUR
- Vesicoureteral Reflux

Surgical referral due to high risk

Follow-Up

- Document test of cure with repeat urine culture
- Patient should be examined

Additional Treatment

Radiation Therapy

- Myelosuppression

Additional Therapies (5)

- Topical therapy for voiding dysfunction
  - Timed voiding, biofeedback
  - Antibiotics for lower urinary tract infection
  - Poliectomy for detrusor sphincter dyssynergia

- Consider suppressive antibiotics in selected cases
  - Nitrofurantoin 1–2 mg/kg PO daily
  - Sulfamethoxazole/trimethoprim (SMZ-TMP)
  - 5–10 mg/kg SMZ, 1–2 mg/kg TMP PO daily (Do not use in infants or with sulfa allergy)
  - Trimethoprim 1–2 mg/kg PO daily
  - Ampicillin or amoxicillin not recommended due to resistance

Complementary & Alternative Therapies (4)

- Consider suppressive antibiotics in selected cases
- Fluoroquinolones
- 3rd- or 4th-generation cephalosporin
- Oral antibiotic therapy vs. IV antibiotics dependent upon severity of infection

- Abdominal pain
- Urinary tract infection
- Urinary tract infection
- Urinary tract infection
- Urinary tract infection

Ongoing Care

Prognosis

- Potential progression of infection

- Follow-up

- Document test of cure with repeat urine culture

- Consider nephrology referral

- Yearly blood pressure assessment

- Document test of cure with repeat urine culture

- Consider nephrology referral

Patient Resources


References


Additional Reading


Clinical/Surgical Pearls

- Complicated UTIs can lead to increased patient morbidity and mortality.
- Treatment plan should be tailored to the specific underlying contributing factors leading to UTI development.
- Prompt institution of broad spectrum antibiotics after urine culture is obtained with subsequent tailoring of antibiotic therapy based on bacteria sensitivities recommended in cases of recurrent or complicated UTIs.
- Maintain a high degree of suspicion for potentially surgically correctable causes. Correction will likely decrease UTI risk.
URINARY TRACT INFECTION (UTI), PEDIATRIC

Kathleen Kieran, MD, FAAP, FACS
Christopher S. Cooper, MD, FAAP, FACS

BASICS

DESCRIPTION
A urinary tract infection (UTI) represents inflammatory changes in the urinary tract caused by the presence of bacteria.

Spectrum of severity, from local infection to systemic changes/urosepsis.

EPIDEMIOLOGY
Incidence
• 180,000 children annually will develop UTI in the United States.
• 0.7% of all pediatric office visits each year (3.5–9% of emergency department visits).
• Overall 2% of febrile infants, 5% of all infants.
• 0.7% of all pediatric office visits each year (3.5–5% of emergency department visits).
• 0.7% of all pediatric office visits each year (3.5–5% of emergency department visits).
• 21% of uncircumcised male infants.
• 5% of female infants.
• 2–3% of circumcised male infants.

Prevalence
Prevalence is variable and closer to an adult level as age groups increase.

RISK FACTORS
• Previous UTI:
  – 100% of infants with a symptomatic UTI will have a recurrence.
  – Older females may have a 40–60% risk of recurrent infection.
• Immunosuppressive states, including diabetes, chemotherapy, and steroid use.
• Anatomic and functional abnormalities of the urinary tract which predispose to urinary stasis:
  – Vesicoureteral reflux, ureterocaliceal, ureteropelvic junction obstruction, bladder diverticula, posterior urethral valves.
  – Neurogenic bladder, dysfunctional voiding/elimination behaviors (e.g., constipation).
• Urologic instrumentation (catheters).
• Other children: Sexual activity.
• Circumcision (1):
  – Uncircumcised males, 1 yr of age have the highest rate of UTI of all gender and age groups (10 times higher than circumcision males).
  – AAP has stopped short of endorsing routine circumcision, but acknowledges apparent protective effect against UTIs and genital cancer.
• Consider circumcision in infant males with UTI.

GENERAL PREVENTION
• Identification and treatment of underlying urologic conditions which may predispose to urinary stasis.

GENETICS
• Incompletely understood.
• Multifactorial, including altered carbohydrate secretion antigens on cell surface molecules which may increase bacterial adherence.

PATHOPHYSIOLOGY
• Usually ascending infections, although hematogenous spread can be seen in infants or immunocompromised populations.
• Colonization of female introitus or male preputial epithelium with intestinal flora.
• The most common pathogen is Escherichia coli (85%–90%).
• Other uropathogens include Klebsiella, Proteus, Enterococcus, Citrobacter, Staphylococcus saprophyticus, and Enterococcus.

• Viral (e.g., adenovirus, BK virus) and fungal (Candida) infections may be seen in immunocompromised patients.
• Both humoral and cellular responses result in inflammation of the urinary tract.
• Bacterial virulence factors include O antigen (part of lipopolysaccharide), K antigen (part of capsule), and P fimbriae contributes to bacterial ascent to the upper tracts, even in the absence of reflux.

ASSOCIATED CONDITIONS
• Dysfunctional elimination including incontinence, holding or retention of urine, and constipation increase risk of UTI.
• Immunocompromise.
• Structural abnormalities of the GU tract.

GENERAL PREVENTION
• Good voiding/elimination habits.
• Treatment of constipation.
• Identification and treatment of underlying urologic conditions which may predispose to urinary stasis.

DIAGNOSIS

HISTORY
• Vague in infants:
• Older children may complain of dysuria, incontinence, changes in voiding habits, flank or abdominal pain, enuresis.
  – Presence, severity, and duration of fever.
• Previous UTIs and how documented (e.g., culture, urinalysis, symptoms).
• Prenatal history including prenatal ultrasounds.
• Other children: Sexual activity.
  – Circumcision (1):
    – Uncircumcised males, 1 yr of age have the highest rate of UTI of all gender and age groups (10 times higher than circumcision males).
    – AAP has stopped short of endorsing routine circumcision, but acknowledges apparent protective effect against UTIs and genital cancer.
• Consider circumcision in infant males with UTI.

PHYSICAL EXAM
• Specific findings in infants are rare; may see fever, failure to thrive, jaundice, or lethargy.
• Older children may have suprapubic, flank, abdominal and/or upper quadrant tenderness.
• PVF also raises concern for infection.
  – Cervical tenderness suggests pyelonephritis.
  – A sterile exam will help rule out epididymitis.
  – Caudal external genital exam to rule out trauma, local irritation, urethral discharge, phimosis, and anatomic abnormalities.
• Urine culture is the gold standard to diagnose UTI.
• Symptomatic bacteriuria (no symptoms, <5 WBC/hpf, but positive culture) should prompt treatment if a pathogenic organism is present.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
• Urine analysis (2):
  – Microscopic exam after dipstick urine analysis.
  – Also yields clues to contamination (epithelial cells).
• Positive leukocyte esterase (LE) indicates WBCs in the urine (up to 95% sensitive in children with symptoms.
• Positive nitrite (many gram-negative bacteria produce this substance) has a sensitivity of 30–45%, but a specificity that nears 100%.
• Positive leukocyte esterase (LE) indicates WBCs in the urine (up to 95% sensitive in children with symptoms.
• Positive nitrite (many gram-negative bacteria produce this substance) has a sensitivity of 30–45%, but a specificity that nears 100%.

• Combination positive nitrite-leukocyte esterase.
• Blood tests are unreliable in diagnosing UTI.
• Asymptomatic bacteriuria (no symptoms, <5 WBC/hpf, but positive culture) should prompt treatment if a pathogenic organism is present.

Imaging
• The need for and timing of imaging following UTI remains controversial.
• Imaging is not required in the acute setting, but may be indicated at follow-up.
• Consider evaluating all children ≤5 yr after their 1st documented UTI, and all girls, regardless of age, with febrile or recurrent infections, particularly with voiding dysfunction.
• Renal/Bladder US should be considered following a febrile UTI.
• Need for and timing of VCUG is controversial. The American Academy of Pediatrics (AAP) recommends VCUG after second febrile UTI unless there is a suspicion of underlying anatomic abnormality.
• 40% of children with a single febrile UTI have VUR.
• Absence of clinical improvement after 48 h of appropriate treatment should raise concern for structural or functional abnormalities.

Sedation may help to obtain a reliable renal ultrasound or VCUG.

In toilet-trained children in whom voiding dysfunction may be a factor, assessment or voiding patterns (e.g., stopwatch) may be helpful.
URINARY TRACT INFECTION (UTI), PEDIATRIC

Diagnosis/Procedures/Surgery
Nonspecific, though cystoscopy may be performed for associated conditions or chronic infections as indicated.

Pathologic Findings
- Cysts and polyps/implants are generally associated with inflammatory response.
- Renal scarring may be manifested by architectural changes including collagen deposition and glomerular loss.

Differential Diagnosis
- UTIs present similarly to other infections:
  - Bacteremia and sepsis
  - Urethritis
  - Pyelonephritis
  - Sexual abuse
  - Vaginitis
- Also consider: Appendicitis, diabetes, dysfunctional voiding/elimination, pregnancy in postpubertal females, urolithiasis, urinary obstruction.

Alert
Findings suggestive of an STI/STD infection should raise concern for sexual abuse.

Treatment
General Measures
- Initial, empirical treatment should be based on clinical suspicion of UTI as well as reliability of patient and family.
- As the symptoms are often vague, a high index of suspicion must be maintained to ensure early detection of pyelonephritis.
- Hospitalization might be required based on patient age and clinical status, although infants <2 mos and nonurologic children with suspected pyelonephritis can be treated as outpatients as long as compliance is not an issue.
- Children with asymptomatic bacteriuria may not require treatment with antibiotics if the urinary system is otherwise normal.

Medication
Alert
- In children, use 7–14-day treatment course (~7 days has been shown to be effective).
- Fluoroquinolones should not be a 1st-line choice for children overall.
- 3rd-generation cephalosporins: Ceftriaxone, Cefixime, Cefdinir.
- Children <2 yr of age should be treated with pharmcodynamic (B/L, P, or combination).
- School-aged children without systemic symptoms may be treated with an oral broad-spectrum antibiotic such as AMX-TMP, nitrofurantoin.
- Appropriate to start broad-spectrum antibiotics while awaiting culture results (5).

Second Line
- Antibiotic course should be tailored by comorbidities, age, and local bacterial resistance patterns.

Surgery/Other Procedures
- May be indicated following resolution of infection if child has specific urinary abnormalities predisposing to or exacerbating effects of urinary tract infection (eg, obstruction, VUR).
- Surgical correction of reflux is aimed at protecting upper tracts and is associated with a decrease in the number of future UTIs.

Additional Treatment
- In children with UTIs and dysfunctional voiding/elimination behaviors, improvement in the latter will often result in fewer recurrent UTIs.
- Regular (eg every 2 h) voiding.
- Avoidance of constipation.

Radiation Therapy
N/A.

Additional Therapies
N/A.

Complementary & Alternative Therapies
- Cranberries may be effective in decreasing bacterial adherence, but there are no specific recommendations for children at present.
- Probiotics may favorably alter gastrointestinal flora, but again there are no specific recommendations for use.

Ongoing Care
- Infants <2 mo (IV therapy preferred).
  - Amoxicillin/trimethoprim: ~7 d; 50–100 mg/kg/24 h IV, q6h; Term infants: 75–150 mg/kg/24 h, q6–8h; Children >1 mos: 200 mg/kg/24 h IV, q6h R or IV
  - Gentamicin: Infants ~7 d; 1200 mg/24 h IV, q8h; Children >1200 mg/24 h, q12h; Children <2.5 mg/kg/dose IV, q12h; Children <2.5 mg/kg/dose IV = q6h, ≤ renal insufficiency.
- 3rd-generation cephalosporin.
- Ceftriaxone: 8 mg/kg PO – daily bid, q12h in renal impairment.
- Ceftriaxone: 7 mg/kg PO bid or 14 mg/kg PO, q12h in renal impairment.
- Ceftobiprol: 9 mg/kg PO, q12h in renal impairment; take on empty stomach (susp).
- Children >2 mo.
  - 3rd generation cephalosporin: Ceftriaxone, Cefixime, Cefdinir.
  - Children <2 yr of age should be treated with pharmcodynamic (B/L, P, or combination).

Patient Resources

References

Additional Reading

See Also (Topic, Algorithm, Media)
- Urinary Tract Infection (UTI), Complicated, Pediatric
- Urinary Tract Infection, Pediatric Algorithm
- Vesicoureteral Reflux, Pediatric

Codes
ICD-9: N39.0 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn
599.0 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn

ICD-10: B96.20 Urinary tract infection as the cause of disease classed elsewhere
N90.9 Urinary tract infection, site not specified
P39.3 Nephrolithic urinary tract infection

Clinical/Surgical Pearls
- A high index of suspicion is often required for an accurate diagnosis of UTI, especially in nonverbal children.
- Treatment of the acute infection should be tailored to the child’s age, comorbidities, and clinical condition, as well as local antibiotic resistance patterns and culture results.
- Surgical intervention is undertaken when conservative management is unlikely to prevent further UTIs and/or protect the kidneys.
- Patients with recurrent febrile infections, VUR, and/or kidney scarring should be followed carefully for development of renal disease.

ICD9
599 Other and unspecified Escherichia coli [E. coli]
771.82 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn

ICD10
B96.20 Urinary tract infection as the cause of disease classed elsewhere
N90.9 Urinary tract infection, site not specified
P39.3 Nephrolithic urinary tract infection

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Urinary Tract Infection (UTI), Complicated, Pediatric
- Urinary Tract Infection, Pediatric Algorithm
- Vesicoureteral Reflux, Pediatric

Codes
ICD-9: N39.0 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn
599.0 Urinary tract infection, site not specified

ICD-10: B96.20 Urinary tract infection as the cause of disease classed elsewhere
N90.9 Urinary tract infection, site not specified
P39.3 Nephrolithic urinary tract infection

Clinical/Surgical Pearls
- A high index of suspicion is often required for an accurate diagnosis of UTI, especially in nonverbal children.
- Treatment of the acute infection should be tailored to the child’s age, comorbidities, and clinical condition, as well as local antibiotic resistance patterns and culture results.
- Surgical intervention is undertaken when conservative management is unlikely to prevent further UTIs and/or protect the kidneys.
- Patients with recurrent febrile infections, VUR, and/or kidney scarring should be followed carefully for development of renal disease.

ICD9
599 Other and unspecified Escherichia coli [E. coli]
771.82 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn

ICD10
B96.20 Urinary tract infection as the cause of disease classed elsewhere
N90.9 Urinary tract infection, site not specified
P39.3 Nephrolithic urinary tract infection

ADDITIONAL READING

See Also (Topic, Algorithm, Media)
- Urinary Tract Infection (UTI), Complicated, Pediatric
- Urinary Tract Infection, Pediatric Algorithm
- Vesicoureteral Reflux, Pediatric

Codes
ICD-9: N39.0 Urinary tract infection, site not specified
771.82 Urinary tract infection of newborn
599.0 Urinary tract infection, site not specified

ICD-10: B96.20 Urinary tract infection as the cause of disease classed elsewhere
N90.9 Urinary tract infection, site not specified
P39.3 Nephrolithic urinary tract infection

Clinical/Surgical Pearls
- A high index of suspicion is often required for an accurate diagnosis of UTI, especially in nonverbal children.
- Treatment of the acute infection should be tailored to the child’s age, comorbidities, and clinical condition, as well as local antibiotic resistance patterns and culture results.
- Surgical intervention is undertaken when conservative management is unlikely to prevent further UTIs and/or protect the kidneys.
- Patients with recurrent febrile infections, VUR, and/or kidney scarring should be followed carefully for development of renal disease.
UROLITHIASIS, ADULT, GENERAL
Margaret S. Pearle, MD, PhD, FACS
Jodi A. Antonelli, MD

BASICS
DESCRIPTION
• Calculus that occurs in the urinary tract
• May be asymptomatic but can also be associated with mild to severe symptoms

EPIDEMIOLOGY
RISK FACTORS
Incidence
• More common in Caucasians than in Hispanics, Asians, or African Americans
• More common in men, increasing in women
Prevalence
• Prevalence in US adults is 8.8% (10.6% for men, 7.1% for women) (1)
• Prevalence gradient increases from North to South and West to East

PATHOPHYSIOLOGY
• Hyperoxaluria—Urine oxalate
• Hypercalciuria—urine Ca
• Calcium (Ca) stones—occur in settings of
• Most common stone—calcium oxalate (60%)
• Comorbidities: chronic diarrheal states, GI surgery, gout, diabetes, recurrent UTIs hyperparathyroidism, cystinuria, type I renal tubular acidosis, sarcoidosis
• Anatomic anomalies: Ureterointestinal junction obstruction, horseshoe kidney, caliceal diverticula, medullary sponge kidney

GENETICS
• Multiple genetic polymorphisms may contribute to calcium stone formation
• Nephritic disorders: Primary hyperoxaluria, cystinuria, Lesch–Nyhan syndrome, xanthinuria, type I renal tubular acidosis

PATHOPHYSIOLOGY
• Most common stone—calcium oxalate (60%)
• Calcium (Ca) stones—occur in settings of hypercalciuria, hyperoxaluria, hypocitraturia, hyperuricosuria
• Hypercalciuria—urine Ca > 200 mg/d
• Absorptive hypercalciuria—Increased intestinal absorption of Ca
• Renal hypercalciuria—Impaired renal reabsorption of Ca
• Nephrocalcinosis—Primary hyperparathyroidism, renal cystic disease
• Hyperoxaluria—Urine oxalate > 40 mg/d
• Primary hyperoxaluria—Excess endogenous oxalate production
• Enteral hyperoxaluria—Increased intestinal absorption of oxalate
• Dietary hyperoxaluria—Overindulgence in oxalate-rich foods, Ca restriction, excess vitamin C supplementation, reduced Oxalobacter formingens (oxalate-degrading intestinal flora)
• Hyperuricosuria—Uric acid (UA) > 600 mg/dl
• Causes: excess animal protein intake, gout, myeloproliferative disorders
• Urate pH < 5.5—Uric acid or calcium stones
• Urate pH > 5.5—Cystine stones
• Hypocitraturia—Urine citrate < 120 mg/dl
• Low urine citrate occurs in states of acidosis—Renal tubular acidosis, chronic diarrhea
• Uric acid stones—Rudolphstein
• Congenital causes—Disorders of renal tubular urine transport, disorders of UA metabolism
• Acquired causes—Obesity, high animal protein intake, volume depletion
• Cystine stones
• Cystinuria—Inherited disorder of impaired renal absorption of cystine
• Infection stones—Composed primarily of meprotein, ammnonium, and phosphate
• Alkaline urine produced by unass-splitting bacteria—Proteus (most common), Enterobacter, Pseudomonas, Staphylococcus
• Miscellaneous stones
• Xanthine—Rudolphstein, inherited disorder of the enzyme (ADH) that catalyzes xanthine to UA, another cause—high-dose Allopurinol use
• Ammonium acid urate—Associated with laxative abuse, inflammatory bowel disease (IBD), hyperlipidemias
• Cystine—Typically radiolucent, associated with infection, may contain protein
• Medullary sponge kidney

ASSOCIATED CONDITIONS
• Chronic diarrheal states, GI surgery, gastric bypass, small bowel resection
• Hyperparathyroidism
• Gastric ulcers
• Pancreatic pseudocysts
• Gallstones
• Cystinuria
• Type I renal tubular acidosis
• Medullary sponge kidney

DIAGNOSIS
HISTORY
• Can be asymptomatic
• Personal/family history of kidney stones
• Gross hematuria
• Pain—Frank, abdomen, ipsilateral groin—Renal colic—Pain in flank when stones occur in ureters
• Acute colics may suggest obstruction
• Nausea/vomiting—may suggest obstruction

PHYSICAL EXAM
• Can be unremarkable
• Elevate heart rate and blood pressure—pain
• Rectal, uterine, rectovaginal, or sigmoid tenderness
• Costovertebral angle tenderness

DIAGNOSTICS TESTS & INTERPRETATION
Lab
• Urinalysis—Microhematuria, pyuria
• Crystalluria—Hexagonal (cystine), coffin lid (MAP), dumbbell (Ca oxalate monohydrate)
• Leukocyturia/felourea—Inflammation and/or infection
• Elevated serum osteocalcin—Bilateral obstruction or solitary kidney

Imaging
• Non-contrast CT of abdomen and pelvis—Gold standard to identify urinary stones
• Low-dose protocol limits radiation exposure
• Provides additional anatomic information: Hydronephrosis, kidney stones, and other visera
• Plain radiography: Not as sensitive or specific as CT for stones, useful for follow-up
• Ultrasound—Often difficult to visualize adult urothelium, first-line for pregnant women, consider transvaginal ultrasound for pregnant women
• Intravenous pyelography (IVP)—Arterial anatomy of collecting system, renal function, obstruction; limited availability, must give IV contrast; CT urography generally replaces this
• MRI—Poor for stones of all types; some value in patients with renal transplant

DIFFERENTIAL DIAGNOSIS
• Any of the following causes may be confused with pain related to urolithiasis:
  • Vascular: Abdominal aortic aneurysm, mesenteric ischemia
  • Gastrointestinal: Appendicitis, bowel obstruction, choledocholithiasis, colic, constipation, diverticulitis/diverticulosis, pancreatitis, peptic ulcer
  • Gynecologic: Uterine fibroids, ovarian torsion/rupture
  • Musculoskeletal—Back pain
• Urolithiasis—Pyelonephritis, urinary tract infection, sloughed renal papilla, ureterointestinal junction obstruction

Stone analysis—Ca oxalate monohydrate or dihydrate, Ca phosphate, uric acid, cystine, struvite, mixed

Differential diagnosis
• Any of the following causes may be confused with pain related to urolithiasis:
  • Vascular: Abdominal aortic aneurysm, mesenteric ischemia
  • Gastrointestinal: Appendicitis, bowel obstruction, choledocholithiasis, colic, constipation, diverticulitis/diverticulosis, pancreatitis, peptic ulcer
  • Gynecologic: Uterine fibroids, ovarian torsion/rupture
  • Musculoskeletal—Back pain
• Urolithiasis—Pyelonephritis, urinary tract infection, sloughed renal papilla, ureterointestinal junction obstruction

Stone analysis—Ca oxalate monohydrate or dihydrate, Ca phosphate, uric acid, cystine, struvite, mixed
TREATMENT

GENERAL MEASURES

ALERT

- Fever, leukocytosis/akoncentration, tachycardia, hypotension, tachypnea, bacteriuria, and/or pyuria with upper tract stone is life-threatening; treat with renal decompression (ureteral stent or nephrostomy tube).
- \*Conservative therapy:
  - Hydration, analgesia, medical expulsive therapy (best evidence for alpha-blockers)
- \*Medical expulsive therapy
  - \% success with conservative measures:
    - 80%—Stone 3–3 mm
    - 50%—Stone 4–5 mm
    - 20%—Stone 6–8 mm
  - Direct instructions to return for fevers, worsening pain, unable to tolerate oral fluids
- \*Relative indications for intervention:
  - Large stone burden—Staghorn or partial staghorn
  - Large or pelvic stone
  - Stone location—Renal pelvis, ureter
  - Concern for infection; severe pain
  - Unable to tolerate oral fluids
  - Renal deterioration, solitary kidney
  - Repeated presentations to emergency room

MEDICATION

First Line

- Analgesics—anti-inflammatory (ibuprofen, ketorolac), acetaminophen, narcotic
- Antibiotics
- \*Antioxidants
- \*Analgesics
- \*Antibiotics
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

Second Line

\*Antimetics if colic is associated with nausea

SURGERY/OFFICE PROCEDURES

- \*Conservative therapy
- \*Medical expulsive therapy
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Note

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

ADDITIONAL TREATMENT

Radiation Therapy

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

COMPLEMENTARY & ALTERNATIVE THERAPIES

GENERAL TREATMENT

- Diet
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Note

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

Patient Monitoring

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

PROGNOSIS

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Note

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

ONGOING CARE

- Diet
- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

ADDITIONAL READING

- See Also (Topic, Algorithm, Media)
  - \*Antioxidants
  - \*Analgesics
  - \*Antibiotics
  - \*Antioxidants
  - \*Analgesics
  - \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

URINOLOGY

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

CODES

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

CLINICAL/SURGICAL PEARLS

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

REFERENCES


ADDITIONAL READING

- See Also (Topic, Algorithm, Media)
  - \*Antioxidants
  - \*Analgesics
  - \*Antibiotics
  - \*Antioxidants
  - \*Analgesics
  - \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

URINOLOGY

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

CODES

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

CLINICAL/SURGICAL PEARLS

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

URINOLOGY

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

cli010

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

URINOLOGY

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Alert

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Warning

- \*Antioxidants
- \*Analgesics
- \*Antibiotics

\*Normal

601
Hypercalciuria may be heterogeneous.

### Pathophysiology

#### Incidence

- **US annual stone incidence:** 164,100
- **Male:** 3:1–2:1
- **Age of peak incidence:** 20–40 yr
- **1 in 10 men, 1 in 20 women lifetime risk**

#### Stone Incidence by Composition

- Calcium oxalate: 30–56%; mixed Ca oxalate and Ca phosphate: 11–31%.

#### Prevalence

- **10–15%** US prevalence of stones
- **Lifetime prevalence of kidney stone disease is estimated at 1–15%, with the probability of having a stone varying according to age, gender, race, and geographic location.**

#### Risk Factors

- **See also Section II: “Urolithiasis, Risk Factors.”**
- **Intrinsic:** Polygenic defect; hypercalciuria inherited as autosomal dominant trait; white males; other ethnicities (IBD, etc.), elevated PTH
- **Extrinsic:** UPI obstruction, horseshoe kidneys
- **Environmental:** Fat malabsorption causes Ca to complex with bile acids and form Ca soap, which decreases free Ca absorption.

#### Baseline Evaluation

- A comprehensive metabolic evaluation (with Ca and Na restriction) prior to fast and load Ca studies; renal hypercalciuria by reducing the suppressive effect of absorbed Ca on parathyroid stimulation

#### Other Causes of Calcium Oxalate Stones

- **Hyperoxaluria:**
  - **Primary hyperoxaluria type I:**
    - Autosomal recessive, defect of AGT
    - 200 mg/24 hr
  - **Primary hyperoxaluria type II:**
    - Autosomal dominant, defect of AGT
    - 45 mg/24 hr

#### Associated Conditions

- **Primary hyperparathyroidism:**
  - Elevated HCT, medullary sponge kidney, UTIs

#### General Prevention

- See “General Measures” below

### Diagnosis

#### History

- **“Flank Pain” and “Urolithiasis, General.”**
- **Review stone history, family history, and the intrinsic and extrinsic risk factors of a patient’s stone.”

#### Physical Exam

- See “Flank Pain” and “Urolithiasis, General.”

### Diagnostic Tests & Interpretation

- **Lab (1):**
  - **Abnormal protocol for low-risk single-stone formers:**
    - Urinary calcium, creatinine, urinary oxalate, citrate, uric acid, sulfate
    - 24-hr urine analysis (Ca, oxalate, citrate, Na, phosphate, magnesium, pH, uric acid, sulfate)

### Urinary Calcium, Oxalate/Phosphate

**John J. Pahira, MD**
GENERAL MEASURES

Imaging

- CT: Most sensitive
- US, KUB, Excretory Urography (EU)
- MRI not useful for calcifications/surgical calculus

Do not use for stone analysis.

Diagnostic Procedures/Surgery

- In deciding which stone formers require a metabolic evaluation, consider the following:
  - 80–90% have predisposing urinary abnormality or underlying disease identified.
  - Treatment programs to be maintained for life.
  - 50–60% patients pass only 1 stone/lifetime.
  - Involve your patient in the decision to perform a workup, explain risk and benefits.

- Criteria for metabolic evaluation:
  - Anatomic abnormality, family history of stones, history of great or major stone complications, history of metabolic stone (uric acid or cystine), infestation stone (intravesical, pure Ca phosphate stone, RTA), or elevated PTH
  - Metabolically active (x-ray evidence of new stone or stone growth in the past year or the documented passage of a new stone or gravel)
  - Osteoporosis or pathologic skeletal fracture
  - Recurrent stone formation
  - Renal insufficiency
  - Significant number of risk factors
  - Tertiary therapy: age at onset <20 yr

Pathologic Findings

- Stone analysis: Varying percent composition from Ca oxalate and/or Ca phosphate
- Crystals: Ca oxalate monohydrate (dihydrate/amorphous), Ca oxalate dihydrate (envelope/bipyramidal), Ca phosphate-apatite (dumbbell/hourglass), Ca oxalate dehydrate

DIFFERENTIAL DIAGNOSIS

- Hypercalciuria: Primary elevated PTH, RTA, vitamin D excess, immobilization, sarcoidosis, metabolic maladies, milk-alkali syndrome, hyperparathyroidism, myeloma, adrenal insufficiency, fetus/infantile administration

- See: "Section I Flank Pain: Upper Urinary Tract."
- See: "Section I Tissue.

TREATMENT

GENERAL MEASURES

- Treat active UTI.
- Medical expulsion therapy for a symptomatic infection stone (struvite), pure Ca phosphate stone, or stone growth in the past year or the documented passage of a new stone or gravel

TREATMENT

MEDICATION (3)

First Line

- Absorptive hypercalciuria type I: Thiazide (not a selective therapy for AIH as it does not decrease intestinal Ca; initial long-term effect:– Hydralazine/Indapamide 25–50 mg b.i.d.
  - Indapamide C. r. 20 (20–40 mg b.i.d.):– Alternates: Indapamide 1.25–2.5 mg/d or furosemide (25–50 mg/d)
  - Restrict dietary oxalate, Na to 2000 mg/d
  - Magnesium supplementation
  - Art type II: Moderate Ca restriction (600 mg/d or 1–2 servings dairy/d); Na restriction; thiazide if not effective; K citrate supplementation
  - Art type III: orthophosphate (Neutra-Phos-K)

- Renal hypercalciuria: Thiazide to increase tubular Ca reabsorption; hydralazine/Indapamide 25–50 mg b.i.d.
  - Indapamide C. r. (20–40 mg b.i.d.)
  - K citrate supplementation (Polykala K syrup 15–30 ml); (Polykala K crystal: 1 packet b.i.d.; Urocit K 10–20 mg b.i.d.); Na restriction (2 g Na diet); be sure urinary Na < 100 mg/d

- Hypouricosuric Ca nephrolithiasis: Increase fluid intake; reduce dietary purine (eg, red meat); urinary alkalization (pH 6.5–7.0); K citrate; reduce endogenous uric acid production (allopurinol 300 mg/d); if serum uric acid > 8 mg/dL; or if uncorrectable hyperuricosuria

- Hyperparathyroidism: Ca nephrolithiasis type K: evidence of renal hypercalciuria, or stone (RTA or elevated PTH)

- See "Section I Flank Pain: Upper Urinary Tract."

- See: "Section I Tissue."

- See: "Section I General."

TREATMENT

ADDITIONAL TREATMENTS

- Additional Therapies
  - Hypercalciuria
  - Complementary & Alternative Therapies

FOLLOW-UP

- Patient Monitoring
- Provide patients with appropriate written dietary handouts
- Patients with recurrent stones on medical therapy require periodic monitoring:
  - Urine analysis, urine pH
  - Serum chemistry if warranted
  - 24-hr urine collection
  - KUB, US, or CT

Patient Resources

Urology Care Foundation: http://www.urologyhealth.org

ADDITIONAL READING


See Also (Topic, Algorithm, Media)

Urolithiasis, Adult, General

Urolithiasis, Calcium Oxalate/Phosphate Image

REFERENCES


CODES

- ICD9
  - 592.9 Urinary calculus, unspecified
  - 592.0 Calculus of kidney
  - 592.3 Urinary calculus, unspecified

- ICD10
  - 592.34 Unspecified disorder of calcium metabolism
  - 592.0 Calcium of kidney
  - 592.9 Urinary calculus, unspecified

- ICD10-CM
  - E83.25 Hyperparathyroidism
  - N20.0 Calcium of kidney
  - N20.9 Urinary calculus, unspecified

- ICD11
  - G92.52 Calcium metabolism

CLINICAL/SURGICAL PEARLS

- A family history of nephrolithiasis is important risk when deciding on a metabolic work-up.
- A slight increased PTH is best indication of renal leak hypercalciuria with normal ATP and persistent hypercalciuria on a restricted diet.
- When starting on a thiazide for hypercalciuria, it is important to check serum calcium in 2–4 wk to rule out an occult hyperparathyroidism.
- Accurate 24 hr urine uric acid cannot be done until the patient is placed on urinary alkalization or acidic urine can cause uric acid to precipitate out of solution causing underestimation.

- Ongoing care
  - Untreated recurrence for Ca oxalate stones: 10% at 1 yr, 35% at 5 yr, 50% at 10 yr.
  - Medical therapy: Decrease new stone formation; elimination >90% and >90% reduction in stone recurrence.
  - Alternates:
    - Ongoing care: see above.
  - Treatment program is to be maintained for life.
  - 80–90% have predisposing urinary abnormality or underlying disease identified.

- Ongoing care
  - Untreated recurrence for Ca oxalate stones: 10% at 1 yr, 35% at 5 yr, 50% at 10 yr.
  - Medical therapy: Decrease new stone formation; elimination >90% and >90% reduction in stone recurrence.
  - Alternates:
    - Ongoing care: see above.
UROLITHIASIS, CYSTINE, AND CYSTINURIA (HYPERCYSTINURIA)
Anthony J. Tracey, MD, MPH
Raju Thomas, MD, MHA, FACS

DESCRIPTION
Cystinuria is an autosomal recessive error of transepithelial transport involving the intestine and the kidneys. Cystinuria is the clinical result of crystallization and stone formation in the urinary tract.

- Excessive urinary excretion secondary to reduced tubular absorption of cystine disulfate (1).
- There is a transport defect of dibasic amino acids including cystine, ornithine, lysine, and arginine (COUAs). (See also Section I: “Urolithiasis.”) (1)
- Cystinuria form when concentrations rise above the saturation point (roughly 250 mg cystine per liter of urine).
- Cystinuria accounts for about 1–2% of adult and 6–8% of pediatric nephrolithiasis (1).
- Historical, three types of cystinuria have been recognized in humans—Type I, Type II, and Type III—on the basis of levels of urinary cystine in obligate heterozygotes; however, this classification correlates poorly with molecular findings; newer genetic classification is available (see below).
- Cystinuria is distinct from cystinosis.

Epidemiology
Incidence
- For patients with cystinuria:
  - An average of one surgical procedure every 3 yr.
  - A mean number of stone episodes of 0.42 and 0.21 per year occurring in men and women, respectively.

Prevalence
- Homozygous: 1 in 15,000 in the United States
- Heterozygous: 1 in 20–200 in the United States
- Libyan Jews: 1 in 2,500 (3)
- Cystinuria is more common in Caucasians.
- Cystine stones are common in the second or third decade of life.
- 20% of these patients develop calculi in childhood.

Risk factors
- Family history (see genetics)

Genetics
- Identification of genetic mutations that cause cystinuria have led to a new classification system based on genotype that is more accurate than the prior phenotypic one.
- Mutations in 2 genes, SLC3A1 and SLC7A9 (3)

RISK FACTORS
- Prevalence
- Incidence
- Description

PATHOPHYSIOLOGY
- Cystine is homodimer of the amino acid cystine. Cystinurics have impaired renal cystine transport, with increased proximal tubular reabsorption of filtered cystine resulting in increased urinary cystine excretion with the consequence of cystine urolithiasis.
- Clinical consequences present only when crystals precipitate (low cystine solubility at normal urinary pH values).
- Cystine stone formers have slightly lower creatinine clearance than other types of stone formers.

ASSOCIATED CONDITIONS
- Deleterious renal acidification
  - Hypercalciuria 19%
  - Hypokaliemia 22%
  - Hypophosphatemia 44%
  - Urolithiasis

GENERAL PREVENTION
- Create high urine volume (<1.3 L/m²/d) to reduce the urinary concentration of cystine to below its solubility limit (200–300 mg/L).
- Alkalize urine to pH of 7.5 ± 0.4 mg/L (glutamic acid, citrate, or sodium bicarbonate) in 3–4 divided doses.
- Avoid alkali (but do not restrict carbonates).
- Restrict sodium and protein.

RISK FACTORS
- Family history (see genetics)
- Prevalence
- Incidence
- Description

DIAGNOSIS
- History
- CT scan of abdomen without contrast
- Imaging
- Diagnostic procedures/Surgery

HISTORY
- Stones in childhood (3)
- Family history of stones (3)
- Presentation of a large branched calculi

PHYSICAL EXAM
- C/S tenderness may be present with acute stone disease.

DIAGNOSTIC TESTS & INTERPRETATION
- Lab
  - Urine is screened for cystine using the cyanide-nitroprusside test (positive = purple hue with cystine >75 mg/dL).
  - Cystine converts cystine to cysteine; this binds nitroprusside then binds resulting in a purple color usually in <10 min.
  - If positive, a 24-hr urine quantitative test is performed.
    - Normal cystine excretion is 30 mg (0.13 mmol/d).
    - Cystinuria >400 mg/dL (1.7 mmol/d) (1).
    - Heterozygous for cystinuria and with the Fanconi syndrome, excrete >250 mg/dL (1 mmol/d) and usually do not form stones.

IMAGING
- CT scan of abdomen without contrast
- Preferred imaging modality

- KUB may show stones with a fuzzy gray appearance (1).
- Stones are less radiopaque than calcium stones that usually well seen.

Physics and Imaging
- More economical than CT scan for monitoring the growth of renal calculi.
- Indicated for children and frequent stone formers to reduce radiation (2).

UROLOGIC FINDINGS
- Renal biopsys is not usually performed. However, renal pathology may include plugging of the ducts of Bellini with cystine crystals, tubular dilation, and focal fibrosis.

DIAGNOSTIC PROCEDURES/SURGERY
- KUB
- N/A
URINARY CALCULI, CYSTINE, AND CYSTINURIA (HYPERCYSTINURIA)

DIFFERENTIAL DIAGNOSIS

- Other forms of urolithiasis (calcium oxalate, uric acid, etc.)
- Any of the following may be confused with pain related to urolithiasis:
  - Vascular: Abdominal arterial aneurysm, mesenteric ischemia
  - Gastrointestinal: Appendix, bowel obstruction, cholecystitis/biliary colic, constipation, diverticulitis/diverticula, gastritis, pancreatitis, peptic ulcer
  - Gynecologic: Septic pregnancy, tubo-ovarian abscess, ovarian torsion/cyst rupture
  - Musculoskeletal: Back pain
  - Urologic: Pyelonephritis, urinary tract infection, sloughed renal papilla, ureterosigmoid junction obstruction

TREATMENT

GENERAL MEASURES

- For existing calculi treatment is similar to other stones based on clinical indication
- Extracorporeal shockwave lithotripsy has been discouraged for stones > 1 cm by some authors (2)
- Cystine stones are often not well fragmented by ESWL (extracorporeal shock wave lithotripsy)
- Multiple treatments are usually required
  - Algorithm for Patients with Renal cystine stones:
    - Percutaneous nephrolithotomy (PNL) for cystine renal calculi larger than 15 mm in diameter
    - Ureteroscopy effective for cystine ureteral stones and for select renal cystine calculi
    - Laparoscopic pyelolithotomy may also be possible for stones in favorable locations of the ureter or renal plexus.
    - ESWL monotherapy for cystine renal calculi 15 mm or smaller (High failure rate)

MEDICATION

First Line

See general prevention

Second Line

- Use chelating agents (bind cystine) only if the conservative methods do not work
- These inorganic cystine solubility in urine via formation of a more soluble mixed-disulfide bond
- These medications have potentially serious side effects and must be monitored
  - Mercaptopropionylglycine (Thiola, Tiopronin)
    - Most frequently used cystine-binding agent
    - Dosage start at 100 mg, orally two times per day, doses titrated to achieve urinary concentrations of cystine less than 250 mg/L urine.
    - Side effects: include asthma, GI distress, rash, joint aches, and mental status changes
  - Etoposide (Etopophrine)
    - Better tolerated than p-penicillamine
  - D-penicillamine (Cuprimine)
    - Binds with cystine to yield a disulfide more soluble than cystine
    - Typically start therapy at 250 mg per day and titrate to effect
    - Typical side effects: nephrotic syndrome, dermatitis, and pancreatitis.

- Captopril: Potential alternative
  - More favorable side effect profile: Fatigue, hypotension, and chronic cough
  - No long-term clinical trials describe the effectiveness of captopril in preventing recurrent cystine stone formation

SURGERY/OTHER PROCEDURES

See General Measures above

ADDITIONAL TREATMENT

Radiation Therapy

- Additional Therapies
  - Complementary & Alternative Therapies

ONGOING CARE

PROGNOSIS

- One study reported 1.22 stone episodes per year (2)
- The medical compliance of patients with cystinuria can be poor.
- A few patients are able to achieve and maintain targeted goals of medical intervention
  - 33% achieved and maintained therapeutic success, as defined by urine cystine concentration less than 300 mg/L.
  - 15% achieved and maintained therapeutic success but subsequently had failure at an average of 16 mo.
- The Renal Stone Consortium has developed a registry and will lead further efforts in managing cystinuria

COMPLICATIONS

- Studies report 1.22 stone episodes per year
- Chronic cystinuria—19%
- Renal impairment—Approximately 70% (2)
- Risk for nephrectomy—10–20%
- End stage renal failure—5%
- Hypertension—10%
- Mental illness and mental retardation (2)

FOLLOW-UP

Patient Monitoring

- Patients should have frequent clinical, radiologic, and laboratory surveillance
  - Patients should follow a diet low in protein and sodium chloride
  - Urinary pH level, and check first-morning urine for cystine crystals
- Regularly check renal function
  - CBC counts, WBC counts, and platelet counts should be monitored for patients on p-penicillamine and tiopronin (2)
- EUS and renal ultrasound should be the routine Surveillance:
  - Annually perform 24-hr urine testing and imaging for patients with stable disease (2)
  - Multidisciplinary approach early in disease
  - Nephrologists
  - Urologists
  - Radiation Therapy

ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Cystinosis
  - Metabolic Stone Evaluation (24-Hour Urine Studies)
  - Sodium Cyanide-Nitroprusside Test
  - Urinaryithiasis, Adult, General
  - Urinaryithiasis, Calcium Oxalate/Phosphate
  - Urinaryithiasis, Cystine and Cystinuria (Hypercystinuria)
  - Urology Care Foundation http://www.urologyhealth.org

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Cystinosis
  - Metabolic Stone Evaluation (24-Hour Urine Studies)
  - Sodium Cyanide-Nitroprusside Test
  - Urinaryithiasis, Adult, General
  - Urinaryithiasis, Calcium Oxalate/Phosphate
  - Urinaryithiasis, Cystine and Cystinuria (Hypercystinuria)
  - Urology Care Foundation http://www.urologyhealth.org

CODES

- ICD9 720.0 Disturbances of amino acid transport
  - 580.9 Urinary calculi, unspecified
- ICD10 E72.01 Cystinuria
  - N20.9 Urinary calculi, unspecified

CLINICAL/SURGICAL PEARLS

- Cystine stones are often not well fragmented by ESWL, and may be considered for cystine renal calculi > 15 mm.
- Consider PCNL for cystine renal calculi larger than 15 mm in diameter.
- Ureteroscopy effective for cystine ureteral stones and for select renal cystine calculi.
UROLITHIASIS, PEDIATRIC, GENERAL CONSIDERATIONS

Gregory E. Tassign, MD, MSc
Douglas A. Canning, MD, FACS

DESCRIPTION

Urolithiasis can be found anywhere in the urinary tract of a child.

Urolithiasis is much less common in children than adults.

Urolithiasis is an increasingly common disease of childhood.

The most common stones in children are calcium (calcium oxalate and calcium phosphate), uric acid, struvite and cystine.

EPIEMIOLOGY

Incidence

In adolescents, the incidence of nephrolithiasis has increased 6–10% per year over the last 20 yr (1,2).

White = African American

Male = Female

Increased incidence in the Southwest United States.

Prevalence

The prevalence is unclear.

RISK FACTORS

When a metabolic evaluation is performed, an abnormality can be identified in 40–50% of children.

Most common metabolic abnormalities are hypercalciuria and hypocitraturia.

PATHOPHYSIOLOGY

Stone formation involves nucleation and growth. Nucleation is the process by which a theoretical nucleus forms, which is then supersaturated with respect to a crystalline phase. Growth occurs when one crystal is able to catalyze the growth of another.

Metabolic evaluation

A metabolic evaluation is performed when a child presents with recurrent urolithiasis.

Phenotypic and genotypic abnormalities are divided into three categories:

1. Inherited abnormalities
2. Secondary metabolic abnormalities
3. Sporadic or idiopathic abnormalities

Inherited abnormalities are divided into the following categories:

A. Autosomal recessive
B. Autosomal dominant
C. X-linked

Special consideration is given to hyperoxaluria and cystinuria.

The most common metabolic abnormalities are hypercalciuria and hypocitraturia.

DIAGNOSTIC TESTS & INTERPRETATION

PHYSICAL EXAM

Lab

Acute Episode: Urinalysis

- Microscopic or microscopic hematuria is found in 85% of children with nephrolithiasis (3).

- Metabolic evaluation

- Following the resolution of the acute stone episode, obtain at least one 24-hr urine collection in children who are toilet trained.

- Analyze for calcium, oxalate, uric acid, sodium, chloride, creatinine levels, volume, pH, and cystine.

- It is essential to evaluate the results with respect to weight and creatinine level to accurately interpret the results.

- Hypercalciuria is defined by a urinary calcium excretion of greater than 4 mg/kg over 24 hr while ingesting a routine diet.

- Urine creatinine excretion (normal 15–25 mg/kg/d) is useful in assessing the adequacy of the urine collection.

- Urine calcium—creatinine ratio (Ca/Cr) from a spot urine sample should be obtained in children who have not been toilet-trained.

- Except for neonates, there is an inverse relationship between age and Ca/Cr.

- At approximately 5 years of age, Ca/Cr approaches 0.21, the upper limit of normal for adults (4).

Imaging

- Ultrasonography: Reliable when it identifies a kidney stone, but it has only moderate sensitivity specifically for stones in the mid-ureter.

- CT: Accurate but delivers ionizing radiation, concerns for increased cancer risk, particularly with exposure at young age.

A reasonable approach is to use US as the initial study. A non-contrast CT is indicated in children with persistent symptoms of nephrolithiasis and a non-diagnostic US.

UROLOGY, PEDIATRICS, GENERAL CONSIDERATIONS

DIAGNOSIS

HISTORY

- Patient: Prematurity, medications, dietary habits, fluid consumption, malignancies, previous iatrogenic disorder/surgery, hematuria

- Family: Cystinuria, primary hyperoxaluria, RTA, uric acid lithiasis

- Abdominal/flank pain ± nausea/vomiting

PHYSICAL EXAM

- Occasional abdominal or flank tenderness

- Growth charts may identify decreased growth patterns associated with certain childhood diseases associated with stones (cystinuria, distal RTA, hyperoxaluria, etc.)
MEDICATION

GENERAL MEASURES

- Indications for surgery: When the presence of an obstructing stone, plain radiography to exclude stones, acute kidney injury, and an obstructing stone in a solitary kidney.
- Evaluate all children for underlying metabolic disorder.
- Goal is to decrease stone-promoting risk factors (urinary calcium, sodium, oxalate, uric acid, and low urine volume), and increase protective factors (urine pH, citrate, magnesium).

Hydration:
- Water preferred; avoid caffeine, sodium, and sugary drinks (sports drinks).

Dietary modifications when applicable
- Goal is to decrease stone-promoting risk factors
- Evaluate all children for underlying metabolic disorder.
- Dietary modifications when applicable

TREATMENT

GENERAL MEASURES

- Indications for surgery: When the presence of an obstructing stone, plain radiography to exclude stones, acute kidney injury, and an obstructing stone in a solitary kidney.
- Evaluate all children for underlying metabolic disorder.
- Goal is to decrease stone-promoting risk factors (urinary calcium, sodium, oxalate, uric acid, and low urine volume), and increase protective factors (urine pH, citrate, magnesium).

Hydration:
- Water preferred; avoid caffeine, sodium, and sugary drinks (sports drinks).

Dietary modifications when applicable
- Goal is to decrease stone-promoting risk factors
- Evaluate all children for underlying metabolic disorder.
- Dietary modifications when applicable

MEDICATION

First Line
- Should a trial of spontaneous passage be indicated, appropriate oral analgesics are important (ie, narcotics).

Second Line
- Hyperuricosuria:
  - Allopurinol (decrease uric acid production): Adult 30–90 mEq/d; children 1–2 mg/kg/d.
- Hypocitraturia:
  - Potassium citrate: Adults 25–100 mg/d, children 1–2 mg/kg/d.
- Hypercalciuria:
  - Limit dietary sodium and milk.
- Uric acid stones:
  - Allopurinol (decrease uric acid production).

Cystinuria
- Create high urine volume (>1.5 L/m²).

Hyperoxaluria
- Limit sodium and oxalate-rich foods (eg, spinach, rhubarb, nuts, tea, bran, strawberries).

Hypomagnesemia
- Magnesium, diuretics.

SURGERY/OTHER PROCEDURES

- The optimal management based on the size, location, and presumptive stone composition, as well as the age, size, and health of the patient.

Complications
- Subcapsular hematoma: Self-limited
- Interstitial fibrosis: Insignificant unless multiple procedures
- Injury to surrounding organs:
- Ureteroscopy:
  - Rigid and flexible endoscopes permit access to almost all areas of the collecting system in nearly all children.
  - Pre-placement of stent is sometimes necessary to passively drain the ureter.

Acute calculous cholecystitis:
- Access sheaths (without pre-stenting) facilitate procedures requiring multiple endoscope passes.
- All forms of lithotripsy are safe; holmium laser most effective.
- Percutaneous nephrolithotomy (PCNL):
  - Appropriate for large intrarenal/pelvicalyceal ureteral stones.
  - Also failed primary procedures (SWL, ureteroscopy), and with associated anatomic abnormalities (congenital, acquired, etc).
  - Access at same time as or prior to surgery:
    - Smaller size as small as possible to allow for successful procedure and to accommodate flow of irrigant around scope.
    - Renal access: best access to stone burden.
    - Multiple tracts are safe.
    - Ureteroscopy: Always when possible to allow for successful procedure and to accommodate flow of irrigant around scope.

Ongoing care

- Adequate hydration to dilute urine.

Follow-up

- Patient monitoring: Repeat 24-h urine 3–4 mo after initial surgery.
- Assess periodically for stone growth or new or recurrent disease with US.

Patient resources


References


See also (Topic, Algorithm, Media)

- Cystinuria
- Hyperuricosuria (Absorptive, Renal, and Resorptive)
- Urolithiasis, Adult, General
- Urolithiasis, Cystine and Cystinuria
- Urolithiasis, Pediatric, General Considerations

Codes

- ICD9: 592.0 Calculus of kidney
- N20.9 Urinary calculus, unspecified

-U-
UROLITHIASIS, RENAL

Aaron G. Boonjindasup, MD, MPH
Raju Thomais, MD, MHA, FACS

BASICS

DESCRIPTION
- Renal urolithiasis refers to kidney stones within the kidney itself (parenchyma, calyces or renal pelvis). The majority of stones in the urinary tract have their origin in the kidney.
- Renal urolithiasis is a significant cause of patient renal morbidity and a major source of medical costs in the United States.
- Calcium oxalate stones are most common; also uric acid, struvite (magnesium ammonium phosphate), cystine, carbonate apatite, etc.

Epidemiology
Incidence
- Estimated to be 10–15% in the United States
- Males are affected 2–3 times more than females
- Peak incidence: 4th–6th decades
- More common in Southeast, Southwest, and Northwest United States
- Increasing incidence with increased obesity
- Accounts for 7–10% of every 1000 hospital visits

Prevalence
- Highest prevalence in Caucasians

Risk Factors
- Calcium stone formation
  - Dietary excess
  - Hyperparathyroidism
  - Inappropriate loss of calcium in urine through malabsorption
- Uric acid stone formation
  - Purine excessive intake
  - Gout
  - Myeloproliferative disorders
- Struvite stones
  - Chronic dehydration
  - Escherichia coli syndrome
  - Ingestion of urolithic drugs
- Cystine stones
  - Inherited disorder of renal tubular reabsorption of cystine (See Urolithiasis, Cystine)

Genetics
- In general, urolithiasis is associated with polygenic defect and partial penetrance
- Cystinuria: Homozygous recessive
- Renal tubular acidosis (RTA): Inherited

Pathophysiology
- Supersaturation: Urine oversaturated with certain types of crystal, which then is precipitated out of solution.
- Saturation level is variably pH dependent based on crystal type
- Inhibitor deficiency: Inhibitors may limit crystal growth and aggregation
- Urinary citrate and magnesium are inhibitors
- Non-infection stones: Calcium oxalate, calcium phosphate (brushite, carbonate apatite), uric acid
- Infection stones: Magnesium ammonium phosphate (struvite), carbonate apatite, ammonium urate
- Genetic defects: Cystine, xanthine, 2,8-dihydroxyadenine (DHA)
- Drug stones: Indinavir, trimethoprim, others

Associated Conditions
- Congenital malformations or anatomical variations of kidney, collecting system, ureter, or bladder may predispose patient to urolithiasis due to stasis and/or impaired urine drainage
- Cystinosis
- Dehydration
- Gout
- Inflammatory bowel disease
- Intravenous pyelography
- Intestinal bypass
- Medullary sponge kidney
- Renal tubular acidosis

General Prevention
- Decreased sodium intake
- Renal tubular acidosis
- Stones may form
- Decreased calcium intake
- Stones may form
- Increased urinary citrate
- Patients with RTA
- Increased magnesium intake
- Patients with RTA
- Decreased protein intake (purine) if at-risk
- Decreased oxalate consumption
- Ingestion of uricosuric drugs
- Patients with gout
- Urine oversaturated with certain types of crystal, which then is precipitated out of solution.
- Saturation level is variably pH dependent based on crystal type
- Inhibitor deficiency: Inhibitors may limit crystal growth and aggregation
- Urinary citrate and magnesium are inhibitors
- Non-infection stones: Calcium oxalate, calcium phosphate (brushite, carbonate apatite), uric acid
- Infection stones: Magnesium ammonium phosphate (struvite), carbonate apatite, ammonium urate
- Genetic defects: Cystine, xanthine, 2,8-dihydroxyadenine (DHA)
- Drug stones: Indinavir, trimethoprim, others

Diagnostic Tests & Interpretation
Lab
- Urinalysis
  - Microscopic hematuria
  - Urine culture (sterile, complete obstruction)
  - Crystaluria may provide important information regarding the type of calculus
- Pyuria
- May suggest concomitant UTI
- Urine glucose and culture
- Authors opinion: Catheterized urine specimen
- Should be collected for urolithiasis, gram- and, culture in all female patients under consideration for surgical intervention
- CBC
  - Sedimentology: Suggests secondary infection
  - Basic metabolic profile
  - Elevated creatinine
  - May be present if bilateral obstruction present
  - Calcium level
  - Glucose: Impaired glycemic control in patients with diabetes especially in setting of infection

Imaging
- Non-contrast low-dose helical computed tomography (CT)
  - KUB study
  - 1st-line test with acute renal colic
  - Can determine degree of hydronephrosis, size, and location of stones
- Intravenous pyelography (IVP)
  - Requires IV contrast
  - Delayed x-rays needed if high-grade obstruction present
  - Some stones radiolucent—not visible on IVP
  - Can provide some assessment of renal function
- Ultrasound
  - Non-invasive, 1st-line evaluation for in patients at risk for X-ray exposure
  - Children, pregnant females
  - Operator-dependent
  - Difficult to visualize ureter in adult
  - Residue index (RI) >0.7 suggestive of obstruction in the setting of acute obstruction
  - Clinical signs—Presence does not rule out partial obstruction

Diagnostic Procedures/Surgery
- Retrograde pyelography
  - Invasive
  - Can assist computed surgical management
- Endoscopic procedures
  - Hydropropulsion
  - Endourology
  - Stone removal

Pathologic Findings
- Hemorrhagic
- Stone deposits and anatomic location of obstruction
- Perinephric stranding on CT

Differential Diagnosis
- Abdominal aortic aneurysm
- Appendicitis
- Bowel obstruction
- Gastritis, pancreatitis, peptic ulcer
- Mesenteric ischemia
- Musculoskeletal back pain
- Pyelonephritis, urinary tract infection
- Cholangitis or biliary colic
- UPI obstruction
- Strangled renal papilla

608
Urolithiasis, Urolithiasis, Urolithiasis

**TREATMENT**

**ALERT**

The presence of pain, fever, leukocytosis, or bacteriuria suggests the possibility of a urinary infection and the potential for an infected obstructed ureter or urethra. Such a condition is potentially life-threatening and should be treated as a surgical emergency.

**GENERAL MEASURES**

- Hydration and adequate pain control
- Patients with likelihood of spontaneously passing a stone (>4–5 mm in size) in the absence of indications for surgical intervention may be sent home with analgesics and a trial of medical expulsion therapy (MET), hydration, analgesics, symptomatic relief
  - Should be instructed to return if pain worsens, or severe vomiting or fever
  - Likelihood of spontaneous stone passage is related to location and size of stone
    - Stones 2–3 mm: 90% probability of passing
    - Stones 4–5 mm: 50% probability of passing
    - Stones 6–8 mm: 20% probability of passing
    - Stones >1 cm: unlikely to pass spontaneously
  - Controversy exists regarding maximum period of observation for partially obstructing stone without development of significant irreversable renal function; generally, within 4–6 wk.
  - Indications for intervention:
    - Fever and/or infection
    - Intense pain
    - Unable to tolerate oral fluid and at risk for dehydration
    - Progressive renal deterioration; obstruction of solitary functioning kidney
  - All urinary tract infections should be treated with culture-sensitive antibiotics prior to surgical treatment

**MEDICATION**

**First Line (L1)**

- Patients with evidence of acute UUT should be treated with broad-spectrum antibiotics (eg, ampicillin and gentamicin, 3rd generation cephalosporin)
- Antimicrobial for acute colic is associated with nausea and vomiting.

**Medical expulsive therapy (MET)**

- α-Blockers (ie, tamsulosin, tamsulosin) or calcium channel blockers (eg, nifedipine) can relax muscle spasm of the ureter and allow stone to pass
- Urine output and stone passage should be monitored with 24-hr urine collection
- Uric acid stones and cystine stones can be dissolved with medical therapy; calcium stones and struvite stones cannot be dissolved
- Uric acid stones: Alkaline urine with potassium citrate or bicarbonate, to maintain urinary pH between 6.5 and 7.0.
- Urine pH >7.5 can precipitate calcium phosphate with resulting stone formation.
- May dissolve up to 1 cm per month

**Second Line (L2)**

- Cystine stones: see Urolithiasis, Cystine

**SURGERY/OTHER PROCEDURES (3)**

- Primary goal is to achieve maximal stone clearance with minimal morbidity.
- Patients with active uropathic obstructed kidney is drained by placement of ureteral stent or percutaneous nephrostomy tube
- Preoperative urine culture should document no infection before stone removal
- Calculi in kidney: Ureteroscopy vs. ESWL with or without stent placement (>1 cm)
  - >2 cm: Percutaneous nephrolithotomy or if >1.5 cm in lower pole
  - Shock-wave lithotripsy (ESWL)
    - Irregular calculus <2 cm
    - Relative contraindications
      - Stone >2 cm
      - Within dependent or obstructed portions of collecting system
      - Body habitus/ankylosis that inhibits imaging and targeting of the stone
      - Lower pole stone
      - Unconnected calyceal or recent anticoagulant use
    - Ureteroscopy
      - Used for lower pole stones or stones resistant to ESWL
    - Effective for treatment of cystine, calcium oxalate monohydrate, and brushite stones
    - Percutaneous nephrolithotomy (PCNL)
      - Stones >2 cm; no bleeding diathesis or obesity
      - Steephorn calculus
    - Laparoscopic and robotic stone surgery for large non-branching calculi
- "Sandwich technique"
  - SWL in combination with other modality

**ADDITIONAL TREATMENT**

**Radiation Therapy**

- Urolithiasis, Radiation Therapy

**ADDITIVE THERAPY**

- Complementary & Alternative Therapies

**ONGOING CARE**

**PROGNOSIS**

- The most important measure to avoid future stone episodes is increased fluid intake.
- Once patient has initial incident, 50% chance that in 5 yr will have recurrent calculus.
- Produce >2 L of urine/day
- 24-hr urine collection for metabolic analysis
- Stone fragment chemical analysis should be performed when possible
- Metabolic worksup after 2nd episode

**COMPLICATIONS**

- Pyelonephritis
- Renal abscess formation
- Surgery carries standard risks of bleeding, infection, urinary stricture.
- Fracture with nephrostomy access

**FOLLOW-UP**

**Patient Monitoring**

- Oral hydration to make 2–2.5 L of urine/day
- Diet low in protein and sodium intake
- Dietary modification and medical intervention tailored to underlying metabolic abnormality can prevent recurrence of stones in 75% patients and significantly reduce new stone formation in up to 98% of patients
- Restriction of oxalate-rich foods such as chocolate, nuts, soybeans, rhubarb, spinach, sweet potatoes, beets.
- Maintenance of adequate intake of dietary calcium

**Patient Resources**


**REFERENCES**


**ADDITIONAL READING**

- See Also (Topic, Algorithm, Media)
  - Metabolic Stone Evaluation (24-Hour Urine Studies)
  - Urolithiasis, Adult, General
  - Urolithiasis, Calcium Oxalate/Phosphate
  - Urolithiasis, Cystine and Cystinuria (Hyperoxaluria)
  - Urolithiasis Image ID
  - Urolithiasis, Pediatric, General
  - Urolithiasis, Staghorn
  - Urolithiasis, Urinary Calculi Algorithm
  - Urolithiasis, Urine Acid

**CODES**

- ICD9
  - 274.11 Uric acid nephrolithiasis
  - 275.49 Other disorders of calcium metabolism
  - 592.0 Calculus of kidney

- ICD10
  - E79.8 Other disorders of purine and pyrimidine metabolism
  - E83.52 Hypercalciuria
  - N20.0 Calculus of kidney

**UROLITHIASIS, RENAL**

**Follow-Up**

- Diet low in protein and sodium intake
- Dietary modification and medical intervention tailored to underlying metabolic abnormality can prevent recurrence of stones in 75% patients and significantly reduce new stone formation in up to 98% of patients
- Restriction of oxalate-rich foods such as chocolate, nuts, soybeans, rhubarb, spinach, sweet potatoes, beets.
- Maintenance of adequate intake of dietary calcium

**Patient Resources**


**REFERENCES**


**ADDITIONAL READING**

- See Also (Topic, Algorithm, Media)
  - Metabolic Stone Evaluation (24-Hour Urine Studies)
  - Urolithiasis, Adult, General
  - Urolithiasis, Calcium Oxalate/Phosphate
  - Urolithiasis, Cystine and Cystinuria (Hyperoxaluria)
  - Urolithiasis Image ID
  - Urolithiasis, Pediatric, General
  - Urolithiasis, Staghorn
  - Urolithiasis, Urinary Calculi Algorithm
  - Urolithiasis, Urine Acid

**CODES**

- ICD9
  - 274.11 Uric acid nephrolithiasis
  - 275.49 Other disorders of calcium metabolism
  - 592.0 Calculus of kidney

- ICD10
  - E79.8 Other disorders of purine and pyrimidine metabolism
  - E83.52 Hypercalciuria
  - N20.0 Calculus of kidney

**CLINICAL/SURGICAL PEARLS**

- Renal stones >1 cm are unlikely to pass spontaneously.
UROLITHIASIS, STAGHORN

Brian M. Benway, MD
Gerald L. Andriole, MD, FACS

**BASICS**

**DESCRIPTION**
- Staghorn calculi are branched stones that occupy a large portion of the collecting system. Typically, they fill the renal pelvis and branch into several or all of the calices.
- Partial staghorn: Fills some but not all of the collecting system
- Complete staghorn: Fills nearly the entire collecting system
- Can be comprised of any of the following stone types, with struvite and calcium carbonate apatite the most commonly seen:
  - Struvite (magnesium ammonium phosphate)
  - Calcium carbonate apatite
  - Cystine
  - Uric acid
  - Calcium oxalate
  - Calcium phosphate
- Some literature refers to staghorn calculi as “coral calculi” or “coral nephrolithiasis” based on its characteristic shape.

**EPIDEMIOLOGY**

**Incidence**
- Not well-defined, with conflicting studies
- More common in women than in men

**Prevalence**
N/A

**RISK FACTORS**
- Chronic indwelling catheter
- Chronic infection
- Dehydration
- Metabolic disorders (hypercalciuria, cystinuria, hyperoxaluria)
- Neurogenic bladder
- Urinary obstruction or reflux
- Urinary diversion

**GENETICS**
N/A

**PATHOPHYSIOLOGY**
- Staghorn calculi are most frequently composed of mixtures of magnesium ammonium phosphate (struvite) and/or calcium carbonate apatite.
- These are also commonly referred to as “infection stones” due to their association with urinary tract infections.
- Strong association with urinary tract infection caused by specific organisms that produce the enzyme urease, which results in the generation of ammonia from urea.

**DIAGNOSIS**

**HISTORY**
- Often asymptomatic
- Discovered incidentally on imaging
- Recurrent or persistent urinary tract infection
- Fever, malaise, weight loss
- Renal insufficiency
- Flank pain
- Hematuria
- Neurogenic bladder
- Urinary diversion
- Metabolic disorders

**PHYSICAL EXAM**
- Costovertebral angle tenderness
- Rarely, palpable mass

**DIAGNOSTIC TESTS & INTERPRETATION**

**Lab**
- CBC
- Basic metabolic panel
- PT/INR
- Urinalysis and culture
- pH > 7.0 may indicate urea-splitting infection
- Culture may demonstrate commonly associated bacteria
- Persistence of a species may indicate a stone harboring infection

**Imaging**
- May be seen on KUB or ultrasound
- CT is gold-standard
- Provides clear information on stone location and configuration
- Evaluates cortical thickness
- Can identify excluded calyces and calyceal diverticula
- Provides information on location of surrounding structures
- Aids selection of access site(s)

**Diagnostic Procedures/Surgery**
- Diagnosed based on imaging studies

**Pathologic Findings**
- Gross pathology—calcium material
- Microscopic evaluation of crystals aids in determination of stone composition

**DIFFERENTIAL DIAGNOSIS**
- Blood clot
- Fibroepithelial polyp
- Fungus ball
- Granuloma
- Herpangina
- Malignancy
- Renal cell carcinoma and other renal malignancy
- Tuberculosis
- Upper tract carcinoma (urothelial, other)
- Xanthogranulomatous pyelonephritis (XGP)
Surgery/Other Procedures

- Acetohydroxamic acid
  - May reduce recurrence of struvite stones
  - Inhibits bacterial urease, denaturing urinary ammonia production
  - Adult dose: 12 mg/kg PO, 3–4 times a day on empty stomach, 1.5 g/d maximum
  - Pediatric dose: 10 mg/kg/day tolerated
  - May have severe side effects including deep discomfort, hallucinations, headache, loss of taste sensation, hallucinations, rash, abdominal discomfort
  - Must follow CBC and liver functions
  - May have severe side effects including deep discomfort, hallucinations, headache, loss of taste sensation, hallucinations, rash, abdominal discomfort
  - Contraindicated in patients with severe renal dysfunction (serum creatinine > 5.0 mg/dL), provided a ureteral stent or intervention is performed, PCNL should be the last definitive intervention for staghorn management.

- Open surgery is not commonly performed. May be used in extraordinary cases where clearance is not expected within a reasonable number of less-invasive procedures.

- Observation associated with significant risk of renal deterioration (28–48%) (2,3)
- Observation carries a high risk of morbidity, including renal deterioration and septic events. Only definitive intervention (stent, percutaneous nephrostomy tube) is appropriate for patients who would not tolerate open surgery.

- Nephrectomy for kidneys with negligible function or Xanthogranulomatous pyelonephritis (XGP)
- Dissolution may be effective in carefully selected patients, but has the potential for significant side effects. It is not presently included in the guidelines for staghorn management.

Additional Treatment

- Radiation Therapy
  - N/A

- Additional Therapies
  - Prophylactic antibiotics to suppress UTI

Complementary & Alternative Therapies

- N/A

ONGOING CARE

PROGNOSIS

- Observation associated with significant risk of renal deterioration (28–48%) (2,3)
- Good prognosis for patients who are rendered stone-free

COMPLICATIONS

- Observation
  - Death
  - Functional renal loss
  - Pyelonephritis
  - Sepsis
- Interventions
  - Anesthesia complications
  - Death
  - Hematoma
  - Hemorrhage
  - Injury to colon, liver, spleen
  - Pneumothorax/hydrothorax
  - Upper tract injury
  - Urinary fistula
  - Uronoma

FOLLOW-UP

Patient Monitoring

- KUB and ultrasound at regular intervals
- Urinoma
- Consider metabolic evaluation (serum studies, 24-h urine study)

Patient Resources

- N/A

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Pyelonephritis, Xanthogranulomatous
- Urinary tract infection (UTI), Complicated, Adult
- Urinary tract infection (UTI), Complicated, Pediatric
- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General
- Urolithiasis, Staghorn Image

CODES

ICD9

- 592.0 Calculus of kidney
- 599.0 Urinary tract infection, site not specified

ICD10

- N39.0 Urinary tract infection, site not specified
- N20.0 Calculus of kidney
- N12 Tubulo-interstitial nephritis, not spcf as acute or chronic
- 611.9 Calculus of kidney
- N39.0 Urinary tract infection, site not specified

CLINICAL/SURGICAL PEARLS

- Staghorn calculi are large branching renal calculi most often associated with urinary tract infections.
- Observation carries a high risk of morbidity, including renal deterioration and sepsis.
- Percutaneous nephrostomy is the gold standard for treatment.
UROLITHIASIS URETERAL

Mohamed S. Ismail, MBChB, MRCS, PhD
Francis Xavier Keeley, Jr., MD, FRCS

BASICS
DESCRIPTION
Urolithiasis ureteral refers to a stone present in the ureter.
- Urinary stones usually present with severe colicky pain that radiates from the loin (flank) to the groin as the stone passes to the lower ureter. Urinary stone can cause obstructive uropathy as well as urosepsis which is a clinical emergency.
- Stone composition:
  - Calcium oxalate: Absorptive hypercalciuria, nephrocalcinosis, renal hypercalciuria, hyperparathyroidism, hypertriglyceridemia
  - Urine acid stones: Gout, myeloproliferative disorders, idiopathic uric acid stones, chemotherapeutic
  - Calcium phosphate and oxalate: Distal renal tubular acidosis
  - Struvite stones: Occur as a result of infection with urease-producing bacteria that breakdown urea into ammonia
  - Cystine stones: Occur in patients with cystinuria or autosomal recessive disorder resulting in reduced absorption of cystine from the proximal tubules
  - Medication stones (rare): Triamterene, indinavir.

ASSOCIATED CONDITIONS
- Primary hyperoxaluria
- Medullary sponge kidney/nephrocalcinosis
- Primary hyperparathyroidism
- Chronic diarrheal states: GI surgery: gastric bypass/banding, small bowel resection
- Distal (type 1) renal tubular acidosis
- Acute cholecystitis
- Upper-tract TCC
- Renal cell carcinoma
- Pyelonephritis
- Acute appendicitis
- Peritonitis
- Pancreatitis
- Abdominal aortic aneurysm
- Ureteropelvic junction obstruction
- Ureteral stone.

GROSS PATHOLOGY
- Operator dependent. Very useful in pregnancy, patients with contrast allergy and children. Can miss small kidney stones. Normal examination does not rule out ureteral stone since stones may not be well seen. Cost and availability also limit its routine use.

DIAGNOSIS
HISTORY
- Acute onset colicky pain that radiates from the loin to the groin
- Patient resists ambulation trying to find a comfortable position
- Lower ureteral stone pain may radiate to the tip of the penis
- Nonspecific haematuria and very rarely macroscopic haematuria
- Previous history of renal stones
- Urinary frequency, urgency, and urinary incontinence are associated with lower ureteral stones

ALERT
- Obstructed infected kidney is a clinical emergency

PHYSICAL EXAM
- The most important aspect of examination of patient with ureteral stone is core body temperature.
- Abdominal examination may reveal tenderness.
- Urosepsis is associated with high temperature, low blood pressure, and tachycardia.

DIAGNOSTIC TESTS & INTERPRETATION
- CBC to test for underlying infection (See General Measures).
- Serum creatinine to detect renal impairment.
- Urine analysis: To check for hematuria, nitrite, and leukocytes.
- X-ray KUB: Only in radio opaque stones. Most practical for conservative management.
- Ultrasound:
  - Operator dependent. Very useful in pregnancy, patients with contrast allergy and children. Can miss small kidney stones. Normal examination does not rule out ureteral stone since stones may not be well seen. Cost and availability also limit its routine use.
- Intravenous urography: May be used to diagnose ureteral stones due to ureteral distortion, but stones usually not well seen. Cost and availability also limit its routine use.
- CT urography: Is the imaging of choice for patient with suspected ureteral stone.

Differential Diagnosis
- Abdominal aortic aneurysm
- Acute appendicitis
- Acute cholecystitis
- Pancreatitis
- Renal cell carcinoma
- Nephrolithiasis
- Urinary tract infection

Pathologic Findings
- Dependent on stone composition

Lab
- Urine analysis: To check for hematuria, nitrite, and leukocytes.
- Serum creatinine to detect renal impairment.
- CBC to test for underlying infection (See General Measures).

Urine analysis: To check for hematuria, nitrite, and leukocytes.
TREATMENT

GENERAL MEASURES

- Unstable calculi which are associated with renal impairment and/or signs of infection are indication for emergency treatment with broad-spectrum antibiotic and decompression of the renal tract.
- Antibiotic therapy is warranted to treat infection and to prevent and treat infection in the presence of obstruction. Failure to provide appropriate postoperative antimicrobial prophylaxis can lead to increased rate of superinfection.

Average stone passage time is 3 wk, stone has not r

Watchful waiting: Small ureteral stones will pass r

Ureteroscopy: Fluoroquinolone, trimethoprim

Broad-spectrum empiric antibiotic in the presence of r

Pain control: Nonsteroidal anti-inflammatory drugs, r

Infected stones warrant close observation to limit r

Percutaneous nephrolithotomy (PCNL): passed within 2 mo is unlikely to pass.

- 47% of stones 6–10 mm in diameter
- 68% of stones 5 mm or less pass spontaneously

Stone size, shape, location, and associated ureteral r

- Adequate renal function reserve
- Well-controlled pain
- For hospital-acquired urosepsis following urologic r

Patient Monitoring
- Patient is followed to detect any further stone formation
- Prevention measures to avoid further stone formation (see general prevention)
- Patients with septic stone picture require at least 14 days of culture appropriate antibiotics

Patient Resources

ADDITIONAL READING

- Belladonna M, Milamar G, Matsumoto G. Efficacy of r

- Bone RC, Balk RA, Cerra FB, et al.; ACCP/SCCM 


CLINICAL/SURGICAL PEARLS

- In the setting of an infected obstructing ureteral calculi, there is no significant difference in outcome whether stented or treated by percutaneous drainage.
- Recent studies suggest that in unstable patients with very large stone burden percutaneous drainage may be preferred.

REFERENCES


UROLITHIASIS URETERAL

TREATMENT

Second Line
- Medical expulsion therapy: U-1-adrenergic 

- Intravenous urography (IVU) or retrograde pyelography (RGP)
- Ultrasound and CTA are preferred for noninvasive examinations. MRU is indicated in case of uncertain diagnosis when IVU is not available.

SUDDEN APPEARANCE OF COMPLICATED STONES

- Clinical presentation of complications may be delayed for several years after the initial onset of symptoms.
- Acute onset of symptoms may be associated with an increase in stone size and clinical presentation.
- Evaluation of the patient with acute onset of symptoms should include a thorough history and physical examination, as well as appropriate imaging studies. In addition, laboratory investigations should be performed to evaluate for potential metabolic abnormalities that may contribute to stone formation.

Malignant Change

- Malignant change in the urinary tract is rare, but can occur in individuals with a history of stone disease. The risk of malignancy appears to be increased in patients with long-standing renal calculi and those with a history of urolithiasis.
- The diagnosis of malignant change is typically made through biopsy and histopathological examination of the affected tissue. Treatment options include surgical resection and chemotherapy or radiation therapy in selected cases.
UROLITHIASIS, URIC ACID
Aaron G. Boonjindasup, MD, MPH
Raju Thomas, MD, MHA, FACS

BASICS
DESCRIPTION
- Urticaria stones that are composed primarily of uric acid and can be found anywhere in the urinary tract.
- Uric acid usually precipitates in acidic urine.

EPIDEMIOLOGY
Incidence
- 1/1000 adults
- Prevalence
- Account for 5–10% of all urinary tract stones
- Incidence

RISK FACTORS
- Persistent acidic urine is most important pathogenic factor.
- Urinary tract infection
- Bowel-related:
  - Crohn disease, regional ileitis
  - Ulcerative colitis, ileostomy, short bowel syndrome
- Hyperuricemia, gout
- Uric acid nephrolithiasis occurs in 10–25% of patients with gout
- Purine gluttony
- Inborn errors of metabolism
  - Lesch–Nyhan syndrome
  - Uric acid transferase deficiency (HGPRT)
  - Hypoxanthine guanine phosphoribosyl transferase deficiency (HGPRT)
- Myeloproliferative states
- Neoplasia
- Histiocytic anemia
- Chemotherapy
- Decreased urinary volume
- Diabetes associated with metabolic syndrome

Genetics
- Autosomal dominant for familial variant

PATHOPHYSIOLOGY (1)
- Uric acid crystallization caused by the supersaturation of urine with respect to undissociated uric acid.
- Free uric acid is 20 x LESS soluble in urine than urate salt.
- At a pH of 5.3, ½ of the uric acid is a urate salt and ½ is free uric acid.
- At pH of 6.5, 90% of the uric acid is soluble.
- Uric acid may serve as a nidus.
- Calcium oxalate stone formation
- Acute and chronic nephropathy due to uric acid crystals in renal tubules.
- May be related to hyperuricemia or gout.

Uricase—enzyme that converts uric acid to allantoin
- Allopurinol—10 to 100 x more soluble in urine than uric acid
- Relationship between obesity, diabetes, and the metabolic syndrome.
- Causes of low urinary pH.
- Low urinary pH in turn is the major urinary risk factor for uric acid stones.
- High plasma uric acid (UA) is a precipitating factor for good and renal calculus as well as a strong risk factor for metabolic syndrome and cardiovascular disease.

ASSOCIATED CONDITIONS
- Obesity with insulin resistance (metabolic syndrome)
- High waist circumference and BMI are associated with higher insulin resistance and leptin production, both reduce uric acid excretion.
- Myeloproliferative disorders
- Congenital disorders
- Lesch–Nyhan syndrome
- Gout
- Inflammatory bowel disease

DIAGNOSIS
HISTORY
- Acute presentation of urolithiasis
  - Pain, fever, chills, nausea, vomiting
  - Purine gluttony
  - Diet high in red meats, fish, poultry
  - Dehydration
  - Poor urine output
  - Poor urine volume
  - Gout
- Up to 20% of patients will have uric acid calculi
- Family history of uric acid stones
- Short bowel syndrome, inflammatory bowel disease, ileostomy
- History of myeloproliferative disorders

PHYSICAL EXAM
Costovertebral angle (CVA) tenderness
- Uric acid > 4.0 mmol/L
- Can often underestimate the total amount of uric acid of pH drops lower than 5.5

DIAGNOSTIC TESTS & INTERPRETATION
Lab
- Serum uric acid level may be normal or elevated
  - > 380 μmol/L, or 6.4 mg/100 mL
- Latent hyperuricemia may require purine loading test
- Urinalysis
  - pH: Acidic. Generally > 5.8
  - Crystals: Coffin-lid crystals
- 24-h urine collection for uric acid
  - Volume < 2 L
  - pH < 6.0
  - Uric acid > 4.0 mmol/L
  - Can often underestimate the total amount of uric acid of pH drops lower than 5.5

Imaging
- Non-contrast abdominal spiral computed tomography (CT): Gold standard
- Plain x-rays
  - Kidneys, ureters, bladder (KUB)
  - Non-contrast abdominal spiral computed tomography (CT)
  - May be related to hyperuricemia or gout.

DIAGNOSTIC PROCEDURE/SURGERY
- Stone analysis
- 24-h urine collection for uric acid

PATHOLOGIC FINDINGS
- Long-term deposition of crystals in the renal parenchyma can cause chronic urate nephropathy.
- Microscopic cause giant cell inflammatory reaction
  - Proteins
  - Inability of the kidney to concentrate urea
  - May have orange appearance when viewed endoscopically

DIFFERENTIAL DIAGNOSIS
- Other renal calculus
- Calcium oxalate monohydrate
- Calcium oxalate dehydrate
- Cystine
- Struvite

- Filling defect if IV urogram is obtained
- Urinary neoplasms
- Blood clot
- Pusball
- Sclerotic renal papillae
- Stricture
- Bladder calculus
- 50% consist of uric acid

- Uric acid of pH drops lower than 5.5
- Uric acid > 4.0 mmol/L
- Can often underestimate the total amount of uric acid of pH drops lower than 5.5

- Non-contrast abdominal spiral computed tomography (CT): Gold standard
- Plain x-rays
  - Kidneys, ureters, bladder (KUB)
  - Non-contrast abdominal spiral computed tomography (CT)
  - May be related to hyperuricemia or gout.
TREATMENT

GENERAL MEASURES (2)

ALERT
- During alkalinization, do not allow urinary pH to chronically rise above 7.0.
- This may cause precipitation of other urinary calcium salts (heterogenous nucleation/epitaxy).
- Acute renal colic should be treated accordingly (see Section "Urolithiasis, adult, general considerations").
- Uric acid stones are often amenable to medical therapy
- Lower protein/no purine diet
- Alkalization of urine
- Medical therapy should only be initiated in moderately symptomatic or asymptomatic patients

MEDICATION

First Line (3)
- Potassium citrate 30–60 mEq/d
- Allopurinol 100–600 mg/d
- Sodium bicarbonate 650 mg q6–8h
- Potassium citrate 30–60 mEq/d

Second Line
- Allopurinol 100–600 mg/d
- Hyperuricemia or urinary uric acid secretion >100 mg/d
- Urate inhibitors: Xanthine oxidase inhibitors (80 mg daily) have been used in the management of hyperuricemia in patients with gout with limited information on uric acid stones. It can reduce uric and uricin.

COMPLIANTIONS

- Sepsis
- Obstructive nephropathy

FOLLOW-UP

Patient Monitoring
- Clinical: pH, crystals, red blood cells (RBCs)/white blood cells (WBCs)
- Urinalysis
- Follow stone size with US or low-dose CT every 3–6 mo on medical therapy

Patient Resources
- Metabolic Stone Evaluation (24 Hour Urine Studies)
- Bladder Calculi
- Pregnancy, Urolithiasis
- Urate, Dietary
- Urolithiasis, Adult, General
- Urolithiasis, Calcium Oxalate/Phosphate
- Urolithiasis, Renal, General
- Urolithiasis, Uric Acid Image

ADDITIONAL TREATMENT

Radiation Therapy

Vital Additional Therapies
- Treat underlying illness
- Evaluate for and treat gout if elevated serum uric acid
- Correct metabolic syndrome though diet and weight reduction
- Febuxostat a relatively new xanthine oxidase inhibitor (80 mg daily) has been used in the management of hyperuricemia in patients with gout with limited information on uric acid stones. It can reduce uric and uricin.

Ongoing Care

PROGNOSIS

Dependent on etiology and stone characteristics

COMPLICATIONS

- Sepsis
- Obstructive nephropathy

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Bladder Calculi
- Metabolic Stone Evaluation (24 Hour Urine Studies)
- Pregnancy, Urolithiasis
- Urate, Dietary
- Urolithiasis, Adult, General
- Urolithiasis, Calcium Oxalate/Phosphate
- Urolithiasis, Renal, General
- Urolithiasis, Uric Acid Image

CODES

ICD9
- 274.11 Uric acid nephrolithiasis
- 592.0 Calculus of kidney
- 790.6 Other abnormal blood chemistry

ICD10
- E89.0 Hyperuricemia w/o signs of inflammatory arthritis and tophaceous dis
- N20.0 Calculus of kidney
- N20.9 Urinary calculus, unspecified

CLINICAL/SURGICAL PEARLS

- Common conditions that increase the risk of uric acid stone formation: gout, chronic diarrhea, diuretics, and metabolic syndrome.
- Uric acid stones are often radiolucent (noncalcified) therefore, plain film often not useful.
- Non-contrast abdominal spiral computed tomography (CT) is considered the gold standard for imaging urolithiasis including uric acid stones.
- The metabolic syndrome causes low urinary pH which in turn is a major urinary risk factor for uric acid stones.
- Alkalinization can dissolve uric acid calculus.
RISK FACTORS

- Advanced age (>65 yr)
- Diabetes, malignancy, immunosuppression, cachexia, immunodeficiency, alcoholism
- Obstructive uropathy, BPH, prostate cancer, stricture, urethral, neuropathic bladder disorders, retroperitoneal masses and fibrosis, sloughed papilla, endometriosis
- Abnormal/urinary anatomy: ureteropelvic junction obstruction, polypycnic kidneys, urethrocèle, vesicoureteral reflux, phimosis
- Inflammatory/infectious diseases:
  - Pyelonephritis, acute bacterial prostatitis, renal abscesses, perinephric abscesses, epididymo-orchitis, Fournier gangrene
- Precipitating interventional/nosocomial events resulting in bacteremia and subsequent sepsis:
  - Indwelling urethral, urologic instrumentation/surgery such as prostate biopsy, transurethral surgery

PATHOPHYSIOLOGY

- Sepsis is a systemic, deleterious host response to infection leading to severe sepsis and septic shock.
- The most common etiology of sepsis is secondary to a bacterial infection with Enterobacteriaceae, Proteus sp., Enterococcus and Klebsiella sp., and Pseudomonas aeruginosa.
- Obstipation in an infected urinary tract further contributes to the development of sepsis.
- The primary initiator of gram-negative bacteria septic shock is endotoxin, a lipopolysaccharide component of the bacterial cell membrane.
- Exotoxins released by some bacteria can initiate septic shock.
- However, the bacteria themselves and cell wall components are primarily responsible for the development of septic shock.
- The intravascular activation of inflammatory systems contributes to the development of septic shock.
- The intravascular activation of inflammatory systems results in overproduction of cytokines such as tumor necrosis factor (TNF) and IL-1.

ASSOCIATED CONDITIONS

- Acute pyelonephritis
- Lower UTI
- Urinary tract infection
- Urogenital instrumentation

GENERAL PREVENTION

- Urine culture and appropriate antibiotic coverage prior to urologic procedure
- To further reduce incidence of nosocomial UTI: remove Foley catheter as soon as it is no longer needed, use aseptic insertion technique, maintain unstructured Foley, use closed urinary drainage systems (13L)

DIAGNOSIS

- History:
  - A thorough history should be obtained, with emphasis on identifying the primary etiology:
    - Classic: presentation of fever, chills, followed by hypotension seen in only ~10% of patients.
    - A history of hypodensification, urethritis, flank pain, UTI, immunocompromised status, urinary retention, and recent urologic instrumentation/procedure is common
  - Evaluate for mental status changes.

- Physical exam:
  - Emphasis on identifying the primary source of the infection
  - Most common findings: Hypothermia, tachycardia, tachypnea, and hypotension
  - Earliest signs of sepsis may be increased respiratory rate with respiratory alkalosis
  - Examine for all urologic and non-urologic sources of bacteremia:
    - Purulent subcutaneous fluid collections, chest exam; costovertebral angle tenderness; abdominal or suprapubic tenderness; examine of the stomach, testes, perineum; prostatic fluctuance; extremities for tenderness or swelling.

DIAGNOSTIC TESTS & INTERPRETATION

- Lab:
  - CBC with differential. Usually shows elevated WBC count with elevated neutrophil count
  - Patients may also have neutropenia
  - Basic metabolic panel (BMP), liver function tests (LFTS), lactate. May show evidence of end-organ dysfunction
  - Blood, urine, and wound culture with a Gram stain for preliminary identification:
    - If possible obtain 2 sets of blood cultures before starting empiric antibiotics
    - Specific organisms causing sepsis are identified in about half of patients

- Imaging:
  - Obtain based on presumptive initiating event and clinical symptoms
  - US can quickly evaluate for hydronephrosis
  - CT scan can evaluate for stones, fluid collections and abscesses within tissue

Diagnostic Procedures/Surgery

Diagnostic procedures should be tailored to identifying the initiating event.

Pathologic Findings

- Positive blood cultures
  - Empyema, meningitis, pyelonephritis
  - Kidney abscess
  - Renal and perineal abscesses
  - Xanthogranulomatous pyelonephritis
  - Lower urinary tract source:
    - Acute bacterial prostatitis
    - Eretal gangrene
  - Epididymitis/urinary tract infection
  - Fournier gangrene
  - Epidural abscess
  - Common non-urologic causes of sepsis:
    - Central line
    - Sepsis, pneumonia
    - Endocarditis, mediastinitis
    - Prostatitis, arthritist
  - Sepsis within a complex urinary tract infection, perineal, peripheral abscesses
  - Septic arthritis
  - Soft tissue infection

UROSEPSIS

Christopher Ameling, MD, FACS
Nick Cowan, MD
Noninfectious conditions that mimic sepsis:
- Acute adrenal insufficiency
- GI bleed
- Myocardial infarction
- Pancreatitis
- Pulmonary embolus
- Renal failure

**TREATMENT**

**GENERAL MEASURES**
- Early goal-directed therapy, “Rivers protocol”:
  - Goal MAP >65 mmHg, CVP 8–12 mmHg, UOP >0.5 mL/kg/h
  - Start empiric IV antibiotics (ABX) within 1 h of recognition of severe sepsis or septic shock
- Volume expansion with isotonic fluids
- Supplemental oxygen with or without intubation and assisted ventilation if indicated
- Vasopressors to achieve hemodynamic goals (norepinephrine preferred to dopamine)
- Maintain glycemic control
  - Keep-glucose <180 mg/dL as intensive glycemic control (85–110 mg/dL) has shown either no change or increased mortality, and increased rates of hypoglycemia (2A)

**ALERT**
Autopsy studies in persons who died in the ICU show that the failure to diagnose and treat infections with antibiotics or surgical drainage is the most common avoidable error.

**MEDICATION**

**First Line**
- Broad-spectrum antibiotic coverage (against both gram-positive and gram-negative bacteria) should be instituted immediately:
  - Vancomycin: 1 g IV q12h
  - Piperacillin + tazobactam: 3.375 g IV q6h
  - Cefepime: 2 g IV q12h
  - Ceftazidime: 1–2 g IV q6–8 h
  - Ceftriaxone: 2 g IV q24 h
  - Meropenem: 1 g IV q8h
  - Piperacillin + tazobactam, imipenem, or meropenem

**Second Line**
- Reassess antimicrobial regimen daily and deescalate when sensitivity results are available.
  - Switch to PO ABX when clinically stable for at least 48 h and usually complete a 7–10-day course based on the cause of the infection.

**SURGERY/OTHER PROCEDURES**
- Patients should undergo surgical drainage of purulent collections, debridement of necrotic tissue, and relief of urinary tract obstruction.
- Retrgrade urethral catheterization and percutaneous nephrostomy effectively relieve obstruction and infection due to urinoma/calculi
- Neither modality has demonstrated superiority in promoting a more rapid recovery

**ADDITIONAL TREATMENT**

**Radiation Therapy**
N/A

**Additional Therapies**
- Definitive correction of any correctible factors when patient stabilized
- Corticosteroids in use in sepsis is complex and current data do not show improved survival in severe sepsis

**COMPLEMENTARY & ALTERNATIVE THERAPIES**
N/A

**ONGOING CARE**

**PROGNOSIS**
- Mortality rates associated with severe sepsis and septic shock are 25–35% and 40–70%, respectively.
- Factors associated with a higher risk of mortality from sepsis: Fever, WBC count, serum creatinine, diabetes mellitus, lactate, and albumin.

**ALERT**
- Mortality rate decreased by 42% when early goal-directed therapy achieved within the first 6 hours for severe sepsis and septic shock.

**COMPLICATIONS**
- Renal insufficiency, hepatic dysfunction, and organ failure, cardiac events, death

**FOLLOW-UP**

**Patient Monitoring**
- Patient should be continued on appropriate ABX coverage for 7–10 days, longer if needed.
- Repeat cultures can be obtained to ensure treatment is adequate.

**Patient Resources**

**REFERENCES**

**ADDITIONAL READING**

**See Also (Topic, Algorithm, Media)**
- Epididymitis
- Fournier Gangrene
- Prostatitis, Acute, Bacterial (NIH I)
- Pyelonephritis, Acute
- Pyelonephritis, Empyema
- Pyelonephritis, Xanthogranulomatous
- Renal and Perirenal Abscess

**CODES**

**ICD9**
- 599.5 Urosepsis, site not specified
- 785.52 Septic shock
- 995.82 Severe sepsis

**ICD10**
- N99.0 Urosepsis, site not specified
- R65.20 Severe sepsis without septic shock
- R65.21 Severe sepsis with septic shock

**CLINICAL/SURGICAL PEARLS**
- Early goal-directed therapy guided by invasive monitoring (mean arterial pressure [MAP], central venous pressure [CVP] and urine output [UOP]) within the first 6 hours after recognition of sepsis.
- Blood culture x2 prior to antibiotics if possible.
- Start empiric ABX within 1 hour of recognition of severe sepsis or shock.
- Initial fluid resuscitation with crystalloid.

**URSEPSIS**
UROSTOMY PROBLEMS

Edouard J. Trabulsi, MD, FACS

Basics

Description
- Urostomy is an intestinal urinary diversion and relies on an external appliance (pouching system) for the collection of urine.
- Urostomy can be made of either small or large intestine, with the detail being the most common bowel segment used:
  - Also called ileal conduit, cutaneous ureterostomy if made up of ileum
  - Colon conduit, if made up of segment of large bowel.
- Very rarely, a urostomy can consist of the unresected rectum, being directly anastomosed to the skin (cutaneous ileostomies). These are uncommon in adults but are sometimes performed in children.
- Complications of the abdominal urinary stoma (urostomy) are the most common problem encountered in the postoperative period in patients undergoing urinary diversion.

Epidemiology
Incidence
- 2.8–19% of patients develop stomal stenosis with Loop ileostomies.
- 10–20% of patients with colon conduits develop stenosis.
- Parastomal hernia:
  - Occurs in 2–6.6% of patients with loop ileostomies.
  - Rare with end ileostomies (1–4%).
  - More common occur with loop stomas (4–20%).
- Nearly all patients will have a stomal-related complication at some point.

Prevalence
N/A

Risk Factors
- Obesity
- Chronic cough
- Wound infection
- Abdominal dissection
- Malnutrition
- Immunosuppression/steroid use
- Poor surgical technique
- Lack of proper stoma care
- Warm weather, excessive sweating, oily skin may cause the skin barrier adhesive to loosen
- Weight gain or loss can alter the topography of the stoma itself and the surrounding skin that may affect the security of the face plate adherence

Genetics
N/A

Pathophysiology
- A pouching system (also called an appliance) collects the urine that exits from the stoma.
- 2 styles of pouching systems are available: 2-piece systems have a face piece and a pouch that can be removed from the barrier; 1-piece pouches fused to skin barrier.
- The faceplate and system should be changed if there is leakage or every 4–7 days depending on individual patient characteristics.
- A properly constructed stoma usually protrudes ~ 0.5 cm from the abdominal wall.
- Initially, a properly constructed stoma will be somewhat edematous. It will reduce slightly in size over several weeks following surgery. This means that the initial hole in the faceplate may change as the edema resolves.
- The stoma is ideally not placed near a skin fold and is sufficiently far from the incision that the appliance will adhere and not leak.
- Early complications usually relate to impaired vascular supply (1):
  1. Stomal necrosis can result in retraction, with a flush ostomy that is difficult to apply an appliance to.
  2. Early stomal retraction can be caused by an insufficient length of bowel segment or improper technique in securing and eversion of the stoma.
- A pouching system (also called an appliance)
  - 2 styles of pouching systems are available:
    - 2-piece systems have a face plate and a pouch
    - 1-piece pouches fused to skin barrier
- Proper selection of pouching system:
  - Compatibility with abdominal contours
  - Proper sizing of the pouch opening to minimize urine exposure on the skin
- When changing the faceplate, the patient should learn to gently push the skin away from the sticky barrier rather than pulling the barrier off the skin.
- An acidic urine will be more protective of the peristomal skin than alkaline urine.

Diagnosis

History
- Timing of diversion
- Weight change: may alter the fit of the faceplate
- Review the care of the stoma and appliance:
  - Frequency of face plate change
  - Frequency of emptying the collection pouch
- Complaints of peristomal skin lesions: blistering, itching, or dermatitis
- Problems with the adhesive, pates, tape, or pouch material

Physical Exam
- Peristomal skin lesions:
  - Irritative parastomal lesions that are manifested by hypopigmentation, hyperpigmentation, and scaling with loss of epidermis.
  - Pseudo-verrucous appear wartlike

- Pseudo-verrucous appear wartlike
**Urostomy Problems**

- Minor bleeding from the exposed mucosa is common. Significant bleeding can be seen in cases of fistula contents.
- Examine for evidence of parastomal herniation:
  - Defect along sacral region of urostomy usually redoublé.
  - Stomal stenosis or hyperkeratosis:
    - Calibrate ostomy with a sterile catheter if stoma stenosis present.
    - Note presence of urinary crystals on the skin.

**Diagnostic Tests & Interpretation**

- Lab
- Imaging
- Usually not necessary

**Differential Diagnosis**

- N/A
- Pathologic Findings

- Useful.

**Diagnostic Procedures/Surgery**

- Catheterization of the stoma with a red rubber catheter and determination if there is retained urine may be useful.

**Pathologic Findings**

- N/A

**Treatment**

**General Measures**

- Proper initial surgical technique will minimize short- and long-term stoma problems.
- Proper stoma care and problem-solving is often accomplished by consultation with a certified ostomy care health provider:
  - Wound, Ostomy and Continence Nursing Certification Board (WONCB) provider:
  - Certification in ostomy nursing
- A proper pouching system should have the following characteristics:
  - Secure, leak-proof seal that lasts 3–7 days
  - Protective of the skin around the stoma
  - Nearly invisible when covered with clothing
  - Easy to put on and take off
  - Convex-style appliances can sometimes compensate for a retracted or flush stoma
  - Many styles and adhesive types may offer options to correct many fit problems.
- A 1-piece ostomy system tends to be more flexible than a 2-piece unit; may help with stomas that are near a deep abdominal fold or crease.
- Ostomy belts can sometimes help with securing the appliance in place and minimize mechanical disruption of the system.
- Gently trimming peristomal hair may help with face plate adherence.

**Follow-Up**

- Patient Monitoring
  - Stomal wound care
  - Care surveillance as per protocol

**Patient Resources**

- Wound, Ostomy and Continence Nursing Society.
  - http://www.wound.org/patient/patients
- Urostomy and Continent Urinary Diversion.

**Reference**


**Additional Reading**

- See Also (Topic, Algorithm, Media)
  - Catheterizable Stoma Problems
  - Intraperineal Anastomotic Stasis
  - Urostomy Problems Image

**ICD-9**

- 597.5 Urological complications, not elsewhere classified

**ICD-10**

- K83.93 Parastomal hernia without mention of obstruction or gangrene
- K97.5 Urological complications, not elsewhere classified

**Clinical/Surgical Pearls**

- Urostomy difficulties are common.
  - A urostomy that is flush with the skin causes significant skin excoriation and complications, so attempt to have the stoma protrude at least 1–2 cm above the skin when creating it in the OR.
  - A convex stoma appliance can be helpful for stoma issues.

- Allergic reaction to adhesive or other components can be addressed by switching to another product.
- Urine crystals on the skin or stoma (white gritty particles) are caused by alkaline urine:
  - Cranberry juice in place of citrus juices (citrus juices make the urine more alkaline)
  - Consider vitamin C daily
  - Some acid ash foods: (make urine acidic) include:
    - Meat, breads and cereals, cheese, corn, cranberries, eggs, macarons, nuts, pasta, prunes, fish, and poultry.
- A 1:1 dilution of water and white vinegar applied with a cloth moistened with the mixture will dissolve the crystals.
- A pouch cover can help keep the skin beyond the pouch hanging down and contacts the skin.

**Medication**

**First Line**

- Antifungal agents: Nystatin or miconazole powder lightly applied twice a day in cases of superficial fungal infection
- Severe allergic reactions to adhesive or appliance may require topical steroids short-term.

**Second Line**

- N/A

**Surgery/Others Procedures**

- Surgical repair for parastomal hernias:
  - High likelihood of recurrence with or without relocation of the fascial opening. Suprapubic synthetic mesh wrap may decrease recurrence.
  - Period of conservative management appropriate; laparoscopic repair reported.
- Surgical revision for stomal stenosis
- Surgical revision of retracted stoma
- Liposuction reported to correct inverted stoma in obese patients
- Liposcopy to remove calcific

**Additional Treatment**

**Radiation Therapy**

- Some limited reports of radiation to treat stomal stenosis–related hyperkeratosis

**Additional Therapies**

- Additional readings on urinary stones.
- Fevervescent stones:
  - Cranberries, eggs, macaroni, nuts, pasta, prunes, fish, and poultry.
- Acidic diet:
  - Cranberries, eggs, macaroni, nuts, pasta, prunes, fish, and poultry.
- Alkaline diet:
  - Most meats, breads, and cereals, cheese, corn, cranberries, eggs, macaroni, nuts, pasta, prunes, fish, and poultry.

**Prognosis**

- Very good when intervention is applied in a timely fashion to prevent irreparable upper tract deterioration from stomal stenosis.

**Complications**

- Recurrent stomal stenosis
- Recurrent parastomal hernia
- Recurrent skin irritation from poor ostomy care
- Appliance leakage

**Ongoing Care**

**Follow-Up**

- Patient Monitoring
  - Stomal wound care
  - Care surveillance as per protocol

**Patient Resources**

- Wound, Ostomy and Continence Nursing Society.
  - http://www.wound.org/patient/patients
- Urostomy and Continent Urinary diversion.

**Reference**


**Additional Reading**


**See Also (Topic, Algorithm, Media)**

- Catheterizable Stoma Problems
  - Intraperineal Anastomotic Stasis
  - Urostomy Problems Image

**ICD9**

- 553.29 Other vesical hernia without mention of obstruction or gangrene
- 997.5 Urological complications, not elsewhere classified

**ICD10**

- K43.5 Parastomal hernia without obstruction or gangrene
- N99.531 Infection of other stoma of urinary tract
- N99.538 Other complication of other stoma of urinary tract

**Clinical/Surgical Pearls**

- Urostomy difficulties are common.
  - A urostomy that is flush with the skin causes significant skin excoriation and complications, so attempt to have the stoma protrude at least 1–2 cm above the skin when creating it in the OR.
  - A convex stoma appliance can be helpful for stoma issues.
VAGINAL MESH EROSION
Jessica M. DeLong, MD
Kurt A. McCammon, MD, FACS

BASICS

DESCRIPTION
- Mesh erosion is 1 of the major complications of prolapse surgery conducted by transvaginal approach.
- Currently, most common mesh used for pubovaginal sling (PVS) and pelvic organ prolapse (POP) repair is polypropylene mesh.
- Most sling erosions diagnosed 1–18 mo postoperatively (mean 9 mo).
- Most common and consistently reported mesh-related complication for POP (1).
- May occur in isolation or in combination with urethral or bladder erosion.
- Note: More specific term may be “vaginal extrusion”.

EPIDEMIOLOGY

Incidence
- 0.012–23% for midurethral slings; varies widely in literature (2).
- Wide variation with POP repair as well.
  – Attributed to type of synthetic material used.
  – Older synthetic materials had higher risk of extrusion due to intrinsic properties.

Prevalence
- Unknown; increasing over time with increasing use of mesh.
  – Likely underreported.

RISK FACTORS

Patient factors
  – Estrogen deficiency.
  – History of local radiation.
  – Early resumption of intercourse.

Operative factors
  – Use of tightly woven, large-diameter mesh.
  – Excessive sling tension or mesh too loose.
  – Perforation of urethra or bladder.
  – Inadequate vaginal closure.
  – Superficial mesh placement.

Genetics
- N/A.

PATHOPHYSIOLOGY

- Not completely understood. Theories:
  – Subclinical infection.
  – Poor wound healing.
  – Iatrogenic injury/technical error.

ASSOCIATED CONDITIONS
- Stress incontinence.
- POP.
- Cystocele.

GENERAL PREVENTION
- Perform intraoperative cystoscopy to minimize risk of urinary tract erosion.
- Appropriate patient selection.
- Rigorous surgical technique.

ALERT
- Be familiar with FDA warnings regarding risks of intravaginal mesh & counsel patients appropriately.

DIAGNOSIS

HISTORY
- Determine timing, details of initial surgical procedure and type of mesh used.
- Patients often present with storage symptoms, vaginal discharge, pelvic pain/dyspareunia, UTI.
- May complain of de novo lower urinary tract symptoms (LUTS).
- Delay in presentation is common.
- Sexual activity/sexual function.

PHYSICAL EXAM
- Pelvic exam.
  – Localize sites of pain.
  – Palpate for exposed mesh.
  – Foul discharge, if present.
- Abdominal exam.
  – Assess for tenderness, suprapubic pain if retropubic sling placed.

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Urine analysis.

Imaging
- Usually not indicated.

DIAGNOSTIC PROCEDURES/SURGERY

- Cystoscopy.
  – Perform if concern for urethral or bladder involvement.
- Urodynamics may be of value to assess lower urinary tract function.
- Check PVR if concern for retention.

Pathologic Findings
- Inflammation, fibrosis.

DIFFERENTIAL DIAGNOSIS

- Urethral mesh erosion.
- Bladder mesh erosion.
- UTI.

TREATMENT

GENERAL MEASURES
- In general treatment is divided into:
  – Conservative.
  – Surgical.
- Some patients may be observed with reasonable success.

MEDICATION

First Line
- Culture-specific antibiotic course if UTI present.
- Vaginal estrogen cream.
  – May be effective for small erosions.
  – Apply small amount to tip of index finger, apply vaginally 2–3 times/ wk.
  – Contraindicated if history of deep venous thrombosis (DVT), estrogen-responsive cancer.

Second Line
- None.

SURGERY/OTHER PROCEDURES

- Transvaginal excision.
  – Only exposed mesh vs. entire mesh.
- Primary approximation of tissue over exposed mesh.
- Martius flap interposition at the discretion of the surgeon.
ADDITIONAL TREATMENT

Radiation Therapy
- N/A

Additional Therapies
- N/A

Complementary & Alternative Therapies
- N/A

ONGOING CARE

PROGNOSIS
- Unclear in literature
  - Recurrent SUI is common and may be alleviated by repeat PVS placement
  - Generally autologous material preferred
  - Pain may not be corrected with mesh removal
  - Expectant management may be successful in up to 42% of patients
  - However, a recent multicenter review of the topic indicated that the majority of women who present for management of synthetic mesh complication after POP or SUI surgery have severe complications that require surgical intervention, with a significant proportion requiring >1 surgical procedure (5).

COMPLICATIONS
- Voiding dysfunction after surgical management of synthetic sling erosion is common (3)
- Sexual dysfunction, male and female dyspareunia
- Persistent pain
- Vesicovaginal fistula formation
  - Recurrent stress urinary incontinence (SUI)
  - Can place 2nd pubo vaginal sling (PVS)

FOLLOW-UP

Patient Monitoring
- Depends upon treatment
  - If patient observed, will need follow-up exams
  - If mesh excised, patient should return if bothersome symptoms

Patient Resources
www.fda.gov—health notification regarding use of surgical mesh for POP and SUI

REFERENCES


ADDITIONAL READING


ADDITIONAL READING


See Also (Topic, Algorithm, Media)
- Vaginoplasty
- Pelvic Organ Prolapse (Cystocele and Enterocele)
- Stress Urinary Incontinence, Female
- Urethral Discharge
- Urethral Sling, Indications and Anatomic Positions
- Urethral Sling, Materials
- Vaginal Mesh Erosion Image

CODES

ICD10
- N59.84 Other specified disorders of urethra
- T83.711A Erosion of implanted vaginal mesh and other prosthetic materials to surrounding organ or tissue
- T96.39 Other mechanical complication of genitourinary device, implant, and graft

ADDITIONAL READING

**GENERAL PREVENTION**
- Avoid local irritants such as perfumed soaps and shower gels, wipes, powders, and sprays.
- Wash external skin with water alone or mild soap.
- Avoid local irritants such as perfumed soaps and laundry detergents, panty liners, etc.
- Vaginal candidiasis: 17–39%
- BV: 22–50%
- Treatment of candidiasis
- Trichomonas: Yellow or yellow-green, malodorous, fishy smell (amine odor)
- BV: White or gray, homogeneous, thin, coats the vaginal walls, can have fishy odor
- KOH instead of saline.
- Fold vaginal sidewall pH can help with diagnosis:
- Premenopausal: normal pH 4–4.5
- Postmenopausal: normal pH 4.7
- Yeast cells or hyphae remain undissolved.
- Vaginal discharge has leukocytes (>10 WBC on microscopic exam)
- Ferrable cervix; symptoms of PID (pelvic pain, fever)
- Discharge from cervix
- Culture is most accurate test for trichomonas
- Wet mount about 60% sensitive
- If suspected but not seen on KOH or wet mount
- NAAT (nucleic acid amplification testing) should be used for diagnosing Chlamydia trachomatis and Neisseria gonorrhoeae with NAAT

**DIFFERENTIAL DIAGNOSIS**
- Basis of mononuclear cell disorder with an unknown etiology
- Tumors or lymphoma
- Localization of symptoms
- Endometriosis
- Endometrial biopsy
- Infection
- Thrombosis
- Premenstrual syndrome
- Autoimmune disease
- Endometrioid carcinoma
- Basal cell adenoma
- Endometrial polyp
- Mullerian duct cyst
- Metastasis from breast, ovary, or colon
- Cervical polyp
- Adenocarcinoma
Pregnancy Considerations

- Bacterial vaginosis (1,2):
  - Metronidazole 500 mg PO BD for 7 days
  - Clindamycin cream 2% applied at bedtime every day for 7 days
- Trichomoniasis:
  - Clindamycin cream 2% applied at bedtime every day for 7 days
  - Topical clindamycin should not be used in the 2nd half of pregnancy

- VVC: if pregnant, the only recommended treatment is topical azole for 7 days (2)
- Trichomoniasis in pregnancy is associated with adverse outcomes, but no strong evidence that treatment improves outcomes, therefore (1, 2):
  - No need to screen
  - No treatment for women who have symptoms
- Metronidazole is pregnancy category B and OK for 2 g single PO dose
- Tinidazole is pregnancy category C
- With both drugs, stop breast-feeding.

SURGERY/OTHER PROCEDURES

N/A

ADDITONAL TREATMENT

Radiation Therapy

N/A

ADDITIONAL READING


See Also (Topic, Algorithm, Media)

- Sexually Transmitted Infections (STI) Sexually Transmitted Diseases (STD), General
- Vaginitis/Vulvovaginitis Image
- Vaginal Discharge Algorithm
- Vaginal Discharge, Urologic Considerations
- Vaginosis

ICD9

- N76.0 Acute vaginitis
- B37.3 Candidiasis of vulva and vagina
- A59.01 Trichomonal vulvovaginitis
- 616.10 Vaginitis and vulvovaginitis, unspecified

REFERENCES


CLINICAL/SURGICAL PEARLS

- Pelvic pain and fever are red flags for pelvic inflammatory disease.
- Avoid alcohol with metronidazole until 24 hr after last dose (72 hr for tinidazole) as it can cause nausea.
- Clindamycin cream may weaken latex condoms and diaphragms for 5 days after use.
- Consider delaying breastfeeding 12–24 hr after metronidazole and 72 hr for tinidazole.
RISK FACTORS

Prevalence
- 15% of males
- Majority left sided (75–90%), 33% bilateral
- Seen in 35–40% of men presenting with primary infertility
- 70–80% with secondary infertility (infertility after previously conceiving a child)
- Not causative of infertility in the majority of men

Incidence
- Decrease in incidence with increasing body mass index (BMI)
- Increased (3–8x) among 1st-degree relatives with varicocele
- Decrease in incidence with increasing body mass index
- If prior to puberty or unilateral right varicocele, only palpable are clinically relevant
- If prior to puberty or unilateral right varicocele, suggests underlying pathology (See Varicocele, Pediatric)

Associated Conditions
- Infertility
- Testicular atrophy
- Rarely, tumor, renal vein thrombus

GENERAL PREVENTION

None

DIAGNOSIS

ACUTE ASYMPTOMATIC

Acute onset suggests obstruction of renal or gonadal vein (possibly secondary to tumor).

HISTORY

- Intra-abdominal
- Pain
- Testicular atrophy
- Infertility
- History of testicular or renal surgery
- History of varicocele

PHYSICAL EXAM

- Examine with patient supine and standing upright, during Valsalva
- Examine in a warm room after patient has been standing for 10 min
- Relieved by recumbency
- Increases with activity (including intercourse)
- Dull ache, heavy sensation, sensation of increased intrascrotal pressure
- Examine with performing Valsalva while in upright position

DIAGNOSTIC TESTS & INTERPRETATION

LAB
- Semen analysis:
  - 3–5 days of sexual abstinence prior to collection
  - "Thrash pattern" on SA
- Consensus <20 million/mL; motility <60%; morphology <14% strict normal forms (oligoasthenoteratozoospermia or OAT)
- FSH >4.5 & DFI indicates varicocele may be impacting sperm production

IMAGING
- Ultrasonography: Valsalva exclude other intrascrotal pathology
- Valsalva: May exclude other intrascrotal pathology
- Valsalva defined as dilation of spermatic plexus veins with Valsalva to caliber of >3 mm

DIFFERENTIAL DIAGNOSIS

- Spermatic cord mass:
  - Spermatocele
  - Sperm granuloma
  - Epidermoid cyst
  - Adenomatoid tumor of the cord
  - Leydig cell tumor
  - Leydig cell adenoma
  - Testis tumor
  - Undescended/retractile testicle
  - Virilizing tumors

- Testicular atrophy
  - Epidermoid cyst
  - Adenomatoid tumor
  - Leydig cell adenoma
  - Benign tumor
  - Malignant tumor
  - Liposarcoma, leiomyosarcoma
  - Metastasis
  - Malignant tumor
  - Leiomyoma
  - Hemangioma
  - Hydrocele/hydrocele of the cord
  - Invasive lymphangiomyoma
  - Invasive leiomyoma

- Incisional hernia
- Inguinal lymphadenopathy
- Epididymitis/epididymo-orchitis

- Epididymitis
- Acute orchitis
- Chronic orchitis
- Epididymo-orchitis

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings

Pathologic Findings
Second Line

Pain: Analgesics (eg, NSAIDs) usually not durable

GENERAL MEASURES

Surgical technique:

Anatomic site of ligation:

Surgical treatment successfully eliminates over 90% of symptomatic varicocele or testicular hypotrophy not noted on both sides in presence of elevated FSH and semen parameters (4). Subclinical varicoceles have questionable impact on fertility, and repair may not improve fertility rates (5). Varicocele recurrence: 5%–15% are also indications for repair.

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

Interventional radiology:

Varicocele recurrence:

Hydrocele rate

Recurrence rates 15–25%

Hydrocele rates

Recurrence rates up to 16%

Hydrocele rate 5–8%

Recurrence rates 1–2%

Nerve injury

Testicular artery injury

Varicocele recurrence:

Hydrocele

Recurrence

Testicular artery injury

Nerve injury

Testicular atrophy

FOLLOW-UP

Patient Monitoring

Varicocele recurrence:

Typically evident within 6–13 mo

Infertility:

Semen analysis (SA) at 3 mo interval; semen should be monitored for at least 1 yr or until pregnancy has been achieved

Young men with varicocele and normal SA should be followed with tests 3A and FSH every 1–2 yr

Patient Resources

www.clinicopedia.com Urologist maintained male infertility, potency, and health blog


REFERENCES


ADDITIONAL READING


6. See Also (Topic, Algorithm, Media)

Infertility, Urology Considerations

Sperm Count and Tumors

Varicocele, Adult Image

Varicocele, Pediatric

ICD-9


625

VARICOCELE, ADULT

TREATMENT

GENERAL MEASURES

Subclinical varicoceles have questionable impact on fertility, and repair may not improve fertility rates (4).

NOASDs and HCO may provide symptomatic relief

Indications for treatment of infertile male (should meet all criteria):

Varicocele palpable on exam

Man with abnormal semen parameters or abnormal sperm function tests

Couple with known infertility

Female has normal or potentially treatable cause of infertility

Treatment will enable natural pregnancy or less invasive assisted reproductive techniques (ART) eg, intrauterine insemination (IUI)

Surgical varicocelectomy significantly improves semen parameters in infertile men with palpable varicocele and abnormal semen parameters (4).

Pain from symptomatic varicocele or testicular hypotrophy (15–20%) are also indications for repair.

MEDICATION

First Line

Pain: Analgesics (eg, NSAIDs) usually not durable therapy

Second Line

None

SURGERY/OTHER PROCEDURES

Surgical treatment successfully eliminates over 90% of varicoceles.

Bilateral repair warranted when varicoceles are noted on both sides in presence of elevated FSH and testicular hypotrophy.

Operative intervention classified by anatomic site of ligation and surgical technique:

Anatomic site of ligation:

Subinguinal microsurgical: The standard in recent years, incision over the cord below the external ring

Number of veins requiring ligation is greater

Microscope and Doppler to protect spermatic artery and lymphatics

Recurrent rates ~1%

Hydrocele rate ~1%

Hydrocele: Inguinal incision, ligation of spermatic veins within inguinal canal

Allows for concurrent hernia repair

Recurrence rates up to 16%

Scrotal: The transcrural approach is considered obsolete.

Retroperitoneal (Palomo or high ligation): Muscle splitting incision, exposure of spermatic vessels with or without preservation of spermatic artery

Mass ligation permitted due to presence of collateral arterial circulation (splanchnic artery)

Recurrence rates 15–25%

Hydrocele rate ~7%

Surgical technique:

Open with or without magnification

Magnification preferred to spare arteries and lymphatics, and allow ligation of small venous tributaries

Subinguinal or inguinal microscopic varicocelectomy offers the best overall outcome (6,7)

Laparoscopic:

High ligation

Recurrence rates <2%

Hydrocele rate 5–8%

5% of patients experience transient anterior thigh numbness

ADDITIONAL TREATMENT

Radiation Therapy

N/A

Additional Therapies

Interventional radiology:

Varicocele recurrence:

Hydrocele rate

Recurrence

Testicular artery injury

Nerve injury

Testicular atrophy

FOLLOW-UP

Patient Monitoring

Varicocele recurrence:

Typically evident within 6–13 mo

Infertility:

Semen analysis (SA) at 3 mo interval; semen should be monitored for at least 1 yr or until pregnancy has been achieved

Young men with varicocele and normal SA should be followed with tests 3A and FSH every 1–2 yr

Patient Resources

www.clinicopedia.com Urologist maintained male infertility, potency, and health blog


REFERENCES


VARICOCELE, PEDIATRIC

Hyeyoung Lee, MD, MS
Harry P. Koo, MD, FAAP, FACS

DESCRIPTION
A pediatric varicocele is defined as an abnormal dilatation of the internal spermatic veins in the pampiniform plexus of the spermatic cord in a male generally <18 yr of age. Usually asymptomatic, may cause testicular hypotrophy.

EPIDEMIOLOGY
Incidence
- Reported frequency of varicoceles in adolescent boys is ~16%, developing as a result of testicular enlargement and consequent increased blood flow in puberty
- Actual incidence may be underestimated and detected later during evaluation of infertility in adulthood

Prevalence
- 8–16% of adolescent males but unusual in prepuberty
- 50% left sided
- 1–7% right sided
- 2% bilateral
- No racial, cultural, or geographic predilection
- Unclear how it affects future fertility or hypotrophy

Risk Factors
- Increased height, and relatively low weight and body mass index
- Congenital incompetence or absence of valves of internal spermatic vein
- Acquired incompetence of valves, extrinsic compression increasing intravascular pressure (eg, inguinal hernia repair, retroperitoneal pathologic process)
- May be associated with generalized venous abnormality

Genetics
- Varicocele prevalence as high as 67% has been reported in sons of fathers with varicocele
- Risk of varicocele in 1st-degree relatives is 2–11%

Pathophysiology
- Unique angle of left spermatic vein entering the left renal vein compared to right spermatic vein entering IVC
- Left spermatic vein is 8–10 cm longer than the right
- “Nuckler” phenomenon of left renal vein passing between aorta and superior mesenteric artery
- Erect posture (no varicocele in four-legged animals)
- Different mechanisms are hypothesized to cause testicular insult

- Hyperthermia: Increased testicular arterial blood flow interferes with countercurrent heat exchange
- Increased testicular temperature affects enzymatic reactions
- Decrease proliferation and increased apoptosis of germ cells
- Heat shock protein A2, oxidative stress patterns, calcium-channel, and SDF-1 expression altered

- Testicular hypotrophy: Significantly testicular volume loss in 30–70% of adolescents with a varicocele:
  - Most rapid growth of testses between ages 11 and 16 yr
  - Testicular hypotrophy reversible in 90% of patients after varicocelectomy

- Venous stasis: Possible oxygen deprivation in testes
- Endocrine imbalance: Abnormal response in patients with varicocele to GnRH stimulation
- Unilateral flow if affects future fertility or hypotrophy

Associated Conditions
Secondary causes can include retroperitoneal tumor, renal mass with renal vein extension, renal vein thrombosis, retroperitoneal fibrosis.

GENERAL PREVENTION
None

DIAGNOSIS

History
- Usually asymptomatic, associated pain reported in 2–11%
- Symptomatic dull ache or fullness in scrotum, worsened with activity
- Occasional testicular pain due to venous congestion
- Change in size with position or Valsalva
- Find out routine pediatric physical exam

Physical Exam
- Examine patient, weight, and supine, with and without Valsalva
- Grading criteria:
  - Grade 0: Subclinical, not visible or palpable, only detected by ultrasound (US)
  - Grade 1: Palpable only with Valsalva
  - Grade II: Palpable but not readily visible
  - Grade III: Visible through scrotal skin

- Ultrasound: Determines size and extent of varicocele

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Semen analysis: Can be performed if Tanner stage 5 or >18 yr old
- Response to GnRH stimulation: Not useful for surgical decision making

Imaging
- Scrotal US
- Color Doppler US can detect subclinical varicoceles that are not palpable
- Decrease in volume of 2 cc or 20% size warrants intervention

- Scrotal vein diameter >2 mm in standing position with Valsalva is noted in up to 96% of boys with grade III varicocele
- Lambert formula: 0.71 (length × width × depth

Pathologic Findings
- Varicocele is known to be associated with high levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and low testosterone levels
- Endothelial proliferation and basement membrane thickening in venules and capillaries
- Germ cell maturation arrest and sloughing of germ cells
- Heat shock protein A2, oxidative stress patterns, calcium-channel, and SDF-1 expression altered

DIAGNOSTIC PROCEDURES/SURGERY
Diagnosis confirmed by physical exam or US
DIFFERENTIAL DIAGNOSIS
- Spermatocoele (seminoma)
- Hydrocele:
  - Communicating
  - Scrotal
- Spermatic cord
- Inguinal hernia
- Lipoma of cord
- Peritesticular fibromyxosarcoma

TREATMENT

GENERAL MEASURES
- Management is either observation or surgical intervention
- Nonoperative treatment can be proposed when the patient or guardian fully understands the need for lifelong follow-up and the potential for progressive subfertility
- Surgical indications in the pediatric population:
  - 2 cm or 20% size discrepancy between testicles based on US or orchidometer measurements
  - Symptomatic
  - Bilateral varicoceles
  - Abnormal semen analysis
  - Solitary testis with varicocele

SURGERY/OTHER PROCEDURES
- Surgical techniques based on comfort and experience of surgeon
- Techniques described in more detail in Section 1: "Varicocele, Adult"
- 50–75% of patients demonstrate catch-up growth, not necessarily meaning improved semen quality
- Testicular artery sparing:
  - High ligation of vessels (Palomo)
  - Retroperitoneal or transperitoneal
  - Should be considered in adolescents
- Preferred in adults because of concerns with infertility
- Doppler can help identify
- Possible decreased fertility

MEDICATION
- N/A

SECONDARY TREATMENT
- Radiation Therapy
  - Varicocele, Adult

ADDITIONAL TREATMENT
- Radiation Therapy
  - N/A
- Additional Therapies
  - N/A
- Complementary & Alternative Therapies
  - N/A

ONGOING CARE

PROGNOSIS
- No definitive evidence that adolescents with varicocele will have impaired fertility in future or that surgical correction will improve/prevent infertility

COMPPLICATIONS
- Recurrence or persistence of varicocele:
  - 1–35% depending on technique (3)
- Postoperative hydrocele (1–9%)
- Testicular atrophy
- Failure of catch-up growth
- Possible decreased fertility

FOLLOW-UP
- Patient Monitoring:
  - If asymptomatic and no testicular size discrepancies, not necessarily meaning improved semen quality
  - Contraindicated for recurrent/persistent varicocele
  - Single port laparoscopic approach provides
  - Laparoscopic and open suprainguinal
  - Scrotal, scrotal, and scrotal
  - Communicating varicocele
  - Provides facilitated artery and lymphatic sparing
  - Low-risk of hydrocele
  - Time consuming
  - Radiographic embolization:
    - Simultaneous in children and adolescents, less successful than open or laparoscopic approach
    - Significant radiation exposure
    - Generally reserved for recurrent/persistent varicocele

REFERENCES

ADDITIONAL READING
- Varicocele, Adult

CODES
- ICD9
  - 459.8 Scrotal varices
  - 456.4 Scrotal varices
  - 752.89 Other specified anomalies of genital organs
- ICD10
  - N6.1 Scrotal varices
  - N6.9 Other specified disorders of veins
  - Q64.8 Other specified congenital malformations of urinary system

CLINICAL/SURGICAL PEARLS
- Varicocele is found in 8–16% of adolescents.
- Genetic susceptibility, thin and tall body habitus, and various abnormalities increase the risk of varicocele.
- Surgical treatment is indicated if testicular hypotrophy, bilateral varicocele, abnormal semen analysis or symptoms.
- Laparoscopic and open supravesical varicocelectomy are almost equally effective.
- Microsurgical approach minimizes risk of hydrocele development.
Genetics of CUAVD less understood

- CBAVD without clinical CF

- CFTR: Most common
  - Mutations of cystic fibrosis transmembrane conductance regulator (CFTR)
  - Function: Chloride channel
  - Sites:
    - Lungs, liver, pancreas, intestines
  - Vas deferens/GU tract

- CFTR mutation
  - Point mutations most common in CF
  - Alter chloride transport
  - Thick, viscous secretions
  - Multi-organ disease in CF
  - Obstruction/regeneration of vasa vs. agenesis.
  - Vas deferens is a derivative of mesonephric (Wolffian) duct.
  - Wolfian abnormalities often seen with AVD
  - Seminal vesicle (SV) hypoplasia or absence
  - Causes low-volume ejaculate.
  - See: Associated Conditions

- CF
  - CBAVD is considered the mildest manifestation of CFTR disease spectrum
  - CF is most severe
    - Nearly all CF patients have CBAVD
  - Genitourinary abnormalities
    - Renal agenesis
  - Abnormalities of mesonephric structures
    - Ejaculatory ducts
    - Vasa deferentia
  - Low testicular volume
    - See more commonly when CFTR mutations not detected (48)
  - May indicate primary testicular cause

GENERAL PREVENTION
CFTR screening of both partners can help assess and manage risk of CF and CBAVD for offspring

POTENTIAL SCREENING TESTING
- CFTR genetic mutation screen
  - Part of evaluation for low-volume azoospermia
  - Evaluates for mild vs. severe mutations
  - Can prove, but not exclude, a congenital form of CF
  - Risk is difficult to predict with some rare CFTR mutations
  - Negative CFTR screen reduces, but does not eliminate, risk of being a carrier
  - Thus, suggest screening in female partner
  - CFTR screening for partner
  - Helps guide genetic counseling regarding CF risk for offspring

- Diagnostic tests & interpretation
  - Lab
    - Potential semen analysis findings:
      - Low volume (<1.5 cc)
      - Azoospermia if bilateral obstruction
      - Acidic pH (increased SV fluid)
      - Seminal fructose might be negative
      - Presence of sperm rules out bilateral obstruction
    - Postejaculatory utrality
      - Evaluates for retrograde ejaculation
    - For all men with vasal agenesis
      - CFTR genetic mutation screen
    - Seminal vesicle (SV) hypoplasia or absence
    - Evaluates for retrograde ejaculation
    - Seminal vesicle (SV) hypoplasia or absence
    - Causes low-volume ejaculate.
- Pathophysiology
  - CFTR
    - Cystic fibrosis transmembrane conductance regulator
    - Function: Chloride channel
    - Sites:
      - Lungs, liver, pancreas, intestines
    - Vas deferens/GU tract
  - CFTR mutation
    - Point mutations most common in CF
    - Alter chloride transport
    - Thick, viscous secretions
    - Multi-organ disease in CF
    - Obstruction/regeneration of vasa vs. agenesis.
    - Vas deferens is a derivative of mesonephric (Wolffian) duct.
    - Wolfian abnormalities often seen with AVD
    - Seminal vesicle (SV) hypoplasia or absence
    - Causes low-volume ejaculate.
    - See: Associated Conditions
- CBAVD
  - CBAVD is considered the mildest manifestation of CFTR disease spectrum
  - CF is most severe
    - Nearly all CF patients have CBAVD
  - Genitourinary abnormalities
    - Renal agenesis
  - Abnormalities of mesonephric structures
    - Ejaculatory ducts
    - Vasa deferentia
  - Low testicular volume
    - See more commonly when CFTR mutations not detected (48)
    - May indicate primary testicular cause

- Diagnostic tests & interpretation
  - Lab
    - Potential semen analysis findings:
      - Low volume (<1.5 cc)
      - Azoospermia if bilateral obstruction
      - Acidic pH (increased SV fluid)
      - Seminal fructose might be negative
      - Presence of sperm rules out bilateral obstruction
    - Postejaculatory utrality
      - Evaluates for retrograde ejaculation
    - For all men with vasal agenesis
      - CFTR genetic mutation screen
    - Seminal vesicle (SV) hypoplasia or absence
    - Evaluates for retrograde ejaculation
    - Seminal vesicle (SV) hypoplasia or absence
    - Causes low-volume ejaculate.
- Pathophysiology
  - CFTR
    - Cystic fibrosis transmembrane conductance regulator
    - Function: Chloride channel
    - Sites:
      - Lungs, liver, pancreas, intestines
    - Vas deferens/GU tract
  - CFTR mutation
    - Point mutations most common in CF
    - Alter chloride transport
    - Thick, viscous secretions
    - Multi-organ disease in CF
    - Obstruction/regeneration of vasa vs. agenesis.
    - Vas deferens is a derivative of mesonephric (Wolffian) duct.
    - Wolfian abnormalities often seen with AVD
    - Seminal vesicle (SV) hypoplasia or absence
    - Causes low-volume ejaculate.
    - See: Associated Conditions
  - CBAVD
    - CBAVD is considered the mildest manifestation of CFTR disease spectrum
    - CF is most severe
      - Nearly all CF patients have CBAVD
    - Genitourinary abnormalities
      - Renal agenesis
    - Abnormalities of mesonephric structures
      - Ejaculatory ducts
      - Vasa deferentia
    - Low testicular volume
      - See more commonly when CFTR mutations not detected (48)
      - May indicate primary testicular cause
    - General Prevention
      - CFTR screening of both partners can help assess and manage risk of CF and CBAVD for offspring
    - Physical Exam
      - Findings in AVD
        - Absent vas deferens (bilateral/unilateral)
        - Absent or hypoplastic body/tail of epididymis
        - Present caput epididymis, often dilated
      - Considerations:
        - Evaluate for skip lesions
        - Check for other causes of infertility
        - Varicocele
        - Azoospermic tests
        - Normal in CBAVD:
          - Tests size (<3.5 cm length, 2–3 cm diameter)
        - Digital rectal exam:
          - Prostate usually normal
          - Tis usually nonpalpable/hypoplastic, may be cyclic
GENERAL MEASURES

- Transrectal ultrasound (TRUS)
  - Allows for evaluation of low-volume azoospermia
  - Not necessary with CBAVD
- Evaluate for ejaculatory duct obstruction
- Normal findings:
  - SV diameter: 0.3–0.5 cm
  - SV length: 1.4–4.6 cm
- Ejaculatory duct diameter: <0.1 cm
- Abnormal findings:
  - SV diameter: >1.5 cm
  - SV length: >4.6 cm
- Vaso-epididymal obstruction
- Varicocele

Differential Diagnosis

- Spermatogenic failure causing azoospermia
  - Congenital/gene causes:
    - 17q12-q21 microdeletions
    - Sex chromosome abnormalities (D4Y male)
    - Undescended testes
  - Inflammatory causes:
    - Gonadotropin exposure
    - Radiation
    - Experimental
- Obstruction causing azoospermia
  - Inflammatory or infectious causes:
    - Tuberculosis
    - Sexually transmitted infections
    - Environmental
    - Radiation
  - Congenital causes:
    - Undescended testes
    - Sex chromosome abnormalities (XY male)
    - Y chromosome microdeletions
  - Drugs:
    - Gonadotropin exposure
    - Radiation

Pathologic Findings

- CF or CBAVD in offspring

Diagnostic Procedures/Surgery

- Vasography
  - Fluoroscopic injection of contrast material
  - Evaluates for sperm retention
- Vasography (see below)
- Transrectal ultrasound (TRUS)
  - Assesses patency of vas/vasa
- Fluoroscopic injection of contrast material
  - Evaluates for ejaculatory duct obstruction
  - Not necessary in CBAVD

Second Line

- Medications used only to treat other conditions
- Fertilization and pregnancy rates with ART in obstructive azoospermia are most closely tied to obstructive azoospermia
- Sperm retrieval techniques (ART)
  - IVF/ICSI
  - Intrauterine insemination
  - See Surgery, below

Sperm retrieval techniques

- Donor semen
- Intravaginal insemination
- ICSI
- Consider referral for genetic counseling regarding CF risk for offspring

SURGERY/OTHER PROCEDURES

- Sperm retrieval for ART
  - Testicular sperm extraction (TESE)
  - Microsurgical epididymal sperm aspiration (MESA)
  - Sperm can be used for IVF or ICSI

ADDITIONAL TREATMENT

- Radiation Therapy
- Additional Therapies
- Complementary & Alternative Therapies

ONGOING CARE

- Ongoing care includes management of infertility
- Continuous monitoring of semen analysis
- Medications used only to treat other conditions

COMPLICATIONS

- Of limited utility in CBAVD since reconstruction of ejaculatory ducts, due to risk of damage/obstruction at vasa entry point
- Of limited utility in CBAVD since reconstruction usually not an option

TREATMENT

- Infertility treatment requires assisted reproductive techniques (ART)
- Sperm retrieval techniques
  - See Surgery, below
- Donor semen
  - Intravaginal insemination
  - ICSI
- Consider referral for genetic counseling regarding CF risk for offspring

PROGNOSIS

- Fertilization and pregnancy rates with ART in obstructive azoospermia
- Penetrance of cystic fibrosis gene mutations.
- Incomplete penetrance of cystic fibrosis gene mutations.
- Low-volume ejaculate in CBAVD and CUAVD is usually not an option

MEDICATION

- First Line
  - Medications used only to treat other conditions
- Fertilization and pregnancy rates with ART in obstructive azoospermia
- Intrauterine insemination
- IVF/ICSI

SECOND LINE

- IVF/ICSI

COMPLEMENTARY & ALTERNATIVE THERAPIES

- Radiation therapy
- Additional therapies

Coding

ICD9
- 752.89 Other specified anomalies of genital organs
- 752.89 Other specified anomalies of genital organs
- 752.89 Other specified anomalies of genital organs
- 752.89 Other specified anomalies of genital organs

ADDITIONAL READING


REFERENCES

VASECTOMY AND POSTVASECTOMY PAIN SYNDROME

Christopher L. Starks, MD
Edmund S. Sabanegh, Jr, MD

BASICS

DESCRIPTION

- Vasectomy is a surgical procedure that creates a disruption of the vas deferens leading to permanent male sterilization
  - Vasectomy is the safest, least expensive, and most reliable form of sterilization (1,2)
- Postvasectomy pain syndrome: Poorly understood and largely unpredictable chronic testicular pain
  - 3 mo duration after vasectomy
  - Variable constellation of symptoms including but not limited to orchialgia, pain with daily activities, and pain with intercourse/jaculation

EPIDEMIOLOGY

Incidence

- Vasectomy: Number of vasectomies performed each year is >150,000–500,000
- Postvasectomy pain syndrome: 15–35% of men may experience persistent mild to troublesome testicular discomfort following vasectomy with 4% experiencing significant long-term testicular pain
- Long-term pain requiring some kind of intervention or surgical therapy occurs in up to 1 in 1,000 vasectomized men

Prevalence

- ~5% of couples of reproductive ages rely on vasectomy for contraception

RISK FACTORS

N/A

GENETICS

N/A

PATHOPHYSIOLOGY

- Vasectomy: Vasectomy involves disrupting the vas deferens via several methods: electrocautery, clips, and/or fascial interposition
  - Vasectomy disrupts the blood-tissue barrier
  - Antisperm antibodies in 60–80% of men
  - Does not appear to result in cell-mediated immunity

- Postvasectomy pain syndrome: Proposed mechanisms:
  - Increased pressure on the testicle and epididymis
  - Nerve entrapment
  - High pressure may cause blowouts of sperm resulting in tender sperm granulomas and epididymal regions

ASSOCIATED CONDITIONS

N/A

GENERAL PREVENTION

No preoperative factors have been identified in the postvasectomy pain syndrome

DIAGNOSIS

HISTORY

- Vasectomy: A careful history ensuring that the patient understands that this is a permanent method of sterilization should occur
  - A directed history including previous scrotal and inguinal surgery
- Postvasectomy pain syndrome: Mean time to onset of pain reported as 2 yr
  - Symptoms associated with postvasectomy pain syndrome include:
    - Persistent pain in the groin, testicle, or epididymis
    - Pain with an erection and/or engaging in sexual activity
    - Decreased libido and/or erections

PHYSICAL EXAM

- Pre-vasectomy: Analysis of testicular histology after vasectomy
  - Routine histologic exam of excised vas segment is not required
- Post-vasectomy pain syndrome: Physical exam commonly reveals:
  - Fullness/tenderness at the proximal vas, epididymis, or at a granuloma site
  - Evidence of sperm granuloma
  - Epididymal tenderness or other masses
  - Evince for evidence of groin hernia

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Nonsteroidal anti-inflammatory medication
  - Usually not necessary
- Ultrasound imaging can confirm epididymal engorgement, thickening, or nodularity

TREATMENT

GENERAL MEASURES

First Line
- Nonsteroidal anti-inflammatory medication
  - Usually not necessary
- Ultrasound imaging can confirm epididymal engorgement, thickening, or nodularity

ALERT

Patients must be fully informed that an alternative form of birth control must be used immediately after vasectomy and until a semen analysis is clear.

DIFFERENTIAL DIAGNOSIS

- Vasectomy: A minimally invasive or “no-scalpel vasectomy” technique should be used
  - Methods of performing vasectomy are based upon surgeon preference. These include:
    - Excision of a portion of the vas
    - Clips vs. suture ligation of vas ends
    - Cautery of mucosa
    - Interposition of the vas ends between fascia (may reduce recanalization)
- Postvasectomy pain syndrome:
  - Conservative therapies are the mainstay: Scrotal support, activity limitation, sitz baths, ice-packs

SECOND LINE
- Tricyclic antidepressants and neuroleptic medication (eg, gabapentin) can be considered

PHYSICAL EXAM

- Pre-vasectomy pain syndrome: Analysis of testicular histology after vasectomy
  - Routine histologic exam of excised vas segment is not required
- Post-vasectomy pain syndrome: Analysis of testicular histology after vasectomy
  - Demonstrates disturbance of the seminiferous tubules, interstitial fibrosis, and reductions in the seminiferous cell population

MEDICATION

First Line
- Nonsteroidal anti-inflammatory medication
  - Usually not necessary
- Ultrasound imaging can confirm epididymal engorgement, thickening, or nodularity

SECOND LINE
- Tricyclic antidepressants and neuroleptic medication (eg, gabapentin) can be considered
VASECTOMY AND POSTVASECTOMY PAIN SYNDROME

SURGERY/OTHER PROCEDURES
- Postvasectomy pain syndrome
- With the failure of long-term conservative management, more invasive treatments: Sperm granuloma excision, denervation of the cord, open-ended vasectomy, epididymectomy, and orchiectomy may be considered
- With pain localized to a sperm granuloma on physical exam, granuloma excision with occlusion of vas with intraluminal cautery usually relieves the pain and reduces the risk of recurrence
- In 1 study up to 50% were pain-free following epididymectomy
- Epididymectomy renders the vasectomy completely irreversible and may jeopardize the blood supply to the testes, which can result in ischemic atrophy
- Vasectomy reversal: There are no controlled trials, but reversal may offer best chances of significant improvement (50% pain free in 1 series). The drawback is that fertility is restored (3)

ADDITIONAL TREATMENT
Radiation Therapy

Additional Therapies
- Postvasectomy pain syndrome
- Men with intractable symptoms might benefit from a multidisciplinary team approach involving a urologist and pain-clinic specialist, including a psychologist
- Many men with chronic orchalgia also had signs of major depression or chemical dependencies (4)
- Spermatic cord blocks
- Local neurolysis/cordotomy
- Transrectal injections into the region of pelvic plexus (5 mL bupivacaine and methyl prednisolone) have been used to manage cases of ischemic atrophy
- Denervation of the cord, clips, suture ligation, cautery, and fascial interposition
- There are rare complications from vasectomy
- Other complications from vasectomy include hematoma and postvasectomy pain syndrome
- Vasectomy should be considered a failure if nonmotile sperm are present at 6 mo after vasectomy

COMMENTS
- Vasectomy should be considered if they do not desire permanent sterilization

ONGOING CARE

PROGNOSIS
- Postvasectomy pain syndrome does not work immediately
- They should use contraceptives and consider themselves fertile until a postvasectomy semen analysis (PVSA) is negative
- Even once vas occlusion is confirmed, the risk of preventing pregnancy is not 100% reliable. Risk of pregnancy is 1 in 2,000 for men who have PVSA showing azospermia or rare nonmotile sperm
- Repeat vasectomy is needed in ~1%
- Despite counseling, up to 5% of men will change their mind postvasectomy and request a vasectomy reversal

COMPLICATIONS
- Bleeding/hematoma: ~1–2%
- Infection: <1%
- Symptomatic sperm granuloma: <1%
- Postvasectomy pain syndrome: 15–33%

FOLLOW-UP

Patient Monitoring
- PVSA should be a first-unsurgated semen sample and should be examined within 1–2 hr of ejaculation
- PVSA can be made by the patient between 8–16 wk after vasectomy
- Acceptable PVSA show azospermia or only rare nonmotile sperm
- Vasectomy should be considered a failure if motile sperms are present at 6 mo

Patient Resources

REFERENCES

ADDITIONAL READING
- See Also (Topic, Algorithm, Media)
- Testis, Pain (Orchalgia)
- Vas Deferens, Obstruction
- Vasectomy Reversal

CODES
ICD9
- 631.18 Other acute postoperative pain
- 608.89 Other specified disorders of male genital organs
- Z16.52 Vasectomy status

ICD10
- C68.18 Other acute postprocedural pain
- N00.8 Other specified disorders of male genital organs
- Z06.2 Vasectomy status

CLINICAL/SURGICAL PEARLS
- A minimally invasive approach to accessing the vas (ie, no scalpel vasectomy) should be used
- There are a variety of methods and techniques that can be used to disrupt the vas bilaterally including excision, clips, subcuticular suture, cautery, and facial incision
- There are rare complications from vasectomy including hematoma and postvasectomy pain syndrome
VESICOURETERAL REFLUX, ADULT
Sanjay S. Kasturi, MD

DESCRIPTION

- Vesicoureteral reflux (VUR) is defined as retrograde passage of urine from the bladder into the ureter and/or renal pelvis and calyces.
- VUR in the presence of bacteria is a risk factor for pyelonephritis and may lead to upper tract pathologic changes, which may be unilateral or bilateral, primary or secondary.
- A more common problem in children, it can be associated with significant morbidity in adults and may be an uncommonly unrecognized cause of hypertension (HTN) in this population.

EPIDEMIOLOGY

Incidence
- 5% of adults have VUR at the time of evaluation.
- Female
- Family history of VUR

Secondary VUR
- Conditions that predispose to secondary VUR (eg, neurologic bladder)
  - Genitourinary TB can cause the ureteral orifices to become fixed and relatively patulous
  - Bacterial cystitis can often cause transient ureteral reflux due to inflammation
  - Patients who have undergone urinary diversion (ileo/colonic conduit) may develop ureteric reflux
  - Congenital deficiency of the intravesical tunnel is the most common etiology

PHYSIOPATHOLOGY

Primary VUR (1)
- Failure of development or breakdown of the distal ureteral antireflux mechanism
- Normally, the distal 4–5 cm of the ureter courses through the muscular wall of the bladder before reaching the bladder trigone
- This tunnel prevents reflux of urine
- Congenital deficiency of the intravesical tunnel is the most common etiology

Secondary VUR
- Disorders that cause elevated intravesical pressure: BPH, spinal cord injury, MS, and other neurologic diseases
- Patients who have undergone urinary diversion (ileo/colonic conduit) or Bladder replacement (prosthetic neobladder, catheterizable diversions) commonly have VUR
- Bacterial cystitis can often cause transient ureteral reflux due to inflammation

Diagnosis

History
- History of VUR in childhood
- Family history of VUR
- Recurrent UTIs
- Simple cystitis leading to fever and flank pain suggestive of pyelonephritis
- Lower urinary tract voiding symptoms, suggesting outlet obstruction or neuropathic bladder

Physical Exam
- CVK tenderness with pyelonephritis
- Digital rectal exam for BPH
- Palpable bladder
- Neurologic impairment
- HTN (if renal compromise)

Diagnostic Tests & Interpretation

Lab
- Blood testing is not necessary, except for severe cases in which renal function should be evaluated.
- Proteinuria (if renal compromise)

Imaging
- US can show hydronephrosis dependent on severity of VUR
- VCUG: Definitive test for identifying and grading the severity of reflux. It may also point toward the cause of VUR
- A nuclear medicine cystogram (indirect VCUG): – Can be performed with MAG3
  - Provides less anatomic information than the VCUG but does not require catheterization

Pathologic Findings
- Renal lesions (scarring) can be associated with higher grades of reflux
- Chronic scarring may, over time, cause HTN

DIFFERENTIAL DIAGNOSIS

- Other causes of flank (renal) pain and infection (eg, renal colic, urosepsis/junction obstruction) (see Section I: “Flank Pain”)
- Other causes of hydroureteronephrosis or ureteral obstruction (see Section I: “Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult”)

Medication

First Line
- Patients with recurrent UTI may benefit from prophylactic antibiotics
- Other causes of VUR (see Section I: “Hydronephrosis/Hydroureteronephrosis, Adult”)
- Early treatment of cystitis can prevent progression to pyelonephritis.
VESICOURETERAL REFLUX, ADULT

Second Line

Secondary VUR may benefit from medical treatment of underlying cause:

– Anticholinergic preparations in detrusor overactivity
– α-Blockade or 5α-reductase inhibition in bladder outlet obstruction

SURGERY/OTHER PROCEDURES

Primary VUR rarely requires surgical intervention in adults; however, where indicated procedures include:

– Endoscopic treatment: Injection of bulking agents below the ureteral orifice:
  ◦ Initial results are good; however, long-term follow-up is scant

Several agents have been used for endoscopic correction of VUR:

◦ Polytetrafluoroethylene (Teflon)
◦ Cross-linked bovine collagen, dextranomer/hyaluronic copolymer (Deflux)

Since the FDA approval of Deflux in 2001, this has been the most commonly used injectable agent for VUR

– Ureteric reimplantation can be undertaken transvesically, extravesically, or by a combination of both:
  ◦ Some common techniques include: Cohen cross-trigonal, Politano–Leadbetter, Lich–Gregoir (extravesical) reimplantations

ADDITIONAL TREATMENT

Complementary & Alternative Therapies
Some data suggest cranberry juice and live-culture yogurt can be effective in preventing UTI

ON GOING CARE

PROGNOSIS
Depends on underlying etiology and severity of VUR

COMPICATIONS (3,4)

– Chronic pyelonephritis
– Reflux nephropathy
– Renal impairment in primary VUR unless pre-existing from childhood, but can be encountered in secondary VUR
– UTI
– Urolithiasis

FOLLOW-UP

Patient Monitoring

Medical follow-up is unnecessary in patients without HTN or proteinuria, unless the patient develops recurring infections, at which point repeat workup is needed

– Patients with intrinsic renal disease due to prior reflux (in childhood) require follow-up of BP, creatinine, and urine protein

Patient Resources

REFERENCES


ADDITIONAL READING


See Also (Topic, Algorithm, Media)

– End-Reflux Classification System
– Hydronephrosis/Hydronephrosis (Dilated Ureter/Renal Pelvis), Adult
– Reflux Nephropathy
– Pyelonephritis, Chronic
– Urinary Tract Infection (UTI), Adult Male
– Urinary Tract Infection (UTI), Complicated, Adult
– Vesicoureteral Reflux, Adult Image

CODES

ICD9

593.70 Vesicoureteral reflux unspecified or without reflux nephropathy
593.721 Vesicoureteral reflux with reflux nephropathy, unilateral
593.729 Vesicoureteral reflux with reflux nephropathy NOS

ICD10

N13.30 Vesicoureteral reflux, unspecified
N13.321 Vesicoureteral reflux with reflux nephropathy without hydronephrosis
N13.322 Vesicoureteral reflux with reflux nephropathy with hydronephrosis

CLINICAL/SURGICAL PEARLS

Women with VUR tend to present with infections, while men tend to present with HTN and proteinuria.
VESICOURETERAL REFLEX, PEDIATRIC

Kathleen Kieran, MD, FAAP, FACS
Christopher S. Cooper, MD, FAAP, FACS

ASSOCIATED CONDITIONS

- Primary VUR: Hydronephrosis, UTI, bladder/bowel dysfunction
  - V: Severe ureteral tortuosity
  - IV: Renal pelvis and calyces with ureteral tortuosity
  - II: Renal pelvis and calyces without dilatation
  - I: Ureter only
- Secondary VUR: Optimizing lower urinary tract function to prevent elevated pressure and decreased bladder compliance

GENETICS

- Likely autosomal dominant with incomplete penetrance
- Seen in 27–51% of siblings of children with VUR, up to 100% in identical twins
- Seen in 50–64% of children of parents with VUR

PATHOPHYSIOLOGY

- The normal ureter enters the bladder at an obtuse angle through the bladder wall; with bladder filling on contraction, the ureter is compressed and retrograde flow of urine (reflux) is prevented.
- Primary VUR is associated with a functionally shortened submucosal tunnel
- Secondary VUR occurs in the setting of abnormal lower urinary tract function with resulting increase in bladder pressures
- VUR is graded on a scale of I–V
  - I: Linear only
  - II: Renal pelvis and calyces without dilatation
  - III: Renal pelvis and calyces with calyceal blunting
  - IV: Renal pelvis and calyces with ureteral tortuosity
  - V: Severe ureteral tortuosity

DIAGNOSTIC TESTS & INTERPRETATION

- Complete physical exam for baseline functional information
  - Neurologic exam for spina bifida
  - Abdominal and pelvic exam:
    - Palpable kidneys secondary to hydronephrosis
    - Palpable bladder secondary to incomplete emptying
  - CVaT tenderness
  - Suprapubic tenderness
  - Circumcision status in males
- Blood pressure should be compared with age-adjusted normative values
- Identify or exclude causes of secondary VUR, eg, neurogenic bladder

DIAGNOSTIC PROCEDURES/SURGERY

- Voided specimen urine samples are more accurate for diagnosis of infection but are more costly and invasive; collect in patients with high index of suspicion based on voided sample or in patients with history of VUR
- Blood cultures sent only when urine analysis or clinical presentation is suspicious for infection
- Serum creatinine and electrolytes are not routinely checked unless significant sonographic anomalies in renal units, history of multiple febrile UTIs, or significant renal scarring on radionuclide imaging; evaluate at initial diagnosis and again only when substantial change in clinical condition

DIAGNOSTIC TESTS & INTERPRETATION

- Voided specimen urine for assessment of proteinuria, evidence of infection
- Catherized urine samples are more accurate for diagnosis of infection but are more costly and invasive; collect in patients with high index of suspicion based on voided sample or in patients with history of VUR
- Cultures sent only when urine analysis or clinical presentation is suspicious for infection

DIAGNOSTIC PROCEDURES/SURGERY

- Diagnosis of renal scarring may suggest presence of VUR but are not sensitive or specific enough for definitive diagnosis
- Renal ultrasound utilized to help define upper tract anatomy, eg, hydronephrosis or duplicated systems, assess quality of renal parenchyma, ensure adequate renal growth
- Renal scintigraphy (DMSA scan) is the gold standard for detection of renal scarring
  - Differential renal function
  - Diagnosis of acute pyelonephritis/scarring

DIFFERENTIAL DIAGNOSIS

- Should be based on the abnormal symptom or clinical finding that prompted the evaluation
  - UTI: Dysuria, lower tract infection vs. pyelonephritis
  - Hydronephrosis: Physiologic hydronephrosis, ureteropelvic junction obstruction, ureteropelvic junction obstruction, congenital megareter
  - Always consider secondary causes when evaluating for VUR

GENERAL MEASURES

- Counsel parents on pathophysiology and natural history of VUR; Causes, contraindications, potential sequelae, likelihood of resolution, risks and benefits of alternative treatment plans
- Spontaneous resolution of primary reflux is common and depends on initial grade of reflux, gender, age, voiding dysfunction, presence of renal scarring, and timing of VUR on VCUG
- Goal of intervention is to prevent renal scarring, recurrent febrile UTI, and long-term complications such as hypertension and renal insufficiency

IMAGING

- Voiding cystourethrogram (VCUG) or radionuclide cystogram
ADDITIONAL TREATMENT

Surgery/Other Procedures

Second Line

Management of elimination habits:
- Use of anticholinergic medications when reflux is refractory to behavioral modification

Surgey/other procedures
- Endoscopic intervention:
  - Can be performed via intra- or extravesical
  - Higher success rate (95–99%)
  - Only 1 currently in use in US: Deflux, Salix
- Surgical intervention recommended for persistent VUR, worsening renal function, recurrent UTIs

Patient Monitoring
- Patients with VUR:
  - Annual complete physical exam with blood pressure check and urinalysis (proteinuria, infection)
  - Imaging: No consensus on interval, but general agreement of renal ultrasound and cystography every 1–2 yr

FOLLOW-UP

Patient Monitoring
- Patients with VUR:
  - Annual complete physical exam with blood pressure check and urinalysis (proteinuria, infection)
  - Imaging: No consensus on interval, but general agreement of renal ultrasound and cystography every 1–2 yr

ICD9
- 582.73 Vesicoureteral reflux unspecified or without reflux nephropathy
- 753.5 Estrophy of urinary bladder
- 756.71 Prune belly syndrome

ICD10
- N13.70 Vesicoureteral reflux, unspecified
- O04.15 Exstrophy of urinary bladder, unspecified
- Q94.9 Prune belly syndrome
ASSOCIATED CONDITIONS
- Genetics
  - Prevalence in USA: About 7,000 people
- Incidence
  - Rare: 1 in 35,000 live births
- Prevalence
  - Prevalence in USA: About 7,000 people
- Risk Factors
  - Inheritance of a mutated VHL allele
  - No gender or racial predilection
- Genetics
  - Autosomal dominant inheritance pattern
  - VHL is a tumor suppression gene on chromosome 3p25–26 (3)
  - Affected individuals inherit 1 copy of a mutated VHL from the affected parent
  - The loss or mutation of the 2nd (initially normal) allele in the cell leads to tumor formation (mechanism known as a 2-hit model)
  - Present technology identifies the mutated gene in 100%
- Pathophysiology
  - Mutated VHL leads to aberrant VHL protein (pVHL)
  - Abnormal pVHL is unable to target hypoxia inducible factor (HIF) for degradation
  - Accumulation of HIF protein upregulates downstream genes such as VEGF, GLUT-1, PGF, TGF-β, HIF, and many others, leading to tumor formation
- Associated Conditions
  - Multifocal and bilateral ccRCC in 50%
  - Renal cysts seen in up to 70%
  - Papillary cystadenomas in about 20%
  - CNS hemangioblastomas in 75%
  - Retinal angiomas in 50–50%
  - Pancreatic cysts seen in up to 60%
  - ELST in 5–10%
  - Papillary cystadenomas of the epididymis or broad ligament in <1%
  - VHL-associated lung cysts/hematomas in <1%
  - VHL-associated ovarian tumors in <1%

GENERAL PREVENTION
- Close surveillance of affected individuals and timely intervention
- Genetic screening of family to initiate early surveillance

DIAGNOSIS

HISTORY
- Early history of RCC or pheochromocytoma, CNS or pancreatic surgery, hearing or vision problems is often elicited
- Patients may present with ≥1 symptoms related to the organ involved
- Renal tumors and cysts:
  - Usually detected incidentally or during screening by imaging in VHL patients
  - May present with hematuria, flank pain, abdominal fullness, weight loss, cachexia in advanced disease
- Pheochromocytoma:
  - Headaches, palpitations, episodic sweating, anxiety attacks, personality changes
  - Severe hypertension (HTN) leading to hemorrhagic stroke
  - May present with weight loss, cachexia, bone pain, or cough in setting of metastatic disease
- May be asymptomatic
- CNS hemangioblastomas:
  - Often asymptomatic
  - Headaches, vertigo, ataxia, vomiting, wide-based gait, sensory loss, seizures
  - Size and location of the lesion(s) often determine symptoms
- Retinal angiomas:
  - Blurred or decreased vision, eye pain
  - If undetected, may present with blindness
- Pancreatic NET and cysts:
  - Most are asymptomatic
  - Diabetes, steatorrhea, and diabetes may occur if panceas is replaced by cysts
  - Early satiety if pancreatic cysts are large and compressing the stomach
  - Bone pain and paraneoplastic jaundice in rare cases of extrinsic compression of the biliary system or metastatic disease
- CNS hemangioblastomas:
  - Nystagmus, papilledema, loss of proprioception, and sensory deficits
- Retinal angiomas:
  - Decreased visual acuity, characteristic retinal hemangioblastomas, and retinal detachment
- Pancreatic NET:
  - Undetected on exam unless large in size, metastatic, or causing obstruction
- ELST:
  - Decrease or loss of hearing
  - Papillary cystadenomas of the epididymis
  - Parasitol tends to develop:
    - Extra-adrenal pheochromocytomas
- Baseline imaging:
  - Elevated plasma and urine catecholamines are seen in patients with pheochromocytoma
  - Increased plasma and urine metanephrines are most commonly elevated in VHL patients
  - Other catecholamines may also be elevated
  - Similar to sporadic ccRCC:
    - Hypercalcemia, erythrocytosis, anemia, or elevated liver function tests (LFTs) may be seen as paraneoplastic lab abnormalities
  - Elevated erythropoietin levels or erythrocytosis may be seen with CNS involvement

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- Elevated plasma and urine catecholamines are seen in patients with pheochromocytoma
- Increased plasma and urine metanephrines are most commonly elevated in VHL patients
- Other catecholamines may also be elevated
- Similar to sporadic ccRCC:
  - Hypercalcemia, erythrocytosis, anemia, or elevated liver function tests (LFTs) may be seen as paraneoplastic lab abnormalities
- Elevated erythropoietin levels or erythrocytosis may be seen with CNS involvement

Imaging
- Bone and spine magnetic resonance imaging (MRI) for detection of CNS hemangioblastomas and ELSTs
- Abdominal imaging: Ultrasound (US) in children, and computed tomography (CT) or MRI in adults; for detection of renal or pancreatic masses, as well as adenial and extra-adrenal pheochromocytomas
- Magnetic resonance imaging (MRI) scan is helpful in localizing active pheochromocytoma
- Chest CT or MRI may be helpful for extra-abdominal pheochromocytomas

Differential Diagnosis
- Genetic testing
  - Occasionally, the glucagon stimulation test or clonidine suppression for pheochromocytoma

Pathologic Findings
- ccRCC
  - Usually multifocal and bilateral
  - May be several hundreds of gross and microscopic lesions in a single kidney
  - Most commonly fumarase nuclear grade II
  - Cysts commonly lined by clear cells
- Papillary cystadenomas of the epididymis
  - Vascular and vascular
  - Frequently multifocal and bilateral
  - Microscopic foci of cells in round clusters
- CNS hemangioblastomas
  - Solitary or multiple lesions in cerebellum, spinal cord, brainstem, or cerebrum
- Benign vascular lesions
Papillary cystadenomas of the epididymis or the pancreas: Benign (1)

Other familial types of hereditary renal carcinoma: Non-VHL familial bilateral multifocal RCC

Multiple endocrine neoplasia type 2 (MEN-2)

Metastatic RCC or other primary

Papillary cystadenomas of the epididymis or the pancreatic NET: Benign (2)

Vigilant surveillance of kidneys, adrenals, pancreas, and renal masses

Succinate dehydrogenase B (SDHB) deficiency: May metastasize to liver or bones unless resected

SDHB deficiency: Increase metastatic potential

No metastasis with solid RCC lesions

Growth rate similar to sporadic counterpart of about 3 mm on average per year

Pancreatic NET: May metastasize to liver or bones unless resected

Pancreatic NET also increase metastatic potential

The type of surgical resection and procedure is determined by tumor size and location

No VHL-specific medical treatment

Surgeries, hearing or vision problems.

Retention angiomas: Laser ablation or cryotherapy

Brain and spinal cord

With CT or MRI for kidneys, adrenal, pancreas; and MRI for brain or spinal cord

MRI for brain or spinal cord

With CT or MRI for kidneys, adrenal, pancreas; and MRI for brain or spinal cord

Surgeries, hearing or vision problems.

Genetic counseling, ophthalmology, neurosurgery, and otolaryngology support as needed

Blindness

Severe neurologic deficit or paralysis

Hypertensive crisis resulting in hemorrhagic stroke

With a fibrous stroma

Well circumscribed but unencapsulated

Microscopic: Nests of polygonal cells with a fibrous stroma

Microscopic: Low-grade papillary

– Bilateral nephrectomies and renal transplantation

– Treatment of pheochromocytoma is preferred

– Higher risk of miscarriage with active pheochromocytoma

– Yearly abdominal US from age 10 yr

– Yearly urinary catecholamines from age 2 yr

– Yearly ophthalmologic exam from birth

Pancreatic NET: Pheochromocytoma

Pheochromocytoma, or pancreatic NET

Ongoing Care

PROGNOSIS

Much depends on the stage of the renal lesions at presentation

Growth rate similar to sporadic counterpart of about 3 mm on average per year

No metastasis with solid RCC lesions <3 cm (2)

Metastatic potential of RCC lesions increases with increase in the size of the lesion, with up to 50% metastasis in those with tumors >6 cm

Pancreatic NET also increase metastatic potential with increase in size

COMPlications

Hyperviscous crisis resulting in hemoragic stroke

Severe neurologic deficit or paralysis

Blindness

Metastatic disease from either RCC, pheochromocytoma, or pancreatic NET

FOLLOW-UP

Patient Monitoring

Radiographic surveillance is performed every 1–2 yr

With CT or MRI for kidneys, adrenal, pancreatic, and MRI for brain or spinal cord

More frequent for faster-growing lesions

Ophthalmology exams yearly

Otology exams every 5 yr

Pediatric considerations

– Yearly ophthalmologic exams from birth

– Yearly urinary catecholamines from age 2 yr

– Yearly abdominal US from age 10 yr

Pregnancy considerations

– Higher risk of miscarriage with active pheochromocytoma

– Treatment of pheochromocytoma is preferred before pregnancy or early in the pregnancy

Patient Resources

www.vhl.org

REFERENCES


ADDITIONAL READING

[637]
WILMS TUMOR (NEPHROBLASTOMA)
Jonathan S. Karpelovsky, MD, PhD
Grahame H.H. Smith, MBBS

ASSOCIATED CONDITIONS
- Congenital anomalies in <15% of Wilms tumors
  - GU anomalies: Renal anomalies, cryptorchidism, hypopigmentation, ureteral duplication, ambiguous genitalia (4%)
  - Hemihyperplasia (3%)
  - Aniridia (1%)
  - Denys–Drash syndrome (male pseudohemaphroditism, renal mesangial sclerosis, renal failure)
  - WAGR syndrome
  - Beckwith–Wiedemann syndrome (macroGLOSSIA, organomegaly, hemihyperplasia)
  - Other: Perlman syndrome, Sotos syndrome, Simpson–Golabi–Behmel syndrome

GENERAL PREVENTION
- N/A

DIAGNOSIS

HISTORY
- Abdominal mass
- Fever, anorexia, weight loss
- Hematuria
- Physical exam
- N/A

PHYSICAL EXAM
- N/A

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- CBC: Anemia, polycythemia
- Liver function tests
- U/B creatinine
- Serum calcium
- Urine analysis: 25% with microhematuria
- Coagulation studies to assess for an acquired von Willebrand disease

Imaging
- Abdominal US: Initial study and if there is any concern about intravascular extension
- CT of abdomen and chest: To detect smaller lesions in either renal unit not detected by US; these imaging to evaluate for pulmonary metastasis
- Bone scan: If history of bone pain or elevated alkaline phosphatase or serum Ca

Diagnostic Procedures/Surgery
- N/A

Pathologic Findings
- Gross: Solid or grapelike, feathery tumor with a pseudocapsule
- Microscopic: (3 features): Stromal (immature spindle cells) and can have muscle cartilage or fat; epithelial (recapitulates kidney with glomerular and tubular), and blastemal (undifferentiated cells)
- Venous invasion in up to 20%; usually single tumor; 7% bilateral and 12% multifocal
- Histology relates to final outcome:
  - Favorable (95%)
  - Unfavorable (5%): Nuclear enlargement (>3-fold), hyperchromasia, abnormal mitoses, unfavorable marker of chemoresistance

DIFFERENTIAL DIAGNOSIS
- Clear cell carcinoma
- Rhabdoid tumor
- Neuroblastoma
- Multilocular cystic nephroma
- Mesioblastic nephroma
- Multicystic dysplastic kidney
- Renal cell carcinoma
- Renal medullary carcinoma

TREATMENT

GENERAL MEASURES
- Multimodality therapy combining surgery, chemotherapy, and radiation
- Treatment decisions based on staging
- Staging relies on anatomic extent of tumor (no genetic, histologic, or biomarkers); higher stages have worse prognosis and require more aggressive therapy
- 2 systems currently used: the NWTS/COG and SIOP; they are difficult to compare directly due to the fact that NWTS/COG is a prechemotherapy staging and SIOP post-chemoadjuvant therapy
- NWTS/COG: Commonly used in USA and Canada; based on surgical evaluation prior to chemotherapy
- SIOP: Commonly used in Europe, based on surgical findings following chemotherapy

MEDICATION

First Line
- SIOP: Studies favor preoperative chemotherapy for 6 wk with vincristine alone or vincristine followed by surgery. Histology and staging are potentially altered but the tumor response to chemotherapy is noted and aids in risk stratification
- Persistent biopsy is not recommended

ASSOCIATED CONDITIONS
- Congenital anomalies in 15% of Wilms tumors
  - GU anomalies: Renal anomalies, cryptorchidism, hypopigmentation, ureteral duplication, ambiguous genitalia (4%)
  - Hemihyperplasia (3%)
  - Aniridia (1%)
  - Denys–Drash syndrome (male pseudohemaphroditism, renal mesangial sclerosis, renal failure)
  - WAGR syndrome
  - Beckwith–Wiedemann syndrome (macroGLOSSIA, organomegaly, hemihyperplasia)
  - Other: Perlman syndrome, Sotos syndrome, Simpson–Golabi–Behmel syndrome

GENERAL PREVENTION
- N/A

DIAGNOSIS

HISTORY
- Abdominal mass
- Fever, anorexia, weight loss
- Hematuria
- Physical exam
- N/A

PHYSICAL EXAM
- N/A

DIAGNOSTIC TESTS & INTERPRETATION

Lab
- CBC: Anemia, polycythemia
- Liver function tests
- U/B creatinine
- Serum calcium
- Urine analysis: 25% with microhematuria
- Coagulation studies to assess for an acquired von Willebrand disease

Imaging
- Abdominal US: Initial study and if there is any concern about intravascular extension
- CT of abdomen and chest: To detect smaller lesions in either renal unit not detected by US; these imaging to evaluate for pulmonary metastasis
- Bone scan: If history of bone pain or elevated alkaline phosphatase or serum Ca

Diagnostic Procedures/Surgery
- N/A

Pathologic Findings
- Gross: Solid or grapelike, feathery tumor with a pseudocapsule
- Microscopic: (3 features): Stromal (immature spindle cells) and can have muscle cartilage or fat; epithelial (recapitulates kidney with glomerular and tubular), and blastemal (undifferentiated cells)
- Venous invasion in up to 20%; usually single tumor; 7% bilateral and 12% multifocal
- Histology relates to final outcome:
  - Favorable (95%)
  - Unfavorable (5%): Nuclear enlargement (>3-fold), hyperchromasia, abnormal mitoses, unfavorable marker of chemoresistance

DIFFERENTIAL DIAGNOSIS
- Clear cell carcinoma
- Rhabdoid tumor
- Neuroblastoma
- Multilocular cystic nephroma
- Mesioblastic nephroma
- Multicystic dysplastic kidney
- Renal cell carcinoma
- Renal medullary carcinoma

TREATMENT

GENERAL MEASURES
- Multimodality therapy combining surgery, chemotherapy, and radiation
- Treatment decisions based on staging
- Staging relies on anatomic extent of tumor (no genetic, histologic, or biomarkers); higher stages have worse prognosis and require more aggressive therapy
- 2 systems currently used: the NWTS/COG and SIOP; they are difficult to compare directly due to the fact that NWTS/COG is a prechemotherapy staging and SIOP post-chemoadjuvant therapy
- NWTS/COG: Commonly used in USA and Canada; based on surgical evaluation prior to chemotherapy
- SIOP: Commonly used in Europe, based on surgical findings following chemotherapy

MEDICATION

First Line
- SIOP: Studies favor preoperative chemotherapy for 6 wk with vincristine alone or vincristine followed by surgery. Histology and staging are potentially altered but the tumor response to chemotherapy is noted and aids in risk stratification
- Persistent biopsy is not recommended
Therapies

Complementary & Alternative treatment based on risk stratification

Additional Therapies

Radiation Therapy

ADDITIONAL TREATMENT

Surgery/Other Procedures

SURGERY/OTHER PROCEDURES

Treatment based on risk stratification

Additional Therapies

Ongoing Therapies

COMPLEMENTARY & ALTERNATIVE THERAPIES

N/A

ONGOING CARE

PROGNOSIS

5-yr overall survival: 90%

4-yr postsurgery overall survival:

- Favorable histology: Stage II: 96%
  Stage III: 95%
  Stage IV: 90%

- Unfavorable histology: Stage II: 83%
  Stage III: 81%
  Stage IV: 72%

- Stage V: 55%

- Unfavorable histology: 12% of patients, but 50% of deaths

- Prognostic factors: Histology, stage, patient age (younger better prognosis, but less significant today due to improved treatments)

- Future treatment will include 1p and 16q loss of heterozygosity in the risk and treatment stratification

COMPLICATIONS

- Surgical:
  - Bowel obstruction (5.1%)
  - Hemorrhage (1.9%)
  - Wound infection (1.4%)
  - Injuries to other visceral organs (1%)

- Medical:
  - Renal impairment: 1% chance from surgical, chemotherapy, and/or radiation
  - Increased in bilateral disease with radiation
  - Unrelated disease risk in patients with disseminated disease

- Radiation:
  - Congestive heart failure in patients treated with doxorubicin and radiation
  - Doxorubicin cardiotoxicity

- Vincristine and doxorubicin-related:
  - Hepatotoxicity
  - Cardiotoxicity

- Vascular injuries (1.4%)

- Wound infection (1.9%)

- Hemorrhage (1.9%)

- highest risk in patients treated with both doxorubicin and radiation: occur in radiation field; mean 16.1 yr post therapy

- Radiation:
  - Short stature, muscle weakness, scoliosis
  - Highest risk in age: -12 mo
  - Thyroid disease and mammary tissue damage in chest radiation

- Pregnancy complications increased in females receiving high-dose abdominal radiation

FOLLOW-UP

Patient Monitoring

- Stages I-IV focal or diffuse anaplasia:
  - Stage II: Favorable histology and stage IV focal or diffuse anaplasia:
    - Abdominal/pelvic radiation: 10.8 Gy
    - Lung radiation: 12.0 Gy
    - Chemotherapy: vincristine, doxorubicin, and cyclophosphamide
  - Stages II-IV focal anaplasia:
    - Abdominal/pelvic radiation: 10.8 Gy
    - Chemotherapy: vincristine, doxorubicin, and cyclophosphamide

- Unfavorable histology:
  - Stage II: 83%
  - Stage III: 81%
  - Stage IV: 72%
  - Stage V: 55%

- Unfavorable histology: 12% of patients, but 50% of deaths

- Prognostic factors: Histology, stage, patient age (younger better prognosis, but less significant today due to improved treatments)

- Future treatment will include 1p and 16q loss of heterozygosity in the risk and treatment stratification

- Surgical:
  - Bowel obstruction (5.1%)
  - Hemorrhage (1.9%)
  - Wound infection (1.4%)
  - Injuries to other visceral organs (1%)

- Medical:
  - Renal impairment: 1% chance from surgical, chemotherapy, and/or radiation
  - Increased in bilateral disease with radiation

- Radiation:
  - Congestive heart failure in patients treated with doxorubicin and radiation
  - Doxorubicin cardiotoxicity

- Vincristine and doxorubicin-related:
  - Hepatotoxicity
  - Cardiotoxicity

- Vascular injuries (1.4%)

- Wound infection (1.9%)

- Hemorrhage (1.9%)

- highest risk in patients treated with both doxorubicin and radiation: occur in radiation field; mean 16.1 yr post therapy

- Radiation:
  - Short stature, muscle weakness, scoliosis
  - Highest risk in age: -12 mo
  - Thyroid disease and mammary tissue damage in chest radiation
  - Pregnancy complications increased in females receiving high-dose abdominal radiation
SECTION II

Short Topics: A to Z

Section Editors: Deborah T. Glassman, MD
Alana M. Murphy, MD
11β-HYDROXYLASE (CYP11B1) DEFICIENCY

DESCRIPTION: Congenital 11β-hydroxylase deficiency (CYP11B1) causes Autosomal recessive disorder that manifests as childhood hypertension, hypokalemia, and muscle weakness. Low plasma renin activity is a hallmark. A deficiency in 11β-hydroxylase leads to low cortisol levels, high aldosterone levels, and adrenal hyperplasia. Affected females are not virilized and may have male-apparent genitalia. Males may be hypogonadal. Diagnosis is made by high levels of deoxycorticosterone and 11-deoxycortisol in serum or their tetrahydro-metabolites in a 24-hr urine. (See also Section I: “Disorders of Sexual Development [DSD].”)

TREATMENT:
- Oral hydrocortisone (10–20 mg/m2/day)
- Refractory hypotension treated with spironolactone, amiloride, and/or calcium channel blockers
- Surgical correction of ambiguous genitalia in females
- Prenatally treated with steroid administration to mother


5α-REDUCTASE DEFICIENCY

DESCRIPTION: An autosomal recessive disorder characterized by a 46XY male with external female phenotype at birth, normally developed Wolffian structures, and bilateral testes residing outside the abdominal cavity. The primary etiology is the loss of 5α-reductase activity in the prostate, seminal vesicles, and the epididymis. 5α-reductase activity is responsible for converting testosterone to dihydrotestosterone (DHT) during fetal development.


ACETAMINOPHEN ABUSE, UROLOGIC CONSIDERATIONS

DESCRIPTION: Bladder outlet obstruction can be defined only by pressure–flow measurement. The Abrams–Griffiths nomogram is an easy method of classifying these data to distinguish between the presence or absence of obstruction. Using the values for maximal flow and the corresponding voiding detrusor pressure, the Abrams–Griffiths nomogram can help determine whether bladder outlet obstruction is present.

The acrosome is a membrane-bound organelle covering the anterior 1/3 of the sperm head. This organelle contains numerous enzymes whose release, termed the acrosome reaction, is required for penetration of the hard zona pelucida of the ovum. It is hypothesized that human sperm bind to the ovum, after which the acrosome reaction is induced by 1 or more of the zona pelucida glycoproteins. Abnormalities of any aspect of this reaction may be a cause of male-factor infertility. Transmission electron microscopy, although the procedure of choice to detect acrosome reaction defects, is labor-intensive and expensive. This test may be recommended in cases of profound abnormalities of head morphology or in the setting of unexplained infertility in patients with poor IVF pregnancy rates. (See also Section II: “Semen Analysis, Technique, and Normal Values.”)

REFERENCE

ACTINOMYOSIS, RENAL
DESCRIPTION
Actinomycosis is a chronic granulomatous infection caused by a gram-positive anaerobic Actinomyces bacteria, usually A. israelii. No pathological findings are common; it can reach the kidney by hematogenous spread or instrumentation. Fibrils and fociules are common. The infection can present as pyrexia with negative urine culture. Imaging can reveal renal abscesses and hydrocephrosis, and the condition has been typically diagnosed postoperatively due to a renal mass prompting nephrectomy. It is diagnosed by gram-positive organisms on culture and prolonged incubation of bacteria. Microscopic exam of the organism can appear as yellow bodies called sulfur granules.

TREATMENT
• N-acetylcysteine has a clear role in preventing liver necrosis but not in the treatment of actinomyces-induced nephrotoxicity.
• Treatment focuses on supportive care, including management of volume status, blood pressure, and electrolyte balance.

REFERENCE

ACQUIRED RENAL CYSTIC DISEASE
DESCRIPTION
The development of renal cysts in patients with long-standing ESRD or severe chronic renal insufficiency. The cause is not known, but an accumulation of toxins unfiltered by dialysis is theorized. Usually asymptomatic. It can present with abdominal pain or hematuria. It is more common in males, and there is a 3–6 times greater incidence of renal cell carcinoma (RCC) compared to the general population (individual risk 4–7%). In dialysis-related RCC, neoplastic cells of acquired cystic disease-associated RCC are positive for alpha-methylacyl-CoA racemase (AMACR), but negative for cytokeratin (CK) 7. The cysts are slow to form and can be seen with a high incidence of metastasis. Risk increases with increased time on dialysis. (See also Section II: “Renal Cysts [Intimal, Peripelvic, Periureteral].”)

TREATMENT
• Close follow-up for early detection of malignancy (periodic imaging).
• Renal transplantation can reverse growth of cysts, but malignancy can still occur.

REFERENCE

ACROSOME REACTION ASSAY
DESCRIPTION
The acrosome is a membrane-bound organelle covering the anterior 1/3 of the sperm head. This organelle contains numerous enzymes whose release, termed the acrosome reaction, is required for penetration of the hard zona pelucida of the ovum. It is hypothesized that human sperm bind to the ovum, after which the acrosome reaction is induced by 1 or more of the zona pelucida glycoproteins. Abnormalities of any aspect of this reaction may be a cause of male-factor infertility. Transmission electron microscopy, although the procedure of choice to detect acrosome reaction defects, is labor-intensive and expensive. This test may be recommended in cases of profound abnormalities of head morphology or in the setting of unexplained infertility in patients with poor IVF pregnancy rates. (See also Section II: “Semen Analysis, Technique, and Normal Values.”)

REFERENCE

ADRENAL CALCIFICATIONS
ADRENAL FIBROMA, METANEPHRIC, PEDIATRIC
DESCRIPTION
Metanephric adenofibroma is a very rare benign tumor, first described as nephrogenic adenofibroma by Henningar and Bedworth in 1952. This tumor appears to affect predominantly young people (mean, 14 yo; range, 20 mo–35 yo). The most common symptom is hematuria, but a significant proportion of patients are asymptomatic. Polyuria is a peculiar incidental finding that resolves after resection of the tumor. The radiologic appearances are nondiagnostic and insubstantial from other solid pediatric renal tumors, particularly Wilms tumor. Histologically, this tumor is characterized by proliferation of benign-appearing mesenchymal cells surrounding multifocal nodules of immature epithelial cells. The latter cells show differentiation toward glandular and papillary structures. The mesenchymal component of metanephric adenofibroma closely resembles congenital mesothelial neoplasms in cytologic appearance. At present, all metanephric adenofibroma lesions should be excised to establish diagnosis, but no further adjuvant therapy is required.

REFERENCES

ADRENAL ANGIOMYOLIPOMA
DESCRIPTION
Angiomyolipoma arising from the adrenal. RCC contains more fat than adenoma. The etiology of this tumor is unknown. In a survey of 200 cases, the mean age was 20 yo. Angiomyolipoma is more common than adenoma, and most occur in the third and fourth decades of life. Histologically it consists of mature fat cells, smooth muscle cells, and thin-walled blood vessels. Management is identical to any adrenal mass: Assessment of functional status of the tumor with surgery if the pathological diagnosis of lesion is >5 cm (risk of malignancy and possibly bleeding). (See also Section I: “Adrenal Mass”, and Section II: “Adrenal: Myelolipoma [Adrenal Myelolipoma].”)

REFERENCE

ADRENAL CALCIFICATIONS
DESCRIPTION
Adrenal calcifications may be the result of hamartoma (secondary to trauma, venous thrombosis, stress, or bleeding diathesis), infective (usually granulomatous diseases), or may be associated with different tumors. Necrosis and calcifications are more common in association with adenocarcinoma but are not diagnostic. Bilateral calcified adrenal glands may be seen in adenocarcinoma or secondary Addison disease. Calcifications may be detected on MRI; however, because of their susceptibility artifact but are much better appreciated on CT images.

REFERENCE
ADRENAL CYSTS AND PSEUDOCYSTS

**ADRENAL CYSTS AND PSEUDOCYSTS**

**DESCRIPTION**
A cyst (0.064–0.18” in autopsy studies) is a cavity filled with fluid. Most are asymptomatic. These cysts can cause GI discomfort, pain if large, and even an acute abdomen with rupture or infection. Four major types are recognized: Endocrinologic, pseudocyst, epithelial, and parasitic; in order of decreasing incidence. Pseudocysts arise primarily from Echinococcus granulosus infection. Adrenal pseudocysts are thought to result from infarction or hemorrhage of a cyst or tumor.

**TREATMENT**
• >3.5 cm: Observation with serial imaging (US or CT or MRI).

**REFERENCE**

**ADRENAL CYTOMEGALY**

**DESCRIPTION**
Found infrequently in children and adults who considered a benign mass lesion, the condition is seen often in Beckwith–Wiedemann syndrome. Other possible associations include hemolytic disease of the newborn, erythroblastosis fetalis, and congenital rubella. It is characterized by the presence of large polyhedral cells with eosinophilic granular cytoplasm and enlarged nuclei in the adrenal cortex. Adrenal cytomegaly rarely forms cysts. This condition is thought to be a degenerative process but not a malignancy, possibly caused by a physiologic condition resulting from functional capacity and proliferation of adenocytes.

**REFERENCE**

**ADRENAL CYSTIC HYPOPLASIA**

**DESCRIPTION**
Incidentally discovered adrenal lesion: Whether it is functioning and whether to observe, screen and do follow-up studies.

**REFERENCE**

**ADRENAL HYPOPLASIA**

**DESCRIPTION**
Reduced ACTH production can result in hypoplasia of the adrenal gland (secondary adrenal hypoplasia); this can occur as a result of lack of pituitary trophic signaling, such as in pituitary agenesis. Congenital adrenal hypoplasia (primary) is an inherited disorder, with several forms identified. The major form of adrenal hypoplasia is Klinefelter syndrome and it is to the BAX-1 (46RH) gene. This gene is in close proximity to other genes encoding for: tyrosine kinase and Osurne. (Both associated with adrenal hypoplasia). Hypogonadotropic hypogonadism is also a common finding. It typically presents in the neonatal period or when adrenal crisis (dehydration, hypotension, hyperkalemia, hypoglycemia, hypoglycemia). Disorders of the external genitalia may include micropenis, undescended testes, or hypospadias. It can be detected by biochemical testing (serum cortisol, corticotropin releasing hormone (CRH) stimulation test, etc). Adrenal renal adrenal screening can also detect adrenal hypoplasia.

**TREATMENT**
Treatment is replacement of adrenal hormones.

**REFERENCE**

**ADRENAL HEMORRHAGE**

**DESCRIPTION**
Adrenal hemorrhage (AH) is a blood echogenic mass. CT scans, and the prevalence increases with age. Most are asymptomatic. Some symptoms include fever, flank or abdominal pain, tachycardia, nausea, vomiting, respiratory distress, and weakness. Ultrasound may be an incidental finding during imaging. AH may result from multiple mechanisms: Stress, sepsis (Winterbottom-Friedenreich syndrome), anticoagulation-related hemostasis, vascular spasm, adrenal venous thrombosis, or heparin-associated thrombocytopenia. Workup may show decreased hemoglobin and electrolytes in order of triphasic incidence. Hypokalemia in 56% of Bilateral AH.

**TREATMENT**
Include replacement of fluids, electrolytes, and blood if anemia is significant. Patients should be started on steroid replacement if adrenal insufficiency is suspected. Surgical exploration may be necessary for uncontrollable hemorrhage, uncertain diagnosis, or if obvious formation is suspected.

**REFERENCE**

**ADRENAL HYPOPLASIA**

**DESCRIPTION**
Reduced ACTH production can result in hypoplasia of the adrenal gland (secondary adrenal hypoplasia); this can occur as a result of lack of pituitary trophic signaling, such as in pituitary agenesis. Congenital adrenal hypoplasia (primary) is an inherited disorder, with several forms identified. The major form of adrenal hypoplasia is Klinefelter syndrome and it is to the BAX-1 (46RH) gene. This gene is in close proximity to other genes encoding for: tyrosine kinase and Osurne. (Both associated with adrenal hypoplasia). Hypogonadotropic hypogonadism is also a common finding. It typically presents in the neonatal period or when adrenal crisis (dehydration, hypotension, hyperkalemia, hypoglycemia, hypoglycemia). Disorders of the external genitalia may include micropenis, undescended testes, or hypospadias. It can be detected by biochemical testing (serum cortisol, corticotropin releasing hormone (CRH) stimulation test, etc). Adrenal renal adrenal screening can also detect adrenal hypoplasia.

**TREATMENT**
Treatment is replacement of adrenal hormones.

**REFERENCE**

**ADRENAL INCIDENTALOMAS**

**DESCRIPTION**
Incidentally discovered adrenal lesions — called “adrenal incidentalomas” — are by-products of increased availability and use of advanced imaging. Adrenal masses are found in approximately 4% of patients undergoing abdominal CT scans, and the prevalence increases with age. Most are nonfunctional, benign adenomas. It is important to consider 2 questions in the evaluation of an adrenal incidentaloma: Whether it is functioning and whether it is malignant. Differential diagnosis includes benign nonfunctioning adenoma, pheochromocytoma, hormonally active tumors such as pheochromocytoma, primary hyperaldosteronism, and Cushing disease (nodular hyperplasia); myelolipoma and malignancies including adrenocortical carcinoma; or metastasis from lungs, breast, colon, kidney, melanoma, or lymphoma. (See also Section 1: “Adrenal Mass.”)

**REFERENCE**

**ADRENAL MYELOLIPOMA**

**ADRENAL MYELOLIPOMA**

**DESCRIPTION**
Referred to as myelolipoma and myelolipoma in the literature, this rare, usually nonfunctioning lesions are composed of adipose and hematopoietic cells. Myelolipomas may be extramedullary hematopoiesis. It is rarely metabolically active (Cushing or Conn syndrome) and usually asymptomatic, except when very large or if hemorrhage occurs. They mostly occur in the adrenal glands, but extra-adrenal myelolipomas have been reported (pulmonary, retroperitoneum). It can be diagnosed radiographically and is more typically incidentally discovered on imaging or autopsy. Ultrasound shows a highly echogenic mass. CT demonstrates focal densities near that of fat (Hounsfield units of ~30 to ~115). MRI T1-weighted images demonstrate high signal intensity, whereas T2-weighted images are moderately intense. The main diagnostic similarity is well differentiated liposarcoma. (See also Section 1: “Adrenal Mass.”)

**TREATMENT**
Excision if symptomatic or if diagnosis cannot be confirmed radiographically or on needle biopsy.

**REFERENCE**

**ADRENAL ONSCYCTOMY**

**DESCRIPTION**
Gonadal neoplasms of the adrenal study, unlike that of the kidney, are rare with only 147 cases described. 80–90% of lesions are nonfunctional and only 10–20% of lesions show malignant elements. Typically occurs from 27–72 yr of age. Most common in women (2:1 ratio compared to men) and the left adrenal gland (3:1 ratio compared to the right). Histologically, lesions are highly granular and eosinophilic due to an abundance of mitochondria. Grossly, they are large, well-rounded, and encapsulated with an average diameter of 8 cm (2–20 cm). When cross sectioned, they have a brown, yellow, or mahogany appearance. Mitoses include breast (most common), lung, kidney, stomach, pancreas, and melanoma. (See also Section 1: “Adrenal Mass.”)

**REFERENCE**
the adrenal lesion can be performed either laparoscopically or using an open technique. If benign, the prognosis is excellent. If malignant, there is a 20–35% 5-yr survival rate. (See also Section I: “Adrenal Insufficiency.”)

REFERENCE

ADRENAITALIS

DESCRIPTION: An inflammation of the adrenal gland that can lead to primary adrenal insufficiency (Addison disease), which accounts for 80% of cases. Tuberculosis is the 2nd leading cause, with the balance made up by fungal infections, hermaphrodite, metastatic neoplasms, sarcoidosis, amyloidosis, and adrenal leukodystrophy. Autoimmune adrenitis can be associated with thyroiditis, diabetes mellitus, pernicious anemia, vitiligo, hypothyroidism, and mucocutaneous candidiasis (autoimmune polyendocrine syndrome type I), also known as candidiasis-hypothyroidism-Addison disease-syndrome), or with autoimmune polyendocrine syndrome type 2 (also known as Schmidt syndrome). HIV with opportunistic CMV adrenitis accounts for an increasing number of cases. (See also Section I: “Adrenal Insufficiency, acute (adrenal crisis) and “Addison Disease.”)

TREATMENT
• Replacement of adrenal and other hormones, as necessary
• Treatment of underlying cause

REFERENCE

ADRENOCORTICAL DISEASE, PRIMARY PIGMENTED NODULAR

DESCRIPTION: Primary pigmented nodular adrenocortical disease (PPAD) is a rare AC syndrome independent form of Cushing syndrome, accounting for ~1% of Cushing syndrome patients. Hypercortisolism is resistant to a dexamethasone suppression test. Typically, bilateral adrenal glands are involved with gross appearance of multiple nodules of varying sizes and pigmented colors. Histologically, the nodules are circumscribed, unencapsulated, and comprised of polygonal cells with an eosinophilic appearance. 25% of patients manifest Carney complex, which includes spotty skin pigmentation, endocrine tumors, and myxoid desmoids. Treatment requires bilateral adrenalectomy as unilateral and partial adrenalectomy has resulted in recurrence. (See Section I: “Cushing Disease and Syndromes.”)

REFERENCE

ADRENODENDRAL SYNDROME

DESCRIPTION: This is the most common cause of disorders of sexual development (DSD) (formerly ambiguous genitalia), caused by an internal error of masculinization involving androgen synthesis. At birth it is a defect in any of the 5 enzymes involved in the cortisol biosynthetic pathway (21-hydroxylase, 11-hydroxylase, 3-hydroxysteroid dehydrogenase, 20,22-desmolase, and 17-hydroxylase), which may result in CAH. Usually presents with an autosomal recessive inheritance. (See also Section I: “Disorders of Sexual Development (DSD).” Section II: “Congenital Adrenal Hypertrophy.”)

SYNONYMS
• CAH
• Female pseudohermaphrodite
• Male pseudohermaphrodite

COMPLICATIONS
• For untreated females:
  – Premature pubic and axillary hair development
  – Rapid osteopathic maturation, premature epiphyseal closure, short adult stature
  – No breast development or menstruation
• For untreated males:
  – Sexual and somatic precocity within 1st 2 yr of life
  – Premature epiphyseal closure, short adult stature
  – Untimely male and female pubertal and secondary sex characteristic
  – Progressive weight loss, dehydration within 1st few weeks of life

TREATMENT
• Early diagnosis with ascertainment of correct sex and prevention of salt wasting and metabolic complications
• Steroid replacement with cortisone, hydrocortisone, or dexamethasone as needed
• Surgical genital reconstruction may be necessary early in life, based on specific findings

REFERENCES

ADRENOLUEKYOSTROPHY

DESCRIPTION: Rare, X-linked recessive metabolic disorder occurring in boys, and characterized by adrenal atrophy and widespread, diffuse cerebral demyelination. It produces mental deterioration, cortical spinal tract dysfunction, and cortical blindness. There is a lab evidence of adrenal cortical dysfunction. 2 phenotypes, with onset in childhood or young adulthood, exhibit hypogonadism. Death inevitably occurs within months of onset. A defect is theorized in peroxisomes, which handle long-chain fatty acids. Concept’s (or mixture of glycerol and long-chain fatty acids) has been tried in this disease, with some delay in neurologic symptoms. Bone marrow transplantation is under study.

REFERENCE

SYNONYM
Formerly Glyeryl trierucate oil

REFERENCE

AGING MALE SURVEY

DESCRIPTION: The Aging Male Survey (AMS) is a questionnaire developed to detect hypogonadism in adult men. It has 3 domains: Psychological, Somatic-vegetative, and Sexual. The minimum and maximum scores are 5 and 25, respectively, for the Psychological and Sexual domains and 7 and 35 for the Somatic-vegetative domain. The higher the score, the more severe the symptoms. The AMS has been shown to have a sensitivity (83%) and specificity (99%) similar to those of the shorter ADAM Survey. (See also Section I: “Andropause [Late Onset Male Hypogonadism]” and Testosterone, Decreased [Hyponogonadism]. Section II: “Androgen Deficiency in the Aging Male (ADAM) and ADAMS Survey.”)

REFERENCE

AL GHIRAB CORPORAL SHUNT

DESCRIPTION: A surgical treatment for the management of priapism refractory to penile aspiration. A small transverse incision is made on the dorsum of the glans. A section of septum between the glans corpora and the corpora cavernosa is removed to create a shunt. (See also Section I: “Priapism” and Section II: “Al Ghorab Corporal Shunt With Burnett “Snake” Maneuver.”

REFERENCE

AL GHIRAB CORPORAL SHUNT WITH BURNETT “SNAKE” MANEUVER

DESCRIPTION: A modification of the Al Ghorab distal corporal glansular shunt for priapism. The Burnett “snake” modification involves passing a 7/8 Hegar dilator through the amputated glans tip of the corpus cavernous bladder. The dilator is passed to the proximal lesion of the corpus cavernous laterally on each side to avoid urothelial injury. Milking of ischemic blood and clot is performed until bright red blood is visualized. A study of 10 patients with a mean follow-up of 7 mo reported that 8 men had no recurrence of priapism. Of the 6 men who had normal erectile function preoperatively, 2 had partial erectile function postoperatively.

REFERENCE
ALAGILLE SYNDROME

DESCRIPTION
An autosomal dominant disorder associated with abnormalities of the liver, heart, eye, skeleton, and kidneys. A characteristic facial appearance is also seen. Renal abnormalities are not specific but include diploia and renal failure. This autosomal dominant disorder is mapped to chromosome 20; it is treated by renal replacement therapy as needed.

SYNONYM
Alagille-Watson syndrome

REFERENCE

ALKALINE PHOSPHATASE, UROLOGIC CONSIDERATIONS

DESCRIPTION
As an enzyme produced in many tissues, such as bone, liver, placenta, and intestine, alkaline phosphatase can monitor the progression of metastatic cancer to bone (such as prostate cancer). Bone (or core) can be distinguished from other sources by its heat lability compared with other forms. This test has also been recommended by some authors as a useful tool for monitoring antineoplastic agents.

REFERENCE

ALKAPTONURIA

DESCRIPTION
An inherited (dominantly expressed) disorder of metabolism of phenylalanine and tyrosine metabolism wherein homogentisic acid (HGA) accumulates in the body and is excreted in a large amount in the urine. If allowed to stand, the urine gradually turns dark (black urine disease). Alkalai can accelerate this process. Ochronosis (deposition of a bluish-black pigment noted in the connective tissue) may lead to arthropathy. Ocular: interstitial, renal failure occurs, opacities, with long-standing disease. Even more rarely, HGA stones can occur. It is caused by a single gene defect, causing absence of HGA release. It is treated by dietary restriction of phenylalanine and tyrosine metabolism of phenylalanine and tyrosine metabolism.

SYNONYM
Bluish-black urine disease

REFERENCE

ALLOPURINOL HYPERSENSITIVITY SYNDROME (AHS)

DESCRIPTION
2% of patients treated with allopurinol will develop minor adverse reactions, including drug eruption, pruritic maculopapular exanthema or minor vasculitis, which often disappear after cessation of treatment. In contrast, AHS is a life threatening and includes at least 2 of the following major criteria:
• Decreasing renal function
• Acute heparinovascular injury
• Cutaneous rash including erythema multiforme (EM), generalized morbilliform eruptions, generalized exfoliative dermatitis (GED), or Steven-Johnson syndrome/ebullis epidermal necrolysis (SS/EN). Diagnostic criteria may also include 1 of the above and at least 1 of the following minor criteria:
  • Fever
  • Eosinophilia
  • Leukocytosis

TREATMENT
Nebulizer alternative for patients with AHS

REFERENCE

ALPLOPOLY

DESCRIPTION
A poorly understood and clinically insignificant condition marked by the loss and subsequent regrowth of pubic hair, possibly due to tight-fitting undergarments.

REFERENCE

- (ALPHA) FETOPROTEIN

DESCRIPTION
A single-chain glycoprotein (MW 70,000) that primarily aids in the management of testicular cancer. It is normally produced by the liver, yolk sac, and fetal testis. Adult level is 5.0–6.0 ng/mL. Serum a-fetoprotein (AFP) levels are normally elevated in the 1st 8 mo of life. The normal adult level is <5 ng/mL. This can be elevated in 39% of cases of embryonal cell carcinoma, 44% of neuroblastoma, and 64% of yolk sac tumors. Other reasons for elevation include resectable hepatocellular carcinoma, hepatocellular neoplasm, fetal death, aplasia termalis, and some cases of benign hepatic disease.

REFERENCE

ALPORT DISEASE/SYNDROME

DESCRIPTION
Alport disease/syndrome consists of hereditary nephritis, high-frequency neural hearing loss, and ocular abnormalities. It can present as hematuria, proteinuria, or anemia. Familial abnormality is crucial in diagnosis. The nephritis is progressive, usually resulting in renal failure by the 3rd decade. Males are more severely affected. It is caused by a genetic mutation on a single locus on the X chromosome, with altered type IV collagen production. Treat with renal replacement therapy, as needed.

REFERENCE

ALSTRÖM–EDWARDS SYNDROME

DESCRIPTION
A progressive autosomal recessive genetic disorder affecting multiple organ systems. It may be detected at birth or in early childhood. Clinically, patients with Alstrom syndrome develop cone–rod dystrophy leading to eventual blindness, have sensorineural deafness, and normal intelligence. Patients develop obesity, endocrine disturbances such as type 2 diabetes mellitus, delayed cardiomyopathy, and progressive renal and hepatic failure. Alstrom syndrome is caused by specific mutations in the ALMS1 gene, located at chromosome 2p13. No specific treatment is available for infertility; renal replacement therapy is indicated as needed.

SYNONYM
Alston syndrome

REFERENCE

ALZHEIMER DISEASE, UROLOGIC CONSIDERATIONS

DESCRIPTION
Alzheimer disease is the principal cause of dementia in the elderly patient population. The urologic manifestations include urinary incontinence, decreased bladder, and erectile dysfunction (ED). Patients may be difficult to treat due to limited cooperation with the treatment plan; toileting schedules can help with early incontinence episodes. Often considered a case of “functional” urinary and fecal incontinence. Current theories regarding the etiology of Alzheimer disease revolve around cortical cholinergic loss. This may also make the treatment of urologic manifestations even more difficult by limiting the use of anticholinergic agents. Rule out other concomitant causes before ascribing urinary tract problems to this disease specifically. (See Section I: “Incontinence, Urinary, Adult Male”; Section I: “Incontinence, Urinary, Adult Female.”)

REFERENCE

AMBIGUOUS GENITALIA

DESCRIPTION
DSO (Disorders of sexual development) refers to a child born with a congenital discrepancy between external genitalia, gonads, and chromosomal sex. In 2006, consensus conference stated that the potentially reparative terms “pseudohermaphrodite,” “hermaphrodite,” and “intersex” be replaced by the more appropriate diagnostically accurate term “DSD.” It is recognized that some DSDs present with abnormalities of the external genitalia. These abnormalities that prompt evaluation occur in approximately 1 in 4,500 live births. These findings may include may
An acid loading test to rule out Excretion of an overabundance of 

REFERENCE


REFERENCES

[CAIS] and Partial [PAIS"]; or "Androgen Resistance Syndrome, Complete 

Section I: "Disorders of Sexual Development [DSD]"

and Section II: "Androgen Insensitivity Syndrome

Nonpalpable gonad as a few examples. (See also 

appearance with a palpable gonad (with or without

Serum bicarbonate values are taken at hours 2 and 4

mellitus (DM) and diabetes insipidus (DI).

diseases that affect the kidney, such as diabetes
tubular acidosis, Fanconi

association with renal tubular acidosis, Fanconi

cancers of the endometrium, ovary, stomach, small 

intestinal, hepatobiliary tract, urinary tract (upper tract

adrenocortical carcinoma (HNPCC or Lynch syndrome). Lynch

exhibiting microsatellite instability (MSI), is 

associated with tumors exhibiting microsatellite instability (MSI), is 

matched repair gene and associated with tumors exhibiting microsatellite instability (MSI), is 

affected patients with renal tubular acidosis. Aminoaciduria is found in

times with the most current version referred to as

used to treat ureteropelvic

REFERENCES

DESCRIPTION

An acid loading test to rule out distal renal tubular acidosis. Performed by giving 0.1 g/kg ammonium chloride oral solution over 45 min

REFERENCE

Piñol V, Castells A, Andreu M, et al. Accuracy of

REFERENCES

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA (AAST) ORGAN SEVERITY SCALES: GENITOURINARY INJURIES

DESCRIPTION

Numerous classifications of traumatic injuries exist, but the most widely used and accepted classification was developed by the American Association for the Surgery of Trauma’s Organ Injury Scaling Committee. (See also Section I: “Bladder Trauma, Perineum, Trauma; Renal Trauma, adult; Urethra, Trauma; Urethra, Trauma.”

REFERENCE


AMINOCIDURIA

DESCRIPTION

Excretion of an overabundance of amino acids in urine, more often due to an inherent error of metabolism. Aminociduria is found in association with renal tubular acidosis, Fanconi syndrome, and other primary renal tubular disturbances. It may also occur secondary to other diseases that affect the kidneys, such as diabetes mellitus (DM) and diabetes insipidus (DI).

REFERENCE


AMMONIUM CHLORIDE LOADING TEST

DESCRIPTION

An acid loading test to rule out distal renal tubular acidosis. Performed by giving 0.1 g/kg ammonium chloride oral solution over 45 min after a 6 hr fast. 100 ml of water are given every hour during the test. Urine pH is measured hourly for 4 hr. Serum bicarbonate values are taken at hours 2 and 4 to ensure adequate acidification (pH<5.6). The normal result is urine pH <5.4; distal RTA exists if pH >5.4. (See also Section II: “Renal Tubular Acidoses.”)

REFERENCE


AMMONIUM URATE UROLITHIASIS

DESCRIPTION

Enzyme defect results in uric acid stones. (see also Section I: “Bladder Trauma, Perineum, Trauma; Renal Trauma, adult; Urethra, Trauma; Urethra, Trauma.”)

REFERENCE

Hossain RZ, Ogawa Y, Hokama S, et al. Urolithiasis in patients with Androgen Insensitivity Syndrome (AIS); or “Androgen Resistance Syndrome, Complete (CAIS) and Partial [PAIS].”

CITRATES: 

AMERSTAD AND BETHESDA CRITERIA FOR LYNCH SYNDROME

DESCRIPTION

Criteria have been developed to aid in the diagnosis of hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome). Lynch syndrome caused by a germline mutation in a mismatch repair gene and associated with tumors exhibiting microsatellite instability (MSI), is

REFERENCE

Used to treat ureteropelvic junction obstruction. The UPJ is declared, and the ureter is reimplanted into the renal pelvis. The widely spatulated ureter is reanastomosed to the renal pelvis with the widely spatulated end of the UPJ being excised. Normal anal sphincter function is restored. (See also Section II: “Bladder Trauma, Perineum, Trauma.”)

REFERENCE


ANAL SPHINCTER TONE AND SENSATION, UROLOGIC CONSIDERATIONS

DESCRIPTION

Anal sphincter tone is a vital part of the GU evaluation, especially in a person with new-onset urinary incontinence. Normal anal sphincter tone is a function of somatic fibers traveling over S2–5 in the pudendal nerve. A hypotonic sphincter suggests a lower motor neuron lesion, whereas a hypertonic sphincter may be an upper motor neuron lesion. The loss of voluntary contraction of the sphincter suggests interruption of centrally directed fibers somewhere between the motor strip of frontal cortex and the pudendal nerve. The bulbocavernous reflex (BCR), which is widely used in evaluating urinary incontinence and ED, requires adequate sphincter contraction in response to squeezing the glass of water.

REFERENCE


ANDERSON-HYNES PYELOPLASTY

DESCRIPTION

Used to treat ureteropelvic junction (UPJ) obstruction. The UPJ is declared, and the ureter is reimplanted into the renal pelvis. The widely spatulated ureter is reanastomosed to the renal pelvis with interrupted chromic suture, and the excised renal pelvis is closed with simple or running suture. After nephrectomy, a ureteral stent is placed. (See also Section II: “Bladder Trauma, Perineum, Trauma.”)

REFERENCE


ANDERSON-HYNES PYELOPLASTY

DESCRIPTION

Used to treat ureteropelvic junction (UPJ) obstruction. The UPJ is declared, and the ureter is reimplanted into the renal pelvis. The widely spatulated ureter is reanastomosed to the renal pelvis with interrupted chromic suture, and the excised renal pelvis is closed with simple or running suture. After nephrectomy, a ureteral stent is placed. (See also Section II: “Bladder Trauma, Perineum, Trauma.”)
ANDREWS PROCEDURE (HYDROCELE)

DESCRIPTION
A technique described in 1907 where the hydrocele sac at the superior portion of the testis is incised 2–3 cm. This step is followed by excision of the edges of the testis, which is wrapped around the cord structure.

SYNONYM
Bottle Operation

REFERENCE

ANDREWS DEFICIENCY IN THE AGING MALE (ADAM) AND ADAM QUESTIONNAIRE

DESCRIPTION
Previously referred to as andropause, this has more recently been described as ADAM. The onset of ADAM is unpredictable, and its manifestations are subtle and variable. It is associated with a decrease in testosterone, but also with decreased growth hormone, insulin, and dehydroepiandrosterone (DHEA). Clinical manifestations include fatigue, depression, decreased libido, and erectile dysfunction (ED), as well as changes in cognition and mood. The ADAM questionnaire is a screening tool to detect late-onset andropause, with a sensitivity and specificity of 88% and 60%, respectively, compared with serum bioavailable testosterone levels. A positive answer represents yes to questions 1 or 7 or to any of the other questions.

The Androgen Deficiency in Aging Male (ADAM) Questionnaire

Yes No 1. Do you have a decrease in libido (sex drive)?
Yes No 2. Do you have a lack of energy?
Yes No 3. Do you have a decrease in strength and/or endurance?
Yes No 4. Have you lost height?
Yes No 5. Have you noticed a decreased enjoyment of life?
Yes No 6. Are you sad and/or grumpy?
Yes No 7. Are your erections less strong?
Yes No 8. Have you noticed a recent deterioration in your ability to play sports?
Yes No 9. Are you falling asleep after dinner?
Yes No 10. Has there been a recent deterioration in your work performance?

REFERENCES

ANDROGEN DEPRIVATION SYNDROME (ADS)/ METABOLIC SYNDROME

DESCRIPTION
Long-term androgen deprivation therapy (ADT), for the treatment of prostate cancer, results in hypogonadism and increased risk of type 2 diabetes mellitus. Furthermore, death from cardiovascular disease (CVD) is the most common cause of prostate cancer-related death in these men. ADS is a spectrum of adverse effects that includes flushing, impotence, loss of libido, emotional lability, anxiety, hyperglycemia, increased triglycerides and cholesterol, muscle atrophy, decreased muscle strength, testosterone atrophy, osteoporosis, depression, anxiety, malaise, fatigue, and memory difficulties. Andrological syndrome defined by the NIH Adult Treatment Panel III criteria is also part of this spectrum and may include abdominal obesity, hypertension, hyperglycemia, hyperinsulinemia, elevated HDL cholesterol, and hypertriglyceridemia. Treatment of the metabolic syndrome includes:

- Management of underlying causes (metabolically and physically inactive): Weight management, increased physical activity
- Treat lipid and nonlipid risk factors if they persist
- Treat hypertension
- Management of underlying causes (metabolically and physically inactive): Weight management, increased physical activity
- Treat lipid and nonlipid risk factors if they persist
- Treat hypertension
- Management of complete (severe) androgen insensitivity is important to target the optimal timing of goserelin acetate. Because the testes produce estradiol, which results in appropriate changes for the female phenotype, it is considered by many preferable to leave the testes in situ until pubertal development is complete. In partial androgen insensitivity, the external genitalia may be ambiguous at birth, but the prototypical phenotype is characterized by perineoscrotal hypospadias, micropenis, and a bifid scrotum. The testes may also be undescended.

Clinical Features of Complete Androgen Insensitivity Syndrome

- Karyotype 46, XY
- Inheritance X-linked recessive
- External genitalia Ambiguous with blind vaginal pouch, undermasculinized, isolated hypoplasia, and primary amenorrhoea
- Wolffian duct derivatives Absent or vestigial
- Gonads Bilateral Tests
- Hormone and metabolic profile Testosterone levels; increased estradiol (Female reference range), FSH levels often normal or slightly increased. Resistance to androgenic and metabolic effects of testosterone

REFERENCES

ANDROGEN INSensitivity SYNDROME (AIS; OR ANDROGEN RESISTANCE SYNDROME, COMPLETE (CAIS) AND PARTIAL (PAIS))

DESCRIPTION
Androgen insensitivity is a disorder of androgen action and a common form of 46,XY DSD. Mutations in the androgen receptor lead to variable defects in virilization or infertility in 46,XY males with testes and normal testosterone formation. Clinical presentation ranges from phenotypic women to variable defects in virilization or infertility in 46,XY males with testes and normal testosterone formation. Clinical presentation ranges from phenotypic women to variable defects in virilization or infertility in 46,XY males with testes and normal testosterone formation. Clinical presentation ranges from phenotypic women to variable defects in virilization or infertility in 46,XY males with testes and normal testosterone formation. Clinical presentation ranges from phenotypic women to variable defects in virilization or infertility in 46,XY males with testes and normal testosterone formation.

Clinical Features of Partial Androgen Insensitivity Syndrome

- Karyotype 46, XY
- Inheritance X-linked recessive
- External genitalia Ambiguous with blind vaginal pouch, undermasculinized, isolated hypoplasia, and primary amenorrhoea
- Wolffian duct derivatives Absent or vestigial
- Gonads Bilateral Tests
- Hormone and metabolic profile Increased LH and testosterone concentrations; increased estradiol (for female reference range). FSH levels may be normal or slightly increased. Partial resistance to androgenic and metabolic effects of testosterone

REFERENCES
ANTIOVARYAN WITHERDRAWN SYNDROME (FLUTAMIDE WITHERDRAWN SYNDROME)

REFERENCE


ANDROGEN/ANABOLIC STEROID ABUSE

DESCRIPTION

Androgens are steroid hormones that include testosterone and its derivatives, including androstenedione, DHT, and dromestosterone. In the medical realm, androgens at physiologic doses treat androgen deficiency due to hypothalamic, pituitary, or testicular disorder of genetic or acquired etiology. The use of androgens at supra-physiologic doses greatly enhances muscle strength, size, and performance, thus promoting its abuse most notably in power sports and body building. While banned by all major sports organizations, androgen abuse is rampant and has been linked to several high-profile athletes. Androgen abuse is a frequent cause of male infertility by suppression of Leydig cell production of testosterone, which results in delayed spermatogenesis. Abnormalities in sperm motility and morphology are commonly seen, and usually recover spontaneously within 4 mo after cessation of abuse.

REFERENCE


ANGIOKERTATOMA OF FORDYCE (PENILE AND SCROTAL ANGIOKERTOMAS)

DESCRIPTION

Vascular malformation of subepidermal blood vessels with an overlying epidermal proliferative reaction. Capillary ectasia is present in the papillary dermis. Typically, numerous dark red to blue dome-shaped papules are linearly arranged on the scrotum and, less commonly, on the penis. In women, 1 larger vulvar papule is typical. Dark red to blue dome–shaped papules are linearly present in the papillary dermis. Typically, numerous subepidermal blood vessels with an overlying eosinophils, and (4) lymphoid infiltrates. These are found: (1) Vacuolated histiocytoid cells, (2) tumor histiocytoid hemangiomas in which 4 features are necessary. Adjuvant radiation may be useful; chemotherapy for adjuvant or metastatic disease is not usually effective.

REFERENCE


ANGIOLUMPHOID HYPERPLASIA, PENILE

DESCRIPTION

A subtype of a broad class of histiocytoid hemangiomas in which 4 features are found: (1) Vasculur histiocytoid cells, (2) tumor vessels that are thick-walled or capillaries consisting of only of histiocytoid endothelial cells, (3) interstitial eosinophils, and (4) lymphoid infiltrates. These are usually confluent to the skin of 1 area of the body.

SYNONYMS

• Fordyce dots (or atypical seborrheic granule)
• Inflammatory angiomatous nodule
• Subcutaneous angiofibroplasia with eosinophilia
• Epithelial hemangioma
• Intravascular atypical vascular proliferation

TREATMENT

Local surgical resection or laser (CO2) ablation.

REFERENCE


ANGIOMYOMA, PERINEAL

DESCRIPTION

Rudimentary lesion of the pelvis with tissue, but may vary due metastasis. Characterized by slow, infiltrative growth. May present as mass in the pelvis. Histologically, demonstrates wavy collagen fibers related to the myxoid change. Multiple prominent blood vessels are also seen. It occurs mainly in females and can be quite locally aggressive, with frequent local recurrence. Treatment is through wide local excision with close postoperative monitoring.

REFERENCE


ANGIOSARCOMA, GENITOURINARY

DESCRIPTION

A very rare malignancy that greatly appears as a well-circumscribed mass or diffusely fungating tumor that may involve any organ. Microscopically, angiosarcoma shows numerous vascular channels. It stains positively for factor V, immunohistochemically. These sarcomas can be widely metastatic and have persistent local recurrence. Bladder angiosarcoma has been reported postirradiation for treatment of other malignancies; chronic lymphedema, foreign bodies, and other causes have been implicated.

TREATMENT

Radical resection of affected area (penectomy, radical resection of affected area). Such a patient may present as mass in the pelvis. Histologically, demonstrates wavy collagen fibers related to the myxoid change. Multiple prominent blood vessels are also seen. It occurs mainly in females and can be quite locally aggressive, with frequent local recurrence. Treatment is through wide local excision with close postoperative monitoring.

REFERENCE


ANTERIOR URETHRAL VALVES

DESCRIPTION

Much less common than posterior urethral valves, this condition is characterized by obstruction of the anterior urethra, usually associated with the posterior urethra. It is caused by a diverticulum acting as valves, although corks without diverticulum have been reported. It usually presents with voiding symptoms or bulging diverticulum on the normal shaft with voiding. Diagnosed by VCUG and renal ultrasound. Retropubic urethropexy may miss the valve. It may be associated with reflux, but less so than with PUV. Renal deterioration is less common than with PUV.

TREATMENT

• Bilateral catheter if urethrae occurs
• Endoscopic valve fulguration or single-stage urethroplasty if urethra is adequate
• Staged urethropexy for large diverticulum
• Vescicoureteral reflux or persistent azotaemia

REFERENCE


ANTIOVARYAN WITHERDRAWN SYNDROME (FLUTAMIDE WITHERDRAWN SYNDROME)

DESCRIPTION

A decrease of PSA levels occurs in 15–40% of patients upon withdrawal of nonsteroidal antiovars in those treated for advanced prostate cancer with total androgen blockade that is rarely
APPROACH TO GENITAL ULCERS

APHTHOUS ULCER, EXTERNAL GENITALIA

DESCRIPTION

Aphthae are localized, painful, shallow, round to oval ulcers often covered by a gray to white, central, superficial, necrotic layer with a pale red border and an erythematous halo. Complex aphthosis involves almost 10% of the oral and/or genital mucosa. Those involving both oral and genital aphthae are termed constant, multiple, oral or oral and genital aphthae. When a disruption occurs in the blood–testis barrier; they may be a cause of infertility. Causes can include ductal obstruction (i.e., varicocele), infection, cryptorchidism, and warfarin, but are often idiopathic. Serum antisperm antibody levels are not as useful as antibodies in the semen, which can be measured by immunobead testing. The higher the percentage of sperm binding to the bead, the lower the probability of pregnancy. Scoring varies by lab, but normal is generally considered to be <10% of sample binding to the bead. Condylomas, antibiotics, steroids, and sperm washing have all been utilized, with variable results. Presently, assisted reproductive techniques (ARTs) such as in vitro fertilization are most effective. See also Section II: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Techniques”; “Semen Analysis, Technique and Normal Values.”

REFERENCE


ARTEMIOVIRUS MALFORMATION

DESCRIPTION

Arensiviruses are in the family Arenaviridae, order Mononegavirales, and are characterized by lipid-enveloped, pleomorphic particles. Arenavirus is a genus that consists of 2 species: Lassa virus and Marburg virus. Arenaviruses are commonly transmitted to humans by infected rodents or bats. Human-to-human transmission can also occur. The current scientific understanding suggests that Arenaviruses are not a major human health concern. However, in 2013, a novel human arenavirus emerged which has caused multiple outbreaks in Sierra Leone, Guinea and Liberia. The disease is characterized by a fever, severe headache, and respiratory tract infection. The disease has a high mortality rate. The arenavirus is transmitted through the bite of infected rodents, and the virus is currently being studied for potential vaccine development.

REFERENCES


ARTERIOVENOUS MALFORMATION (AVM)

DESCRIPTION

Arteriovenous malformations (AVMs) are rare vascular anomalies characterized by the coexistence of arterial and venous blood vessels lacking an intermediate capillary bed. AVMs can occur anywhere in the body, but the most common sites are the brain, scalp, and lower extremities. They can cause local effects such as pain, swelling, or disfigurement, as well as systemic effects such as organ dysfunction and bleeding. Treatment options for AVMs include surgical resection, embolization, and radiosurgery. The goal of treatment is to eliminate or reduce the size of the AVM, thereby improving symptoms and preventing complications.

REFERENCES


ARTERIOVENOUS FISTULA (AVF), RENAL OR ARTERIOVENOUS MALFORMATION (AVM)

DESCRIPTION

Racial AVF or AVM are uncommon lesions. They can be congenital, acquired, or idiopathic. Most (70%) are symptomatic and occur as a result of renal biopsy, blunt or penetrating trauma,
ASPERGILLOSIS, GENITOURINARY

DESCRIPTION
Only Candida infections are more common opportunistic infections in the urologic population than aspergillosis. It affects patients with diabetes and malignancy, and immunosuppressed patients (HIV, renal transplant). It can cause renal parenchymal disease or obstructive uropathy. The prostate has been a rare site of infection. Renal aspergillosis or pseudotumor has been reported in patients with AIDS. Striae can be negative, but aspiration and cytology can demonstrate typical septated hyphal. Therapy is systemic amphotericin B at least 3 mg/kg, or voriconazole. Amphotericin B in suspension is given through a central venous catheter. Amphotericin B in suspension has been the most successful approach to therapy. Through a retrograde ureteral catheter instillation of a solution of amphotericin B in sterile water is infused at 40 ml/h. Shade the solution to limit degradation. Monitor pressure with a pop-off mechanism at 25 cm water. (See also Section II: Fungal Infections, Genitourinary.)

REFERENCE

ASPERMINA

DESCRIPTION
A condition of no ejaculate, which should be differentiated from aspermia, where an ejaculate is present but the sperm are absent from the fluid. (See also Section II: Infertility, Urologic Considerations) and “Ejaculatory Disturbances (Delay, Decreased, or Absent).” Section II: “Semen Analysis, Technique, and Normal Values.” Section II: “Semen Analysis, Abnormal Findings, and Terminology.”

CAUSES
• Complete bilateral obstruction of ejaculatory duct
• Congenital anomalies, imperforate anus, and other congenital anomalies
• Medication (Hypogonadal, α-blockers, methyldopa, imipramine)
• Radical prostatectomy (RP)
• Retrograde ejaculation; failure of seminal emission

REFERENCE
plastic sperm injection by testicular sperm in pa-
bients with aspermia or azoospermia after cancer 

ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

DESCRIPTION
ART includes all fertility treatments in which both eggs and sperm are handled. Although the Centers for Disease Control and Prevention does not include treatments in which only sperm are handled, there are various methods of sperm retrieval as defined below:

• Percutaneous epididymal sperm aspiration (PESA): Aspiration of sperm from epididymal percutaneously
• Microsurgical epididymal sperm aspiration (MESA): Done by open surgery
• Testicular sperm aspiration (TESA): Done percutaneously
• Testicular sperm extraction (TESE): Done through open biopsy of testicular tissue

• Intratissue insemination (II) or Artificial insemination (AI). Also not ART by strict definition; however these are methods for fertility performed during ovulation by inserting a catheter into the cervix or as injecting concentrated sperm into the uterus, thereby bypassing the cervical mucus barrier.

The following are classical methods of ART:

• Gamete intraturbulap transfer (GIFT): Oocytes and sperm are retrieved, the semen is concentrated, then both are placed into the fallopian tube by laparoscopy.
• In vitro fertilization (IVF): Fertilization by either including sperm with oocytes or by inserting a single live sperm into an oocyte with a micropipette called intracytoplasmic sperm injection (ICSI). The resultant embryo is transplanted to the uterus or fallopian tube with a catheter through the cervix.

In 2017, after IVF of an egg, the resultant embryo is placed into the fallopian tube laparoscopically, instead of through the cervix.

REFERENCE

ASTHENOSPERMIA

DESCRIPTION
A general term for defects in sperm movement, usually a decrease in sperm motility to <30–40% of normal. It can be detected on semen analysis and can be a cause of male factor infertility. (See also Section II: Infertility, Urologic Considerations, Section II: “Semen Analysis, Abnormal Findings, and Terminology.”)

CAUSES
• Antibody antibodies
• Hypogonadotropic state
• Hypogonadism
• Immotile cilia (Kartagener syndrome and immotile cilia syndrome)
• Infection
ATHLETIC HEMATURIA

- Partial ejaculatory duct obstruction (EDO)
- Varicocele (most common surgically correctable abnormality)

TREATMENT

- Aimed at offending agent (ie, antibiotics for infection, sperm washing for antibodies, varicocelectomy)
- Has been noted in vitamins C and E and other low-radical scavengers

REFERENCE


ATHLETIC HEMATURIA

DESCRIPTION

Hematoma, microscopic, or gross, can be noted in athletes engaged in high-intensity or long-duration exercise. Usually benign in course. Repeated episodes of hematuria may cause anemia in some athletes. Theorized causes include stress from hematosis, renal ischemia, release of a hemolyzing factor, direct trauma to bladder or kidney, dehydration, myoglobinuria, increased circulating, and HOBs. Treatment includes adherence to sensible training guidelines and hydration.

SYNONYMS

- Sport-related hematuria
- Exercise-induced hematuria

REFERENCE


ATOPIC DERMATITIS (ECZEMA), UROLOGIC CONSIDERATIONS

DESCRIPTION

Also called eczema, disseminated nervous, atopic eczema, or “itchy-pruritic” skin disease. This chronic pruritic inflammatory condition affects characteristic sites. In adults, the genitalia is a common site. Patients present with itching, excoriations, edema, erythema, and scaling. As the disease progresses, the skin undergoes lichenification (thickening). The cause is unknown, but there is a familial association with this and other atopic disorders (allergic rhinitis, asthma).

TREATMENT

Topical corticosteroids as triamcinolone 0.1% BID nighttime sedation with antihistamines or other agent. Treat stress and remove irritants (soaps, cleansers, fabric made of wool or nylon).

REFERENCE


ATTENTIVE DIGITAL RECTAL EXAM

DESCRIPTION

Utilized to obtain prostate specific antigen in urine to identify DNA, RNA, protein, and metabolite based biomarkers for the detection of prostate cancer. Clinical studies have identified PCA3 and TMPRSS2:ERG fusion transcripts as promising RNA markers for cancer detection and possibly prognosis. A “light prostate massage” should be performed, including firm pressure to depress the gland by 1 cm. A total of 3 strokes per lobe should be performed from base to apex and from lateral to median line. (See Attentive digital rectal exam [DRE] image.)

REFERENCE


ATYPICAL ADEMOMATOUS HYPERPLASIA OF THE PROSTATE (ADENOSIS)

DESCRIPTION

Some lesions can be confused with low-grade prostate cancer on small-needle biopsy samples. The differential diagnosis of these confusing pseudoneoplastic lesions includes atypical adenomatous hyperplasia of the prostate (AAH), sclerosing adenosis, postatrophic hyperplasia, basal cell hyperplasia, and others that must be differentiated from low-grade prostate carcinoma. Histologically, AAH is a crowded focus of small glands. It has not yet been definitively associated with an increased risk of prostate cancer. AAH is no longer considered a premalignant lesion but rather a benign small glandular process of the transition zone that simulates adenocarcinoma. It is recommended to stain for α1B and α1D, which detect basal cell-specific α1. If basal cell staining is present, this helps to rule out carcinoma. Although the biologic significance of AAH is uncertain, its tight microscopic appearance and immunophenotype allow it to be distinguished from carcinoma in most cases. The lesion appears to be distinct from atypical small acinar proliferation (ASAP), which appears to be more associated with prostate cancer (in AAH, reactivity is not usually indicated). See also Section II: “Atypical Small Acinar Hyperplasia, Prostate (ASAP);” Section III: “Postatrophic hyperplasia of the Prostate Gland.”

SYNONYM

- Small gland hyperplasia
- Atypical adenosis
- Atypical small acinar hyperplasia

REFERENCE


ATYPICAL SMALL ACINAR PROLIFERATION, PROSTATE (ASAP)

DESCRIPTION

Prostate needle biopsies occasionally contain cells identified as ASAP that are suspicious for but not diagnostic of malignancy. About 2% of contemporary prostate needle biopsy specimens contain collections of small acini that are suspicious for cancer but that fall below the diagnostic threshold and are often reported as “ASAP suspicious for but not diagnostic of malignancy.” Prostate cancer has been identified in specimens from subsequent biopsies in up to 60% of cases of ASAP indicating this finding is a significant predictor of cancer. Identification of ASAP (with or without high-grade PIN) warrants repeat biopsy for confirm of subsequent invasive prostate carcinoma. (See also Section I: “Prostatic Intratubular Neoplasia;” Section II: “Atypical Adenomatous Hyperplasia and Postatrophic Hyperplasia of the Prostata.”)

REFERENCE


AUA (AMERICAN UROLOGIC ASSOCIATION) SYMPTOM INDEX FOR BPH

DESCRIPTION

Also called the BPH symptom index, and the AUA symptom score or AUA-5, this standardized instrument assesses the degree of lower urinary tract symptoms (LUTS) due to BPH in men, as well as guides response to treatment. Originally developed by the AUA, it is now widely used. (See Section VII: Reference tables: AUA Symptom/International Prostate Symptom Score [IPSS].) The AUA Index consists of 7 questions that assess emptying, frequency, intermittency, urgency, weak streams, and straining, with each graded on a scale of 0–5. Scores can range from 0–35. The index currently categorizes symptoms as:

- Mild (score ≤7)
- Moderate (score 8–19)
- Severe (score ≥20)

The International Prostate Symptom Score (IPSS) is identical to the AUA index, except that it adds a single question to assess the quality of life based on the patient’s perception of the problem. This is scored from 0 (“improved”) to 6 (“worse”). It is suggested that patients with mild symptoms (IPSS ≤7) and patients with moderate or severe symptoms (IPSS >7) who are not bothered by their symptoms (ie, symptoms do not interfere with daily activities) should be managed by watchful waiting, although a wide range of patients with bothersome moderate to severe symptoms prefer this strategy as well. Today, most patients undergo medical management (ie, blockers with or without 5α-reductase inhibitors or 5α-reductase alone prior to any surgical intervention). Surgical options include TURP, transurethral incision of the prostate, open prostatectomy, or minimally invasive therapies (such as transurethral microwave thermotherapy, transurethral needle ablation, and laser-induced photodynamic therapy). (See Section II: “International Prostate Symptom Score (IPSS);” Section VII: “AUA Symptom Index for BPH.”)

REFERENCE


AZOOSPERMIA

DESCRIPTION

The absence of viable sperm on semen analysis and a documented cause of male factor infertility. Azoospermia can be obstructive or nonobstructive. When 1st noted, the sample should be centrifuged and the pellet examined for the presence of sperm. If present, a workup for oligospermia should be performed. A postejaculate urine analysis should be obtained to rule out retrograde ejaculation (ie, the urine contains significant numbers of sperm).
10–15 HPF). If absent, a physical exam for the presence of vasa deferentia and hormone studies are indicated. Treatment is based on the underlying cause. (See also Section I: “Infertility, Urologic Considerations.”) Section II: “Semen Analysis, Abnormal Findings, and Terminology.”

CAUSES
- Congenital absence of vasa deferentia
- Ductal obstruction
- Germ cell failure
- Gonadotoxicity
- Hypoplasmatropic hypogonadism
- Idiopathic
- Testicular failure (Klinefelter syndrome)

REFERENCE

BACK PAIN, UROLOGIC CONSIDERATIONS
DESCRIPTION The differential diagnosis of back pain includes several potential urologic etiologies:
- Cauda equina syndrome is a surgical emergency. Common findings are bladder dysfunction (especially urinary retention) and saddle anesthesia, in addition to sciatica and weakness.
- Endocrine: Adrenal hyperplasia or infarction
- Gynecologic: Neoplasm of uterus or ovary, endometriosis
- Infection: Tuberculosis, osteomyelitis, subarachnoid or spinal abscess
- Medication: Tadalafil—incidence of back pain and/or arthralgia
- Neoplastic: Myeloma, Hodgkin disease, carcinoma of breast, prostate, lung
- Neurologic: Trauma: Injury to bone, joint, internal organs, or ligament
- Orthopedic: Osteomyelitis, fractures
- Psychogenic: Travel anxiety
- Spinal: Intraspinal tumors
- Spondylosis
- Vascular: Vascular thrombosis or embolus

REFERENCES

BALKAN KNEPHROPATHY
DESCRIPTION An immunologic nephropathy endemic to the Balkan Republics of Yugoslavia, Bulgaria, and Romania, and that afflicts mainly the middle-aged rural populations. It is slowly progressive, and may eventually lead to ESRD. Anemia, polyclonality, and hypertransfusion can be seen. Renal biopsy has no specific markers for the disease. Balkan endemic nephropathy is caused by eating bread that is contaminated with a toxin called aristolochic acid, which comes from a plant called Aristolochia. Balkan endemic nephropathy can occur in multiple family members, but it is not an inherited condition. A strong association with increased incidence of upper tract transitional cell carcinoma (TCC) has been documented, although bladder TCC incidence is normal. Treatment involves aggressive surveillance for TCC and renal replacement therapy, as necessary. (See also Section II: “Aristolochic acid” [Tang et al].)

REFERENCE

BANFF CLASSIFICATION, TRANSPLANT REJECTION
DESCRIPTION A classification method developed in 1993 for standardization of criteria in the histologic diagnosis of renal allograft rejection. The Banff classification characterizes renal biopsy findings into a scheme that outlines possible clinical approaches to manage the rejection. (See also Section I: “Transplant Rejection, Renal.”)

REFERENCE

BARCET-REDMAN HYPOSPADIAS REPAIR
DESCRIPTION In a modification of the Mathieu procedure, this repair mobilizes the posterior urethral plate and splits the glans in addition to the penile flap. The full thickness penile and urethral plate grafts are tailored together and laid to rest in the new urethral groove.

REFERENCE

BARIATRIC SURGERY, UROLOGIC CONSIDERATIONS
DESCRIPTION Bariatric surgery, the 1st bariatric procedure, produced severe hyperkalemia secondary to tubular atrophy. Modern bariatric surgery utilizes gastric restrictive procedures and sometimes bypass of variable amounts of small intestine, such as Roux-en-Y gastric bypass and biliopancreatic diversion. Modern bariatric surgery is associated with less malabsorption compared to jejunoileal bypass; however, contemporary bariatric bypass patients continue to have hyperkalemia, hypertriglyceridemia, and lower urine volumes, which result in an increased risk of calculus formation.

REFERENCE
BASHFUL BLADDER (PARURESSIS, SHY BLADDER SYNDROME, “PEE-SHY”)

DESCRIPTION

This is the inability to urinate with others present, such as in a public restroom. It is a relatively common disorder but little is understood about the phobia. According to DSM-III TR, this disorder is classified as social phobia.

REFERENCE


BFG REFRACTORY TRANSITIONAL CELL CARCINOMA (TCC)

DESCRIPTION

TCC that recur after treatment with intravesical BCG treatment. Failure of initial intravesical therapy may be managed by further intravesical therapy or cystectomy. With more aggressive therapy indicated for high-risk patients having superficial invasion (T1), high-grade lesions or concomitant carcinoma in situ (CIS). Patients with high-risk features who fail a 2nd course of BCG have a very high-risk of progression to muscle-invasive TCC. In addition, relapses after >2 courses of BCG appear to be associated with poor outcomes, despite subsequent aggressive therapy. Several different salvage therapies, including intravesical interferon alone or in combination with BCG, valrubicin, mitomycin C, gemcitabine, and other chemotherapeutic agents, as well as photodynamic therapy, have been described for BCG failures. salvage therapies have poor response rates; however, and radical cystectomy remains the “gold standard” for the salvage of failed intravesical therapy in high-risk patients. (See Also Section II: “Bladder Cancer, General.”)

REFERENCE


BCL-2, UROLOGIC CONSIDERATIONS

DESCRIPTION

The protein product of the gene bcl-2-2 acts as an apoptotic blocking agent. It appears to be required for normal morphogenesis of the kidney, and may be unimportant as a prognostic factor in RCC. It is seen in higher levels in prostatic intraductal hyperplasia but is variable in prostate cancer. Levels increase during XRT. Expression is increased in high-grade bladder tumors.

REFERENCE


BECKWITH–WIEDEMANN SYNDROME

DESCRIPTION

This condition is characterized by macrosomia, abdominal wall defects, adrenal cytomegaly, and neonatal hypoglycemia. Other characteristic features include gigantism, variable creases and pits, facial rashes, and prominent eyes with infraorbital recessions. Neonatal hypoglycemia is frequent, of which Wilms tumors, adrenal cortical carcinoma, and hepatoblastoma are most common. Mental retardation is not associated. Most cases are sporadic, but a genetic cause related to mutation or deletion of imprinted genes within the chromosome 15p15.5 region. The mode of inheritance of BWS is complex. Focalis patterns include: autosomal dominant inheritance with variable expressivity, contiguous gene duplication at 15p11, and genomic imprinting resulting from a defective or absent copy of the maternally derived gene. Several lines of evidence support that BWS may be causally associated with right overexpression of the paternally imprinted IGF2 gene. Some suggest a slightly increased risk in babies born by assisted reproduction. Close follow-up early in life is recommended for tumor surveillance as 1 of the most serious findings is the increased risk of neoplasia. In 1 series the majority of tumors were Wilms tumors (67%), followed by hepatoblastomas (11%), rhabdomyosarcomas (5%), and neuroblastomas (4%).

SYNONYM

EMCN syndrome (exomphalos, macrosomia, and gigantism)

REFERENCES


REFERENCES


BEER NEPHROURETERECTOMY

DESCRIPTION

Refers to a retroperitoneal 2-incision approach to a nephroureterectomy through a flank and a separate Gibson or a midline Czerny incision.

REFERENCE


BELLINI DUCT CARCINOMA (COLLECTING DUCT CARCINOMA)

DESCRIPTION

A variant of RCC in which the cell of origin is the collecting duct. Very few cases are reported in literature. Immunohistochemically, the lesion stains with high–molecular-weight keratin and lectin. Histologically, cells demonstrate intracytoplasmic mucinoic material, which is not seen in RCC. Radial nephrectomy for localized disease is the treatment of choice. Chemotherapy is used (interferon–ω-based) for metastatic disease. (See also Section I: “Renal Mass.”) (Image 9-4)

REFERENCE


BEER POTOMANIA

DESCRIPTION

A hypo-osmolality syndrome of beer drinkers, usually with hypoglycemia. Patients with beer potomania have a history of significant beer drinking, often lifelong, in conjunction with a poor diet. This may occur because beer has very little sodium and no protein, and the condition is potentially augmented by the possibility of inappropriate antidiuretic hormone (ADH) secretion.

TREATMENT

Fluid restriction, (CI) monitoring, and serial serum sodium levels, with slow correction of hypoglycemia.

REFERENCE


BEHÇET DISEASE

DESCRIPTION

This is a multisystem vasculitis that is most active during youth; adulthood syndrome characterized by oral and genital ulcers (vulvar and perianal), uveitis, vascular involvement (venous thrombosis, vasculitis), and normocytic normochromic anemia. Lesions on the genitalia are hyperemic and can be painful. Other genital ulcers, such as syphilis, herpes, and chancroid, must be ruled out. Oral ulcers are treated with local moisture-retaining dressings, topical anesthetics, and corticosteroids. Rebutepine is used to treat oropharyngeal ulcers. For severe mucocutaneous lesions, immunosuppressive systemic agents (steroids, azathioprine, penicillin-G, dapsone, interferon-α, colchicine, and thalidomide) have demonstrated benefits.

REFERENCE


BRENNER TUMOR

DESCRIPTION

A renal neoplasm initially described by Dr. Elmer Belt, who described his technique for performing radical perineal prostatectomy in 1939. Dr. Belt described a new approach to the prostate through the perineum between the longitudinal fibers of the rectum and the circular fibers of the external anal sphincter. This approach dramatically decreased blood loss. However, Dr. Belt also recommended leaving behind the apex of the prostate to achieve better urinary control, and opening the anterior layer of the Denonvillier fascia during the dissection.

REFERENCE

BENCHKROU N ILEAL VALVE
DESCRIPTION
A hydraulic valve is used as the continence mechanism in ileal or ileocecal reservoirs. As the reservoir fills, increased pressure occurs in the valve, which is created by imagining an ileal segment that then serves as the effenter continent limb.

REFERENCE

BERGER DISEASE (LG NPHROPATHY)
DESCRIPTION
Sometimes referred to as “hyaluronic immunoglobulin A nephropathy,” this condition was 1st described by Berger and Hinglas in 1966. As the most common primary glomerulonephritis, it exhibits a wide variation in manifestation, ranging from a benign, indolent course to rapidly progressive renal failure. Commonly presents with hematuria, proteinuria, and abnormal urine sediment. Diagnosed by renal biopsy demonstrating LG deposits in the mesangium on immunofluorescence staining.

TREATMENT
• Recent promise seen in corticosteroids, fish oil, and ACE inhibitors
• Renal transplant for cases of renal failure

REFERENCE
Sometimes referred to as

BERGERMAN SIGN
DESCRIPTION
In ultrasonic radiography, the Bergman sign occurs when the ureter is dilated immediately below a neoplasm, rather than collapsed, immediately below a neoplasm, rather than collapsed, as shown in a chalice shape. Retrograde pyelography demonstrates the chalice appearance; a ureteral catheter tends to curl in this segment. The Bergman sign is pathognomonic for neoplasm.

REFERENCE

β-HCG (HUMAN CHORIONIC GONADOTROPIN)
DESCRIPTION
β-HCG is a polypeptide of a molecular weight of 38,000 and a half-life of 2 days. It is produced normally by the syncytiotrophoblast cells in pregnancy. β-HCG is composed of 2 subunits, α and β. The α subunit is identical to a subunit of LH. Urologic uses include staging and follow-up of testicular cancer (elevated in 100% of choriocarcinoma, 7% of seminoma, 60% of embryonal carcinomas). Has been produced by urethral tumors and secreting polynymipharynx. Therapeutically can be given exogenously to stimulate low-grade cells in secondary hypogonadism and facilitate descent of undescended testicles when administered over several weeks. Typical regimen is 500–2,500 U IM 2 times a week for 4 wk. The HCG test is used to diagnose anorexia in undescended testicles; a failure to increase testosterone after administration suggests anorchia. (See also Section I: “Tests, Carcin, General”;

REFERENCE

BIOFEEDBACK, UROLOGIC CONSIDERATIONS
DESCRIPTION
Any method of training the body while receiving feedback on the specific function being trained. Biofeedback ranges from “low tech” (eg, vaginal cones for incontinence) to sophisticated electronic systems (utilizing EMG or pressure probes). Biofeedback is applied in urology for improvement of urinary incontinence, generally by strengthening pelvic floor muscles, and for treatment of dysfunctional voiding. Biofeedback has also been used to teach patients to stop uncontrolled detrusor contractions, teach relaxation of the pelvic floor, and promote normal voiding in children.

REFERENCE

BIOFILM, UROLOGIC CONSIDERATIONS
DESCRIPTION
When microorganisms adhere to the surface of an urologic device (catheter, ureteral stent, implant) and create a matrix of extracellular polymeric substance, Biofilms provide resistance to antimicrobial agents by preventing penetration through the film and thereby limiting access to bacteria. Bacteria protected by a biofilm can also have low expression of antimicrobial binding proteins and activation of intrinsic resistance genes. Biofilm bacteria can typically withstand 1,000–1,500× the concentration of antimicrobial agents utilized to kill nonfilm bacteria. Numerous strategies to avoid biofilm formation are currently being researched. Options include modifying biomaterial surface properties,
DESCRIPTION

Bites to the penis can result in significant injury. Of animal bites, the most common is the dog bite. These can be potentially severe, with deep tissue destruction. In the cases of animal bites, patients tend to present early, and usually the wound can be closed after copious irrigation and any necessary debridement is performed. Broad-spectrum antibiotics should be administered, and wound closure is generally avoided. (See also Section I: “Penis, Trauma.”)

REFERENCES


BIOTHESIOMETRY, PENILE

DESCRIPTION

A simple, inexpensive method of testing the sensory threshold when evaluating neurogenic causes of impotence. It is performed by measuring sensory thresholds, usually in at least 3 different areas of the body, such as the medial malleolus, fingertips, and glans penis. Probably not as accurate and reproducible as other forms of neurologic testing, such as vibral-evoked potentials, pudendal-evoked potentials, and BCR latency. (See also Section I: “Erectile Dysfunction/Impotence, General.”)

REFERENCE


BIRT-HOGG-DUBÉ SYNDROME

DESCRIPTION

Birt-Hogg-Dubé (BHD) syndrome is a rare, autosomal dominant disorder 1st described in 1977. It is caused by germline mutations in the BHD (FH1) gene that lies within the chromosomal band 17p11.2 and encodes for a tumor suppressor protein, folliculin. Folliculin is highly expressed in a variety of tissues, including the skin, kidney, and lung (stromal cells and type I pneumocytes). BHD syndrome is the cutaneous triad of fibrofolliculomas (hamartoma of the hair follicle), trichodiscomas, skin tags, and a propensity for renal tumors. The renal tumors are often chromophobe RCC, oncocytoma, or hybrid of these tumors. However, many will develop clear cell tumors as well. These tumors are more likely to be multiple and bilateral. (See also Section I: “Renal Cell Carcinoma, General.”)

REFERENCE


BITES TO PENIS, ANIMAL, AND HUMAN

DESCRIPTION

Bites to the penis can result in significant injury. Of animal bites, the most common is the dog bite. These can be potentially severe, with deep tissue destruction. In the cases of animal bites, patients tend to present early, and usually the wound can be closed after copious irrigation and any necessary debridement is performed. Broad-spectrum antibiotics should be administered, and wound closure is generally avoided. (See also Section I: “Penis, Trauma.”)

REFERENCES


BLACK-WATER FEVER

DESCRIPTION

Black-water fever is a clinical entity characterized by acute intraocular hemolysis, classically occurring after the introduction of quinine for treatment of malaria. It is a rare but serious condition, in which hemolytic and anemia produce characteristically dark-colored urine. The condition has become rare since 1950, when quinine was replaced by chloroquine. Currently, it has reemerged from the development of resistance to chloroquine. Treatment of black-water fever is supportive, including stopping the offending drug, blood transfusion for severe anemia, and a short course of steroids. (See also Section I: “Malaria, Considerations.”)

REFERENCE


BLADDER AGNESIS

DESCRIPTION

Rare and usually virutal congenital abnormality that has been reported in >20 living patients. Associated abnormalities include renal agenesis, urotelial uterum, crossed fused renal ectopia, malrotation of the gut, colon duplication, anal atresia, imperforated anal canal, and bicornuate uterus. It is caused by a unsgenital virus abnormality during week 5–7 of development.

TREATMENT

• Separation of urinary and fecal stream
• Other reconstructive surgery as appropriate

REFERENCES


BLADDER AUGMENTATION

DESCRIPTION

Bladder segments are most commonly used to improve bladder capacity and manage poorly compliant bladders. The goal is to protect upper urinary tract drainage and maintain renal function. Augmentation cystoplasty is utilized mainly in patients with disorders of the neuologic system (e.g., spinal cord injury [SCI], multiple sclerosis [MS], myelodysplasia). Modifications with bladder neck reconstruction and/or addition of continent channels (interstomal or Monti channel) can be utilized to facilitate both continence and ease in drainage. Complications associated with bladder augmentation include failure to adequately improve bladder capacity, metabolic disturbances, mucous plugging, urinary tract infections, bladder calculi, vesicourethral reflux, bladder perforation, and malignancy (usually adenocarcinoma most commonly located at the region of the anastomosis).

REFERENCE


BLADDER CANCER, INTRAVESICAL AGENTS

DESCRIPTION

Either immunotherapy agents, such as BCG, or chemotherapy agents, such as mitomycin C, are instilled directly into the bladder for the treatment of either carcinoma in situ or high-grade superficial urothelial carcinoma. Adjunct intravesical chemotherapy regimens have been shown to decrease recurrence rates but no clear improvement in overall progression has been demonstrated. Patients who fail intravesical therapy should be evaluated for extirpative treatment. (See also Section I: “Bladder Cancer, General.” “Bladder Cancer, Nephrometic Invasive Bladder Cancer [Ta, T1],” and “Bladder Cancer, Urthelial, Superficial Carcinoma in Situ [T1 NMIBC].”

REFERENCES

656

**BLADDER EARS**

**DESCRIPTION** Primary choriocarcinoma of the bladder is exceedingly rare. Only 7 cases are described in the literature. Most cases present with hematuria and may also have gynecomastia. Metastasis and juxtacystic invasion were seen in the majority of reported cases. A full metastatic workup including social exam and ultrasonogram are mandatory. 3 of the 7 cases were treated with resection and then chemotherapy, and all showed good response (1 patient died of pulmonary embolus during therapy), the other 4 patients died of the disease. (See also Section 1 “Bladder Cancer, General”).


**BLADDER CONTRACTILITY INDEX (BCI)**

**DESCRIPTION** A urodynamic variable. BCI = \( P_{\text{det}}/Q_{\text{max}} < 100 \) defines low detrusor pressure. \( P_{\text{det}} = 10Q_{\text{max}}/1000 \) is the maximum detrusor pressure at maximum flow rate and \( P_{\text{det}}/Q_{\text{max}} \) is the detrusor pressure at maximum flow. Poor detrusor contractility is defined as BCI < 100, normal contractility is BCI between 100 and 150, and strong bladder contractility is BCI > 150.


**BLADDER DIVERTICULUM**

**DESCRIPTION** A bladder diverticulum is a herniation of the urothelial mucosa through the detrusor muscle. Bladder diverticula may be congenital or acquired. Most acquired diverticula are associated with long-standing bladder outlet obstruction (high intravesical pressures) and are most commonly seen in elderly men with benign prostatic hyperplasia or other forms of bladder outlet resistance; it is rare in women. The condition usually evolves from bladder wall trabeculation, to cellule, and finally a diverticulum, typically located on the lateral wall and away from the dome. Since the acquired diverticula have no muscle wall components, they do not empty well and cause urinary stasis with increased risk of infection, stones, and uterine prolapse (urovaginal hernia). The lack of a muscular wall makes urethral carcinoma more likely to extend outside the bladder’s cavity. Congenital bladder diverticula are uncommon and occur almost exclusively in boys. When next to the ureteral orifice (low diverticula), this can result in vesicoureteric reflux on that side. Treatment usually involves correction of the outlet obstruction to reduce high-pressure voiding. Diverticulectomy (open or laparoscopic) can be performed for recurrent infection or bladder calculus. Treatment for cancers within diverticula may include transurethral resection (can be complicated by narrow orifices and thin diverticular wall), laser ablation, diverticulectomy, partial cystectomy, and radical cystectomy with or without intravesical therapy (Image 4).


**BLADDER EARS**

**DESCRIPTION**Transient bladder outpouchings into the trigonal orifice of male infants <6 mo old. This close association of the bladder with the internal ring resolves spontaneously. Inguinal hernorrhaphy in male infants can result in significant bladder damage if bladder ears are present. The condition is differentiated from bladder diverticula by absence of a definable neck.

**REFERENCE**
**BLADDER FILLING DEFECTS**

**DESCRIPTION**
Filling defect on a contrast study of the urinary bladder (cytography) may be the result of:
- Air: Artifactual, postinstrumentation, wessoniometric fistula
- Benign tumor: Prostatic enlargement, inverted papilloma, endometriosis
- Blood clot
- Calculus
- Congenital: Ureterocele
- Extravasitic compression by pelvic organ or mass, pelvic lipomatosis
- Fungal ball (Bazex)
- Infective, inflammatory: Inflammatory edema
- Instruments (catheter), foreign body
- Malignant tumor: Bladder and prostate malignancies, tumors invading urinary bladder from contiguous organs (e.g. uterine, colon)
- Radiologic artifact: Fold in nondistended bladder

See also Section I: “Bladder calculus (neural calculus)” and Section II: “Bladder Mass, Differential Diagnosis.” (Image E)

**SYNONYM**
- Bladder cystocoele

**REFERENCE**

**BLADDER HYPOPLASIA**

**DESCRIPTION**
Lack of urinary bladder development, leading to inadequate function and storage capacity. Hypoplasia is caused either by failure of production or storage of urine, or from complete obliterates of the bladder. Causes include: congenital: renal dysplasia, tuberculosis, bilateral renal agenesis, severe renal dysplasia, and bilateral ureteral ectopia. Bladder reconstruction with bowel-segments can be attempted.

**REFERENCE**

**BLADDER, LYMPHOMA**

**DESCRIPTION**
In lymphoma, involvement of the bladder is usually secondary to systemic disease. Primary lymphoma of the bladder is rare, and carries an excellent prognosis. Most patients are female in the 7th–8th decades. Patients typically present with gross hematuria. The tumors can be single or multiple, sessile or papillary. Most common types are large-cell and small-cell lymphocytic lymphoma and further classified as MAC (medial corticomedullary 8-cell lymphoma). Lymphomas thought to result from chronic inflammation. Many patients in recent series have chronic cystitis. Radiotherapy has been the treatment of choice for localized lymphoma; otherwise, systemic therapy is undertaken if the bladder is not the primary site.

**REFERENCE**

**BLADDER, LEIOMYOMA**

**DESCRIPTION**
A benign spindle cell lesion in the bladder wall. Although these tumors are very rare, they are the most common bladder mesenchymal tumor. The tumors can be single or multiple, sessile or papillary. Most common types are large-cell leiomyosarcoma, myxoid sarcomatoid carcinoma, and myxoid leiomyosarcoma. Resection is the treatment.

**REFERENCE**

**BLADDER, INFLAMMATORY PSEUDOTUMOR**

**DESCRIPTION**
A benign spindle cell lesion in patients who have not had surgery (as opposed to postoperative spindle cell nodules). Most patients are from 20–50 yo and present with gross hematuria. The lesion is nodular or pedunculated, but some may be sessile and invade the muscularis propria. This is a benign lesion, but it must be differentiated from myoid sarcomatoid carcinoma and mesothelial lesions. Resection is the treatment.

**REFERENCE**

**BLADDER, LEIOMYOSARCOMA**

**DESCRIPTION**
Though very rare, it is the most common mesenchymal tumor of the bladder, constituting 0.1% of all bladder neoplasms. Usually incidentally discovered, though if large or pedunculated may present with bladder outlet obstruction. Seen more commonly in females. Generally heterogeneous and smoothly marginated on ultrasound and CT. MRI better and shows the submucosal origin, usually has low T2 and intermediate T1 signal.

**TREATMENT**
- Partial cystectomy can be required for large lesions or primary and secondary involvement by leukemia has been reported.

**REFERENCE**

**BLADDER, RADIATION CUSTODIAL TUMOR**

**DESCRIPTION**
Benign tumor: Prostatic enlargement, inverted papilloma, endometriosis

**REFERENCE**

**BLADDER, HYPOPLASIA**

**DESCRIPTION**
Most are found in the inguinal or femoral region and are often associated with bladder outlet obstruction in men. It is estimated that up to 4% of all inguinal hernias can contain some degree of bladder herniation. Rarely, massive herniation may be found, with significant portions on the bladder and distal ureter descending into the contents; bladder obstruction and distraction has been reported. In women, herniation of the bladder into the anterior vaginal wall is technically a rectocoele. Treatment is repair of inguinal hernia, with reduction of bladder herniation. Bladder outlet obstruction should be identified and treated in males as this may contribute to the original herniation and subsequent recurrences.

**REFERENCE**
**BLADDER SARCOMA (LEIOMYOSARCOMA/RHABDOMYOSARCOMA)**

**BLADDER NECK CONTRACTURE**

**DESCRIPTION**
Scarred and stenotic of the bladder neck is most commonly as a postoperative complication of transurethral resection of the prostate or radical prostatectomy at the site of vesical urethral anastomosis. Bladder neck contracture may lead to decreased urinary flow, high-pressure voiding, urinary retention, urinary tract infections, and incontinence. Factors associated with this complication include urinary leak at the anastomosis, poor muscle approximation, suture retraction, ischemia, or foreign bodies such as surgical clips. Postoperative radiation may contribute. Radiation monotherapy can cause contracture with the presentation from 12–36 mo after completion. Management consists of dilution, endoscopic incision (saw, cold cut, electrocautery) or resection, and, in severe cases, open repair utilizing a Y-V plasty. Occasionally, intermittent self-catheterization may be needed to maintain patency.

**REFERENCE**

**BLADDER NECK HYPERTROPHY**

**DESCRIPTION**
Hypertrophy of the bladder neck is non-inflammatory bladder neck hypertrophy. It may have a role in clinical practice in the future. It consists of 8 questions divided into broad areas: Urge to urinate, urinary frequency, and bladder pain and pressure. For the scoring, a single score is created by summing all 8 items to create a total score ranging from 0–38.

**REFERENCE**

**BLADDER, NEUROFIBROMA**

**DESCRIPTION**
A rare benign tumor of the nerve sheath from overgrowth of Schwann cells, these lesions originate in the bladder from ganglia in the wall. They can present in childhood as obstruction or voiding symptoms. Malignant degeneration is rare. The condition is spread or related to neurofibromatosis. Conservative resection, as needed, is the usual treatment. With severe obstruction or intolerable symptoms, cystectomy may be needed.

**REFERENCE**

**BLADDER OUTLET OBSTRUCTION INDEX (BOOI)**

**DESCRIPTION**
Based on the International Continence Society (ICS) nomogram for identifying bladder outlet obstruction during urodynamic evaluation. The ICS nomogram categorizes patients with LUTS into obstructed, equivocal (or slightly obstructed) or unaffected based on the maximum detrusor pressure during voiding versus the maximum flow rate.

**REFERENCE**

**BLADDER PAIN/INTERSTITIAL CYSTITS SYMPTOM SCORE (BPIC-SS)**

**DESCRIPTION**
BPIC-SS is a questionnaire to select bladder pain syndrome/intestinal cystitis patients for clinical trials. It may have a role in clinical practice in the future. It consists of 8 questions divided into broad areas: Urge to urinate, urinary frequency, and bladder pain and pressure. For the scoring, a single score is created by summing all 8 items to create a total score ranging from 0–38.

**Bladder Pain/Intestinal Cystitis Symptom Score (BPIC-SS)**

**Concept** Item

Urine to urinate: In the past 7 days, how often did you still feel the need to urinate just after you urinated? In the past 7 days, how often did you urinate after you urinated, how often was it because of pain in your bladder?

Urinary frequency: In the past 7 days, how often were you by having to get up during the night to urinate? In the past 7 days, how often were you having to get up during the day to urinate?

Bladder pain and pressure: In the past 7 days, how often do you have a feeling of pressure in your bladder? In the past 7 days, how often did you have pain in your bladder? Select the number that describes your worst bladder pain in the past 7 days.


**REFERENCE**

**BLADDER, PARAGANGLIOMA**

**DESCRIPTION**
Similar to pheochromocytoma in other areas of body. 10% are malignant. They are thought to arise from paraganglion cells in bladder, usually around the trigone. Most are hormonally active and can present with hypertension during bladder filling and firing. Can appear as a submucosal tumor on cystoscopy. Late metastasis can occur, so long-term follow-up is warranted.

**TREATMENT**
• Partial cystectomy is the treatment of choice
• TUR may cause a hypertensive crisis

**REFERENCE**

**BLADDER, PHEOCHROMOCYTOMA**

**DESCRIPTION**
Similar to pheochromocytoma in other areas of body. 10% are malignant. They are thought to arise from paraganglion cells in bladder, usually around the trigone. Most are hormonally active and can present with hypertension during bladder filling and firing. Can appear as a submucosal tumor on cystoscopy. Late metastasis can occur, so long-term follow-up is warranted.

**TREATMENT**
• Partial cystectomy is the treatment of choice
• TUR may cause a hypertensive crisis

**REFERENCE**
BLADDER SMALL CELL CARCINOMA (OAT CELL, SIGNET RING)

For pediatric rhabdomyosarcoma, a multimodal approach utilizing surgery, radiation, and chemotherapy is employed, with improving rates of bladder preservation and improving prognosis. Metastatic disease treatment remains controversial with resection, radiation, and chemotherapy with single-agent chemotherapy in refractory disease. See also Section II: “Bladder Cancer, General.”

REFERENCES

BLADDER SMALL CELL CARCINOMA (OAT CELL, SIGNET RING)

DESCRIPTION
Small cell carcinoma or oat cell carcinoma is an aggressive malignancy derived from either neuroendocrine or pluripotent cells. This tumor most commonly arises in the lung, but may occur in multiple locations including the bladder and less frequently the prostate. Neuroendocrine tumor of the bladder is rare, with ∼283 cases reported in the literature. It can be seen alone or in conjunction with other tumor types, most frequently TCC. Small cell carcinoma of the bladder presents as any other bladder tumor, most frequently with hematuria. The diagnosis is made pathologically, the tumor usually appearing with invasive disease (94% in 1 series), and often with metastatic disease (97% in same series). Most common sites of metastases are the lymph nodes, liver, bone, lung, and brain. Due to the high rate of early dissemination, chemotherapy is the mainstay of treatment, with radical cystectomy often performed afterward. The tumor also appears responsive to combined chemotherapy and radiation. Prognosis is generally worse than for urothelial carcinoma. See also Section I: “Bladder Cancer, General.” (Image 9)

SYNONYMS
• Small cell carcinoma
• Neuroendocrine tumor
• Oat cell carcinoma

TREATMENT
• Partial or radical cystectomy
• Platinum-based chemotherapy has achieved partial regression

REFERENCE

BLADDER, TEARDROP

DESCRIPTION
Diffuse pelvic pathology can compress the bladder into a teardrop configuration on various imaging studies, such as urodynamic urography or cystogram. Causes include pelvic hematoma, pelvic herniation, pelvic adenopathy, and enlarged pelvic

vascularity (usually caused by vena cava obstruction). Occasionally, a muscular patient with a hyper trophyd Repose muscle can exhibit this finding.

REFERENCE

BLADDER TRABECULATION AND CELLULES

DESCRIPTION
Trabeculation is a cystoscopic appearance of hypertrophy of smooth muscle bundles in the muscular propria layer of the bladder wall, which occurs over time due to high-pressure voiding in the setting of bladder outlet obstruction. The obstruction may be due to anatomic obstruction such as benign prostatic hyperplasia (BPH) in the adult or posterior urethral valves in the child, or to neurogenic dysfunction such as detrusor-sphincter dysynchrony. It is a manifestation of increased collagen deposition in the bladder wall. More extreme degrees of trabeculation are termed “cellules.” These small pockets are caused when the bladder muscosa is pushed between the collagen and muscle fibers of the bladder wall. Cellules may progress to form an acquired bladder diverticulum. (See also Section II: “Bladder Diverticulum.”) (Image 9)

REFERENCES

BLADDER, VILLOUS ADENOMA

DESCRIPTION
This tumor has a histologic appearance identical to villous adenoma of the colon. It can also be seen in the stomach. Cystoscopically, it appears neoplastic and papillary. Histologically, a mucous-secreting epithelium with goblet cells is seen. It is treated by transurethral resection with possible cystectomy. If invasion is suspected.

REFERENCE

BLADDER WALL CALCIFICATION, DIFFERENTIAL DIAGNOSIS

DESCRIPTION
Bladder wall calcification is a relatively uncommon finding. The differential includes:
• Amiodarone
• Bilharzia (urinary schistosomiasis)
• Cyclophosphamide-induced cystitis
• Encapsulated cysts
• Mitomycin C intravesical treatment
• Tuberculosis
• Urethral carcinoma

REFERENCE

BLADDER WALL THICKENING, DIFFERENTIAL DIAGNOSIS

DESCRIPTION
Bladder wall thickening can be seen on US, CT, or MRI. The differential includes:
• Bacterial cystitis
• Bilharzial infection (urinary schistosomiasis)
• Bladder cancer (urothelial carcinoma)
• Bladder fistula (Crohn disease, diverticulitis)
• Hemorrhagic cystitis
• High-pressure storage voiding (bladder outlet obstruction, neurogenic bladder)
• Systemic lupus erythematosus
• Tuberculosis (Image 9)

REFERENCES

BLASTOMYCOSIS, GENITOURINARY

DESCRIPTION
Blastomyces dermatitidis is endemic in the Ohio, Mississippi, and Missouri river basins. It is an opportunistic infection in immunosuppressed patients, particularly associated with prolonged steroid use (>2 mo), HIV, solid tumors treated with radiation or chemotherapy, and end-stage renal and hepatic disease. GU blastomycosis tends to involve the prostate and epididymis, and produces voiding complaints. Genitourinary disease may be seen in 20–30% of disseminated infections. Prostatic abscesses can be seen, up to 30% can have epididymal involvement. GU blastomycosis is a manifestation of systemic disease; it has been reported to be transmitted by sexual relations to the GU system of the partner. Diagnosis may be made by isolation of fungus from the urine, semen, or tissue. Detection of Blastomycosis A antigen by immunodiffusion may be helpful in diagnosis. Other serologic testing with enzymeimmunosassay and radioimmunoassay have high sensitivity (85–88%) and specificity (100%).

TREATMENT
• Standard therapy for disseminated infection is long-term amphotericin B
• Long-term ketoconazole (12 mg) at 400 mg/day may be effective for prostatic/lipidicystitis
• Imoconazole may be effective in local uncomplicated infections

REFERENCES
Bleomycin Toxicity

DESCRIPTION

Bleomycin is a combination chemotherapy for testicular cancer as well as cervical, ovarian, SCC, and lymphoma, induces single- and double-strand breaks in DNA called scission. Pulmonary fibrosis (fibroelastic alveolitis) is a potentially lethal toxicity, it can develop 1–4 mo after treatment and has been reported to occur beyond 6 mo. Bleomycin may also cause hypersensitivity pneumonitis and nodular pulmonary densities. Skin changes, alopecia, and stomatitis are common. Vascular toxicity, anaphylaxis, and Raynaud phenomenon have been reported. Clinical indications of pulmonary toxicity may include any of the following: Cough (prolonged), dyspnea, pleural chest pain, fever, tachypnea, sinks, loss of restriction, and hypopnea. Renal insufficiency is a risk factor for bleomycin toxicity (90% eliminated by the kidney).

TREATMENT

- Discontinue drug with suspected bleomycin-induced injury; vincristine may help some cases.
- Attention to minimizing oxygen concentration and hydration status during surgery is essential.

REFERENCE


Blue Diaper Syndrome

DESCRIPTION

Deficit in tryptophan absorption in which the urine contains indoles, giving it a blue color. Similar to Hartnup disease, a chronic course is usual. Hypoglycemia of the optic disc and abnormal eye movements have also been reported.

SYNONYMS

- Familial hypercalcemia with nephrocalcinosis and indurated skin
- Tryptophan malabsorption
- Phenylketonuria

TREATMENT

Low-tryptophan diet; no treatment known for underlying defect.

REFERENCE


Blue Dot Sign

DESCRIPTION

A blue discoloration seen through the scrotal wall when the testes are tented against the skin. Indicates the presence of torsion of the appendix testis itself. If torsion of the cord can be ruled out by skin. It has been reported in lesions with adenoscincoma.

REFERENCE


Blue Nevus (Melanosis), Urologic Considerations

DESCRIPTION

Beige melanotic lesion of the prostate that may be differentiated from multiplicity melanoma. It is usually an incidental finding after TURP. In prostate, the term blue nevus has been used when melanin is confined to atrophic or elongated melanocytes in the stroma, whereas the term melanosis has been used for those prostatic lesions that have melanin in both the stromal melanocytes and glandular epithelium. It has been reported in lesions with adenocarcinoma.

REFERENCE


Body Mass Index (BMI), Urologic Considerations

DESCRIPTION

The BMI is defined as the weight (in kilograms) divided by the height (in meters)². BMI is used to categorize obesity (see table). Higher BMI carries many increased health risks, including diabetes and coronary artery disease. Obesity and elevated BMI have many detrimental effects and associations in urology. Elevated BMI has been shown to be an independent risk factor for incontinence in females and for adverse outcomes in prostate cancer. BMI has been clearly correlated with incidence and risk of formation of renal calculi in both men and women. It has been implicated in ED, with reduction of BMI correlating with improved IIEF score. Increased BMI as a marker of obesity implies increased difficulty in many open, laparoscopic, and percutaneous procedures. A BMI calculator from the NIH is available online at:\n
http://www.nhlbisupport.com/bmi/.

(See also Section II: “Obesity, Urologic Considerations.”)

REFERENCE


Classification of Overweight and Obesity by BMI

<table>
<thead>
<tr>
<th>Obesity Class</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5–24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0–29.9</td>
</tr>
<tr>
<td>Obesity I</td>
<td>30.0–34.9</td>
</tr>
<tr>
<td>Obesity II</td>
<td>35.0–39.9</td>
</tr>
<tr>
<td>Extreme obesity</td>
<td>≥40</td>
</tr>
</tbody>
</table>

REFERENCES


Bone Marrow/STEM Cell Transplantation, Urologic Considerations

DESCRIPTION

High-dose chemotherapy regimens used for bone marrow transplantation and stem cell transplantation are accompanied by multiple toxic side effects. The most common urologic complication is hemorrhagic cystitis (HC), with an incidence ranging from 7–68%. HC is commonly seen in a dose-dependent manner after the administration of cyclophosphamide and Fludarabine. Both medications have the same metabolite, acrolein. HC can further be caused by busulfan, pelvic irradiation, thrombocytopenia, and the presence of a urinary viral infection (adenovirus, BK virus, cytomegalovirus [CMV], polyoma virus). Early onset HC is seen due to acrolein exposure, late HC is associated with viral etiologies. Other possible urologic sequelae of high-dose chemotherapy exposures include bladder fibrosis, fistula, bladder contractures, chronic urinary tract infections, pyelgia, and secondary malignancies. A preservative measure for HC is preservation with 2-merscaptoethane sodium sulfate (Mesaon) and hydration. Catheter drainage and continuous bladder irrigation may prevent acrolein exposure to bladder urothelium. Urinary bladder syndrome and urolc acid stone development are also possible.

REFERENCE


Bone Metastasis, Urologic Considerations

DESCRIPTION

Bone metastasis is a common problem in patients with malignancies. Prostate cancer has a predilection to metastasize to bone but bone metastases are also seen from renal cell carcinoma, osteosclerotic carcinoma, and adrenocortical carcinoma is also seen. An elevated alkaline phosphatase suggests bone lesions. The diagnosis often involves a radiographic bone scan with confirmatory imaging study and possibly biopsy. Bone metastases are associated with pain (which may be severe), pathological fractures, and possible spinal compression (often referred to as skeletal-related events or SRE). These lesions often require treatment independently from the primary tumor. Options for treatment include chemotherapy, surgery, and external beam radiation. Radiation therapy is often highly successful at controlling local bony symptoms and radiosteard carbamates such as strontium-89 are useful for palliation of more extensive bone metastasis. Radium 223 ([223Ra]) an α-emitter has been approved for bone metastases, prostate cancer and can improve quality of life and extend survival in metastatic castrate resistant prostate cancer. In prostate cancer in particular, bisphosphonate therapy such as zoledronic acid, and...
osteoclast targeting agents such as denosumab are used to prevent progression and skeletal-related complications and may be effective at preventing occurrence of bone metastases (Image 0).

REFERENCES

BONE MINERAL DENSITY, UROLOGIC CONSIDERATIONS
DESCRIPTION: Prolonged ADT for prostate cancer is associated with decreased bone mineral density (BMD) and osteoporosis, leading to disabling skeletal fractures. Bisphosphonate therapy (zoledronic acid, alendronate, others), smoking cessation, weight-bearing exercise, and vitamin D and calcium supplementation can help improve BMD during androgen ablation therapy. (See also Section II: "Osteoporosis and Osteopenia, Urologic Considerations.") Some recommend that BMD should be monitored during androgen-deprivation therapy using BMD scans (dual energy x-ray absorptiometry or DEXA).

- T-score: The number of standard deviations (SD) by which the patient’s bone mass falls above or below the mean peak bone mass for a 30-year-old healthy adult. For every 1.0 decrease in T-score, relative risk of fracture increases ~1.5–2.5-fold.
- Z-score: Interpretation of T-scores: Normal: –1 to –2.5; Osteopenia: ≤ –1 to 2.5; Osteoporosis: ≤ –2.5; Severe osteoporosis: ≤ –3 and ≤ 1 fracture


BONE SCAN, UROLOGIC CONSIDERATIONS
DESCRIPTION: The radionucleotide bone scan is a sensitive test for bone metastases and is obtained during the initial staging or in the setting of recidivism or metastatic disease in urologic malignancies (prostate, renal, renal, and adrenocortical carcinoma). A standard bone scan is generally performed by acquiring multiple images of the skeleton 3–4 h after injection of technetium-labeled methylene-diphosphonate (MDA). Due to low specificity, if a lesion is identified, particularly when solitary, further investigation is necessary using confirmatory testing. This may be done with plain radiographs, CT, or MRI. Bone scans are extensively used in prostate cancer to detect and follow bone metastases. In prostate cancer patients with extensive bone metastases, the bone scan may have a “super scan” appearance, in which the focal lesions coalesce to produce diffuse increased uptake. An increase in the contrast between bone and soft tissue and faint or absent renal images are the typical appearances seen on a “super scan.” (Image 0)


RONEY TEST (MARSHALL TEST)
DESCRIPTION: A clinical test used for ~50 yr for the diagnosis of stress incontinence and for the selection of patients for incontinence surgery. As originally described, the test consists of 2 parts:
- The patient coughs with a full bladder, and simultaneous urine loss from the urethra is visually confirmed. The examiner elevates the bladder neck with a finger on either side of the urethra while the patient coughs again.
- If the patient is then continent, the test is considered positive and the patient is thought to have an anatomic defect correctable by surgical excision of the bladder neck. Bonney cautioned that the fingers must be carefully placed to avoid compressing the urethra in the immediate postoperative period.


BORS-COMARR CLASSIFICATION OF VOIDING DYSFUNCTION
DESCRIPTION: Based on observations noted with spinal cord injury patients. The system takes into account 3 main factors:
- Anatomic location of the lesion (upper motor neuron, lower motor neuron)
- Completeness of the lesion (partial vs. complete SCI)
- Presence of residual urine, which would mean “unbalanced,” according to the definition
- Best applied to patients with a complete neurologic lesion after spinal shock has resolved.


BOWENOID PAPULOSIS
DESCRIPTION: Bowenoid papulosis is an uncommon skin lesion affecting the genital, groin, and perianal areas of young, sexually active adult men and women. The histology appearance resembles anogenital actinic keratosis, but the lesions usually follow a benign clinical course, and spontaneous regression is observed. Evolution of the lesions to invasive carcinoma is rare. The papules are asymptomatic, discrete, small (average 4 mm in diameter), flat, reddish violaceous or brown, often cockrocker, and usually have a smooth, warty surface. Many patients have a history of genital infection with viral warts or herpes simplex. Genital warts are primarily caused by HPV types 6 and 11; treatment should be conservative. Individual lesions can be adequately treated with excision, cryosurgery, or laser surgery, much as ordinary warts, without the need for wide surgical excision. Alternatively, lesions may be treated with 3–5 wk with 5% 5-fluorouracil cream or imiquimod cream (QD).

and diminution of the radiation dose to the prostate.

organ, especially in cases of patent foramen ovale, regarding this process are possible injury to the end diagnosed incidentally on imaging studies. 2 concerns frequently involved in embolization. Because of their 0.8 mm in diameter and, due to its small size, is more emboli exist through a patent foramen ovale. The is the lung, but reports of coronary artery and hepatic 0.7–55% of all cases. The most common target organ seed displacement and embolization ranging from Multiple investigations have yielded varying rates of prominent periprostatic veins and traveling centrally. seeds, when placed into periprostatic tissue, have been noted to migrate, at times entering the prostate cancer via image-guided implantation of

Nguyen BD. Cardiac and hepatic seed implant

REFERENCE

BOYARSKY GUIDELINES FOR BPH
DESCRIPTION: To provide reproducible guidelines for the severity of symptoms of prostate, BPH, and LUTS, score questionnaire forms have been developed. Traditional assess questions tool include the Seattle–Maden–Pointer System and the Boyarsky Guidelines. These have been generally replaced by the AUA or IPSS questionnaires, but are used in several ongoing follow-up studies of BPH therapies.

REFERENCE

BOYCE NEPHROTOMY (ANATROPHIC NEPHROLITHOTOMY)
DESCRIPTION: The longitudinal anatomic nephrolithotomy [lens advantage of a nearly avascular plane in the kidney (Bridle white line), which can be used to remove staghorn calculus (Boyce anatrophic nephrolithotomy). The incision site in the lateral posterior surface of the kidney can be accurately identified by injecting indigo carmine in the posterior renal artery branch. Once the capsule is incised, the parenchyma is divided with the blunt end of the knife in the proper plane. Traditionally used for staghorn calculus.

REFERENCE

BRACHYTHERAPY SEED EMBOLUS
DESCRIPTION: Brachytherapy is used to treat prostate cancer via image-guided implantation of radioactive seeds of iodine-125 or palladium-103. These seeds, when placed into periprostatic tissue, have been noted to migrate, at times entering the prominent periprostatic veins and traveling centrally. Multiple investigations have yielded varying rates of seed displacement and embolization ranging from 0.7–55% of all cases. The most common target organ is the lung, but reports of coronary artery and hepatic emboli exist through a patent foramen ovale. The iodine-125 seed measures 4.5 mm in length and 0.8 mm in diameter and, due to its small size, is more frequently involved in embolization. Because of their size, these emboli are often asymptomatic and are diagnosed incidentally on imaging studies. 2 concerns regarding this process are possible injury to the end organ, especially in cases of patent foramen ovale, and diminution of the radiation dose to the prostate.

REFERENCE

BRAND METASTASIS, UROLOGIC CONSIDERATIONS
DESCRIPTION: Brain metastasis disease can be seen with several urologic malignancies, most commonly with renal cell carcinoma and germ cell tumors (GCT). They generally are poor prognostic indicators. Patients may be asymptomatic with occult disease or display neurologic symptoms such as headache, nausea, and vomiting, mental status changes, seizures, or focal signs. Patients presenting with neurologic symptoms and neurologic signs should be worked up for brain metastases. CT Scan is generally quick and readily available, but MRI has higher sensitivity and is better at distinguishing metastases from other intracranial processes. Due to their close impact on quality of life, these often require prompt treatment usually via radiation therapy or surgical removal.

REFERENCE

BRENNER TUMORS
DESCRIPTION: These are tumors of variable malignant potential of the ovary. Extravasation and testicular origins have been reported, and they usually present as an ovarian mass. Light microscopy demonstrates distinctive nests of transitional cells indistinguishable from urothelium. Classified as typical, metaplastic, proliferating, or malignant, these lesions usually stain for carcinoembryonic antigen (CEA). Theorized origin is from a metaplastic process of coelomic epithelium. Usually, surgical removal is used to assess malignant potential.

REFERENCE

BRICKER URETAL ANASTOMOSIS
DESCRIPTION: A direct ureter-to-small bowel end-to-side refluxing anastomosis incorporating full-thickness ureteral and intestinal wall. It is used in local suit construction.

REFERENCE

BRIGHAM SLING (URETHROPERYX)
DESCRIPTION: Used to treat stress incontinence in women. A combined endoscopic needle sling procedure that utilizes a Versa facial strip placed at the bladder neck through a vaginal incision. The facial sling is held in place with needles placed through the anterior abdominal wall, similar to the Scarpel and Raz suspension needle procedures. (See also Section I: "Conventional, Urethra, Adult Female.")

REFERENCE

BRINK SCORE
DESCRIPTION: A digital test of pelvic muscle strength for evaluation of a pelvic muscle exercise program. Factors of perceived pressure, alteration of the vertical plane of the pelvis was timed to form a 3-point scale. Currently used in pelvic floor physical therapy regimens.

REFERENCE

BRITISH TESTICULAR TUMOR CLASSIFICATION
DESCRIPTION: Used mainly in Great Britain, and based on the concept that all nonseminomatous tumors represent displaced, nonorganized embryonic blastomeres and are therefore teratomas. Disperse lesions are classified under a common category. The World Health Organization classification is used in most of the rest of the world.

REFERENCE

BRONCHOGENIC CYST, RETROPERITONEAL
DESCRIPTION: Bronchogenic cysts are congenital abnormalities arising from remnants of the primitive foregut, which gives rise to the respiratory diverticula. Generally asymptomatic and benign, these lesions are often incidentally discovered. The true prevalence is unknown due to their asymptomatic nature. Retroperitoneal location is exceedingly rare with only approximately 60 cases reported in the literature. Most retroperitoneal bronchogenic cysts are located near the left adrenal gland or paraaortic. Anatomopathologic criteria include pseudostratified, ciliated columnar epithelium with cartilage, smooth muscle or serous glands. May become larger over time due to continued epithelial secretion, infection, perforation, hemorrhage, and malignant degeneration are possible and surgical extirpation is recommended. Definitive diagnosis can only be made histopathologically. (See also Section I: "Retroperitoneal Masses, Male, and Cysts.")

REFERENCE

BRUNN BUDS AND NESTS (VON BRUNN NESTS)
DESCRIPTION: Variant of bladder epithelium, noted in the development of normal bladders. Brunn buds are an invagination of surface epithelium into the lamina propria. Brunn buds represent a further invagination of epithelial cells present within the lamina propria of the normal bladder. They are not a normal finding and may represent a cystic lesion. The presence of Brunn buds is used to differentiate between a true and a false cyst. The presence of Brunn buds is used to differentiate between a true and a false cyst.

REFERENCES
BRUSHITE (CALCIUM MONOHYDROGEN PHOSPHATE)

DESCRIPTION
Brushite is a calcium phosphate cement used as a bulking agent.

REFERENCES

BULBOCavernous Reflex

DESCRIPTION
The bulbocavernous reflex is elicited by squeezing the glans penis and observing for anal contraction. It is a reflex that is mediated by the pudendal nerve, which is innervated by the S2–S4 spinal roots. The afferent limb of the reflex arc is from the sacral neurologic integrity. The reflex is commonly used in elderly patients with SUI related to nerve damage.

REFERENCES

BRUSHITE (CALCIUM MONOHYDROGEN PHOSPHATE)

DESCRIPTION
Brushite is a calcium phosphate cement used as a bulking agent.

REFERENCES

BULBOCavernous Reflex

DESCRIPTION
The bulbocavernous reflex is elicited by squeezing the glans penis and observing for anal contraction. It is a reflex that is mediated by the pudendal nerve, which is innervated by the S2–S4 spinal roots. The afferent limb of the reflex arc is from the sacral neurologic integrity. The reflex is commonly used in elderly patients with SUI related to nerve damage.

REFERENCES

Table: Bulking Agents, Injectable

<table>
<thead>
<tr>
<th>Material</th>
<th>Brand Name</th>
<th>Description</th>
</tr>
</thead>
</table>
| Combination of calcium hydroxyapatite (CaHA) and calcium carbonate/hydroxylapatite carrier gel | Coaptite | Calcium is a principal component of human bone and tooth and has been used in multiple orthopedic and dental applications. It is demonstrated bone formation and is soft enough to avoid fibrotic infiltration. 

Gluatarylate cross-linked bovine collagen | GAV Collagen | Highly purified 35% suspension of bovine collagen (95% type I collagen and 1–5% type II collagen). Does not cause granuloma formation or migration to distant body sites. Begins to degrade in 12 wk; completely degraded in 19 mo, but the injected material transforms into living connective tissue. 

Pyrolytic carbon-coated zirconium beads | Durosphere | Nonresorbable pyrolytic carbon-coated zirconium beads are much larger (212–500 μm) than either PTFE or silicone polymer beads. Are suspended in a highly viscous silicone gel, which is soft enough to avoid fibrotic infiltration. 

Ethylene vinyl alcohol (EVOH) | Tegress | Permanently implanted nonpyrogenic, injectable bulking agent (EVOH). The resulting mixture is FDA-approved for management of intrinsic sphincteric deficiency in women. 

Silicone polymers | Macroplastique | Biocompatible and biodegradable implant. The dextranomer microspheres range from 80–250 μm in size. 

Dextranomer microspheres | Deflux | Viscous gel of dextranomer microspheres (50 mg/mL) in a carrier gel of nonanimal stabilized hyaluronic acid, constituting a bioresorbable and biodegradable implant. The dextranomer microspheres range from 80–250 μm in size. 

REFERENCES

REFERENCES

REFERENCES

REFERENCES

REFERENCES

REFERENCES
REFERENCE

BURCH COLPOSUSPENSION
DESCRIPTION
The pubocervical fascia at the level of the bladder neck is folded to Cooper’s ligament bilaterally, usually through a parametrial incision and a retropubic exposure. It is used in treatment of stress incontinence in women.

REFERENCE

BUSCHKE-LOWENSTEIN TUMOR
DESCRIPTION
Benign malignant perineal or perianal lesion, which may be large and exophytic. May cause urethral erosion and fistulae. Can be very locally invasive and metastasize to lymph nodes. Microscopically, broad rete pegs, filled with benign squamous cells and surrounded by a layer of inflammatory cells, are noted. A possible role of HPV 6 and 11 in the development is theorized. Treatment is by local excision after proven diagnosis. See also Section 1: “Condyloma Acuminata (Venereal Warts)” and “Penis, Lesion.”

SYNONYMS
• Verrucous carcinoma
• Giant condyloma acuminata

REFERENCE

CALCYPHALYSIS
DESCRIPTION
Calciphylaxis, also known as calcific uremic arteriosclerosis, is a rare cutaneous systemic disease seen with advanced chronic kidney disease. The classical cutaneous picture is a necrotic and progressive skin ulcer (necrotic pattern), primarily in the lower legs and susceptible to local infection. It is a product of mural calcification and occlusion of cutaneous and subcutaneous arteries and arterioles. Calciphylaxis has been reported to occur in 1–4.5% of patients in dialysis, mostly in hemodialysis, with predominance in patients who are obese, diabetic, or have liver disease, are using systemic corticosteroids or have a calcium-phosphate product of >70 mmol²/L. Calciphylaxis is reported to be a lethal complication with an estimated 1-yr survival rate of 48.8%. Mortality is usually reported as a result of local and systemic infections and sepsis.

REFERENCE

REFERENCES

CALCIFICATIONS, ADENOMAL AND PELVIC TUMOR
DESCRIPTION
Adenomatous and pelvic calcifications are a common finding on plain radiographs and CT. The differential is very broad and includes renal, adrenal and bladder calculi, vascular calcifications (atherosclerosis and phlebothrombosis), calcified tumors, lymph nodes, seminal vesicles, vas deferens, and infectious processes (TB) (Image 4).

REFERENCE

CALCIFICATIONS, BLADDER
DESCRIPTION
Bladder calcifications on CT or plain radiography:
• Intraluminal: Bladder calculi, 7% of bladder calcifications, may be small stones, encrusted cystitis, foreign body, iatrogenic (postop sutures, retained prostate chips, catheter fragments, hair [due to chronic self-catheterization], following intravesical BCG or mitomycin)
• Bladder wall: Infections (tuberculosis, schistosomiasis), squamous cell carcinoma, cyclophosphamide-induced cystitis, prior radiation treatment, amyloidosis

REFERENCE

CALCIFICATIONS, PROSTATE
DESCRIPTION
Calcifications within the prostate are fairly common and can be detected in over 50% of older men. In 1 series, of normal men calcifications were found in 23.1% of men aged 20-29 yr compared with 83% for men aged 60-69 yr. Prostatic calcification or calcified nodules are rare. On Doppler imaging they create a prominent “twinkle” artifact. Prostatic calculi usually coexist with prostatitis or BPH in elderly men. BUN along with sodium is thought to be decreased in the setting of increased renal clearance. In renal failure, BUN and creatinine levels are increased, and anemia is usually associated. With anemia, BUN levels decrease in patients with renal disease (diabetic nephropathy, amyloidosis, chronic kidney disease). The serum BUN level depends on both the rate of production and the rate of renal clearance. A decreased level of BUN in renal failure is due to loss of renal mass, and it is not an indication of adequacy of dialysis treatment. Amyloidosis, cyclophosphamide-induced cystitis, prior radiation treatment, amyloidosis

REFERENCE


CALCIFICATIONS, RENAL
DESCRIPTION
May represent calcified renal calculi or calcified cystic or solid renal neoplasms. RCC is detectable on plain radiography and calcified renal calculi can be identified on plain radiographs and CT. The differential is very broad and includes papillary tip calcifications, calcified renal pelvis TCC, nephrocalcinosis, calcified renal artery, and tuberculosis (Image 4).

REFERENCE

CALCINOSIS, IDIOPATHIC SCROTAL
DESCRIPTION
Occur in pre-existing epididymal cysts or in the testis without cysts. Usually affects young men. Multiple cysts ≤2 cm are not uncommon. Calculations range in size from a few millimeters to 3 cm. They may represent epididymal cysts that have, over time, lost their normal wall and calcified. Surgical excision is curative if symptomatic.

REFERENCE
Oral calcium supplementation may be used for a variety of conditions, including osteoporosis. Because calcium carbonate and calcium phosphate are widely used but poorly absorbed from the intestinal tract, these can increase urinary calcium excretion and promote calcium oxalate/phosphate stone disease. Calcium citrate (Citracal) has 950 mg of calcium citrate and 200 mg of elemental calcium in each tablet and increases urinary calcium excretion. However, this formulation also increases urinary citrate excretion, which potentially offsets the lithogenic potential of the calcium supplement–induced hypercalciuria. If calcium supplementation is to be considered to prevent osteoporosis, calcium citrate preparations should be used. In women with a history of stone disease, consider a 24-hr urine collection to identify those who will become or remain hypercalciuric while receiving calcium citrate or slow-release potassium phosphate can be used.

CAMEY I AND II ORTHOTOPIC URINARY DIVERSION

DESCRIPTION In the Camey I procedure, a 40-cm segment of the ileum is chosen for an orthotopic urinary diversion that can reach the urethra. A subcutaneous ventral ileal anastomosis is carried out on each end of the final segment. In the Camey II version, the initial Camey I diversion is modified by using 65 cm of ileum, which is detubularized along its antimesenteric border. It is folded into a U-shape configuration, the adjoining sides of the U are sutured, and the resulting bowel is then folded again to create a pouch anastomosed to the urethra with a Lefort ileal ureterostomy.


CANAL OF NUCK HYDROCELE AND CYST (FEMALE HYDROCELE)

DESCRIPTION In the female, the labia majores are homologous to the scrotum in the male. The labia majores contain the terminal portion of the round ligaments of the uterus and an obliterated remnant of peritoneum similar to the tunica vaginalis, which may persist as the canal of Nuck. A hydrocele (fluid collection) may rarely form in the canal of Nuck.


CANDIDIASIS—CUTANEOUS, EXTERNAL GENITALIA

DESCRIPTION Candida albicans, the most common Candida fungus, rarely colonizes normal skin. Risk factors include the elderly, damaged skin, diabetes, broad-spectrum antibiotic use, steroids, pregnancy, and immunosuppression. Can involve warm, moist areas such as distal urethra, scrotum, inguinal region, glans penis of uncircumcised male and causes burning, itching, redness, dysuria, and pruritis in females (vulvovaginitis). Vesiculobulbar plaques that enlarge and rupture can progress to maceration and erythema. There are distinct nod borders, often with satellite lesions with vesicular discharge being white and thick. Microscopic exam of scrapings or discharge with potassium hydroxide or Gram stain reveals hyphae/pseudohyphae. (For systemic candida, see Section 3, “Fungal Infections, Genitourinary.”)

TREATMENT

• Keep affected areas dry and exposed to air
• Men: Topical Nystatin, 100,000 U/L, microscopic cream QOD
• Women: microscopic cream QOD
• Avoid tight or restrictive clothing
• Women: Nystatin oral Solution or Microconazole cream 100 mg for 3–7 days, others
• More severe infections may require long-term ketoconazole


CAPTOPRIL TEST

DESCRIPTION As a functional test for renovascular hypertension, plasma renin activity (PRA) is measured before and 1 hr after the administration of 20 mg of captopril. The test is considered positive if all of the following occur: Postcaptopril PRA > 12 ng/mL/h, an absolute increase in PRA > 10 ng/mL/h, and a 400% increase in baseline PRA (150% increase if the baseline PRA was >3 ng/mL/h). A positive captopril test points to renovascular hypertension. The test has a sensitivity of ~74% and a specificity of 89%. All diuretics and ACE inhibitors must be discontinued 1 wk prior to the test, and a normal or low-sodium diet is necessary.


CARCINOID TUMORS, GENITOURINARY

DESCRIPTION Very rare in the GU tract, carcinoid tumors have been described in the kidneys, ovaries, uterine cervix, urethra, testes, and bladder, and may have associated carcinoid syndrome. They are usually small, 5–10 mm, and rarely metastasize; carcinoma, adenocarcinoma, and carcinoid tumors are the most common histologic types. The most common sites of occurrence are the bladder, ureter, and renal pelvis.


CARCINOSARCOMA, BLADDER

DESCRIPTION Rare tumor exhibiting elements of epithelial and mesenchymal origin. These usually are fast growing, invasive tumors. Epithelial elements are typically TCC, but they can be any of the other tumor types. Mesenchymal elements are usually spindle cells with evidence of chondroid, osteoid, smooth muscle, or rhabdomyoblastic differentiation. Usually presents with painless, gross hematuria.

TREATMENT

• Transurethral resection or radical cystectomy, as appropriate
• Chemotherapy and radiotherapy for metastatic disease, but outcomes are poor (Image 10)

Carcinoma, Prostate

**DESCRIPTION**
Very rare tumor, similar to the carcinomas of the bladder. These tumors are mixtures of epithelial and sarcomatous elements. The epithelial element in the prostate, however, is adenocarcinoma. Most differentiate from colloid tumors, which are separate coexisting tumors of differing cell types. True carcinomas have an intermediary of cells in the same tumor. Has been described following radiation therapy. Treatment is RR, if organ-confined.

**REFERENCES**

Carney Syndrome (Carney Complex)

**DESCRIPTION**
Also called familial myxoma, the syndrome is characterized by skin pigmentary abnormalities, myxomas, endocrine tumors or overactivity, and schwannomas. Primary pigmented nodular adenocortical disease or PNAAD, which causes Cushing syndrome, is the most frequently observed endocrine tumor in Carney Complex or CNC, occurring in approximately 25%. Pale brown to black lentigines are the most common presenting feature of CNC, and typically increase in number at puberty. Cardiac myxomas occur at a young age. Large-cell myofibroblastomas of the GISTs of the stomach, lung chondroma, paraganglioma, adrenal gland, leiomyoma are syndrome-defining tumors. Of the classic triad, GIST is the most common presenting lesion (75%), followed by lung chondroma (15%) and paragangliomatous tumor (10%). 1/3 of patients had a normal serum PMS level, 1/3 had low serum PMS level, and 1/3 had elevated serum PMS level.

**REFERENCES**

Carcinoma, Urethral

**DESCRIPTION**
An inflammatory lesion of the distal urethra that usually presents as a non-cavitating bladder mass in the postmenopausal woman. Usually reassembles in appearance and covered by mucosa, the lesion protrudes from the urethral meatus. The lesion may thrombose or necrose and may present with spotting of the underwear or even pain. Treatment may involve local estrogen replacement or simple excision. Excision should be considered for any atypical appearing lesions as pathologically significant lesions such as melanoma have been known to mimic this lesion. (See also Section 1: “Urethra, Mass.”)

**REFERENCES**

Causal Procedure

**DESCRIPTION**
A variant of the Yamp-Mont real tube, which is often too short to reach from the bladder to the skin surface. This procedure involves a long (12 cm) catheterizable tube (12–16 Fr) from a short (3.5 cm) segment of bowel, usually ileum. It was designed to take the place of the appendix or colon as a continent channel for intermittent catheterization of the bladder utilizing the Mitrofanoff principle. To increase the canal length, as may be necessary in obese children, Caasle used an intestinal segment that is twice as long, partially split in the middle, and then opened the segment in a spiral fashion on opposite sides to make a longer strip that can be tabulated in continuity. The long-term results of the Caasle tube are comparable to those of the appendix and Yamp-Mont tube in terms of durability, continence, and complication rate (Image 9).

**REFERENCES**

Catenary Syndrome

**DESCRIPTION**
Synonym of tumors affecting at least 5 organs, the stomach, the lung, the paragangliotic system, the adrenal and the endocrine system. Generally seen in young females, 80% of patients present before age 30 and 85% are females. Gastrointestinal stromal tumors (GIST) of the stomach, lung chondroma, paraganglioma, adrenal adenoma, phaeochromocytoma, and epithelial leiomyoma are syndrome-defining tumors. Of the classic triad, GIST is the most common presenting lesion (75%), followed by lung chondroma (15%) and paragangliomatous tumor (10%). 1/3 of patients had a normal serum PMS level, 1/3 had low serum PMS level, and 1/3 had elevated serum PMS level.

**REFERENCES**

Cavernosography

**ADMISSION**
A test used to evaluate veno-occlusive dysfunction. It is performed by the injection of contrast material into the corpora cavernosa after the injection of a pharmacologic agent, such as papaverine, to stimulate relaxation. Any evaluated leakage of contrast material outside the corpora could be a defect in the veno-occlusive mechanism.Typical leak points include the glans, corpus spongiosum, superficial or deep dorsal veins, and cavernous and curvular veins.

**REFERENCES**

Caudo Equina Syndrome

**DESCRIPTION**
A term applied to the clinical picture resulting from compression of the cauda equina (or “horse tail”) by nerve roots or discal material to the level of spinal cord termination. This indicates peripheral sensory loss, loss of anal and urethral sphincter control, and loss of ejaculation. The most common causes of this condition are posterior, central lumbar disc herniation, spinal stenosis, tumor, and trauma. Caudo equina syndrome is present in 1–5% of all prolapsed lumbar discs. Characteristically, the affected patient has an acontractile detrusor with no bladder sensation, and often an inactive sphincter EMG. Treatment consists of surgical relief of pressure, although the neurological deficit can be permanent. On follow-up urodynamics, an acontractile detrusor and variable EMG activity may persist.

**REFERENCES**

Caudal Regression Syndrome

**DESCRIPTION**
First described by Duhamel in 1961, this syndrome is caused by disorder embryogenesis during the 4th–5th wk of gestation. It features a wide array of abnormalities: consisting on the vertebral, urogenital and lower spine areas. Severe cases demonstrate fusion of the lower limbs, sacral agenesis, imperforate anus, and absent GU tract (except gonads). In less severe cases, imperforate anus and/or sacral agenesis are seen. In these, in turn, are associated with voiding dysfunction, Veicoceutal reflux is also quite common. Managing the myriad problems requires a multidisciplinary approach.

**SYNONYMS**
- Caudal dysplasia sequence
- Urorectovaginal syndrome

**REFERENCES**

Cystectomy

**DESCRIPTION**
Removal of the urinary bladder. May be performed in cases of bladder cancer, bladder fistula, non-functioning bladder, or other indications. It is performed by a urologist and involves the removal of the bladder and a portion of the posterior abdominal wall. The incision is made through the abdominal wall, and the bladder is removed. The ureters are implanted into the iliac vessels. A urinary diversion is created to allow for urination. The procedure may be performed open or laparoscopically. It is typically indicated for localized or recurrent bladder cancer.

**REFERENCES**

Cat Eye Syndrome

**DESCRIPTION**
Also called Slocum-Fraccaro syndrome, a rare, congenital syndrome with features of colobomas of the iris and nasal area with fissurae, downward-sloping palpebral fissures, preauricular pits and/or pili, frequent occurrence of heart and renal malformations, and normal or near normal mental development. The ulterior abnormalities reported include various renal malformations, eg, absence of 1 or both kidneys, hydronephrosis, supernumerary kidneys or renal hypoplasia, choicic pelvirectal, horacic kidney, hydronephrosis, and veicoceutal reflux, and an associated additional chromosome 22. Close monitoring for possible pelvirectal is warranted.

**REFERENCES**
CAVERNOSOMETRY

DESCRIPTION
A test used to evaluate veno-occlusive leak in ED. Performed by 1st stimulating erection, either by visual or injection of a pharmacologic agent. Intracorporal pressure measurements are then recorded. The inability to raise intracorporeal pressure to levels equal to systolic blood pressure or a rapid drop of pressure after cessation of injection is indicative of veno-occlusive dysfunction.

REFERENCE


CECIL URETHRAL STRICTURE REPAIR

DESCRIPTION
The stricture is 1st excised, and the defect is closed with urethral skin. In the 2nd stage, a neourethra is created by tabularizing the urethra and represent a subtype of ureterocele.

REFERENCE


CECOUREROTEOCLE

DESCRIPTION
A ureterocele is a congenital saccular dilatation of the terminal portion of the ureter. Cystoureteroceles are elongated beyond the ureteroureteral orifice by tunneling beneath the trigone and the urethra and represent a suble of ureterocele.

REFERENCE


CELLO SCROTUM
DESCRIPTION
A described function medical condition in which a cello player irritates the scrotum. It is a dinosaur.

REFERENCE


CEREBRAL PALSY, UROLOGIC CONSIDERATIONS

DESCRIPTION
Cerebral palsy is a broad term describing a generally nonprogressive brain dysfunction occurring perinatally (up to age 3) by some definition with the consequences of long-term cerebral dysfunction. The etiology is thought to involve injury, infection, or a period of anoxia. The range of symptoms is broad, from mild mental retardation to severe developmental and motor delay. Surprisingly little is written about the exact urologic manifestation of cerebral palsy, and even the incidence of urologic dysfunction is unclear. In some series, up to 36% of patients with cerebral palsy had lower urinary tract dysfunction. In another series, the most common symptom involved incontinence (75%), frequency (56%), and urgency (37%). The most common urodynamically defined dysfunction was detrusor overactivity (DSO) (87% of those undergoing urodynamics), with 25% of these exhibiting apparent outlet resistance dysuria. (See also Section I: “Neurogenic Bladder: General Considerations.”)

REFERENCE


CERVICAL CANCER, UROLOGIC CONSIDERATIONS

DESCRIPTION
Metastatic complications regarding cervical cancer treatment are well documented. If pelvic exenteration is performed, urinary diversion is obligatory. Radical hysterectomy has risks of ureteral and bladder damage, which may result in a fistula. Radiation therapy also can be mobilized, with radiation cystitis, ureteral stricture, and fistula possibly resulting. The increased risk of bladder cancer after radiation therapy is controversial. (See also Section VII: “TNM Staging.”)

REFERENCE


CHANCROID
DESCRIPTION
An STD/STI caused by Haemophilus ducreyi and relatively uncommon in the United States but a concern (STID/STI) in developing countries. The combination of a painful genital ulcer and tender suprapubic iliac adenopathy suggests the diagnosis of chancroid. H. ducreyi is a gram-negative cocccobacilli and resembles a “school of fish” on Gram stain (clumping in long parallel strands). Incubation is 4–10 days and the ulcer is 1–2 cm, necrotic, purulent, and ragged with radiation adenopathy in over 50%.Sites include the dorsal penis in men and labia and vagina in women. Diagnosis is based on clinical findings. No FDA-cleared PCR test for H. ducreyi is available in the United States, but such testing can be performed by clinical labs that have developed their own PCR test and have conducted a CLIA verification study. A probable diagnosis of chancroid, for both clinical and surveillance purposes, can be made if all of the following criteria are met: (1) the patient has 1 or more painful genital ulcers; (2) the patient has no evidence of Treponema pallidum infection by darkfield exam of ulcer exudate or by a serologic test for syphilis performed at least 7 days after onset of ulcer; (3) the clinical presentation, appearance of genital ulcers and, if present, regional lymphadenopathy are typical for chancroid; and (4) a test for HSV performed on the ulcer exudate is negative.

TREATMENT
Recommended treatment is a single-dose of azithromycin 1 g PO or ceftriaxone 250 mg IM or ciprofloxacin 500 mg PO BID x 3 days (contraindicated if pregnant) or tetracycline or erythromycin base 500 mg PO TID x 7 days. (See also Section I: “Sexually Transmitted Infections [STIs] and Sexually Transmitted Diseases [STDs, General.”)

REFERENCE


CHARCOT-BOETTCHER CRYSSTALS AND FILAMENTS
DESCRIPTION
A normal ultrastructural component of human Semel cells observable with electron microscopy. Can be used to establish Sertoli origin in atypical sex cord-stromal tumors.

REFERENCE


CHARGE ASSOCIATION
DESCRIPTION
CHARGE refers to the association of coloboma, congenital heart disease, choanal atresia, retardation growth and development, structural brain abnormalities, and ear abnormal. Of urogenital interest is the association with genital hypoplasia, secondary to low androgen levels. Mostly sporadic, but a familial form has been reported. It is theorized to originate during a developmental error of neural crest elements at about the 6th wk. Early management of sensory defects is important. Androgen replacement is used for genital hypoplasia.

REFERENCE


CHEMOTHERAPY TOXICITY, UROLOGIC CONSIDERATIONS
DESCRIPTION
All chemotherapeutic agents have potentially significant toxicities and side effects. For the urologic surgeon, certain toxicities may be more commonly encountered. Both commonly used chemotherapeutic regimens for urothelial carcinoma, methotrexate/vinblastine/adriamycin/cisplatinum and gemcitabine/cisplatinum have significant nephrotoxicity, which can be problematic for older patients or patients with renal insufficiency or malignant ureteral obstruction. Blinomycin, used for nonmalignant germ cell tumors as part of the bleomycin, etoposide, cisplatin (BEP) regimen causes pulmonary toxicity. If postchemotherapy retroperitoneal lymphadenectomy is necessary, the anesthesiologist should be counseled to avoid high inspired oxygen concentrations and minimize crystalloid fluid resuscitation, as these factors may exacerbate bleomycin-related pulmonary toxicity. Cyclophosphamide may cause hemorrhagic cystitis, because of its toxic downstream metabolites, acrolein, which is excreted into the urine. Administering the agent Metha decreases this toxicity. Cyclophosphamide also increases the risk of subsequent bladder cancer up to 9 fold. (See also Section II: “Blinomycin Toxicity.”)
CHRONIC KIDNEY DISEASE

DESCRIPTION
Chronic kidney disease (CKD) is a diagnosis that can be made in either a man or a woman. Guidelines define CKD as FFR for at least 3 of the preceding 6 mo in the absence of other identifiable causes. Older terms used include prostatodynia and abacterial prostatitis.

Males: Guidelines define CP/CPPS for at least 3 of the preceding 6 mo in the absence of other identifiable causes. Sometimes referred to as chronic prostatitis/chronic pelvic pain syndrome (CPPS/CP) is a chronic syndrome. The symptomatology is based on urologic symptoms and/or pelvic pain or discomfort. While the term “prostatitis” is often used it is unclear to what degree the prostate is the cause of symptoms. Nonbacterial prostatitis occurs in men with no history of urinary tract infection and negative bacterial cultures of urine and prostatic fluid. The inflammatory type (PH I.A. Chronic prostatitis/pelvic pain syndrome, (inflammatory) presents with GU or rectal pain or voiding symptoms; the prostatic fluid contains inflammatory cells. Men with the noninflammatory type (PH II.B. Chronic prostatitis/pelvic pain syndrome, noninflammatory), whose prostatic fluid has no leukocytes, have similar symptoms, but pelvic pain is usually the predominant complaint. (See section I: Prostatitis, Chronic, Nonbacterial, Inflammatory (NH CP/CPPS III A), Section I: Prostatitis, Chronic, Nonbacterial, Noninflammatory (NH CP/CPPS III B), Section II: Pelvic Pain, Male.)

TREATMENT
- Empic 8–12 wk course of antibiotics
- Consider prostatitis massage. If no response
- High-dose α-blockers (Flomax, Cardura, Hytrin)
- Anti-inflammatory agents, lifestyle changes, stress reduction, holistic therapies

REFERENCE

CHRONIC PELVIC PAIN SYNDROME (CPPS) IN FEMALES

DESCRIPTION
A radiologic change in the bladder wall caused by detrusor or muscle hypertrophy and fibrosis as a result of detrusor-sphincter dyssynergia. Also called proctococele appearance.

REFERENCE

CHRONIC PROSTATITIS/PELVIC PAIN SYNDROME (CPPS/CP) IN MALES

DESCRIPTION
Chronic pelvic pain syndrome (CPPS) is a diagnosis that can be made in either a man or a woman. Guidelines define CPPS/CP as FFR for at least 3 of the preceding 6 mo in the absence of other identifiable causes. Other terms used include prostatodynia and abacterial prostatitis.

Males: Guidelines define CP/CPPS for at least 3 of the preceding 6 mo in the absence of other identifiable causes. Sometimes referred to as chronic prostatitis/chronic pelvic pain syndrome (CPPS/CP) is a chronic syndrome. The symptomatology is based on urologic symptoms and/or pelvic pain or discomfort. While the term “prostatitis” is often used it is unclear to what degree the prostate is the cause of symptoms. Nonbacterial prostatitis occurs in men with no history of urinary tract infection and negative bacterial cultures of urine and prostatic fluid. The inflammatory type (NH I.A. Chronic prostatitis/pelvic pain syndrome, (inflammatory) presents with GU or rectal pain or voiding symptoms; the prostatic fluid contains inflammatory cells. Men with the noninflammatory type (NH II.B. Chronic prostatitis/pelvic pain syndrome, noninflammatory), whose prostatic fluid has no leukocytes, have similar symptoms, but pelvic pain is

TREATMENT
- Empic 8–12 wk course of antibiotics
- Consider prostatitis massage. If no response
- High-dose α-blockers (Flomax, Cardura, Hytrin)
- Anti-inflammatory agents, lifestyle changes, stress reduction, holistic therapies

REFERENCE

CHRONIC PELVIC PAIN SYNDROME (CPPS) IN FEMALES

DESCRIPTION
A radiologic change in the bladder wall caused by detrusor or muscle hypertrophy and fibrosis as a result of detrusor-sphincter dyssynergia. Also called proctococele appearance.

REFERENCE
Conditions Associated with Chronic Pelvic Pain in Women

**Gynecologic**
- Endometriosis
- Chronic pelvic inflammatory disease
- Pelvic adhesions
- Pelvic congestion (pelvic varicosities)
- Adenomyosis
- Ovarian remnant syndrome
- Residual ovary syndrome
- Leiomyoma
- Endometriolysis
- Neoplasia
- Tuberculosis: salpingitis
- Benign cystic mesothelioma
- Postoperative pelvic cysts

**Mental health issues**
- Somatization
- Substance abuse
- Physical and sexual abuse
- Depression

**Sleep disorders**
- Urinary tract
  - Interstitial cystitis/painful bladder syndrome
  - Recurrent urinary tract infection
  - Urethral diverticulum
  - Chronic urethral syndrome
- Neoplasia
- Radiation cystitis

**Gastrointestinal tract**
- Inflammatory bowel disease and other causes of colitis
  - Diverticulitis
  - Chronic intermittent bowel obstruction
- Neoplasia
  - Chronic constipation
  - Colitis disease (fattic, sprue)
- Musculoskeletal
  - Pelvic floor myalgia
- Chronic rheumatic heart disease
  - Heart failure
  - Hypertrophy
  - Abnormal posture
- Fatigue
- Peripartum pelvic pain syndrome

**Neurologic disorders**
- Numbness, especially of the lower extremities
- Lower back pain (lumbar syndrome)
- Herniated nucleus pulposus
- Neoplasia
- Neurapraxia
  - Abdominal epi-epi
- Abdominal migraine

**CIRCUMCISION, FEMALE**

**DESCRIPTION**
Female genital cutting, also known as female circumcision or genital mutilation, is a culturally determined practice, predominantly performed in parts of Africa and Asia. The World Health Organization classified female genital cutting into 4 types of procedures.

- **Type I** consists of excision of the prepuce, with or without excision of part or all of the clitoris.
- **Type II** involves clitoridectomy and partial or total excision of the labia minora.
- **Type III**, or infibulation, includes removing part or all of the external genitalia and reapproximation of the remnant labia majora, leaving a small neocervix.
- **Type IV** involves other forms of injuries to the genital region including pricking, piercing, stitching, burning, scraping, or any other manipulation of the external genitalia.

**TREATMENT**
- Short-term urologic problems with the procedure include urethral edema and urinary retention potential. Long-term problems include dysmenorrhea, dyspareunia, and increased risk of urinary tract infection.

**REFERENCE**
Nour NM. Female genital cutting (circumcision). In UpToDate.com, Accessed March 8, 2014.

**CISPLATIN TOXICITY**

**DESCRIPTION**
Cisplatin is a very commonly used antitumor agent with significant adverse effects. Administered in urology for urethral carcinoma and testicular cancer, its nephrotoxicity is cumulative and dose-dependent, and commonly limits use. Other significant effects include myelosuppression, ototoxicity, GI disturbances, and neurotoxicity. See also Section II: “Chemotherapy Toxicity, Urologic Considerations.”

**TREATMENT**
- Antidiuretic has been used to limit toxicity.

**REFERENCE**
Nour NM. Female genital cutting (circumcision). In UpToDate.com, Accessed March 8, 2014.

**CHYLOCELE**

**DESCRIPTION**
Also called chylous hydrocele, chylocele is a rare form of lymphatic fluid drainage into the tunica vaginalis around the testis. The fluid is usually described as milky and contains leukocytes. This may result from lymphatic disruption secondary to diseases such as filariasis. Filariasis affects 120 million people in >80 countries and is caused by Wuchereria bancrofti, which is transmitted by mosquitoes. Chyloceles usually do not resolve after needle aspiration and require the underlying cause to be surgically or medically addressed. Freedom from infection at the time of surgery is critical for a favorable outcome. (See also “Section I: Scrotum and Testicle, Mass.”)

**TREATMENT**
- Vertical scrotal incision with complete excision of tunica vaginalis to use.
- Orchidectomy and choridectomy for severe cases
- Medical treatment of filariasis (diethylcarbamazine, ivermectin, praziquantel)

**REFERENCE**

**CHRONIC PROSTATITIS SYMPTOM INDEX (CPSI)/NIH-CPSI (NATIONAL INSTITUTES OF HEALTH CPSI)**

**DESCRIPTION**
The National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), a reliable validated instrument developed by the NIH Chronic Prostatitis Collaborative Research Network to aid in the quantification of chronic prostatitis symptoms. The NIH-CPSI is intended for clinical practice as well as research protocols. The instrument contains 9 questions. The major domains relate to pain (location, severity, frequency), the nature of voiding (irritative and obstructive symptoms), and the impact of prostatitis on quality of life. The goal of this multi-institutional collaborative effort was to define and measure the symptoms of chronic prostatitis and their impact on the daily lives of patients. The test is self-administered and can be completed in 5 min. Higher scores indicate worse outcomes in all domains, with a possible maximum score of 43. (See also Section I: “Prostatitis, Chronic Bacterial.”)

**REFERENCES**

**CHURG-STRAUSS SYNDROME**

**DESCRIPTION**
Also called allergic angiitis and granulomatosis, this is a vasculitis characterized by extravasatory microscoplic granulomas in the large, heart, GI tract, and skin. Histologically, necrotizing and eosinophilic infiltrate is accompanied by histiocytes are seen. Both necrotizing and eosinophilic granulomatous vasculitis usually involve small arteries and veins, often with a history of atopy. Patients present with fever and weight loss. Eosinophilia, anemia, and an elevated ESR are found. The prostate may be involved by the granulomatous process. Treatment involving corticosteroids with cytotoxic drugs is being investigated.

**REFERENCE**

**CHYLOCELE**

**DESCRIPTION**
Also called chylous hydrocele, chylocele is a rare form of lymphatic fluid drainage into the tunica vaginalis around the testis. The fluid is usually described as milky and contains leukocytes. This may result from lymphatic disruption secondary to diseases such as filariasis. Filariasis affects 120 million people in >80 countries and is caused by Wuchereria bancrofti, which is transmitted by mosquitoes. Chyloceles usually do not resolve after needle aspiration and require the underlying cause to be surgically or medically addressed. Freedom from infection at the time of surgery is critical for a favorable outcome. (See also “Section I: Scrotum and Testicle, Mass.”)

**TREATMENT**
- Vertical scrotal incision with complete excision of tunica vaginalis to use.
- Orchidectomy and choridectomy for severe cases
- Medical treatment of filariasis (diethylcarbamazine, ivermectin, praziquantel)

**REFERENCE**
DESCRIPTION
Anatomically the clitoris is composed of the glans clitoris and the crus, its dimensions are generally independent of BMI, age, and height. Average length of the glans clitoris is 5.1 ± 1.4 mm. Total average of clitoral length from the tip of the glans to the insertion of the crus on the pubis is 16.0 ± 4.3 mm. Multiparous women have slightly larger clitoral dimensions than nulliparous women with a total length on average 0.9 mm greater and a glans length 0.5 mm greater. (See also Section II: “Clitoromegaly.”)

REFERENCE

CLITORAL PRIAPISM
DESCRIPTION
A rare condition that is associated with an extended duration of clitoral erection due to local engorgement of clitoral tissue causing clitoral or vulvar pain. The prolonged erection is not associated with sexual stimulation, and can last from minutes to days. It has been associated with medications: α-blockers, inhibitors of serotonin reuptake (SSRIs antidepressants), and non-SSRI antidepressants and with TCC: obstructing venules and lymphatic outflow. Stopping the offending agent can result in resolution within 24–72 h. Other treatments include: Imipramine, NSAIDs, ice packs, spasms, and, rarely, intracavernous injection of alprostadil. (See also Section II: “Clitoromegaly.”)

REFERENCE

CLITOROMEGALY
DESCRIPTION
Abnormal enlargement of the clitoris is most frequently seen in children born with chromosomal abnormalities. It can also be seen in constitutional growth disorders, such as gigantism or acromegaly. It is most commonly a manifestation of CAH. The underlying cause must be addressed. (See also Section II: “Disorders of Sexual Development-CAH.”)

REFERENCE

CLOSTRIDIUM DIFFICILE COCCIDIOIDOMYCOSIS, GENITOURINARY
DESCRIPTION
A test sometimes used to rule out pneumococcal infection. Clindamycin (0.3 mg) is administered and plasma pneumococcal levels are then measured. Those patients with essential hypertension with an elevation of nonpneumococcal levels will experience a 50% decrease in this carotid sinus reflex level. Patients with pheochromocytoma will not be suppressed. Patients should not be taking diuretics, β-blockers, or tricyclic antidepressants; α-blockers do not interfere with the test.

REFERENCE

CLITORAL LENGTH
DESCRIPTION
An enlarged clitoris is most frequently seen in children born with chromosomal abnormalities. It can also be seen in constitutional growth disorders, such as gigantism or acromegaly. It is most commonly a manifestation of CAH. The underlying cause must be addressed. (See also Section II: “Disorders of Sexual Development-CAH.”)

REFERENCE

CLOSTRIDIOIDES DIFFICILE COLITIS, UROLOGIC CONSIDERATIONS
DESCRIPTION
Also known as pseudomembranous enterocolitis, this is a potentially life-threatening infection of the colon due to overgrowth of C. difficile. It can be precipitated by antibiotic therapy – most commonly fluoroquinolones, clindamycin, cephalosporins, and penicillins – but any antibiotic can be implicated. This suppression of normal bowel flora by antibiotics and overgrowth of C. difficile has been reported in association with bowel preparation prior to elective surgery, as well as in addition to the use of antibiotics for any indication. Watery diarrhea and abdominal pain are the main symptoms of C. difficile infection, but it can range from asymptomatic carrier state, diarrhea with colitis, or pseudomembranous colitis (endoscopic evidence of “pseudomembranes”), to severe life-threatening disease with toxic megacolon. Low-grade fever and leukocytosis are common. It is diagnosed by clinical endoscopic findings, culture of organism, or detection of toxin in stool. Enzyme immunoassay (EIA) allows the direct detection of C. difficile toxin and is the test of choice.

TREATMENT
• Removal of antibiotic therapy, if antibiotic therapy is essential, attempt to use an agent with lesser likelihood of causing C. difficile overgrowth. (aminoglycosides, macrolides, sulfonamides, tetracycline, or vancomycin).
• Metronidazole (500 mg TD or 250 mg QD) is recommended as initial treatment of less severe cases, if needed, IV metronidazole 500 mg q8h; treat for 10–14 days with follow-up toxin assay.
• Alternatively, oral vancomycin 125 mg QID.

REFERENCE

CLOSTRIDIUM DIFFICILE INTESTINAL SYNDROME
DESCRIPTION
The radiologic appearance on an intravenous urogram (IVU) of an intravesical ureterocele of a single ureter in an adult, also called spring onion sign. The dilated ureterocele, filled with contrast material, protrudes into the bladder, which is also filled with contrast material, but is separated from it by a thin radiolucent halo. The ureterocele might be congenital or acquired, as in cases of trauma or inflammation.

REFERENCE

COCCIDIOIDES DIFFICILE, GENITOURINARY
DESCRIPTION
Outbreaks of Coccidioides immitis infection are common when people are exposed to soil that contains the spore. An opportunistic infection more common in patients <5 and >50 yo. It is associated with AIDS, cerebrospinal, and chemotherapeutic for malignancy. After pulmonary inoculation, the patient can develop erythema nodosum (valley bums or valley fever). Chest radiographs demonstrate infiltrates with cavitation. Serologic tests are available to help establish the diagnosis. Disseminated disease involves the kidney in up to 65%, the adrenal in 16–32%, and the prostate in 6%. Renal coccidioidomycosis may cause similar changes, as seen in renal TB (mottled calyces, hyperechoic lesions, ureteral stricture, and calcifications). Prostatic infection with occasional abscesses and clot infections with fistulae have been reported. Epididymal and prostatic involvement can demonstrate necrotizing and nonnecrotizing granulomas. Therapy includes up to 2 g of amphotericin B with 1 year of ketoconazole (200 mg)
COHEN (“CROSS-TRIGONAL”) URETERAL REIMPLANTATION

REFERENCE

COLOM AND RECTAL CANCER, UROLOGIC CONSIDERATIONS
DESCRIPTION
Colon cancer may present as locally invasive lesions that involve the bladder and/or prostate. En bloc resection (pelvic exenteration) of the bladder and rectum is sometimes indicated. In colorectal malignancies, a 2–12% incidence of ischemic extension into the adjacent organs has been reported, with the bladder as the most commonly involved organ. In women, the interruption of the uterus between the colon and bladder makes the incidence lower. In cases of more proximal colon cancers, ureteral and renal involvement may require localization with ureteral catheters. After extensive colorectal dissection, extrapelvic and bladder dissection may occur secondary to disruption of the pelvic plexus up to 70% of the time. (See also Section VII: “Urologist-Bladder.”) (TNM.)

REFERENCE

COLUMN OF BERTIN, HYPERTROPHIED
DESCRIPTION
A normal anatomic structure of the kidney, which, if enlarged, can be mistaken for a renal mass. It normally appears as granular material in the renal sinus, which is simply cortex. The column of Bertini is located between the pyramids. (See also Section II: “Nuclear Pseudotumors.”)

REFERENCE

COMPARTMENT SYNDROME, UROLOGIC CONSIDERATIONS
DESCRIPTION
Compartment syndrome is defined by the rise in pressure in a tissue compartment compromising circulation, can result in devastating consequences, especially in the urologic setting. Reports of compartment syndrome leading to rhabdomyolysis, renal failure, and limb loss have been reported with the dorsal lithotomy position, flank position during open or laparoscopic procedures, prolonged reconstructive pediatric procedures, and urothelial and penile surgeries. Recently there has been an increase in reports relating to robotic prostatectomy. In abdominal compartment syndrome, a Foley catheter can be used to provide continuous abdominal compartment pressure readings.

The etiology of compartment syndrome is multifactorial and prevention is the mainstay of treatment. Positioning and other efforts to prevent acute lower extremity compartment syndrome include limiting the time of leg elevation, positioning the leg below the level of the arium and postoperative monitoring of patients at risk. Pulse oximetry to detect hypoperfusion has been reported. The 6 “Ps” associated with compartment syndrome are: Pain out of proportion based on exam, paresthesia, palmar, paralysis, paresthesia, and pain. Fasciotomy may be necessary to relieve pressure and restore extremity perfusion. Although debated, measured compartment pressure of 30 mm Hg is generally accepted indication for lower extremity fasciotomy. (See also Section I: “Rhabdomyolysis.”)

REFERENCE

CONDYLOMATA LATA
DESCRIPTION
Also called flat condyloma, these moist or mucous papules are found in the skin folds of the groins. They secrete serous fluid and can be covered by a layer of epidemial cells. They represent the hematogenous spread of syphilis. (See also Section I: “Syphilis.”) (Image 49)

TREATMENT
• Single dose of penicillin G (benzyl penicillin)
• 2.4 million units IM-PR
• IM olsalazine, 1,000 mg/d for 10 days OR
• Oral tetracycline 500 mg QID for 14 days OR
• Oral dapsone 100 mg BID for 14 days

REFERENCE

CONGENITAL ADRENAL HYPERPLASIA (CAH)
DESCRIPTION
The adrenal cortex secretes 2 components, DHEA and androstenedione, that require androgenic effects, each...


**CONTACT DERMATITIS, UROLOGIC CONSIDERATIONS**

characterized by a deficiency or total lack of a particular enzyme involved in the biosynthesis of cortisol steroids, particularly cortisol. Steroidogenesis is then channelled into other pathways, leading to increased production of androgens, which accounts for virilization. Simultaneously, the deficiency of cortisol results in increased secretion of ACTH, resulting in adrenal hyperplasia. Certain enzyme defects may also impair aldosterone secretion, adding salt-wasting to the virilizing syndrome. The most commonly recognized forms are 21-hydroxylase deficiency (21-OH deficiency), 11-hydroxylase deficiency (11-OH deficiency), 18-hydroxylase deficiency (18-OH deficiency), and 17α-hydroxylase deficiency. (See also Section I: “Dysfunctional Elimination Syndrome.”)

<table>
<thead>
<tr>
<th>Hormones:</th>
<th>21-Hydroxylase Deficiency</th>
<th>11-Hydroxylase Deficiency</th>
<th>17α-Hydroxylase Deficiency</th>
<th>3β-Hydroxysteroid Synthase Deficiency</th>
<th>Lipid Hypothesis</th>
<th>Aldosterone Synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOC, deoxycorticosterone; DHEA, dehydroepiandrosterone; 18-OHB, 18-hydroxycorticosterone.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**REFERENCES**


**CONGENITAL NEPHROSIS/NEPHROTIC SYNDROME**

**DESCRIPTION** Congenital nephrotic syndrome is a rare condition affecting children in the 1st months of life. Familial incidence occurs as an autosomal recessive mode of inheritance. This disease is seen most frequently in Finland (1:8,000 live births). Clinical manifestations include wide anterior and posterior fontanelles, generalized edema, abdominal distension, anasarca, and malnutrition. Characteristic lab findings include proteinuria, hypoalbuminemia, hypercholesterolemia, and hyperlipidemia. Long-term survival is dependent on transplantation. Treatment of bowel dysfunction alone can resolve chronic constipation and fecal incontinence in some children. It is important to rule out neurologic and bowel disease as causes of constipation before making the diagnosis of functional constipation. (See also Section II: “Dysfunctional Elimination Syndrome.”)

**TREATMENT**

- Diet changes
- Diuretics, stool softeners
- Toilet schedules

**REFERENCES**


**CONTACT DERMATITIS, UROLOGIC CONSIDERATIONS**

**DESCRIPTION** Contact dermatitis is caused by an external irritant or allergen and the patient complains of itching and burning or itching. The findings include inflammation, scaling, and crust formation. Extreme reactions can result in blisters and vesicles. Allergic agents typically induce dermatitis after repeated contact with the skin.
CONTRAST-INDUCED NEPHROPATHY (CIN)

DESCRIPTION
An acute and usually reversible form of acute kidney injury following the administration of radiocontrast media. Onset is often 12–24 hr after the contrast study, with renal recovery typically beginning within 3–5 days. It is nonoliguric. The process behaves as a clinical acute tubular necrosis (ATN) with decreased GFR and increased FENa. Risk factors include renal insufficiency (Cr > 1.5 mg/dl), GFR < 60 ml/min, diabetes, heart failure, dehydration, and multiple contrast studies within 72 hr. The mechanisms of the injury are thought to be renal vasoconstriction with resulting tubular hypoxemia and direct cytotoxic effects of contrast material. Older agents are hyperosmolar and toxic, and carry a higher risk of nephrotoxicity, whereas newer agents are iso-osmolar and nonionic and have a lower risk of renal injury. (See also Section II: “Contrast-Induced Nephropathy” and Section VII: “Nephrotoxic Drug-Induced Nephropathy.”)

TREATMENT
Preventative— Avoid contrast material if possible; consider alternative imaging modalities such as ultrasound or CT/MRI without contrast. Avoid dehydration and NSAIDs, as both increase renal vasoconstriction.

Patch testing of uninvolved skin to common sensitizing agents for the genital skin is performed. Severe reactions (rarely) may require debridement and grafting.

Contrast-induced nephropathy diagnosed following a procedure should be managed as ATN:
– Do not biopsy kidney. Injury is usually transient.
– Carefully control fluid and electrolyte balance; hemodialysis is usually unnecessary.
– Avoid further nephrotoxic insults and/or medications.

REFERENCE

CORTICAL NECROSIS, ACUTE (RENAL CORTICAL NECROSIS)

DESCRIPTION
Acute cortical necrosis is a rare form of acute renal failure (ARF) characterized by necrosis of the cortex with sparing of the medulla. It is thought to be the result of selective arterial spasm of the cortical vasculature with continued perfusion of the renal medulla via the medullary arterioles. Pathologically, necrosis of the glomeruli, tubules, and arterioles occurs. A cortical rim sign can be seen on contrast-enhanced CT scan, indicating spared perfusion of the renal capsule. Factors that can predispose a patient to acute cortical necrosis include shock, prerenal azotemia, peritonitis, infection, and toxins. (See also Section II: “Renal Failure.”)

REFERENCE

COSTOVERTEBRAL ANGLE TENDERNESS
DESCRIPTION
Costovertebral-angle (CVA) tenderness is a clinical sign elicited by percussion of the CVA and often accompanied by symptoms of flank pain. The CVA is defined by the area formed by the 12th rib and vertebral column. CVA tenderness is a manifestation of renal capsule distension resulting in irritation ofafferent T11–L2 nerve roots. Common causes include pyelonephritis, perirenal abscess, urachitis, acute hydrocephrosis, renal artery occlusion, and renal vein thrombosis. (See also Section I: “Flank Pain.”)

REFERENCE

COUGH STRESS TEST
DESCRIPTION
The cough stress test involves filling the patient’s bladder to at least 300 ml or to subjectively fullness. The patient is then asked to cough as the physician directly visualizes the urethral meatus. The test can be performed with the patient in an upright position or in dorsal lithotomy on an exam table (supine stress test). If urine leakage is noted, the test is positive. The cough stress test has been compared with other more sophisticated testing methods (multichannel urodynamic studies) and has demonstrated good sensitivity and specificity. This test can be used not only as part of the clinician’s physical exam, but as an outcome measure after treatment.

REFERENCE

COWPER DUCT CYST
DESCRIPTION
The Cowper glands are paired perineal structures located in the urogenital diaphragm and are drained by 2–3-cm-long ducts that empty into the bulbous urethra through small, brisk openings. These glands secrete a clear fluid that functions as a lubricant and a coagulation factor for semen during ejaculation and to neutralize traces of acidic urine in the urethra. Abnormalities of these glands and their ducts may result from obstruction and, less frequently, trauma and infection. This diagnosis should be considered in any male presenting with intumescence or obstructive urinary symptoms, particularly when there is a complaint of persistent postvoid dribbling or incontinence. Urography and urodynamic studies are the diagnostic studies of choice.

SYNONYMS
• Cowper glands
• Bulbourethral gland ductextrase

TREATMENT
Endoscopic amputating of the glandulae (translucidae) into the bulbous urethra
CT SCAN, UROLOGIC CONSIDERATIONS

REFERENCE

COWPER GLAND CARCINOMA
DESCRIPTION
Rare tumor that can present with obstructive symptoms, pain with defecation, or constipation. Most have a palpable perineal mass. Microscopically, these appear as adenocarcinomas. However, local necrosis and tissue destruction may prevent exact localization of the site of origin. Combined surgical and radiation therapy has been employed.

REFERENCE

COWPERITIS (INFLAMMATION OF BULBOURETHRAL GLAND)
DESCRIPTION
Normally, the bulbar urethral glands are palpable. A gland lies on each side of the membranous urethra, between the inferior edge of the prostate and the inner border of the anal canal. When they are inflamed, they are irregularly tender and palpable. In chronic inflammation, they enlarge from the size of a pea to that of a hazelnut. With a finger in the rectum, the thumb is held outside on the median raphe of the scrotum just anterior to the anus and the tip of the index finger is placed in the suprapubic area and pressing into the abdomen. Both hands are then pressed downward into the pelvis. It may not always be an effective technique to empty the bladder, since the external urethral sphincter may contract during the maneuver.

SYNONYM
Manual compression of bladder

REFERENCE

CREMASTERIC REFLEX
DESCRIPTION
The cremasteric reflex is a useful sign in the evaluation of the acute scrotum. The classic presentation of testicular torsion is sudden onset of severe unilateral pain, often associated with nausea or vomiting. The normal reflex consists of cremasteric contraction with elevation of the testis, elicited by stroking the pubocanal upper medial thigh. The innervation is carried via the genito-inguinal nerve. The reflex was previously reported to be absent in 100% of cases of testicular torsion; however, there have been reported cases of preserved cremasteric reflex in the setting of testicular torsion. As such, the presence or absence of this reflex should not influence the decision to perform a scrotal exploration when there is a clinical suspicion of torsion.

REFERENCE

CRIRIFORM CLEAR CELL HYPERPLASIA OF THE PROSTATE
DESCRIPTION
This condition may be misdiagnosed as cribriform prostate carcinoma, but anticytokeratin staining of the basal cell layer distinguishes the 2 lesions. Also, hyperplasic cells lack cytologic atypia, which is in contrast to carcinoma. The natural history is unknown; the lesion is usually found in the central area of the gland.

REFERENCE

CRYPTOCOCCUS, GENITOURINARY
DESCRIPTION
An opportunistic fungal infection, Cryptococcal meningitis thrives in areas inhabited by birds. A pulmonary site is most common primary infection site, but immunocompromised patients can develop disseminated disease (AIDS, transplant). Adrenal insufficiency has been reported, but the most common sites of GV involvement are the prostate and kidney. The prostate may be a reservoir in patients with AIDS. Epididymitis and perine involvement have also been reported. GU involvement is considered a manifestation of systemic disease. (See also Section I: “Fungal Infections, Genitourinary.”)

TREATMENT
• Systemic antifungal therapy with fl uconazole or itraconazole, fluconazole, fluconazole, or combination of drugs
• Surgical drainage of large abscesses may be considered.

REFERENCE

CRITICAL-INDUCED ACUTE KIDNEY INJURY (ACUTE RENAL FAILURE)
DESCRIPTION
Acute tubular necrosis of crystals poorly soluble in human urine can lead to AKI. This form of AKI most commonly occurs as a result of acute uric acid nephropathy (tumor lysis syndrome) or following the administration of other drugs, such as aminoglycosides, methotrexate, indinavir, lamivudine, efavirenz, etoposide, and high doses of Vitamin C. The presentation is usually asymptomatic and detected by worsening serum creatinine, although renal colic symptoms may be present. Severe volume depletion (preserved state) is the most important predisposing factor to crystal induced AKI when patients are receiving the above medications. Likewise, the 1st step in treatment is correction of volume status, usually with isotonic saline and loop diuretics in order to wash out crystals. (See also Section I: “Acute Kidney Injury, Adult (Renal Failure, Acute”).)

REFERENCE

REFERENCE

COWPER GLAND CARCINOMA
DESCRIPTION
Rare tumor that can present with obstructive symptoms, pain with defecation, or constipation. Most have a palpable perineal mass. Microscopically, these appear as adenocarcinomas. However, local necrosis and tissue destruction may prevent exact localization of the site of origin. Combined surgical and radiation therapy has been employed.

REFERENCE

COWPERITIS (INFLAMMATION OF BULBOURETHRAL GLAND)
DESCRIPTION
Normally, the bulbar urethral glands are palpable. A gland lies on each side of the membranous urethra, between the inferior edge of the prostate and the inner border of the anal canal. When they are inflamed, they are irregularly tender and palpable. In chronic inflammation, they enlarge from the size of a pea to that of a hazelnut. With a finger in the rectum, the thumb is held outside on the median raphe of the scrotum just anterior to the anus and the tip of the index finger is placed in the suprapubic area and pressing into the abdomen. Both hands are then pressed downward into the pelvis. It may not always be an effective technique to empty the bladder, since the external urethral sphincter may contract during the maneuver.

SYNONYM
Manual compression of bladder

REFERENCE

CREMASTERIC REFLEX
DESCRIPTION
The cremasteric reflex is a useful sign in the evaluation of the acute scrotum. The classic presentation of testicular torsion is sudden onset of severe unilateral pain, often associated with nausea or vomiting. The normal reflex consists of cremasteric contraction with elevation of the testis, elicited by stroking the pubocanal upper medial thigh. The innervation is carried via the genito-inguinal nerve. The reflex was previously reported to be absent in 100% of cases of testicular torsion; however, there have been reported cases of preserved cremasteric reflex in the setting of testicular torsion. As such, the presence or absence of this reflex should not influence the decision to perform a scrotal exploration when there is a clinical suspicion of torsion.

REFERENCE

CRIRIFORM CLEAR CELL HYPERPLASIA OF THE PROSTATE
DESCRIPTION
This condition may be misdiagnosed as cribriform prostate carcinoma, but anticytokeratin staining of the basal cell layer distinguishes the 2 lesions. Also, hyperplasic cells lack cytologic atypia, which is in contrast to carcinoma. The natural history is unknown; the lesion is usually found in the central area of the gland.

REFERENCE

CRYPTOCOCCUS, GENITOURINARY
DESCRIPTION
An opportunistic fungal infection, Cryptococcal meningitis thrives in areas inhabited by birds. A pulmonary site is most common primary infection site, but immunocompromised patients can develop disseminated disease (AIDS, transplant). Adrenal insufficiency has been reported, but the most common sites of GV involvement are the prostate and kidney. The prostate may be a reservoir in patients with AIDS. Epididymitis and perine involvement have also been reported. GU involvement is considered a manifestation of systemic disease. (See also Section I: “Fungal Infections, Genitourinary.”)

TREATMENT
• Systemic antifungal therapy with fl uconazole or itraconazole, fluconazole, fluconazole, or combination of drugs
• Surgical drainage of large abscesses may be considered.

REFERENCE

CRITICAL-INDUCED ACUTE KIDNEY INJURY (ACUTE RENAL FAILURE)
DESCRIPTION
Acute tubular necrosis of crystals poorly soluble in human urine can lead to AKI. This form of AKI most commonly occurs as a result of acute uric acid nephropathy (tumor lysis syndrome) or following the administration of other drugs, such as aminoglycosides, methotrexate, indinavir, lamivudine, efavirenz, etoposide, and high doses of Vitamin C. The presentation is usually asymptomatic and detected by worsening serum creatinine, although renal colic symptoms may be present. Severe volume depletion (preserved state) is the most important predisposing factor to crystal induced AKI when patients are receiving the above medications. Likewise, the 1st step in treatment is correction of volume status, usually with isotonic saline and loop diuretics in order to wash out crystals. (See also Section I: “Acute Kidney Injury, Adult (Renal Failure, Acute”).)

REFERENCE
CULP-DEWEERD PYELOPLASTY

- Standard chest x-ray (2 views): 0.06–0.25 mSv
- Natural source: Annual (Germany): 2.4 mSv/yr
- Survival of Hiroshima and Nagasaki Atomic bombings: 50–150 mSv
- Mean lethal dose radiation (V20% within 60 days): 3,500–4,000 mSv

REFERENCES

CULP-DEWEERD PYELOPLASTY
DESCRIPTION
A pyeloplasty technique best suited for management of UPI obstruction in the setting of a long segment of obstructed proximal ureter. A Culp incision is carried out over the anterior and medial aspect of the renal pelvis and continued down across a point beyond the UPI obstruction. The apex of the flap is brought down to the apex of the ureterostomy, where a 5-0 chromic suture is placed. The posterior and anterior anastomoses are completed with interrupted 5-0 chromic sutures.

REFERENCE

CUNNINGHAM CLAMP
DESCRIPTION
A clamp device designed to compress the urethra and prevent urinary incontinence in males only. The clamp is usually placed on the midshaft of the penis and requires the user to have manual dexterity, intact penile skin, good cognition, and a sensate penis and bladder. The clamp comes in small, medium, and large sizes. It is inexpensive and the most commonly used clamp device. Other types are commercially available based on this urethral compression concept.

REFERENCE

CYCLOPHOSPHAMIDE (CYTOXAN) TOXICITY
DESCRIPTION
Cyclophosphamide (sometimes referred to historically by the former brand name Cytoxan) is an alkylating chemotherapeutic agent used to treat many blood cell cancers and as an effective immunosuppressant for other diseases such as rheumatoid arthritis. Common side effects include bone marrow suppression, alopecia, leukopenia, and nausea. However, Cytoxan has unique toxicities, including the development of hemorrhagic cystitis and secondary cancers such as uterine carcinoma of the bladder and leukemia. Acrolein, a metabolite of Cytoxan, is the major cause of acute hemorrhagic cystitis (and thought to be the cause of long-term increased risk of uterine carcinoma in patients treated with Cytoxan). Hemorrhagic cystitis can be prevented by administering Mesna at the time of Cytoxan readministration. Mesna binds the toxic metabolites acrolein. (See also Section 1: “Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation”), Section II: “Chemotherapy Toxicity, Urologic Considerations.”)

TREATMENT
- Mesna can be given either PO or IV, and its routine concurrent use is recommended in the treatment of patients receiving cyclophosphamide and ifosfamide. It should be discontinued when hemorrhagic cystitis is present as it can prevent the development of the cystitis but is ineffective in treating active bleeding.
- Hydration: Forced saline diuresis and the medication Mesna were similar in preventing the incidence of cyclophosphamide-induced hemorrhagic cystitis in some studies. – ASCO recommends that patients receiving high-dose cyclophosphamide in the setting of hematopoietic cell transplantation receive Mesna in conjunction with saline diuresis.

REFERENCES

CYSTADENOCACARINOMA, GENITOURINARY
DESCRIPTION
Comrnonly seen in other organ systems, such as the ovaries, pancreas, appendix, and thyroid. In the GU system, cystadenocarcinoma has been reported in testes, prostate, paratesticular structures, and kidney. Grossly, multicystic, multicystic masses are noted. Microscopically, cuboidal to columnar epithelium is seen lining the cysts. These cells can secrete various mucinous substances. Exfoliative cells will demonstrate multilayering of epithelium, nuclear atypia, and invasion of surrounding stroma. It is treated by primary surgical resection.

REFERENCE

CYSTADENOCAARINOMA, GENITOURINARY
DESCRIPTION
A benign cystic epithelial-lined mass that has been described in the kidney, seminal vesicle, prostate, and epididymis (most common GU tract site). It is often described as a papillary cystadenoma and represents benign epithelial hyperplasia. It usually causes very few symptoms. Ultrasound can be bilateral, and 2/3 may be associated with Von Hippel-Lindau syndrome. Grossly, the lesion appears cystic. Microscopically, it demonstrates cells with dense, vacuolated cytoplasm arranged in glandular or papillary structures. It appears as a cystic-to-solid mass at the head of the epididymis on ultrasound. Treatment is observation or radical orchidectomy, if the diagnosis is in doubt.

REFERENCE

CYSTADENOCAARINOMA, RETROPERITONEAL
DESCRIPTION
Primary retroperitoneal tumors of mucinous type are extremely rare. They can be sub-divided into cystadenoma (a benign cystic epithelial-lined mass), borderline, and cystadenocarcinoma (multicystic cystic masses with multilayer epithelium, nuclear atypia, and invasion of surrounding stroma). Prompt diagnosis is important, as the majority of cystadenocarcinomas are malignant. Presenting symptoms can be vague. Given their malignant nature, they should be considered in the differential diagnosis of chronic abdominal pain. Cross-sectional abdominal imaging is the primary diagnostic modality. Radical resection remains the treatment of choice. (See also Section 1: “Retroperitoneal Mass, Fluid and Cysts.”)

REFERENCE

CYSTIN C
DESCRIPTION
A 13 kDa nonglycosylated endogenous protein found in all nucleated cells that has a constant rate of production unaffected by diet. Its clearance is not affected by renal tubular function. It is currently not clearly available, but it likely replaces serum creatinine as the standard test in GFR measurement.

REFERENCE

CYSTIC FIBROSIS, UROLOGIC CONSIDERATIONS
DESCRIPTION
In this genetic disease affecting 1 in 2,000 Caucasian births, defective chloride transport across the epithelium occurs. This leads to complications involving the pancreas, liver, salivary glands, and lungs. Unusual findings include bilateral absence of the vas deferens, leading to infertility. Abnormal development of the mesonephric system, inguinal hernias, hydropsalpinx, and undescended testes are also seen. Risk of testicular cancer may be increased. (See also Section 1: “Vas Deferens, Congenital Absence.”)
CYSTITIS, RADIATION

DESCRIPTION Radiation cystitis can be caused during the course of pelvic radiation treatment. Patients may experience urgency, frequency, dysuria, and urination of small volumes. Bladder spasm may also be present. This can


CYSTITIS, EOSINOPHILIC

DESCRIPTION A rare and severe form of allergic cystitis. Symptoms include hematuria, urgency, dysuria, and suprapubic discomfort. Urine analysis may show eosinophilia. Cytoscopic findings may reveal raised plaques or ulcers that mimic CIS or invasive bladder cancer. Bladder biopsy revealing eosinophilic infiltrate is pathognomonic. Potential causes include food or drug allergies (including methotrexate, anisakis acid, and thiotepa). Parasitic infections should also be considered as etiologies. Some confusion in the literature exists between this entity and granulomatous cystitis. Conservative medical management with oral antibiotics, antihistamines, and steroids with an allergy evaluation are required. See also Section II: “Cystitis Granulomatous.”

TREATMENT
• Conservative medical management with oral antibiotics, antihistamines, and steroids
• A full allergy evaluation is required


 CYSTITIS, EOSINOPHILIC

REFERENCES

CYSTITIS, POLYPOID AND PAPILLARY

DESCRIPTION These benign lesions may appear cystoscopically as papillary urothelial neoplasms and are a reaction to urothelial injury. Polypoid cystitis becomes papillary cystitis when the condition becomes chronic. Similar lesions occur throughout the urothelial tract and are referred to as polypoid urothelium, polypoid urothelial cystitis. They are seen in the urethra, ureters, and renal pelvis, respectively, and are the most diagnostically similar lesions. Clinical settings for this diagnosis include evaluation of gross hematuria, bladder and/or urethral stones, prostatic cancer with radiation therapy, history of urethral carcinoma treatment, long-term urinary stents, and colorectal fibrosis. Proper diagnosis relies on low-power microscopic identification of the reactive process with an infiltrated background that is edematous or densely fibrous with predominantly simple, nonatrophic, broad-based fronds of relatively normal-thickness urothelium. If the tissue is examined at higher power, some foci may appear to resemble a urothelial neoplasm. Treatment is directed at the inciting cause.


CYSTITIS, RADIATION

DESCRIPTION Radiation cystitis can be caused during the course of pelvic radiation treatment. Patients may experience urgency, frequency, dysuria, and urination of small volumes. Bladder spasm may also be present. This can


CYSTITIS, GRANULOMATOUS

DESCRIPTION Granulomatous cystitis (sometimes called eosinophilic cystitis) or eosinophilic granulomatous cystitis in the literature, thus leading to some confusion of this entity is a rare ale cystitis of the bladder of granulomatous cystitis in patients who often have a significant allergic history. In women, other forms of irritable cystitis, such as interstitial cystitis, TB, and bladder neoplasms. The cause is unknown, but believed to be various antigens that form immune complexes and stimulate eosinophilic infiltration. It can be seen in some patients. The use of intravesical BCG for bladder cancer as a tissue factor, edematous bladder with histopathological plaques, ulcers, and submucosal hemorrhage. Microscopy reveals fibrosis and inflammatory cells with extensive eosinophilic infiltration of bladder wall. Patients present with frequency, dysuria, and hematuria.

TREATMENT
• Condition is usually benign with self-limited course
• Optimal management is unclear; usually NSAIDs, steroids, and antihistamines

REFERENCES
Progress to hemorrhagic cystitis with diffuse bladder mucosal inflammation and hemorrhage. The initial response of the bladder to radiation exposure results in an edematous and friable bladder. There can be extensive endarteritis with friable mucosa. Long-term radiation cystitis may present with delayed bleeding remote from the exposure to radiation (6 mo–20 yr after). The hallmark is intractability that bleeds easily, however when bladder bleeding occurs long-term, bladder cancer should be ruled out. Life-threatening hemorrhage is a possible consequence of radiation-induced hemorrhagic cystitis. Amiodarone has shown potential in prevention of GI and acute bladder toxicity from radiation. (See Section I: "Cystitis, Hemorrhagic Infectious, Noninfectious, Radiation.")

**TREATMENT**

- Establish source with evacuation of clots is the initial intervention along with the connection of any coagulopathy if present should be the initial conservative management based on the clinical presentation.
- Endoscopic electrocautery or laser ablation of bleeding site
- Intravesical album
- Hyperbaric oxygen (100% oxygen at higher than atmospheric pressure) 60–95% effective
- Perfusion polypeptide 100 mg 3 times a day, conjugated estrogens
- Intravesical instillation of formalin (32% solution of formaldehyde) in the absence of reflux
- Refractory life-threatening hemorrhage may require more aggressive intervention: Using selective embolization of the vessel or internal iliac arteries, diversion of the urinary stream (nephrostomy tubes, ileal conduit) with or without cystectomy (Image 4: Quantiﬁcation, POP-Q).

**REFERENCES**


---

**Cystitis, Viral**

**DESCRIPTION**

Viruses are increasingly recognized as the cause of lower UTIs—especially hemorrhagic cystitis—among immunocompromised patients. Viral cystitis is usually self-limited.

**TREATMENT**

In immunocompromised patients, the use of antiviral agents (cidofovir, valaciclovir, ribavirin) administered by PO, IV, or intravesical routes is recommended.

**REFERENCE**


---

**Cystocele Grading: Baden-Walker, Pelvic Organ Prolapse Quantification (POP-Q)**

**DESCRIPTION**

The grading and evaluation of cystoceles have evolved from the Baden-Walker grading scale to the current Pelvic Organ Prolapse Quantification (POP-Q) system. Although the 2 staging systems are widely used in clinical practice, POP-Q is more commonly used in the literature. The classic Baden-Walker grading system was 1st described in 1968. POP-Q was later developed in 1996. Both staging systems base the degree of prolapse on the leading edge during a Valsalva maneuver. (See also Section II: Pelvic Grading ([Image 3: Pelvic Grading: Pelvic Organ Prolapse Classification]).)

**Baden-Walker Grading**

- Grade 0: No prolapse
- Grade 1: Leading edge descends halfway from the hymen.
- Grade 2: Leading edge descends to the hymen.
- Grade 3: Leading edge descends past the hymen.
- Grade 4: Procidentia or vault erosion

**POP-Q Staging**

- Stage 0: No prolapse
- Stage I: Leading edge is > 1 cm above the hymen
- Stage II: Leading edge is between 1 cm above and 1 cm below the hymen.
- Stage III: Leading edge is < 1 cm below the hymen but less than total vaginal length – 2 cm (TVL; total vaginal length) – 2 cm
- Stage IV: Leading edge is below hymen by more than TVL – 2 cm

**REFERENCES**


---

**Cystoscopy Processing**

**DESCRIPTION**

Cystoscopic evaluations are a major component of urological practice used for both diagnostic and therapeutic procedures. The American Urologic Association (AUA) and Society of Urologic Nurses and Associates (SUNA) have issued joint recommendations for reproducible cystoscopes. The key findings are summarized here:

- Cystoscopes are “semi-critical” devices requiring high-level disinfection and sterilization between patients. High-level disinfection differs from sterilization; high-level disinfection does not kill large numbers of bacterial spores; sterilization is the complete destruction of all microbial life.

- Bacterial cystitis is usually self-limited.
DEEP VENOUS THROMBOEMBOLISM (DVT) PROPHYLAXIS: AUA GUIDELINES

DAYTIME FREQUENCY SYNDROME (POLLAKIURIA)

DESCRIPTION The complaint of frequent daytime voiding (pollakiuria (from the Greek pollakis, meaning often) is a fairly common pediatric complaint. Other terms to describe the condition include extraordinary daytime urinary frequency, and in early literature, slam urinary tract infection. It is seen somewhat more often in boys between 4 and 10 yr. In children the differential includes UTI, diabetes mellitus, detrusor instability (DI), obstruction, and bladder detrusor instability. If no cause can be determined simple behavioral regimens have demonstrated effectiveness including reassuring the parents and child and waiting for the condition to self-resolve. Reducing dietary intake of oxalate-rich beverages such as tea and acidic juices such as apple in children who consume large amounts of them, along with liberal intake of water, have been proposed as ancillary approaches. The child needs to learn to ignore the urges and postpone voiding with some type of reward system.


DEEP VENOUS THROMBOEMBOLISM (DVT) PROPHYLAXIS: AUA GUIDELINES

DESCRIPTION Venous thromboembolism (DVT) or PE can occur in 1–5% of patients after major urologic surgery. Risk factors include advanced age, prior venous thromboembolism, cancer, hypercoagulable states, immobilization, obesity, smoking, pelvic dissection, lithotomy position, and many others. Bleeding risk must be weighed against the benefits of prophylaxis. Risk of PE can be divided into low, moderate, and high risk. Reduced risk decreases with additional risk factors.

Low risk: Minor surgery, <40 yo, no additional risk factors

Moderate risk: Risk surgery with additional risk factors or patients 40–60 yo with no additional risk factors

High risk: Patients >60 yo or OR patients 40–60 yo with additional risk factors

RECOMMENDATIONS

• Transurethral or low-risk procedures: Early and continuous prophylaxis with additional risk factors

• Moderate risk: Heparin 5,000 U SQ q8h start post op OR Enoxaparin 40 mg SQ daily (if CrCL <30 mL/min 30 mg)

• High risk: Heparin 5,000 U SQ q8h start post op OR Enoxaparin 40 mg SQ daily (if CrCL <30 mL/min 30 mg)

• Very high risk: Patients with multiple risk factors

Cytokinin Staining

DESCRIPTION Commonly used in prostate cancer diagnosis (to differentiate PIN from basal cell hyperplasia or distinguish various forms of acinar proliferations that are not cancer on needle biopsy) (Michel, which indicates basal cell-specific CK, is commonly used. If basal cell staining is present, this helps to rule out carcinoma. It is also used to examine lymph node or peritumoral tissues for prostate cancer and may increase the accuracy of lymph node staging. It has shown promise in breast cancer staging, where up to 1/3 of patients have unsuspected micrometastases: Correlation to preoperative serum prostate-specific antigen. This section is utilized. Other effects include voiding dysfunction by invading peripheral nerves. CMV cytolsis has been reported to occur in AIDS, and it is 1 of the 10/18 infections that can cause fatal immunosuppression. CMV has been associated with peripheral renal vein thrombosis, and it can be a cause of virally induced hemorrhagic cystitis. Ganciclovir has been effective in transplant patients. (See also Section I: “Immunocompromised Patients, Urologic Considerations.”)

REFERENCES


Cytology, Prostate

DESCRIPTION Exam of cells, usually obtained by fine-needle aspiration (PNA), for the detection of malignancy. Characteristics that can be determined include cellularity, ploidy status, cell cycle distribution, and cytologic grade. Its advantages over standard pathologic techniques involve ease and rapidity of technique, when used in combination with flow cytometry, it seems to increase accuracy. The findings must be read by an experienced cytotechnologist to ensure reliability. The use of this technique has declined greatly in favor of needle biopsy. (See also Section II: “Needle-Needle Aspiration, Prostate.”)

REFERENCES


Cytology, Urinary

DESCRIPTION Microscopic exam of the urine, usually performed for the detection of malignant cells during follow-up of urothelial carcinoma. Criteria for malignancy include increased cytolytic-to-nuclear ratio, eccentric nucleus, nuclear pleomorphism and irregularity, hyperchromasia, chromatin clumping, nuclear crowding and overlapping, prominent nucleoli, mitotic figures, lack of cytolytic vacuolization, and loss of cell cohesion. Highly accurate (90%) in high-grade carcinoma and CIS but less than (50–50%) accurate in low-grade bladder cancer. It is also useful in detecting unsuspected residual tumor and may predict future tumor recurrence after transurethral resection (image 8).

REFERENCES


In the office setting, high level disinfection (using glutaraldehyde or another chemical disinfectant) should include precleaning, leak testing, cleaning, disinfection, rinsing, and drying.

Glutaraldehyde “soak times” are 20–45 min. With no precleaning a 45-min glutaraldehyde soak is required. A 20-min soak is adequate if recommended reprosection steps are followed prior to immersion in glutaraldehyde.

One chemical disinfectant (ortho-phthalaldehyde [OPA]) has been associated with anaphylaxis in cystoscopes.

One chemical disinfectant (ortho-phthalaldehyde [OPA]) has been associated with anaphylaxis in cystoscopes.
DEHYDROEPIANDROSTERONE (DHEA) AND DHEA SULFATE (DHEA-S) BLOOD TEST

REFERENCE

DEHYDROEPIANDROSTERONE (DHEA) AND DHEA SULFATE (DHEA-S) BLOOD TEST

DESCRIPTION
Because they are produced in the adrenal cortex, serum levels of DHEA and the sulfated form (DHEA-S) reflect adrenal gland function. Normal values range differ by age and sex. Common clinical reasons to measure these levels include female virilism, premature puberty, Cushing, and adrenal cancer. DHEA-S is the major form in serum. Generally, blood levels of both forms decrease in the aging male, and replacement has been linked with improved outcomes in Alzheimer disease and systemic lupus.

TREATMENT
• Androgenic medication
• β-Blocker medication
• Behavioral modifications
• Address underlying cause of dementia

REFERENCE

DENT DISEASE

DESCRIPTION
Characterized by hypercalciuria, nephrocalcinosis, kidney stones, renal failure, and rickets. It is a disorder of the proximal tubule with an X-linked recessive inheritance. Symptomatic disease is almost exclusively confined to males. Typical childhood presentation is polyuria, microscopic hematuria, asymptomatic proteinuria, or renal failure. Treatment is focused on reducing the hypercalciuria. (See Section II: “Hypercalciuria [Absorptive, Renal, and Resorptive].”)

REFERENCE

DENYS-DRASH SYNDROME (DDS), UROLOGIC CONSIDERATIONS

DESCRIPTION
Also called Drash syndrome; a rare disorder consisting of congenital nephropathy, Wilms tumor, and DDS (male pseudohemaphroditism) resulting from WT1 gene mutations on chromosome 11p13. Patients develop hypertension, end stage renal disease (ESRD), and gonadoblastomas in their dysgenetic gonads.

TREATMENT
• Early prophylactic bilateral nephrectomy
• Gonadectomy
• Chemotherapy based on National Wilms Tumor protocol
• Renal transplantation after 2 yr of disease free on dialysis

REFERENCE

DERMATITIS HERPETIFORMIS

DESCRIPTION
Dermatitis herpetiformis (also called Duhring disease) is an autoimmune blistering disorder associated with gluten sensitivity, and autoimmune and lymphoproliferative disorders. It is characterized by grouped erosions, urticarial plaques, and papules with vesicles, and has been described on the external genitalia. It is extremely pruritic, and the vesicles are often excoriated to erosions by the time of physical exam. Diagnosis is made by the presence of IgA deposits in the upper papillary dermis seen on direct immunofluorescence of a skin biopsy specimen. The mainstay of treatment are dapsone and a gluten-free diet.

REFERENCE

DERMATOPHYTE, EXTERNAL GENITALIA

DESCRIPTION
Dermatophytes are the most common type of fungi that cause skin and nail infections, and they can involve the external genitalia. The irritation is often caused by the dermatophyte, Trichophyton rubrum. They typically present in those adults with excessive perspiration as a major risk factor. Skin manifestations include red, raised, sharply defined, itchy lesions in the groin that may extend to the buttocks, inner thighs, and external genitalia. Warm weather and tight clothing encourage fungal growth. Also consider treating tinea pedis (“athlete’s foot”), as this is often the original site of the offending organism.

SYNONYMS
• Tinea cruris
• Ringworm
• Jock itch

TREATMENT
• Weight loss, improved personal hygiene; tarsol, cornstomach, or other desiccant powders to keep the area dry
• Topical antifungals (powders, ointments, lotions, solutions) such as terbinafine (Lamisil), clotrimazole (Lotrimin, Mycelex), econazole (Spectazole), ciclopirox (Lopex)

REFERENCE

DERMOMA CYST, TESTICULAR

DESCRIPTION
Cysts (epidermoid cyst) are benign intratesticular neoplasms and a variant of cystic teratomas that contain ectodermic derivatives. Patients present with a palpable, firm, nontender testicular mass. Case reports indicate occurrence over a wide range of ages, from 5–85 yr. Dermoid cysts are typically well encapsulated and unilocular. They occur more often in the right testicle (upper/lower pole) and are usually treated with focal excision or excision.

REFERENCE

DERMOMID CYST, TESTICULAR

DESCRIPTION
Cysts (epidermoid cyst) are benign intratesticular neoplasms and a variant of cystic teratomas that contain ectodermic derivatives. Patients present with a palpable, firm, nontender testicular mass. Case reports indicate occurrence over a wide range of ages, from 5–85 yr. Dermoid cysts are typically well encapsulated and unilocular. They occur more often in the right testicle (upper/lower pole) and are usually treated with focal excision or excision.
DESMOPLASTIC SMALL ROUND CELL TUMOR

DESCRIPTION

Rare, usually very aggressive neuroectodermal tumor that typically presents in the abdominal cavity but may involve the GU system. Those patients with GU involvement tend to be younger men. Histologically, irregular nests of small round cells surrounded by fibrous connective tissue are seen. Immunohistochemical studies reveal both epithelial and nonepithelial origins. Associated with a unique translocation between chromosomes 11 and 22, that involves EWSR1 and WT1 genes. Prognosis is poorly poor, largely due to majority of patients presenting with metastatic disease. Surgical resection and multidisciplinary chemotherapy have been employed with poor success.

REFERENCE


DE TONI-FANCONI-DEBRE SYNDROME

DESCRIPTION

Syndrome of multiple defects of tubular function, characterized by aminoaciduria, phagohistolysis, glycosuria, osteodystrophia, and renal tubular acidosis. The proximal renal tubule is shortened and replaced by a thin tubular structure, constituting the swan-neck deformity.

TREATMENT

• Replacement of cation defects (especially potassium)
• Correction of acidosis with bicarbonate or citrate
• Replacement of phosphate loss with isosonic neutral phosphate solution
• Encouragement of liberal calcium intake with added vitamin D

REFERENCE


DETRUSOR OVERACTIVITY

DESCRIPTION

Evolutory or unihabitited contraction of the detrusor muscle (as seen with multichannel urodynamics) in the absence of a neurologic cause. According to the Incontinence Society definition: DO is an anaerobic observation characterized by involuntary detrusor contraction during the filling phase which may be spontaneous or provoked. Clinically, DO usually presents as urinary urgency, with or without urinary frequency, urgency incontinence. (See also Section I: “Overactive Bladder.”) The etiology of DO can be either neurogenic or idiopathic.

SYNONYM

Overactive bladder

TREATMENT

• Behavioral modification: Fluid restriction, avoidance of bladder irritant
• Pelvic floor exercises
• Anticholinergic/antimuscarinic therapy
• Alpha-adrenergic receptor antagonist therapy
• Botulinum toxin type A

• Sacral neuromodulation
• Posterior tibial nerve stimulation
• Surgical treatments: Resection/cystotomy, augmentation cystoplasty

REFERENCES


DEXAMETHASONE SUPPRESSION TEST

DESCRIPTION

The dexamethasone suppression test is designed to diagnose and differentiate among the various types of Cushing syndrome and other hypercortisolism states. Results indicate of Cushing disease involve no change in cortisol on low-dose dexamethasone but inhibition of cortisol on high-dose dexamethasone. If the cortisol levels are unchanged from both low- and high-dose dexamethasone, then a cortisol-secreting adenocortical tumor is suspected or an ectopic ACTH source. Occasionally, other conditions (such as major depression, alcoholism, stress, obesity, kidney failure, pregnancy, or uncontrolled diabetes) may interfere with cortisol levels.

The low-dose test depends on the fact that only minimal change in cortisol is usually present in Cushing disease, whereas patients with Cushing disease will show no change in cortisol on low-dose dexamethasone but marked suppression on high-dose dexamethasone. Typically, the test is performed in the morning on an empty stomach after fasting. A single oral dose of dexamethasone, 0.5 mg, is administered 1 h before the cortisol sample is obtained on day 1. This represents the low-dose dexamethasone test.

REFERENCES


DIET CRISIS

DESCRIPTION

The most severe manifestation of nephropathies, originally described by Leof in 1864. Classically described as catabolic candal pain, nausea, chills, septicemia, oliguria, and transient hematuria or proteinuria. Nephropathy secondary to vascular obstruction of the ureter is the postulated cause. Physical exam reveals an enlarged, tender kidney.

TREATMENT

• Manual reduction of the ptotic kidney was initially used
• Nephropathy has been used for nephropathies and was 1 of the most commonly performed operations of the early 20th century, uncommon procedure today

REFERENCE


DIMERCAPTOSUCCINIC ACID (DMSA) RENAL SCAN

DESCRIPTION

DMSA allows the visualization of detailed renal cortical anatomy because it accumulates in the kidney at the proximal renal tubules and is slowly excreted in the urine. DMSA renal imaging is the most sensitive radiologic study used to detect pyelonephritic changes and scarring in the kidneys.

REFERENCE


DIURETIC RENOGRAM

DESCRIPTION

A noninvasive nuclear medicine study that provides functional information regarding upper urinary tract obstruction (sometimes referred to as “Latex renogram”). This test is most commonly utilized to determine obstruction in the setting of hypertension. A tubular agent is preferred, therefore IODI is widely used for its high extraction fraction, rapid parenchymal transit, low radiation absorbed dose, and excellent imaging properties. The recommended dose of 15 microCurie (200 MBq) is sufficient for children. Use of higher doses of 30 microCurie (100 MBq) is not recommended. The test is performed in the morning after a 3–4 h fast. A diuretic agent, typically furosemide, is given and the renal scan is performed in the supine position. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h.

REFERENCES

A noninvasive renal diagnostic test that provides functional information regarding upper urinary tract obstruction (sometimes referred to as “Latex renogram”). This test is most commonly utilized to determine obstruction in the setting of hypertension. A tubular agent is preferred, therefore IODI is widely used for its high extraction fraction, rapid parenchymal transit, low radiation absorbed dose, and excellent imaging properties. The recommended dose of 15 microCurie (200 MBq) is sufficient for children. Use of higher doses of 30 microCurie (100 MBq) is not recommended. The test is performed in the morning after a 3–4 h fast. A diuretic agent, typically furosemide, is given and the renal scan is performed in the supine position. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h.

REFERENCES

A noninvasive renal diagnostic test that provides functional information regarding upper urinary tract obstruction (sometimes referred to as “Latex renogram”). This test is most commonly utilized to determine obstruction in the setting of hypertension. A tubular agent is preferred, therefore IODI is widely used for its high extraction fraction, rapid parenchymal transit, low radiation absorbed dose, and excellent imaging properties. The recommended dose of 15 microCurie (200 MBq) is sufficient for children. Use of higher doses of 30 microCurie (100 MBq) is not recommended. The test is performed in the morning after a 3–4 h fast. A diuretic agent, typically furosemide, is given and the renal scan is performed in the supine position. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h.

REFERENCES

A noninvasive renal diagnostic test that provides functional information regarding upper urinary tract obstruction (sometimes referred to as “Latex renogram”). This test is most commonly utilized to determine obstruction in the setting of hypertension. A tubular agent is preferred, therefore IODI is widely used for its high extraction fraction, rapid parenchymal transit, low radiation absorbed dose, and excellent imaging properties. The recommended dose of 15 microCurie (200 MBq) is sufficient for children. Use of higher doses of 30 microCurie (100 MBq) is not recommended. The test is performed in the morning after a 3–4 h fast. A diuretic agent, typically furosemide, is given and the renal scan is performed in the supine position. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h. The renal scan is repeated at 20 min intervals for up to 1 h.
A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

Dysfunctional voiding is characterized by an intermittent and/or fluctuating flow rate due to incoordinate intermittent contractions of the periurethral striated muscle during voiding in neurologically normal individuals. Although dysfunctional voiding is not a very specific term, it is preferred to terms such as “nonneurogenic neurogenic bladder.” Other terms such as “dysfunctional detrusor sphincter dyssynergia,” or “dysfunctional neurologically normal voiding dysfunction,” may be preferable. However, the term dysfunctional voiding is very well established. The condition occurs most frequently in children. While it is felt that pelvic floor contractions are responsible, it is possible that the intraurethral striated muscle may be important. It was originally described by Hinman and Bauman in 1973 after a review of similar reported cases. Upper tract damage can occur. Diagnosis is through videourodynamics. (See also Section II: “Hinman Syndrome (Hinman–Allen Syndrome).”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A complaint of loss of urine that occurs after completion of voiding, thought to be caused by retained urine in the urethra distal to the sphincter in men and retained urine in the vagina or vesical vault distal in women. In men, it is a complaint associated clinically with BPH, following radical prostatectomy and stricture disease. Recent data suggest it may be a surrogate for median lobe hypertrophy in BPH.

REFERENCE

A normal anatomic variant of the left kidney consisting of a bulge of normal tissue that mimics a tumor. Dromedary humps arise from the superosteal aspect of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

Dysfunctional voiding is characterized by an intermittent and/or fluctuating flow rate due to incoordinate intermittent contractions of the periurethral striated muscle during voiding in neurologically normal individuals. Although dysfunctional voiding is not a very specific term, it is preferred to terms such as “nonneurogenic neurogenic bladder.” Other terms such as “dysfunctional detrusor sphincter dyssynergia,” or “dysfunctional neurologically normal voiding dysfunction,” may be preferable. However, the term dysfunctional voiding is very well established. The condition occurs most frequently in children. While it is felt that pelvic floor contractions are responsible, it is possible that the intraurethral striated muscle may be important. It was originally described by Hinman and Bauman in 1973 after a review of similar reported cases. Upper tract damage can occur. Diagnosis is through videourodynamics. (See also Section II: “Hinman Syndrome (Hinman–Allen Syndrome).”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: “Renal Pseudotumor.”)

REFERENCE

A normal anatomic variant of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or intravenous pyelography. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the domesticated camel. (See also Section II: ”...
The presence of ecchymosis in the flank region (Gray-Turner sign) is a physical sign of retroperitoneal bleeding. Common associations may include renal trauma, ruptured abdominal aortic aneurysm, and acute pancreatitis.

**REFERENCE**


---

**EICHOCINOCOCUS, RENAL**

**DESCRIPTION** Renal hydatid disease is a parasitic tapeworm infestation that results in renal cysts that occupy space and cause local mass symptoms. This infection is caused by the larval stage of the cestode *Echinococcus granulosus*, whose definitive host is the dog and the principal intermediate is the sheep. Common symptoms include flank pain, hematuria, and local pressure. The diagnosis of renal echinococcus requires a high index of suspicion and despite a complete clinical history, serologic, radiologic, and urine data, the yield is only 50%. Radiographic findings include a calcified, oval or linear cystic mass in the kidney. During cyst excision, great care must be taken to not spill or rupture the cyst, because the liberated parasites could be spread and cause anaphylaxis. (See also Section II: “Hydatid Cysts.”)

**SYNONYMS**

- Cystic hydatid disease
- Hydatid cyst

**TREATMENT**

- Surgical excision of intact cyst, with care not to spill or rupture the cyst
- Medical treatment is reserved for noncurable cases (albendazole 400 mg twice daily for 4–6 mo)

**REFERENCE**


---

**EDEMA, LOWER EXTREMITY, UROLOGIC CONSIDERATIONS**

**DESCRIPTION** Edema of the lower extremity can occur iatrogenic, physiologic, or psychogenic in nature. It may result in cardiopulmonary problems. Uterine and vaginal edema may be observed in patients undergoing urologic surgery, they should be euthyroid prior to their intervention. Thyroidectomy or thyroid storm can present with fever, laryngospasm, confusion, and cardiovascular collapse. Hyponatremia is generally associated with an increased sensitivity to medications such as anesthetic agents and narcotics; its severe form can be associated with myoclonic dystonia, opsoclonus, electrocerebral imbalance, and decreased gastrointestinal motility.

**REFERENCE**


---

**ECHNOMYSIS, FLANK**

**DESCRIPTION** The presence of ecchymosis in the flank region (Gray-Turner sign) is a physical sign of retroperitoneal bleeding. Common associations may include renal trauma, ruptured abdominal aortic aneurysm, and acute pancreatitis.

**REFERENCE**


---

**EDWARD SYNDROME**

**DESCRIPTION** Also known as trisomy 18, it is the 2nd most common autosomal trisomy after Down syndrome. Characterized by structural heart defects, kidney malformations, esophageal atresia, nephroblastoma, facio-cutaneous naevi, and genital hypoplasia among other signs. High incidence of urogenital abnormalities noted with adrenal kidney in about 20% of cases; hydronephrosis, hypospadias, and inguinal hernia are also common. Up to 90% of patients die within the 1st yr of life, usually secondary to cardiopulmonary problems. Urinary and vaginal abnormalities are common in females.

**REFERENCE**


---

**EJACULATION, PAINFUL**

**DESCRIPTION** So called “female ejaculation” is the expulsion of fluid by females during or before sexual orgasm. The prevalence varies between 10–54%, whereas the amount of fluid ranges from 1–900 mL. There are natural sexual responses but may also represent symptoms of urinary incontinence. The term encompasses various phenomena with different underlying pathophysiologic mechanisms noted below:

- **Vaginal lubrication**: Vaginal fluid is forced out by the contractions of perineal muscles.
- **Ejaculation**: Either organic expulsion of semen or well-synchronized expulsion of the “female prostate” (known as Skene glands), or organic expulsion of diluted urine (squirtng/gushing), or the combination of both.
- **Cystic incontinence**: Leakage of urine that occurs during penetrations or orgasm. Usually associated with stress or urge urinary incontinence.
- **Penetration incontinence**: occurs more frequently and is usually caused by SD. Urodynamic diagnoses of detrusor overactivity (DO) and SUI are observed in organic incontinence. (See also Section I: “Incontinence, Urinary, Adult Female”, Section II: “Cystic Incontinence [Cystal leakage/Irritative Incontinence Incontinence]”)

**REFERENCE**


---

683

---

**EJACULATION, PAINFUL**

**DESCRIPTION** The incidence of pain associated with or immediately after ejaculation is 1–8%. Can be urogenetic, physiologic, or psychogenic in nature. Ejaculatory or postorgasmic pain is believed to arise from interference with the coordination of the muscles of the pelvic floor and male genita that are responsible for semen transport during ejaculation. (See also Section II: “Disparuresia.”)
EJACULATORY ANHEDONIA

CAUSES

- Prostatitis
- BPH
- Ejaculatory duct obstruction (EDO) by calculi
- Postoperative (prostatectomy)
- Antidepressants
- Pelvic neuropathy

TREATMENT

- α-Adrenergic inhibitors
- Rule out and treat EDO
- Pelvic nerve injection with bupivacaine/trimethaphan
- Pelvic nerve release

REFERENCE


EJACULATORY ANHEDONIA

DESCRIPTION

A rare condition, affecting males predominantly, in which ejaculation occurs without an accompanying sense of erotic pleasure. Most common causes are psychogenic in origin or related to ESHI antidepressant usage.

REFERENCE


EJACULATORY DUCT OBSTRUCTION (EDO)

DESCRIPTION

EDO is found in 1–5% of infertile men, producing azoospermia with low-volume, acidic ejaculate that has no fructose. Obstruction of the ejaculatory ducts prevents the emission of sperm and seminal fluid into the posterior urethra during ejaculation. Congenital causes include utricular, mullerian and Wolff duct cysts, ejaculatory duct stenosis, or atresia. Acquired causes include infection, calculus, trauma, or prior instrumentation. Physical exam is usually normal, with the occasional palpable malleable mass or dilated seminal vesicles. Semen analysis shows low-volume, acidic, frank, absent fructose, and failure to coagulate. Transrectal ultrasonography (TRUS) demonstrates a cystic, miliary structure within the prostate, with dilated seminal vesicles. When TRUS is equivocal, additional tests include TRUS-guided seminal vesicle aspiration (demonstrates abundant spermatozoa) or aspiration biopsy. (See also Section II: "Ejaculatory dysfunction.")

TREATMENT

Through transrectal resection of ejaculatory duct, in which the ejaculatory duct is unroofed by transrectal resection at the level of the verumontanum, until efflux from the ducts is seen.

REFERENCE


ELECTROEJACULATION

DESCRIPTION

Procedure for obtaining sperm for ARTs in patients who cannot ejaculate on their own, such as SCI patients, typically used after failure of vibratory perineal stimulation. General anesthesia is used, except in cases of complete spinal cord compromise. A transrectal probe is positioned with electrodes against the anterior rectal wall. Electrical stimulation causes ejaculation and erection in ~85% of patients. Retrosigmoidoscopy is performed before and after the procedure to rule out renal injury. Blood pressure monitoring is essential during the procedure for patients who may have autonomic hyperreflexia.

REFERENCE


ELECTROMYOGRAPHY, EXTERNAL SPHINCTER

DESCRIPTION

Generally, electromyography is the measurement of bioelectric potentials generated by the depolarization of muscle. During voiding, the activity of the external sphincter can be monitored by transperineal needle electrodes or surface electrodes. During filling, there should be maximum decrease in activity, which will reach maximum near capacity. During voiding, there should be a persistent cessation of sphincter activity. At the end of the voiding phase, sphincter activity returns to baseline. To assess external sphincter activity, the patient may be asked to interrupt voiding in the middle of the stream, at which point there should be an abrupt increase in sphincter activity sufficient to stop the flow. Abnormal EMG patterns may be detected in detrusor sphincter dyssynergia and dysfunctional voiding. EMG monitoring may also be used during biofeedback therapy for dysfunctional voiding.

REFERENCE


ELEJALDE SYNDROME

DESCRIPTION

Also known as ano-congenital perineal dysplasia, this exceedingly rare autosomal recessive syndrome is characterized by crouzon- and fibroblast hyperplasia in organs such as skin, larynx, and pancreas. High birth weight, craniofacial disproportion, polyphalantergy, sphenoid abnormalities, hypertrophic nephrosis, and renal cysts are also common features.

REFERENCE


ELEPHANTIASIS, SCROTUM (ELEPHANTIASIS SCRITTI)

DESCRIPTION

Also called rhinophyma scroti, this is the end result of a progressive lymphatic obstruction in which the scrotum and penis can become massively enlarged. Usually associated with filariasis, which is uncommon in the United States. Differential includes filariasis and other infectious causes; malignancy obstructing lymphatics; surgical therapy that has altered lymphatic drainage; and idiopathic, such as Milroy disease. (See also Section I: "Edema, External Genitalis (lymphedema, Pene-Scrotal Edema)", Section II: "Filariasis, Urologic Considerations." and Image O1)

TREATMENT

- Drugs therapy for any infective etiology
- Surgery for retraction of redundant scrotum with flap coverage of testes

REFERENCE


ENCOPRESIS, UROLOGIC CONSIDERATIONS

DESCRIPTION

Children who are inconsistent of stool, even with minor fecal soiling, usually have significant constipation. Occult pathology of the bowel and/or urogenital system may be ruled out as a possible cause. Encopresis usually is helpful in identifying bowel problems when the parents of a child are not aware of the child's stool habits. Children with encopresis and constipation have a higher risk of UTI and urinary incontinence. Successful treatment of functional constipation will usually resolve encopresis and associated urinary tract problems. The term “total incontinence” is sometime used as the preferred term over encopresis or soiling. (See also Section I: “Dysfunctional Elimination Syndromes.”)

TREATMENT

- Diet changes
- Laxatives, stool softeners
- Toilet schedules

REFERENCE


ENCRUPTED CYSTITIS AND PYELITIS

DESCRIPTION

Exacerbatory urinary-tract condition of the bladder and pelvic urogenital system characterized by inflammation with calcium deposits (struvite and apatite calculi). Commonly, the presence of alkaline urine, infection by urea-splitting Corynebacterium urealyticum (formerly called Corynebacterium group D2), a multiple antibiotic-resistant urea-splitting bacterium, is the most frequently incriminated agent, and recent history of a urologic procedure in a immunocompromised host (eg, renal transplant) is found. Clinical manifestations of encrusted cystitis are often febrile, dysuria, and gross hematuria. Encrusted pyelitis may have lumbar pain in addition to symptoms of encrusted cystitis. Imaging on US and CT may reveal calcific encrustations with thick-walled edematous bladder and/or pelvisceral cavity. Calculations within appear on plain abdominal radiographs unless associated with staghorn calculus. The endoscopic appearance is of calciﬁed within plaques adherent to a severely inflamed and ulcerated mucosa. Bacteriologic diagnosis of Corynebacterium group D2 requires culture for 48–72 hr at 37°C on media enriched with 5% carbon dioxide (CO2) or sheep blood agar.

REFERENCE

This rare mucinous analog of Wilson W, Taubert KA, Gewitz M, et al. Prevention of Antimicrobial prophylaxis for REFERENCE.

López-Medrano F, García-Bravo M, Morales JM, et al. REFERENCE. are much more likely to cause infectious endocarditis that bacteremia resulting from random daily activities exceed the benefit. The AHA guidelines concluded every patient is imperative in preventing this challenging complication.

ENCROCUTED URETERAL STENT DESCRIPTION Indwelling ureteral stents are routinely employed for the prevention and treatment of ureteral obstruction secondary to intrinsic, extrinsic, and idiopathic causes such as urethrakinks, strictures, and/or malignancy. Indwelling tube users affect rate of encrustation: Consensus is that stents should not remain in place longer than 3–6 mo (high degree of variation according to different series). Reported risk factors include urethral tract infections (urease-producing microorganisms) and pregnancy. Site and degree of encrustation will guide the approach appropriate use in single or multiple, for this purpose several grading systems and management algorithms have been proposed. Good communication between physician and patient in preventing this challenging complication.

ENDOCRIDS (SBE) PROPHYLAXIS, UROLOGIC CONSIDERATIONS DESCRIPTION Antimicrobial prophylaxis for urology procedures: policy to prevent infectious endocarditis is no longer recommended by the American Heart Association: the risk of adverse events exceed the benefit. The AHA guidelines concluded that bacteria resulting from random daily activities are much more likely to cause infectious endocarditis than bacteria associated with GU procedures.


ENDOCRIVICOSIS, BLADDER DESCRIPTION This rare micronodular analog of endometriosis histologically demonstrates glandular lesions characterized by a prominent endometrioid-type epithelium that may involve the urinary bladder in women of reproductive age. Typically are observed in the posterior wall of the bladder or the dome. Lack of awareness may lead to confusion with a adenocarcinoma, particularly of urothelial origin given its location. Because of this, these are presumed to have an underlying malignancy and are treated surgically. Patients usually present with irritative voiding symptoms and pelvic pain. Transurethral resection of partial hysterectomy is curative, and close follow-up is recommended.


ENDOMETRIOSIS, GENITOURINARY DESCRIPTION Endometriosis is a condition in which endometrial tissue is found outside the uterus. Most common sites in the GU system are the Bladder and distal 3rd of rectum. Other symptoms are variable and may include dysmenorrhea and pelvic pain with or without urinary symptoms of gross hematuria, flank pain, frequency, or urgency. Urinary symptoms may or may not be exacerbated with menstruation, and the classic symptom of “cyclical hematua” is uncommon. Diagnosis is through TVPCT-urography and urine analysis, laparoscopy to inspect the pelvis and obtain tissue biopsy, or cystoscopy or ureteroscopy to evaluate hematuria and dilated biopsy.

TREATMENT

• Hormonal therapy with oral contraceptives, danazol, or GnRH agonists
• Surgery when medical treatment fails
• Partial cystectomy, ureterolysis, ureteric reimplantation, or uretal lancing may be performed


EPICA-2 (EARLY PROSTATE CANCER ANTIGEN) DESCRIPTION A nuclear matrix protein (NMP) that showed promise as a new serum-based biomarker of prostate cancer, which was postulated to have better sensitivity and specificity than PSA. However, at the request of the authors (Leman et al., Urology, 2012; 79(2):490–499), the original article was retracted as there were inconsistencies in validating their data collection.


EPIDERIDYMIS, METASTASIS TO DESCRIPTION This is a benign tumor that accounts for 1/3 of all primary epidermoid tumors. Epidermoid cysts are seen in up to 2% of patients with von Hippel-Lindau disease and are often bilateral with this syndrome. They have a cystic appearance on ultrasound and can be up to 6 cm. Cut surface is gray-brown and contain fluid. The histologic appearance is that of divided tubules with a single or double layer of cuboidal or low columnar epithelium. Rarely can be mistaken for metastatic RCC. Papillary cystadenomas and benign and generally asymptomatic and no treatment is required. (See also Section I: “Scrotum and Testicle, SCROTAL Mass” and “Spermatocele”; Section II: “Epididymal Cysts.”)


EPIDEMIDYAL CYST, TESTICLE DESCRIPTION Epidermoid cysts account for ~1% of all testicular tumors. Producing keratinizing, squamous cell-lined cysts supported by fibrous tissue, these cysts are considered special cases of teratoma since only a single germinal layer and not the required 2 layers is represented. Benign in behavior, cystic US is supportive of the diagnosis but not usually definitive. (See also Section I: “Scrotum and Testicle, Mass.”)

TREATMENT

• Impalpable orchidectomy
• Some advocate organ-preservation surgery if the diagnosis is definitively proven by frozen section.


EPIDMYAL CYSTADENOMA/ PAPILLARY CYSTADENOMA DESCRIPTION This is a benign tumor that accounts for 1/3 of all primary epidermoid tumors. Epidermoid cystadenomas are seen in up to 2% of patients with von Hippel-Lindau disease and are often bilateral with this syndrome. They have a cystic appearance on ultrasound and can be up to 6 cm. Cut surface is gray-brown and contain fluid. The histologic appearance is that of divided tubules with a single or double layer of cuboidal or low columnar epithelium. Rarely can be mistaken for metastatic RCC. Papillary cystadenomas and benign and generally asymptomatic and no treatment is required. (See also Section I: “Scrotum and Testicle, Mass,” “Spermatocele,” and “von Hippel-Lindau Disease/Tumours” and Section II: “Epidermoid Cysts.”)


EPIDMYLIS, METASTASIS TO DESCRIPTION Employed rare, with primary sites reported to include colon, stomach, kidney, prostate, carcinoid, and pancreatic tumors. Prognosis is related to that of the primary disease. Patients can present with pain and swelling or an incidental finding on orchidectomy for prostate cancer. 4 mechanisms for spread have been proposed, including direct extension, retrograde venous extension, orthograde lymphatic extension, and arterial embolism.

REFERENCE
EPIDIDYMS, OBSTRUCTION

REFERENCE

EPIDIDYMS, OBSTRUCTION

DESCRIPTION
A cause of obstructive azoospermia. Most common cause is vasectomy, which results in a fixed obstruction and elevated vesiculogram pressures resulting in the dilation of the epididymal tubules. Other causes include trauma, congenital malformation of the vas and epididymis, infection, inflammatory damage to the epididymis, and idiopathic. Epididymospermatocele is the treatment of choice. (See also Section 1: “Infertility, Urologic Considerations” and “Vas Defects, Congenital Abnormalities,” Section A: “Azoospermia.”)

REFERENCE

EPITHELOID HEMANGIOMA, PENIS AND SCROTUM

DESCRIPTION
Rare vascular lesion, typically arising on the head and distal extremities, whose pathogenesis is not fully understood. Genital involvement has rarely been reported. These lesions do not recur following excision and no metastasis has been reported. Macroscopically, the lesions are described as an inflammatory red to brown nodule. Microscopically, the lesions are characterized by endothelial cells arranged in nests surrounded by immature vessels and eosinophilic cell stroma. Differential diagnosis includes epithelioid hemangioma, epithelioid hemangioendothelioma, epithelioid hemangioendothelioma, Kimura’s disease, and bacillary angiomatosis. Treatment is local excision.

REFERENCE

ECTRICAL DYSFUNCTION INVENTORY OF TREATMENT SURVEY (EDITS)

DESCRIPTION
A validated satisfaction questionnaire for both patient (11 items) and partner (15 items) based on their subjective evaluation of the treatment for ED. Few of the disease-specific instruments used to assess ED address sexual dysfunction-related quality of life, psychosocial impact, and satisfaction. EDITS attempts to address both patient and partner satisfaction with ED treatment, in addition to sexual dysfunction.

REFERENCE

ERECTILE DYSFUNCTION SCORE (EHS) FOR ED

DESCRIPTION
The EHS was developed as a single-item, patient-reported outcome to quantify erection hardness data. It is easy to use and highly responsive to treatment. Psychometric analysis supports its use as a simple, valid, reliable, and responsive tool for the assessment of erection hardness in clinical research.

REFERENCE

ERYSPHELAS, EXTERNAL GENITALIA

DESCRIPTION
Superficial bacterial infection of the dermis, with sudden demarcated lymphatic involvement. The infection affects extremes of age, and the most common site of involvement is the face. Typically heralded by pain, superficial erythema, and plaque-like edema with a sharply defined margin to normal skin, it may often be described as a “pool of orange appearance. The clinician must differentiate erysipelas from cellulitis and furunculonecrosis (exclusion of this diagnosis is a priority in all cutaneous infections of the external genitalia). It is usually caused by Group A hemolytic streptococcus (S. pyogenes), or rarely S. aurous.

TREATMENT
- Mild infection: PO penicillin, macrolides, or clindamycin
- Severe infection: Parenteral penicillin or vancomycin

REFERENCE

ERYTHEMA MULTIFORME (EM), EXTERNAL GENITALIA

DESCRIPTION
EM is a common acquired blistering skin condition that affects all age groups, ethnicities, and sexes. EM minor is a mild subtype that usually is confined to skin and oral involvement. EM major (Stevens–Johnson syndrome) affects skin and often other mucocutaneous-lined surfaces including the eyes, oral cavity, and external genitalia. The hallmark of EM is a target lesion, a circular erythematous macular lesion resembling a bull’s-eye. Commonly occurring on the hands. Painful rash is characteristic, and macules, papules, urticaria, vesicles, bullae, pustules, or pachydermae are characteristic. In EM major, large tracts of skin and oral mucosa may be denuded, along with conjunctivitis, and GI and upper GI involvement. HSV is the most common cause but virtually any infectious agent or drug can cause EM. Main differential is toxic epidermal necrolysis.

TREATMENT
- EM minor: Warm compress with topical astringent, topical aciclovir (for HSV-related EM)

REFERENCE

ERYTHRASMA

DESCRIPTION
Superficial, asymptomatic cutaneous infection by the diphtheroid Corynebacterium minutissimum. Physical exam reveals a sharply demarcated, round to oval plaques with scales in the intertriginous or interdigital regions. Wood’s lamp examination with a Wood’s light will reveal a characteristic yellow-orange fluorescence. Historically, only the stratum corneum is affected, with all other layers normal. More common in tropical climates. Despite there being no consensus on the ideal treatment for the condition, usually it consists of topical or oral antibiotic therapy for 14 days (erythromycin or tetracycline). Recent evidence suggests single-dose clindamycin may be an alternative regimen.

REFERENCE
RARE ENTITY REPRESENTING 3–5% OF EGG
K, Khoury A. The exstrophy-epispadias complex. REFERENCE
EEC is a rare congenital urogenital anomaly with a spectrum of complexity ranging from epispadias and bladder exstrophy to cloacal exstrophy. Incidence of bladder exstrophy is between 1 in 10,000 and 1 in 50,000 live births, with a male predominance. The risk of recurrence is in a family is 1 in 100. The condition is believed to be due to failure of the cloacal membrane to be reinforced by growth of mesoderm, therefore preventing the midline separation of mesenchymal tissues and lower abdominal wall development. The cloacal membrane ruptures prematurely and, depending on the stage of development during which the rupture occurs, a variant of the complex will result. Most anomalies relate to defects of the abdominal wall, bladder, genitalia, pelvic bones, rectum, and anus. See also Section I. “Epispadias” and “Exstrophy, Bladder (Classic Exstrophy).”

TREATMENT
• Immediate at birth: Prevent irritation/trauma to exposed urorectal surface (eg, “Swan wrap”)
• Surgical reconstruction must consider appearance of lower abdomen and genitalia, pelvic bone reconstruction, continence, and subsequent sexual function
• Staged reconstruction: Early bladder, abdominal wall, and posterior urothelial closure, with osteotomy. Epispadias repair begins at 2–3 mo. Reconstruction of continent bladder neck and urethral channel, usually at age 4–5 yr
• Single-stage reconstruction

REFERENCE

EXTRAGONADAL GERM CELL TUMORS (EGCT)
DESCRIPTION Rare entity representing 3–5% of all GCT. There is a clinical association with Klinefelter syndrome, and testicular ultrasound is necessary to exclude primary tumor in the testes (or ovaries in females). Primary EGCT are usually midline in decreasing frequency: Medulloblastoma, retroperitoneal, pineal/suprasellar region, and the sacrococcygeal region. All tumor types are reported, with von Hippel-Linderheim being most common. They can present with widespread dissemination, and advanced metastasis with few symptoms. Transformation to sarcoma or carcinoma has been reported with chemotherapy resistance common in these cases. 1 or both testicular tumor markers (pHCG or AFP) are elevated in >85% of cases of EGCT. Management of EGCT parallels that of metastatic testicular GCT, however EGCT have a worse prognosis.

TREATMENT
• Surgical excision, F feasible
• Chemotherapy, irradiation, or combination based on histology and in general follows testicular cancer regimens.

REFERENCE

EXTRAMAMMARY PAGET DISEASE, UROLOGIC CONSIDERATIONS
DESCRIPTION A rare cutaneous malignancy arising from ducts of apocrine-gland bearing skin. Most often involving the anogenital region, more commonly seen in the elderly and women. The condition presents with a well-circumscribed erythematous scaly patch, similar in appearance to mammary Paget disease. There is a 10% association with underlying metastatic GI (most commonly bladder) or GI (most common colon) malignancy. Differential diagnoses include SCC in situ of malignant melanoma.

TREATMENT
• Surgical excision with wide margin, Mohs microsurgical excision, or radiation
• Screen for occult GI and GI malignancy

REFERENCE

EXTRAMEDULLARY HEMATOPOIESIS, RENAL
DESCRIPTION This is a reactive process in response to the failure of hematopoiesis in the bone marrow. It commonly occurs in organs such as the liver, spleen, and kidney. It commonly occurs in the presence of myelofibrosis (most common), chronic myeloproliferative disorder, polycythemia vera, and essential thrombocytosis. Considered a cause of renal parenchymal, a renal mass in association with any of these disorders should raise the possibility of an extramedullary hematopoiesis. Biopsy confirmation is usually required.

REFERENCE

FABRY DISEASE/SYNDROME
DESCRIPTION Fabry disease is a rare X-linked disorder characterized by the deficient activity of the lysosomal enzyme α-galactosidase A. Progressive accumulation of the substrate (globotriaosylceramide GL-3) leads to progressive organ failure and premature death. Findings consist of multiple cutaneous lesions (angokeratoma corpus circumflexum), neural specification, and progressive renal insufficiency. Symptoms of severe burning pain in the extremities usually begin in the 1st decade, and can cause fibrile episodes. Cardiovascular effects include coronary artery disease and congestive heart failure. Renal failure leads to anemia and hypertension in the 3rd–5th decades.

TREATMENT
• Enzyme replacement therapy with agalsidase-beta

REFERENCE

FAMILIAL TESTOTOXICOSIS
DESCRIPTION Cause of testicular pain, infertility inherited as an autosomal dominant pattern. Markedly elevated levels of testosterone with normal LH secretion are noted, but sleep-associated LH pulses are absent. Patients typically present with family history and testicular enlargement around ages 3–4. Diagnosis is a lack of testosterone response to HCG administration, despite a measurable increase in LH. Hypertension of Leydig cells is noted by biopsy. Ketoticoticotic, antiandrogens, aromatase inhibitors, and/or medroxyprogesterone acetate have been used in different combinations with success.

REFERENCE

FANCONI SYNDROME
DESCRIPTION An acquired or inherited disorder characterized by abnormalities of renal proximal tubular function, including hyperuricemia, phosphaturia, aminoaciduria, and bicarbonaturic wasting. The aminoaciduria is generalized, and deficits in uric acid, water, potassium, and sodium absorption can also occur. The basic abnormality is unknown. Acquired disease is caused by deacetylase or inhibited tetrahydrobiopterin, renal transplantation, multiple myeloma, amyloidosis, introduction with heavy metals or other chemotherapeutic agents, and vitamin D deficiency, inherited form (usually seen with other disorders) presents in infancy with proximal tubular acidosis, hypophosphatemic rickets, hypokalemia, polyuria, and polydipsia. In nephropathic form, failure to thrive and growth retardation are common, with progressive renal failure. Diagnosed by demonstrating the abnormalities of renal function.

REFERENCE

FANCONI SYNDROME
DESCRIPTION An acquired or inherited disorder characterized by abnormalities of renal proximal tubular function, including hyperuricemia, phosphaturia, aminoaciduria, and bicarbonaturic wasting. The aminoaciduria is generalized, and deficits in uric acid, water, potassium, and sodium absorption can also occur. The basic abnormality is unknown. Acquired disease is caused by deacetylase or inhibited tetrahydrobiopterin, renal transplantation, multiple myeloma, amyloidosis, introduction with heavy metals or other chemotherapeutic agents, and vitamin D deficiency, inherited form (usually seen with other disorders) presents in infancy with proximal tubular acidosis, hypophosphatemic rickets, hypokalemia, polyuria, and polydipsia. In nephropathic form, failure to thrive and growth retardation are common, with progressive renal failure. Diagnosed by demonstrating the abnormalities of renal function.

REFERENCE
FATTY CASTS

TREATMENT
• Stomach bicarbonate for acidosis
• Renal transplantation has been successful

REFERENCES


FATTY CASTS
DESCRIPTION
Fatty casts contain fat globules embedded within tubular epithelial casts. Polished light microscopy may reveal "Mallory's cross" appearance if cholesterol is present. These are most commonly associated with nephrotic syndrome, but occasionally seen also after long-bone fractures, and classically seen in fat embolus syndrome.

REFERENCE

FECAL INCONTINENCE, UROLOGIC CONSIDERATIONS
DESCRIPTION
Numerous studies have identified a relationship between urinary symptoms and fecal incontinence. In the Nurses’ Health Study of over 64,000 women ages 63–87 yr, the prevalence of dual urinary and fecal incontinence was 7% (fecal incontinence alone was 4% and urinary incontinence alone was 38%). Risk factors for dual incontinence in women included: age >80 yr; depression; neurologic disorders; functional limitations; multiparity; and childbirth of a heavy newborn (>9.5 lb). As compared with white race, black race was associated with a decreased risk of dual incontinence. Men and women with overactive bladder (OAB) are significantly more likely to report having chronic constipation or fecal incontinence compared with those without OAB. Causes of OAB include vaginal delivery with anal sphincter damage, surgical trauma, diabetes mellitus, decreased rectal compliance (ulcerative proctitis and radiation proctitis), impaired rectal sensation (diabetes, HIV, dementia, malignancies, myelopathy, SCI), fecal impaction, medications, mood disorders, and diabetes mellitus. Fecal incontinence can be caused by any condition that impairs the recto-anal inhibitory reflex or the puborectalis reflex. Fecal incontinence can be acute, transient, or chronic. While incontinence itself is not a serious medical condition, it is a significant source of anxiety and distress for both individuals and their caregivers.

REFERENCE

FECALULIA
DESCRIPTION
The presence of fecal matter passed per urethra, suggestive of a fistulous communication between the urinary and intestinal tracts. Ectopic ureters include a pathologic process such as Crohn’s disease, diverticulitis, and cancer, or iatrogenic causes such as perineal surgery, radiation, or trauma. Initial evaluation should include cross-sectional imaging in the form of CT (modality of choice) or MRI to help delineate the location of the fistulous tract.

REFERENCE

FEMALE HYPOACTIVE SEXUAL DESIRE DISORDER
DESCRIPTION
Female sexual dysfunction has been defined in the DSM-IV manual as persistently or occasionally deficient or absent sexual fantasies and desire for sexual activity that causes marked distress or interpersonal dysfunction. Prevalence ranges from 39–43% in recent studies. The operational definition of desirosexual is currently being reviewed. The DSM V is scheduled for release in May 2013.

CAUSES
• Impaired: Hypothalamic/hippocampal dysfunction, menopause, chronic or antidepressive pills
• Musculoskeletal: Hypo- or hyperactivity of pelvic floor
• Neurologic: Spinal cord injury (SCI), other nervous system disorders (MS, CVA)
• Psychogenic: Relationship problems, poor body image/esteem, mood disorders
• Vasomotoric: Post blood flow, pelvic atherosclerosis, trauma
• Iatrogenic: Medication use (antidepressants, esp. SSRIs)

TREATMENT
• Education: Desire-arousal-orgasm axis, emotional intimacy, anatomic explanation
• Lifestyle modification: Stress management, adequate rest, regular exercise
• Pharmacology: Topical vaginal estrogens improve vaginal lubrication and atrophy, but have shown no effect on sexual desire. Testosterone (300 g/d transdermally) has shown benefit in postmenopausal women, but remains unapproved by the FDA. Phosphodiesterase inhibitors have not shown improvement for women with diminished desire.

REFERENCE

FEMALE SEX FUNCTION INDEX (FSFI)
DESCRIPTION
The FSFI is a validated questionnaire to assess female sexual function. It was developed for the specific purpose of assessing domains of sexual functioning (e.g., desire, sexual arousal, lubrication, orgasm, satisfaction, pain) in clinical practice. It was not designed for use as a diagnostic instrument and should not be used as a subscale for a complete sex history in clinical evaluation. The FSFI was validated in 2 groups of women, including subjects with sexual arousal disorder (determined by history) and age-matched controls. The instrument reliably differentiated these 2 groups in all domains of sexual functioning.

REFERENCE

FEMINIZING GENITOPLASTY
DESCRIPTION
Surgical treatment of a ambiguous genitalia may be indicated in the genetic female with external genitalia of female phenotype. The most common cause of virilization in the female newborn is CAH. Preputial genitoplasty may be performed early in infancy to facilitate gender-appropriate upbringing, or delayed until adolescence when the patient can participate in consent. Extensive counseling of parents of any infant with a disorder of sexual development is critical before considering genitoplasty. Goals of surgery are to create external genitalia with an aesthetic female appearance, and permit sexual function and, if possible, fertility. See also Section II “Disorders of Sexual Development (DDS)”, Section II “Congenital Adrenal Hyperplasia.”

REFERENCE

FERTILE EUNUCH DISEASE/SYNDROME
DESCRIPTION
Syndrome characterized by persistent androgen deficiency or aromatase deficiency caused by luteinizing hormone deficiency or Müllerian inhibitory activity. FSH secretion is present. However, spermatogenesis usually is not entirely blocked in these men, and they are usually fertile. Because there is only relative gonadotropin deficiency and some spermatozoa are present, treatment with LH-like activity (hCG) stimulates Leydig cell testosterone production and aromatizes androgen deficiency, stimulating spermatogenesis sufficient for induction of fertility.

REFERENCE

FIBROEPITHELIAL POLYP, GENITOURINARY
DESCRIPTION
The most common benign uterine tumor, arising from the upper 1/3 of the uterine cervix. These polyps resemble a smooth nodule or may be pedunculated. Histologically, a central fibrous core surrounded by normal or hyperplastic epithelium is seen. Patients present with menorrhagia and hematuria, usually as a young adult. Radiographically, smooth filling defects are seen. Hydrocoeleuroterus can be seen.
seen, as well as ultrasound interrogation. They can recur locally.

TREATMENT
Ultrasound-guided aspiration, open unroofing with prosectorially, or partial unroofing. If the diagnosis cannot be confirmed preoperatively, the lesion should be excised completely. Any doubt about the nature of the lesion should lead to excision. If the diagnosis is confirmed preoperatively, the lesion can be aspirated to relieve symptoms.

REFERENCE

FIBROEPITHELIAL POLYP, PENIS

DESCRIPTION
Fibroepithelial polyp of the penis is a benign tumor found in a small group of men with priapism. Histologically, it is a fibrovascular lesion composed of fibroblasts and elongated, thin-walled vessels. The lesion is usually asymptomatic but can be painful in the case of priapism. Surgical excision is generally recommended.

TREATMENT
Surgical excision is the treatment of choice. Recurrence is rare. The lesion can be managed conservatively in asymptomatic patients with follow-up. Complete excision is necessary for symptomatic patients.

REFERENCE

FIBROHAMSAMTORA OF INFANCY

DESCRIPTION
Common in both sexes, fibrous hamartoma of infancy is a benign tumor that usually appears in the first few months of life. It is composed of a mixture of fibrous and myxoid tissue, and is often associated with skin lesions. The prognosis is favorable, and most lesions regress spontaneously within the first year of life.

REFERENCE

FIBROS PSEUDOTUMOR OF TESTICULAR TISSUE

DESCRIPTION
Fibrosarcoma of the testis is a rare tumor that arises from the germ cell line. It is characterized by the presence of fibrous tissue and is often associated with other testicular abnormalities. The treatment is surgical excision, and the prognosis is generally good with early detection and treatment.

REFERENCE

FISH: URINARY FLUORESCENT IN SITU HYBRIDIZATION (UROVYNSION TEST)

SYNONYMS
Fibrous pseudotumor
Fibroepithelial polyp
Reactive periarteritis

TREATMENT
Surgical excision is usually necessary to confirm diagnosis but local excision can be considered.

REFERENCE

FIDUCIAL MARKERS

DESCRIPTION
External beam radiotherapy is a valuable tool in the treatment of localized prostate cancer. This form of treatment is limited by the difficulty in accurately localizing the prostate gland. The implantation of intraprostatic gold fiducial markers under transrectal ultrasound guidance is a safe outpatient procedure that aids in identifying anatomic structures of interest during radiation treatment (most importantly the prostate-rectal interface). Markers are usually cylindrical and appear as white spots with a hollow bore needle. Surface features prevent migration. The proportionality regimen is similar to that used for ultrasound-guided prostate biopsy. Prophylactic antibiotics are administered, anticoagulant medications withheld 7 days before procedure, and cleansing enemas given to empty the rectal vault. Patients are routinely placed in the left lateral decubitus position. A transrectal ultrasound probe is utilized to calculate prostate volume in the standard fashion. Local anesthesia should be placed bilaterally at the level of the neurovascular bundles. An 18-gauge implant needle is utilized to place fiducial markers into the right base, left base, and apex of the prostate. Standard prostate biopsy discharge instructions are given. Patients then follow up with a radiologist oncologist for pretreatment planning imaging and subsequent radiation therapy (image Q).

REFERENCE

FILARIASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION
Filariasis is transmitted by mosquitos, most commonly Wuchereria bancrofti, endemic to areas of the Caribbean, Venezuela, Colombia, the Guianas, Brazil, Central America, sub-Saharan Africa, North Africa, Turkey, and Asia. Filariasis (Bancroftian, Malayan, and Timorian) is often asymptomatic. The parasite causes symptoms due to inflammation and dysfunction of the lymphatics, where the adult worms develop (liver, head, neck, lymph, and lymphatics). In lymphatic disease, manifestations usually occur 3–7 y after acquisition. Occasionally, moderate lymphopenia, particularly involving the inguinal lymph nodes, occurs. Inflammation of the lymphatics of the extremities and genitalia leads to renegade adenolymphangitis. Epididymitis, orchitis, and hydrocele can also occur, along with fever, chills, and other nonspecific systemic symptoms. Lymphatic dysfunction, with resulting chronic progressive edema of the limbs and genitalia, is relatively infrequent in children. Elephantsiasis can result from fibrosis caused by chronic dysfunction of the lymphatic channels. Chyluria can occur as a manifestation of bancroftian filariasis. Lymphatic filariasis must be diagnosed clinically because serologic tests are not available, and in elephantsiasis the microfilariae may no longer be present. Eosinophilia of 25% frequently occurs in early disease. (See also Section I, “Edema, External Genitalia [Penis] [Testicular Edema].”)

TREATMENT
• Pentastibanazin citrate is the drug of choice. The late obstructive phase of the disease is not affected by chemotherapy.
• Ivermectin, an investigational drug in the United States, is effective against the microfilariae of W. bancrofti, but is unlikely to become the drug of choice for lymphatic filariasis.
• Complex, decongestive physiotherapy may be effective in treating elephantiasis.
• Plastic surgical repair of the genitalia gives variable results.
• Chylioma originating in the bladder responds to fulguration; chylioma originating in the kidney is much more difficult to correct.

REFERENCE

FINE-NEEDLE ASPIRATION (FNA) OF PROSTATE

DESCRIPTION
In the detection of prostatic carcinoma, FNA cytology of the prostate has largely replaced by core needle biopsy of the prostate, as cytology does not allow Gleason grading. However, the detection rates of prostatic carcinoma by either core needle biopsy or FNA appear to be comparable. Largely replaced by core biopsy techniques. (See also Section II, “Urology, Prostate.”)

REFERENCE

FISH: URINARY FLUORESCENT IN SITU HYBRIDIZATION (UROVYNSION TEST)

DESCRIPTION
Cytogenetic studies describe frequent alterations in chromosomes 1, 3, 4, 7, 8, 9, 11, 17, etc., in prostatic carcinoma. FISH allows the study of genetic abnormalities within formalin-fixed cancer cells. UroVysion test is a multitargeted multicolor-FISH assay that stains exfoliated cells from urine specimen with probes for chromosome 3, 7, 17, and Y, and 15, and allows observation of the cells under a fluorescence microscope. Reported sensitivity of UroVysion test is higher for higher-grade tumors (93–97%) and CIS (almost 100%), but with low-grade low-stage tumors (36–57%). Specificity is high (89–96%). A false-positive UroVysion test may predict for future recurrence or simply reflect ultrasound that is not at risk of malignant transformation. A study to detect bladder cancer in a high-risk population showed FISH to be comparable to urine cytology with a higher false-positive rate (Image Q).
**FISTULA, ENTEROVESICAL**

**DESCRIPTION** An abnormal communication between the bowel (such as colo-vesical fistula) and urinary bladder due to various inflammatory and neoplastic causes. Usually presents with fecaluria, pneumaturia, and/or recurrent UTI. Differential diagnosis includes vesicovaginal fistula (VVF), ureterovaginal fistula (UVF), and endometriosis associated with urethrovaginal fistula.

**TREATMENT**
- Surgical excision of fistulous tract and repair
- Conservative management

**REFERENCE**

---

**FISTULA, URETEROARTERIAL**

**DESCRIPTION** May present with microscopic hematuria, intermittent gross hematuria, or torrential bleeding in a patient with associated risk factors. General guideline to reduce the risk of fistula development is the use of the smallest caliber, softest flexible ureteric stent for the shortest possible period. In a stable patient, CT retrograde ureteropyelography, and angiography may be non-specific but aid in planning reconstructive options. Removal of stones and ureteral manipulation should be performed with caution and in a facility where immediate angiographic or surgical intervention is available.

**TREATMENT**
- If stable, early reconstruction of vascular and urinary structures:
  - Vascular occlusion with angiographic stent or embolization; OR
  - Vascular ligation, with or without bypass procedure
  - Ureter reimplantation (urothelial re-implantation, cutaneous ureterostomy, transverse ureteroureterostomy, or urethral Sling with nephrostomy)
  - Endovascular stenting is increasingly used in lieu of open techniques due to the high operative risk and morbidity in patients with ureterocutaneous fistula
- In the actively bleeding patient, immediate surgical intervention or angiographic occlusion

**REFERENCE**

---

**FISTULA, VESICOVAGINAL AND URETEROVAGINAL**

**DESCRIPTION** Vesicovaginal fistula (VVF) is an abnormal communication between the urinary bladder and vagina that may be associated with ureterovaginal fistula (UVF) in 12%. Patients present with urinary incontinence, with prior history of recent pelvic or gynecologic surgery or other causes.

**CAUSES**
- Iatrogenic following obstetric and gynecologic surgery
- Pelvic malignancy
- Pelvic radiation
- Infections: Pelvic and abdominal infections
- Penetrating trauma
- Foreign body

**DIAGNOSIS**
- Pelvic exam
- Cystoscopy with cytology and/or retrograde pyelography
- Contrast imaging (eg, CT urogram with delayed imaging, CT cystography)

**TREATMENT**
- UVF should be managed by reimplantation of ureter. Before undergoing a ureteral reimplantation, a patient with associated risk factors, such as diabetes, hypertension, and obesity, should undergo a pelvic exam to rule out the possibility of a synchronous pelvic malignancy. If a UVF requires primary repair, a multiple-layer closure can be achieved through a transabdominal or transvaginal approach. If diagnosis has been
Baumann DP, Butler CE. Lateral abdominal wall herniation is rare, and the intercostal nerves during incision and closure. Care should be taken to avoid injury to the intercostal nerves during incision and closure. Flank “bulge” is not a true hernia and is believed to be due to laxity of the transversus and internal oblique muscles, caused by injury to the intercostal nerves during incision and closure.

Flank hernia following nephrectomy

DESCRIPTION True flank hernias are rare, and careful palpation may reveal the fascial edges. Obesity, immunocompromised states, and poor nutrition status are risk factors. Frank “bulge” is not a true hernia and is believed to be due to laxity of the transversus and internal oblique abdominal wall muscles, caused by injury to the intercostal nerves, in particular the 11th intercostal, and accumulated in part by unopposed contraction of contralateral musculature. About 15% of patients develop flank bulge after a renal resection.

TREATMENT

• Flank hernia: Generally should be repaired with or without mesh, based on surgeon preference, patient comorbidities, and clinical factors specific to each case. If the patient is asymptomatic or debilitated, a corset can be offered.

• Flank bulge: Repair seldom needed except for cosmetic reasons.

REFERENCES


Fluorescent (Blue Light) Cystoscopy

DESCRIPTION Drugs for fluorescence diagnosis, such as 5-ALA and hexaminolevulinate (Hexvix [EU]; Cypho [US]), are placed intravesically where they preferentially stain multilayer or papillomatous tissue and emit a red fluorescence when excited by visible blue light. Requires specific endoscopic equipment. Fitted with the blue light, camera, and lens with filters. In a meta-analysis, Fluorescent cystoscopy (92.4%) sensitivity was superior to white-light cystoscopy (80.3%). Reports have shown fluorescent cystoscopy to be limited by specificity, which is equivalent to or poorer than white-light cystoscopy. Fluorescent cystoscopy can enhance the diagnosis of patients with positive cytology and no visible lesion on white-light cystoscopy, and for surveillance of high-risk bladder cancers and/or CIS.

REFERENCES


Foley Y-V PyeloPlasty

DESCRIPTION The triangular portion of the Y is incised in the dependent portion of the pelvis, with the apex pointing to the stricture, and a single 2- to 3-cm longitudinal incision is continued from the apex anteriorly down across the stricture to complete the Y configuration. The apex of the triangle flap is then brought down to the lower apex of the ureterostomy and a 5-0 chronic stay suture is placed. Interrupted 5-0 chronic sutures are used to complete the anastomosis. Used for UPU repair.

REFERENCES


Fordyce Spots (Ectopic Sebaceous Glands), Penis

DESCRIPTION Fordyce spots are ectopic sebaceous glands on the lips and buccal and genital mucosa (glans penis and labia minor). Lesions are multicentric and yellowish in color with slightly elevated papules and plaques with sizes ranging from 1–3 mm. Most patients are asymptomatic but some consider receiving treatment for cosmetic reasons since the lesions do not resolve spontaneously. 5-Fluorouracil can be used for ablation.

REFERENCES


Foreign Body, Bladder and Urethra

DESCRIPTION Almost every conceivable foreign body has been inserted into the urinary bladder and urethra, usually for erotic exploration and curiosity, or because of psychiatric disorder or mental retardation. Amnonian paraphilic catfish (Candiru) and leeches have also been reported to enter the urethra while bathing in a river. Symptoms include urinary pain, dysuria, urinary retention, hematuria, frequency, painful voiding, weak stream, and sepsis. (See also Section II: “Bladder filling defects.”)

REFERENCES


Fluorescent, Indications, and Technique

DESCRIPTION Formalin (37% formaldehyde) instillation is an option in the management of hemorrhagic cystitis, which is refractory to more conservative measures. A solution of 50 mL of 1% formalin is typically utilized. Instillation must be done in the operating room and usually with general anesthesia, as the procedure may cause pain. Prior to instillation, a cystogram must be performed to rule out vesicoureteral reflux. If reflux is present, then formalin may cause damage to the ureters and intrarenal collecting system. Use of Fogarty catheters to occlude the ureters in the case of reflux is reported. Bladder fibrosis with reduced capacity and increased urinary frequency is a common outcome after formalin instillation. (See also Section II: Cystitis, Hemorrhagic.)

REFERENCES


FOSSA NAVICULARIS DIVERTICULUM

DESCRIPTION For described by Guérin (1864), the diverticulum is partially separated from the urethra by a septum. On voiding cystourethrography (VCUG), it can often be seen as a small spherical collection of contrast at the tip of the penis. It is thought to result embryologically from an incomplete breakdown of the wall between the ectoderm and the urothelium being formed by the nephrost girlfriend. It is a common anatomic finding with rare symptoms, including dysuria, gross hematuria, spotting of blood, or hematospermia.

SYNONYMS

• Valve of Guérin

• Dorsal-urethral diverticulum

• Lacuna magna

TREATMENT

If symptomatic, the wall can be divided with tenotomy scissors or under direct vision with a resectoscope.

REFERENCES

FOWLER SYNDROME (PRIMARY DISORDER OF URETHRAL SPHINCTER RELAXATION)

DESCRIPTION

REFERENCE

FOWLER–STEPHENS SYNDROME

DESCRIPTION
This procedure is used in the treatment of high intravesical reflux. It entails ligating the spermatic vessels and ferring on the plexus that the urethra will narrow into the vesical and crometric cataracts. The operation was originally described as a 2-stage procedure in which the ureters are divided, and the left side is brought through the right, and division is completed in the manner, after which the 2 stages are performed to have a slight better success rate (95% for 2 stages vs. 80% for 1 stage). It is commonly performed using laparoscopy.

REFERENCES


FRACTURE RISK ASSOCIATED WITH PROSTATE CANCER AND ANDROGEN DEPRIVATION THERAPY

DESCRIPTION
Androgen deprivation therapy (ADT) treatment of prostate cancer leads to a hypergonadal state. This state predisposes men to osteopenia or osteoporosis with subsequent increased risk of fracture. There is a direct correlation between length of time on ADT and risk of fracture. I study reported that after 5 yr on ADT, the risk of fracture rises nearly 7% compared to controls.

TREATMENT
Men being treated with ADT should be considered for a baseline DXA scan to assess bone mineral density (BMD). Increased weight bearing exercise and cessation of smoking should be encouraged. Also, calcium and vitamin D supplementation can help improve BMD. Daily supplementation of calcium (1,200 mg/d) with vitamin D (400–800 IU/d) is recommended. Systemic therapy (bisphosphonate or denosumab) has been shown to play a role in the prevention of osteoporosis and reduce fracture risk. Denosumab is approved for men on ADT or with osteoporosis 60 mg SC Q 6 mos (Prolia). Bisphosphonates such as zoledronic acid (Reclast) can be given IV 5 mg, alendronate (Fosamax, Fosamax Plus O) and risedronate (Actonel) are given orally weekly. Alternative dosing times are given with the presence of bone metastases to decrease skeletal related events (SREs). Denosumab (Pamab) is given 4 mg SC monthly and zoledronic acid (Zometa) is administered IV 4 mg monthly.

REFERENCES

Fragile X Syndrome

DESCRIPTION
The most common cause of inherited mental retardation. The affected gene encodes a protein known as FMR1, which is required for normal cognitive development, facial dysmorphism and behavioral and microcephaly (MC). The Fragile X syndrome is an autosomal dominant disorder with associated mental retardation.

REFERENCE

FRALEY SYNDROME

DESCRIPTION
A condition in which urinary obstruction of the superior infundibulum might lead to hydronephrosis, bleeding, and intermittent frank pain or infection. Patients who experience symptoms related to urinary obstruction may be admitted to intensive care units. It is important to rule out an underlying cause such as urethral stricture or intussusception before surgery. Treatment is usually surgical, and the cecum of the cecum can be used to correct the obstruction.

TREATMENT
Surgery can provide relief in severely symptomatic patients. Various techniques including infundibulo-infundibulostomy, infundibulopexy, and infundibuloplasty have been reported to be successful in treating symptoms.

REFERENCES

French Catheter Scale

DESCRIPTION
Used to measure the outer diameter of catheters, endoscopes, and other instruments. The diameter in millimeters of the instrument is determined by doubling the French size by 3 (eg, an 18 Fr catheter has a diameter of 6 mm). The system was introduced by a 19th-century French medical instrument manufacturer. (See Section VII: “Catheter Guide.”)

REFERENCE

FREQUENCY, URINARY SYNDROME

DESCRIPTION
Urinary frequency is defined as the patient’s perception that he/she voids too often by day. Although often associated with an overactive bladder and/or bladder outlet obstruction, urinary frequency is 1 of many complaints included in the non-specific, nondiagnostic symptom complex known as lower urinary tract symptoms or LUTS. Frequency is further categorized as 1 of the storage symptoms (experienced during the bladder filling phase or the storage phase of micturition), as opposed to a voiding or postmicturition symptom.

REFERENCE

FREQUENCY-DYSURIA SYNDROME

DESCRIPTION
Occurring in children and women, this is also referred to as the “urethral syndrome.” Patients present with complaints of frequency and dysuria, but evaluation finds no infectious, urologic, functional, or pharmacologic abnormalities. Because this term is so nonspecific, it is not a currently accepted meaningful term for diagnosis or treatment planning. In childhood, hyperactive was theorized in and adults, fastidial organisms were once thought to be the cause. See also Section II “Urinary Syndrome.”

REFERENCE
**FURMAN NUCLEAR GRADING CLASSIFICATION, RENAL CELL CARCINOMA (RCC)**

**DESCRIPTION**
A classification used to grade renal cell carcinoma, based on the concept that nuclear features correlate with survival. This scale consists of 4 grades based on size, contour, and conspicuousness of nucleoli. Large series have confirmed the correlation with survival. Grade 1 is round with minute or absent nucleoli. Grade 2 is slightly irregular nucleoli about 15 μm, with nucleoli visible at 400×. Grade 3 is more irregular nucleoli, 25 μm, with nucleoli visible at 100×. Grade 4 is similar to grade 3, with bizarre features noted. There is a noted correlation between tumor size and Furman grade (image not provided).

**REFERENCE**

**FUNGURIA**

**DESCRIPTION**
Funguria (sometimes called candiduria) refers to fungus in the urine (fungal UTI of the urinary bladder) or kidney. It is a common nosocomial infection. Organisms are typically *C. albicans* and *C. glabrata*. Other organisms can involve the kidney through disseminated infection (eg, *Aspergillus* sp., *Fusarium*, others). Associated predisposing factors include catheters, antibiotics, diabetes mellitus, hospitalization, and immunosuppressed states. Urinary colonization is usually asymptomatic, whereas invasive fungal infection of bladder may have irritative voiding symptoms. Fungal infection of the kidney is often nephroscopic in origin from other sources or the GI tract, fungal renal or perirenal abscesses present similar to pyelonephritis. Infection should be suspected when urine microscopy shows budding fungal hyphae. Positive fungal urine culture demands investigation. (See Section I: “Fungal Infections, the GI tract; fungal renal or perirenal abscesses.”)

**REFERENCE**

**GAMETE INTRAFALLOPIAN TRANSFER (GIFT)**

**DESCRIPTION**
GIFT is similar to IVF but is rarely performed currently with the improved pregnancy rates in IVF. Current indications for GIFT include patients who have no evidence of menstrual or ovulatory abnormalities when they are unable to conceive spontaneously. The treatment involves inserting 2–3 embryos into the fallopian tubes on the day of embryo transfer (if embryo transfer is contraindicated in IVF, the technique may be modified for this indication). It provides a 20–30% pregnancy rate per cycle compared to 10–15% in IVF.

**REFERENCE**

**GANGLIONEUROBLASTOMA, ADRENAL**

**DESCRIPTION**
Extremely rare tumor originating from neural crest cells, this ganglioneuroblastoma exists on a spectrum of diseases between neuroblastoma and ganglioneuroma. It is seen in approximately 1% of children with neuroblastoma and can be solitary or multifocal. Diagnosis is by surgical excision. Treatment is by surgical resection.

**REFERENCE**

**GANGLIONEUROMA, ADRENAL**

**DESCRIPTION**
A tumor originating from neural crest cells, this is the benign counterpart of neuroblastoma. It does not metastasize, but can locally recur after resection and be locally aggressive. It most commonly presents as an abdominal mass. Histologically, the lesion is composed of ganglion cells with abundant cytoplasm and large nuclei. Treatment is by surgical resection.

**REFERENCE**

**GENITAL AROUSAL DISORDER (PERSISTENT)**

**DESCRIPTION**
A condition of spontaneous, intrusive, and frequently unwanted genital arousal associated with urogenital maldevelopment, usually located posterior to the urinary bladder. It is caused by a failure of separation of the urogenital fold of the mesonephric duct that leads to persistence of the Gartner duct, often with cystic dilation. The Gartner duct is associated with pelvic pain, dyspareunia, and resultant infection and related problems.

**REFERENCE**

**GARTNER DUCT CYST**

**DESCRIPTION**
Gartner duct cyst is a rare congenital anomaly associated with urogenital maldevelopment, usually located posterior to the urinary bladder. It is caused by a failure of separation of the urogenital fold of the mesonephric duct that leads to persistence of the Gartner duct, often with cystic dilation. The Gartner duct is associated with pelvic pain, dyspareunia, and related problems. The cyst may be bilateral in cases of heminephrogenesis and is rare in patients with complete renal agenesis or hypoplastic kidney. The treatment is by surgical excision of the cyst and closure of any associated urinary sinus, reconstruction of bladder neck and urethra, and reimplantation of ipsilateral and/or contralateral ureter in a nonfunctioning renal unit and antireflux procedure.

**REFERENCE**

**GENITAL AROUSAL DISORDER (PERSISTENT)**

**DESCRIPTION**
A condition of spontaneous, intrusive, and frequently unwanted genital arousal associated with urogenital maldevelopment, usually located posterior to the urinary bladder. It is caused by a failure of separation of the urogenital fold of the mesonephric duct that leads to persistence of the Gartner duct, often with cystic dilation. The Gartner duct is associated with pelvic pain, dyspareunia, and related problems. The cyst may be bilateral in cases of heminephrogenesis and is rare in patients with complete renal agenesis or hypoplastic kidney. The treatment is by surgical excision of the cyst and closure of any associated urinary sinus, reconstruction of bladder neck and urethra, and reimplantation of ipsilateral and/or contralateral ureter in a nonfunctioning renal unit and antireflux procedure.

**REFERENCE**
GENITAL ULCERS
DESCRIPTION: Ulcers may be due to multiple causes: Infection, Behçet syndrome, syphilis, malignancy, colitis, and carcinoma in situ are all possible causes. They are most commonly a manifestation of sexually transmitted infections, including chancroid, genital herpes, lymphogranuloma, and primary syphilis. Characteristics of the ulcers associated with sexually transmitted infections are as follows:

- Chancroid: Tender papule that turns painful which has a pustular ulcer underneath; may be single or multiple
- Genital herpes: Multiple painful vesicles
- Lymphogranuloma: A small painless papule or vesicle that ulcerates
- Primary syphilis: Painless, indurated ulcer; usually single

TREATMENT
If a sexually transmitted infection is suspected, empiric antibiotic therapy should be initiated even before confirmatory testing. Chancroid is treated with a single oral dose of azithromycin, or a single intramuscular dose of ceftriaxone, or oral erythromycin for 7 days. Genital herpes is treated with antiviral drugs such as Acyclovir. Lymphogranuloma is usually treated with tetracycline or erythromycin. Primary syphilis is treated with a single dose of intramuscular penicillin G, or a single dose of oral azithromycin in a penicillin-allergic patient. See also Section I: “Sexually Transmitted Infections [STIs].” Sexually Transmitted Diseases (STDs), General."

REFERENCES

GENITOURINARY PAIN INDEX (GUPI)
DESCRIPTION: GUPI is a validated 9 question instrument to assess severity of symptoms, in men and women with urolologic pain conditions. The GUPI can differentiate men with chronic prostatitis or interstitial cystitis, those with other symptomatic conditions (diabetes, frequency, chronic cystitis), and those with none of these diagnoses. It can discriminate between women with interstitial cystitis, those with incontinence, and those with none of these diagnoses.

REFERENCES

GENOMIC TESTING, PROSTATE CANCER
DESCRIPTION: A variety of genomic tests have been recently approved. The more common tests are shown in the table. All rely on either needle biopsy or radical prostatectomy tissue analysis. Their role in the definitive management of patients with prostate cancer is currently evolving.

Common Prostate Cancer Genomic Tests
Comparisons

<table>
<thead>
<tr>
<th>ConfirmMDx (MDxHealth)</th>
<th>Decipher (Genomic Health)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td>Treatment decisions after radical prostatectomy</td>
</tr>
<tr>
<td>Outcome predicted</td>
<td>Presence or absence of occult cancer; direct follow-up biopsy based on &quot;halo&quot; effect</td>
</tr>
<tr>
<td>Assay</td>
<td>3 epigenetic modification markers</td>
</tr>
<tr>
<td>Prostate (Myriad)</td>
<td>22 genetic markers on RP specimen</td>
</tr>
<tr>
<td>Oncotype DX (Genomic Health)</td>
<td>17 gene Genomic Prostate Score (GPS)</td>
</tr>
<tr>
<td>Indications</td>
<td>Risk assessment on biopsy; active surveillance decision</td>
</tr>
<tr>
<td>Outcome predicted</td>
<td>Progesterone receptors, P53, metastasis, recurrence, progression</td>
</tr>
<tr>
<td>Assay</td>
<td>46 gene Cell Cycle Progression (CCP) panel</td>
</tr>
</tbody>
</table>

GENITAL PIERCING, UROLOGIC CONSIDERATIONS
DESCRIPTION: Urologists must be familiar with complications from genital piercing. In males, piercings include the penile glans, shaft, urethra, and scrotum. In females, complications include the mons pubis, labia, clitoris, and labial folds. In females are also performed. Complications include:

- Transmission of infectious agent: HIV, Hepatitis B and C, or an STD
- Bleeding
- Cellulitis
- "Cutting-out" or erosion
- Propionibacterium acnes
- Recurrence of condyloma accuminatum
- Urethral fistula
- Hypertrophic scarring, keloid
- Trauma during intercourse: To partner or self

REFERENCES

GENITAL SKIN LOSS
DESCRIPTION: Genital skin loss is most commonly iatrogenic, as the result of skin denudement for reconstructing infection by polymicrobial infection—Fournier gangrene. Skin loss can less commonly occur as a result of trauma, usually blunt; however, penetrating trauma can also result in skin loss. Burns can also lead to genital skin loss.

TREATMENT
Reconstruction is the mainstay of treatment. In the case of skin loss due to denudement for infection, the infection should be stable prior to reconstruction being performed. In the case of penile skin loss in an uncircumcised male, a flap using redundant foreskin being performed. In the case of penile skin loss in an uncircumcised male, a flap using redundant foreskin may be harvested to address a proximal defect. Flaps utilizing skin from a penile keratotic plaque may be used in this setting. If a donor site is available, a full thickness skin graft can be used to address both penile and crural skin defects. Vacuum-assisted closure therapy has been effective in early management with skin-grafts (see also Section I: “Scrotum and Testicle, Trauma.”)

REFERENCES

GERM CELL APLASIA (SEER TO CELL ONLY SYNDROME)
DESCRIPTION: Total absence of germ cells within a normal interstitium. Patients present with infertility, and usually with small to normal testes and azoospermic semen specimens. Phenotypically, these patients are normally virilized males. Histologically, Sertoli cells line the seminiferous tubules with a complete absence of germ cells and normal interstitium. Plasma FSH is usually elevated due to the absence of germ cells. Plasma testosterone and LH are normal. Diagnosis is based on an elevated FSH and PRL of the tests. Aplasia may represent the endpoint of various etiologies, resulting in this histologic appearance. Adoption or use of donor sperm is necessary if children are desired.

REFERENCES
Gestational Age Assessment, Urologic Considerations

Description: Gestational age assessment can be derived from 3 clinical methods: (1) physical exam, (2) ultrasound, and (3) history, using the date of the last menstrual period (LMP) to calculate the estimated date of delivery (EDD) or EDD. Clinical assessment of gestational age in a newborn reflects the “menstrual age.” Studies have shown ultrasound to be superior to physical exam or history. Rapid determination of gestational age in the delivery room includes assessment of all areas of the feet, breast nodules, umbilicus, hair, and the external genitalia of males. Babinski born 36 wk and earlier the toes are usually partially descended, the scrotum is small with very few rugae. Term infants (39 wk and beyond) should have the toes fully descended, the scrotum should appear normal sized with prominent rugae.


Gibbon Classification of Voiding Dysfunction

Description: Historic classification based in large part on the system proposed by Ross-Comarr. 5 categories are proposed to be important: (1) Full general and neurologic diagnosis, (2) state of the bladder function, (3) state of the renal function in children with rare exception to as enuresis risoria, is urinary leakage that occurs exclusively occurs in girls. It is characterized by large-volume voids. These children have normal bladder function when the child is not laughing. The disorder is thought to be mediated by the central nervous system and has similarities to detrusor instability.

TREATMENT
- Treatment of this condition is not well studied
  - Anticholinergics (eg, oxybutynin)
  - Methylphenidate
- Biofeedback was effective in 1 series in patients refractory to medical management


Gill-Vernet Extended Pyelolithotomy

Description: An open approach to remove a large renal calculus, such as a staghorn calculus. Using a flank incision, the kidney is exposed and fixed at the upper pole, lower pole and posteriorly. The ureter is identified and traced to the renal pelvis. The renal pelvis is incised and the incision can be continued to include the calixi to allow for removal of more significant calculi.


Gill-Vernet Orthotopic Urinary Diversion

Description: A continuous segment of terminal ileum, cecum, and ascending colon is isolated. The unit is rotated 180° to allow anastomosis of the reduced end of the ascending colon to the urethra and the ureters to the terminal ileum.


Gill-Vernet Ureteral Reimplantation

Description: Through a transvesical approach, the ureters are dissected free from the hiatus. The principle involves advancing the ureters across the trigone to the midesophagus such that both ureters are intraurethral. A single incision is made in the trigone mucosa, which will allow to join traction sutures from each ureter that are anchored in the midline.


Gittelman Syndrome

Description: Gittelman syndrome is an autosomal recessive disorder characterized by hypertelorism, hypertelorism, and hypogonadism with mental retardation. It is caused by loss of function mutations of a thiazide sensitive sodium-chloride symporter found in the distal convoluted tubule of the kidney.

TREATMENT
- Replacement of respective electrolytes.


Gittes Needle Urethroscopy

Description: Needle used to treat female stress incontinence. A Stamey needle is delivered through a stab incision at the upper border of the pubis, then transferred under digital guidance through the anterior vaginal wall at the level of the bladder neck. A No. 2 prolene suture is used to suspend the bladder neck on both sides, and the vaginal sutures eventually cut through the wall and become buried in the incision. A single incision pubovaginal suspension as an adjunct to other pelvic-floor surgery. Obstet Gynecol. 1999;93(5):844–847.

Gleason Grade, Tertiary Pattern

Description: The standard Gleason grading system reports the primary and secondary Gleason pattern. The tertiary pattern (3rd most prevalent) is noted if it is high grade. Retrospective data suggest that a high-grade tertiary component after RP, even when present in a small percentage of total tumor volume, has prognostic significance. It’s presence is associated with biochemical recurrence and adverse pathologic features such as seminal vesicle invasion, extraprostatic extension, and positive surgical margins.


Gleason Grading/Scoring System

Description: A widely accepted system to describe the aggressiveness of prostate adenocarcinoma was developed by Dr. Donald Gleason between 1969 and 1974, in which prostate cancer mortality data were correlated to low-magnification architectural patterns of prostate carcinoma. 5 grades are described, ranging from well differentiated to undifferentiated. To account for variations within tumors, 2 grades are recorded. The predominant, or primary, grade and the less extensive, or secondary, grade. These are summarized to give the Gleason score. Gleason score is added together to obtain
GLEASON GRADING SYSTEM, MODIFIED

a Gleason grade of (3 + 4 = 7). The Gleason score is a strong independent predictor of cancer behavior and treatment outcome for prostate cancer patients. Pattern 3 is separated from pattern 4 because no statistically significant differences between Gleason score 6 from Gleason score 7 tumors, with the latter having a significantly worse prognosis.

Gleason pattern 1: Very well-circumscribed nodule of single, separate, closely packed, back-to-back glands. There is no infiltration into adjacent benign prostatic tissue. The glands are fairly large, round or oval, and are approximately equal in size and shape. Gleason pattern 1 is usually found in transition zone carcinomas and is rare. When present, it is usually associated with a pattern 2 tumor. Distinction from pattern 2 is not critical, as they have a similar prognosis.

Gleason pattern 2: Usually, but not always, seen in transition zone carcinomas. Well-circumscribed nodule of single, separate glands with the glands more loosely arranged and not as uniform as in pattern 1. Minimal invasion by neoplastic glands into the surrounding benign prostatic tissue. The cells are smoothly rounded or oval with open lumens and are not angular, as seen in pattern 3. The cytoplasm is more abundant and pale staining than intermediate-grade tumors.

Gleason pattern 3: Infiltrative with extension into adjacent benign prostatic tissue. The glands vary in size and shape and are often elongated or angular. These small glands are often called microglands and are usually smaller than Gleason pattern 1 or 2 glands. However, some of the glands of pattern 3 may be moderate to large sized. The small glands of pattern 3, in contrast to small poorly defined glands of pattern 4, are distinct glandular units and should be able to draw all imaginary circles around each of them. Crinoid glands may also be Gleason pattern 3. These small glands are irregularly larger than benign glands and having regular outer contours. They resemble interstitial cribriform carcinoma of the breast. Crinoid pattern 3 is distinct from Gleason pattern 4, interstitial cribriform proliferations, and prostatic duct adenocarcinoma.

Gleason pattern 4: The glands are no longer single and separate as seen in pattern 1–3. They are fused, poorly defined with only occasional luminal formation, or cribriform. Fused glands are chains, nests, or masses of glands that are no longer completely separated by intervening stroma. Fused glands contain more strands of residual stroma that may give the appearance of partial separation of the glands. Consequently, fused glands may have a scalloped appearance peripherally. The “reperinfracturate” pattern described by Desjardins is an uncommon variant of fused glands and resembles RCC. Cribriform glands of pattern 4 are either large cribriform glands (cribiform sheets) or small cribiform glands with irregular infiltrating borders. The small cribiform glands with irregular infiltrating borders of pattern 4 must be distinguished from cribriform pattern 3, in which the small cribiform glands have regular borders. Fragments of cribriform carcinoma in needle biopsies of the prostate imply a cribriform cancer and are designated pattern 4.

Gleason pattern 5: The tumor has virtually no glandular differentiation. It is composed of solid sheets, solid cords, or single cells. Nests of tumor with central comedo necrosis are also classified as pattern 5. It is controversial whether cribriform glands of cancer that otherwise would be considered Gleason pattern 4 should be considered Gleason pattern 5 if comedocarcinosis is present. Separating poorly defined pattern 4 glands from costs and nests of tumor with virtually no glandular differentiation or with only vacuoles is a problem, but usually not critical because any combination of the 2 patterns will lead to a Gleason score of 6–10, all of which are poorly differentiated (Image 2).

REFERENCE

GLEASON GRADING SYSTEM, MODIFIED

DESCRIPTION
The International Society of Urologic Pathology held a consensus conference in 2005 at which the "3rd Gleason grading system" for prostatic carcinoma from 1968 underwent its first major revision. With this modified grading system, a shift of the most frequent Gleason scores from 6–7a to 3–4–5 in biopsy specimens and an increased degree of agreement between specimen of biopsies and radical prostatectomies with carcinoma of the prostate could be demonstrated. After modified grading of GS 3 + 4 = 7a tumors, 95% were stage pT2, whereas 79% of GS 4 + 3 = 7b tumors were stage pT2–pT3. In cases with PSA <10 ng/mL, and tumor extent <20%, the most frequent Gleason scores were 6 and 7a. Cases with serum PSA >10 ng/mL, or tumor extent >20% had higher scores (Grades 4 or 5). Cancers with tumor involution of <1 mm in 1 of 12 cores and PSA <10 ng/mL, were mainly low grade (GS scores 6 and 7a) and may correspond to so-called insignificant carcinoma of the prostate. Using the modified Gleason grading system, grade, stage extent, and serum PSA showed good correlations and characterize the difference between low- and high-grade malignancy of the prostate.

REFERENCE

GLEINN-ANDERSON URETTERONEO CYSTOSTOMY

DESCRIPTION
Through a transvesical approach, the ureter is mobilized from its hilus and advanced toward the bladder neck through a submucosal tunnel, where it is reimplanted. Used to treat vesicoureteral reflux or resection of a ureteral orifice.

REFERENCE

GLOMERULOCYSTIC KIDNEY DISEASE (CORTICAL MICROCYSTIC DISEASE)

DESCRIPTION
Rare, bilateral cystic kidney disease that can be inherited (autosomal dominant) or sporadic. Presents most commonly in childhood with bilateral flank masses, which are large kidneys with many cysts. Seen rarely in adults with hypertension, hematuria, and end stage renal disease (ESRD). Cysts are confined to the cortex and arise from the Bowman space. Renal biopsy may be necessary to confirm diagnosis. Radiologically, the lesions are similar to autosomal dominant polycystic kidney disease (ADPKD). Treatment is supportive, with renal replacement therapy if renal failure occurs.

REFERENCE

GLomerulosclerosis

DESCRIPTION
An accumulation of homogeneous eosinophilic material in the glomerulus, made up of plasma proteins that have escaped from the plasma into glomerular structure; this is a light microscopic feature known as hyalinization. This change contributes to obliteration of capillary lumina of the glomerular tuft, a feature of glomerulosclerosis. Hyalinization and glomerulosclerosis are a consequence of endocardial or capillary wall injury and the end result of various forms of glomerular damage.

REFERENCE

GLUCAGON STIMULATION

DESCRIPTION
Indicated when the diagnosis of pheochromocytoma is highly suspected by history and clinical findings, but blood pressure is normal and diagnostic biochemical tests are equivocal (polaroid lines and modified adrenaline). The mode of action is the stimulation of glucagon-sensitive adenylate cyclase receptors expressed on the tumor, which can lead to dangerous rises in blood pressure; thus, this test is rarely used. A physician must be present throughout the test, and it should only be performed in patients whose blood pressure is well controlled, such as in plasma normotensive to >3–5-fold or >2,000 ng/mL is diagnostic of pheochromocytoma.

REFERENCE

GLUCOSURIA, RENAL

DESCRIPTION
Normal urine contains small amounts of glucose. Increased amounts represent either insufficient handling by the tubule or hyperglycemia. Diabetes is the most common cause of glycosuria. Causes of primary glycosuria are either intestinal glycosuria–galactosuria malabsorption or benign familial renal glycosuria. Some substances are known to cause false positive glucose readings on dipstick, such as ascorbic acid and salicylates. Medications such as ACE inhibitors may also have a direct effect on the kidney and cause glycosuria. Pregnancy can be
GOLDSMITH SYNDROME
DESCRIPTION Rare syndrome with principal features of kidney, liver, and brain abnormalities. The kidneys are cystic and large bilaterally. Histologic lesions of the liver are typical with a double band of fibrous tissue without bile ducts. The brain shows the Dandy-Walker malformation, which is the cystic dilatation of the 4th ventricle, secondary to obstruction of the foramina of Luschka and Magendie. Renal replacement therapy is indicated, and hydrocephalus requires a short areometry.

GONADAL DYSGENESIS, PURE
DESCRIPTION Gonadal dysgenesis syndrome includes Turner syndrome (45, X0), 46, XX “pseudosexual” gonadal dysgenesis, mixed gonadal dysgenesis (45, X0/46, XY), partial gonadal dysgenesis (aka, dysgenetic mixed gonadal dysgenesis), and bilateral vanishing testis syndrome. It is the 2nd most common cause of ambiguous genitalia in the newborn after CAH. Mixed gonadal dysgenesis is characterized by unilateral tests, often intra-abdominal, contralateral streaked gonads, and persistent müllerian structures with varying degrees of inadequate masculinization (“testis plus streak gonad”). A streak gonad is dysgenetic and resembles ovarian stromal tissue, but no germ cells are present. US usually testis is 45, X0/46, XY mosaicism. Phenotype is variable, ranging from a female with Turner syndrome to ambiguous genitalia, to (rarely) normal-appearing males. Almost all have a uterus, vagina, and tubal fimbriae, but with varying degrees of phallic development, labioscrotal fusion, and undescended testes. Increased risk exists of gonadoblastoma (incidence 20%) in either dystrophic tissue or streak gonad (more frequently tested), as well as an increased risk of Wilms tumor. Clinical diagnosis is birth and with confirmatory karyotyping. (See also Section I: "Disorders of Sexual Development [DSD]"; Section II: "Gonadal Dysgenesis, Pure.")
TREATMENT
- Determine gender assignment, based upon potential for normal function of external genitalia and gonads
- Perform appropriate sex and growth hormone replacement

GOODPASTURE SYNDROME
DESCRIPTION Characterized by a triad of pulmonary hemorrhage, iron deficiency anemia, and glomerulonephritis (GN), representing <1% of all cases of GN. Anti-GBM antibody deposition in the lungs and kidney is the cause. Antibody production appears to be self-limited. Histologically, it shows focal proliferative and necrotizing glomerular lesions that progress rapidly to diffuse proliferation with crescents. Immunohistochemical studies show diffuse linear deposition of IgG along the GBM. Primarily a disease of young white males (male:female, 6:1) with a mean age of 21. About 1/3 of patients die of pulmonary involvement. Renal involvement is usually severe and progressive, with rapid development of oliguria and renal failure.
TREATMENT
- Steroid pulse therapy with prednisone
- Plasma exchange therapy to remove circulating anti-GBM antibody
- Cyclophosphamide to inhibit further antibody formation
- Renal replacement therapy for ESRD

GOODWIN URETERAL ANASTOMOSIS
DESCRIPTION Through a transcutaneous approach, a nonhealing anastomosis is performed by raising a tunnel of muscosa with a mosquito hemostat for a 3–4 cm distance, then exiting the bowel wall. The ureter is grasped and pulled through the tunnel. The spatulated ureter is anastomosed to the colorectal muscosa while incorporating some muscularis for security.
SYNONYMS
• Nevoid basal-cell carcinoma syndrome
• Basal cell-nevoid syndrome

REFERENCE

GOUT, UROLOGIC CONSIDERATIONS

DESCRIPTION
An inherited disorder of purine metabolism characterized by elevated serum urate levels and severe recurrent arthritis, gout leads to an increased risk of urate urolithiasis and uric acid nephropathy. Most patients with uric acid stones, however, do not have gout. About 25% of patients with gout will develop a stone. Gout may also produce a type IV RTA, resulting in hyperkalemia and a mild metabolic acidosis. (See Section I: “Renal Tubular Acidosis”, Section I: “Urinophilia, Uric Acid Acidosis”.)

TREATMENT
• Alkalization of urine and increasing urine output help prevent stones.
• Allopurinol or following a low-purine diet will help prevent stones.

REFERENCE

GUONERVEUR SYNDROME
DESCRIPTION
Classic presentation of vesicovaginal fistula, with suprapubic pain, urinary frequency, dysuria, and tenesmus.

REFERENCE

GRANULOMA INGUINALE (DONOVANOSIS)
DESCRIPTION
Ulcerative disease of the genitals with significant scirrhous lymphadenopathy, caused by Klebsiella granulomatis (formerly known as Calymmatobacterium granulomatis). The disease occurs rarely in the United States and is endemic in some tropical and developing areas (India, Papua, New Guinea, the Caribbean, central Australia, and southern Africa). Clinically, the disease is commonly characterized as painless, slowly progressive ulcerative lesions on the genitals or perineum without regional lymphadenopathy; subcutaneous granulomas (pseudolymph nodes) may also occur. The lesions are highly vascular (i.e., red, soft appearance) and bleed easily on contact. Ulceration at site inoculation may be on the genitals or extragenital sites, and prominent lymphadenopathy often results in further skin ulceration over the nodules. Ultrasound results in lymphadenoma and genital involvement. See also Section I: “Sexually Transmitted Infections (STI); Sexually Transmitted Diseases (STD)”. Diagnosis is based on rapid Giemsa stained-smear of ulcer (RapiDiff), to look for Donovan bodies. For smear-negative cases, biopsy of the ulcer is necessary. Culture and PCR are available only in specialized centers.

TREATMENT
• Diocycline 150 mg orally twice a day for at least 3 wk and until all lesions have completely healed.
• Alternative regimens (treat until all lesions healed):
  • Azithromycin 1 g orally once per week for at least 3 wk or
  • Ofloxacin 750 mg orally twice a day for at least 3 wk.

REFERENCE

Worowski KA, Berenson S. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines. 2010: Available online. RR-12, 1–110.

GRANULOSA CELL TUMORS
DESCRIPTION
The most common ovarian neoplasm. Usually small, cystic, unilateral, and secretes estrogens. Often presents in childhood as precocious puberty or as postmenopausal bleeding in older women. During the reproductive years, prolonged and irregular bleeding and a pelvic mass are most common. These tumors can also present with urinary symptoms, and they can rarely be present in the testes.

TREATMENT
• Surgical excision is usually curative.
• Close follow-up of the contralateral ovary is necessary.

REFERENCE

GRANULOCYTIC EVIDENCE OF SEXUAL SATISFACTION
DESCRIPTION
A validated psychometric instrument intended for heterosexual couples or individuals. The questionnaire is based on a 28-item scale, with separate forms for men and women. It contains subcales of ED, organic disorders, vaginismus, and male and female nonsensuality. It may be used in individuals undergoing marital or sex therapy.

REFERENCE

GROIN HERNIA, PEDIATRIC
DESCRIPTION
The most common surgry in the pediatric age group. Most hernias in this population are indirect and congenital. The incidence is higher in persons born with a male to female ratio of 6:1. The hernia is formed from the persistence of the processus vavghanii and can present as a communicating hydrocele, hydrocele of the cord, simple hydrocele, or hydrocele of the cord.

REFERENCE

GRAVITATION DISORDER
DESCRIPTION
Also known as resistive manueulation, usually peaks at 4 yo but can be seen at as young as 3 mos of age. The disorder may occur in the absence of genital manipulation and can consist of vocalizations with quiet grunting, diaphoresis, and pressure on the perineum with characteristic posturing of the lower extremities. The patient is commonly referred for seizures or a movement disorder because of the recurrent paroxysmal movements.

REFERENCE

GRISSEX SEX FUNCTION INDEX (GOLombok–Rust INVENTORY OF SEXUAL SATISFACTION)
DESCRIPTION
A validated psychometric instrument intended for heterosexual couples or individuals. The questionnaire is based on a 28-item scale, with separate forms for men and women. It contains subcales of ED, organic disorders, vaginismus, and male and female nonsensuality. It may be used in individuals undergoing marital or sex therapy.

REFERENCE
**HEIKEL–PARKKULAINEN REFUX CLASSIFICATION SYSTEM**

**REFERENCE**


**HAND FOOT SYNDROME**

**DESCRIPTION**

Many oncologic medications have been implicated (such as capecitabine, fluorouracil, others), but this condition appears to be a relatively common problem with multikinase inhibitors such as sunitinib and sorafenib, which are used to treat tumors such as metastatic renal cell carcinoma (RCC).

**SYMPTOMS**

- Palm–plantar erythrodysesthesia (PPE)
- Malignant palmar–plantar toxicity

**TREATMENT**

- Reduce exposure of hands and feet to friction and heat (ie, hot water, avoid pressure on feet, avoid using tools, cool hands and feet with an ice pack, moisturizing creams).

- Stopping the medication temporarily reduces the symptoms. The drug can often be restarted at a lower dose.

**REFERENCES**


Hauptmann Pouch

**DESCRIPTION**

This ileal neobladder is created from 70 cm of ileum, starting 15 cm from the ileocecal junction. The bowel is opened up along the antimesenteric border, and lesions are seen in the transitional areas (ie, urothelial, gland, and peripheral areas). Lesions heal without scarring. Treatment involves antibiotics for superinfection, steroids, and dermabrasion.

**REFERENCES**


**HAILEY–HAILEY DISEASE (OXENFAMILIAL PEMPHIGOID)**

**DESCRIPTION**

Autoimmune skin disease arising from mutations of the ATP2C1 gene. The appearance begins as a fluid vesicle or bulla with associated itching, irritation, and a possible odor. The lesions may erupt and leave crusted erosions, and some may have a dry center and inflammatory periphery. The onset usually occurs within the 2nd–3rd decades of life, and lesions are seen in intertriginous areas (ie, axillary fold, groin, and perilveal areas). Lesions heal without scarring. Treatment involves antibiotics for superinfection, steroids, and dermabrasion.

**REFERENCES**


**HALD–BRADLEY CLASSIFICATION OF VOIDING DYSFUNCTION**

**DESCRIPTION**

Based on the anatomic location of the urologic lesion, voiding dysfunction is broken down into 3 classes: (1) suprapubic, (2) supravesical spiral, (3) influence, (4) peripheral autonomic neuropathy, and (5) muscular lesions. Examples include coordinated voiding with hyperreflexia in suprapubic lesions, whereas muscular lesions may be a decompensated bladder from long-standing bladder outlet obstruction.

**REFERENCES**


**KIDNEY**

**DESCRIPTION**

The kidney is subject to the majority of external injuries in the GI system. Hematuria is a good indicator of injury but its amount or absence does not eliminate renal injury or does it dictate the degree of injury. Any degree of hematuria in penetrating trauma should prompt imaging. Kidney injury is graded from I–V in accordance with the American Association for Surgery of Trauma Organ Injury Severity Scale for the Kidney. In carefully selected patients, management can be nonoperative, with careful observation or segmental embolization used. Absolute indications for surgical exploration include expanding perirenal hematoma, evidence of persistent renal bleeding, and palpable perineal hematoma. Relative indications include urinary extravasation, irreversible tissue, delayed diagnosis of arterial injury, segmental arterial injury, and incomplete staging. (See also Section I: “Renal Trauma, Adult.” Section I: “Renal Trauma, Pediatric,” Section II: “American Association for Surgery of Trauma Organ Injury Severity Scale.”)

**REFERENCES**


**EXTERNAL GENITALIA**

**DESCRIPTION**

Refers to an enlarging mature teratoma or a growing teratoma syndrome: urogenital syndrome. GROWING TERATOMA SYNDROME

**DESCRIPTION**

Refers to an enlarging mature teratoma or a growing teratoma syndrome: urogenital syndrome. The genitalia have several characteristics that are somewhat protective against sustained injury. Characteristics such as the salinity of skin, flaccidity, and multiple sources of blood supply assist with dampening the blow of trauma and help with reconstruction efforts. Nevertheless, the location of major vasculature and visceral organs make these injuries potentially life-threatening. Greater than 50% of injuries to the penis have urethral injuries and 75% have other significant associated injuries. A majority of these injuries require exploration with capsular irrigation, excision of foreign material, antibiotics, and primary closure. In injuries to the urethra, imaging such as retrograde urethrogram should be implemented and, if warranted, abdominal pelvic imaging should be obtained. (See also Section I: “Penis, Trauma,” Section I: “Scrotum and Testicle, Trauma.”)

**REFERENCES**


**GUAILLAN–BARRY (TRANSVERSE MYELITIS) SYNDROME: UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

Also known as acute inflammatory demyelinating polyradiculoneuropathy, an inflammatory demyelinating disorder of the autonomic and peripheral nerve systems. It is thought to be triggered by a bacterial or viral antigen, causing the immune system to cross-react and attack neural tissue. Symptoms may include muscle weakness, respiratory difficulties, autonomic neuropathy, and cardiac, bowel, bladder, and sexual dysfunction. Lower urinary tract dysfunction can range from urgency and stress incontinence to urinary retention.

**TREATMENT**

- Manage lower urinary tract dysfunction (Clean intermittent catheterization [CIC], anticholinergics, etc.)
- Intravenous immunoglobulin

**REFERENCE**


**GUN SHOT WOUND, EXTERNAL GENITALIA**

**DESCRIPTION**

The genitalia have several characteristics that are somewhat protective against sustained injury. Characteristics such as the salinity of skin, flaccidity, and multiple sources of blood supply assist with dampening the blow of trauma and help with reconstruction efforts. Nevertheless, the location of major vasculature and visceral organs make these injuries potentially life-threatening. Greater than 50% of injuries to the penis have urethral injuries and 75% have other significant associated injuries. A majority of these injuries require exploration with capsular irrigation, excision of foreign material, antibiotics, and primary closure. In injuries to the urethra, imaging such as retrograde urethrogram should be implemented and, if warranted, abdominal pelvic imaging should be obtained. (See also Section I: “Penis, Trauma,” Section I: “Scrotum and Testicle, Trauma.”)

**REFERENCES**


**REFERENCES**


**HEIKEL–PARKKULAINEN REFUX CLASSIFICATION SYSTEM**

**REFERENCE**


**HAULMANN POUCH**

**DESCRIPTION**

This ileal neobladder is created from 70 cm of ileum, starting 15 cm from the ileocecal junction. The bowel is opened up along the antimesenteric border, and lesions are seen in intertriginous areas (ie, axillary fold, groin, and peripheral areas). Lesions heal without scarring. Treatment involves antibiotics for superinfection, steroids, and dermabrasion.

**REFERENCES**


**REFERENCES**


**HAND FOOT SYNDROME**

**DESCRIPTION**

Many oncologic medications have been implicated (such as capecitabine, fluorouracil, others), but this condition appears to be a relatively common problem with multikinase inhibitors such as sunitinib and sorafenib, which are used to treat tumors such as metastatic renal cell carcinoma (RCC).

**SYMPTOMS**

- Palm–plantar erythrodysesthesia (PPE)
- Malignant palmar–plantar toxicity

**TREATMENT**

- Reduce exposure of hands and feet to friction and heat (ie, hot water, avoid pressure on feet, avoid using tools, cool hands and feet with an ice pack, moisturizing creams).

- Stopping the medication temporarily reduces the symptoms. The drug can often be restarted at a lower dose.

**REFERENCES**


**HAULMANN POUCH**

**DESCRIPTION**

This ileal neobladder is created from 70 cm of ileum, starting 15 cm from the ileocecal junction. The bowel is opened up along the antimesenteric border, and lesions are seen in intertriginous areas (ie, axillary fold, groin, and peripheral areas). Lesions heal without scarring. Treatment involves antibiotics for superinfection, steroids, and dermabrasion.

**REFERENCES**


**HEIKEL–PARKKULAINEN REFUX CLASSIFICATION SYSTEM**

**REFERENCE**


**REFERENCES**

HEMATOCELE

DESCRIPTION
Collection of blood within the layers of the tunica vaginalis. Hematocele can present as scrotal swelling and may be asymptomatic. It may be difficult to distinguish from tumors, in which case transcutaneous ultrasonography (US) is helpful. Causes include trauma, infection, bleeding disorders, tumors, and rarely uremia. (See also Section I: “Scrotum and Testicle, Trauma.”)

TREATMENT
Conservative management if patient asymptomatic and diagnosis confirmed. Often, diagnosis by surgical exploration is described mostly in adults after a history of trauma, infection, bleeding disorders, tumors, and rarely uremia.

REFERENCE

HEMATUROA, ATHLETIC (RUNNERS’ HEMATURIA)

DESCRIPTION
Described mostly in adults after strenuous exercise. The phenomenon of gross or microscopic hematuria can occur in contact or noncontact sports. The WBCs seen in the urine may be glomerular or nonglomerular in shape. The cause of the hematuria can be from trauma of the posterior bladder wall hitting against the bladder base. Nontraumatic causes are hypothesized to be from changes secondary to the vasodilatation of the glomerular and renal vessels or to constriction of the effluent glomerular arterioles resulting in increased filtration pressures in the kidney. The hematuria should be distinguished from myoglobinuria and hemoglobinuria.

SYNONYMS
• Sports hematuria
• Athletically induced hematuria

TREATMENT
• Should be limited and provoked by strenuous exercise.
• Co-existing urologic pathology should be ruled out.

REFERENCE

HEMATURIA–DIURESIS SYNDROME

DESCRIPTION
Hematuria–diuresis syndrome is the most common reported complication of gastrocystoplasty. The syndrome of diuresis and hematuria is defined as or a combination of the following symptoms: bladder spasm or suprapubic, penile or perineal pain, coffee brown or bright red hematuria without infections, skin irritation or excoriations, and diuresis without infections.

REFERENCE

HEMATURIA–LOIN PAIN SYNDROME

DESCRIPTION
A cause of recurrent gross hematuria that may be confused with IgA nephropathy, loin pain–hematuria syndrome generally affects young women and is characterized by recurrent episodes of gross hematuria associated with dull unilateral or bilateral loin pain and sometimes low-grade fever. BP and renal function are usually normal. The syndrome has been associated most often with the use of oral contraceptive agents and generally resolves when these agents are discontinued. Renal autotransplantation has been described as a treatment modality.

REFERENCE

HEMIZONA ASSAY

DESCRIPTION
This assay assesses the ability of sperm to bind to the zona pellucida of the egg. It is performed by dividing intact zona pellucida and incubating it separately with donor sperm and the patient’s sperm. A hemizona index is derived by dividing the number of bound donor sperm by the number of bound patient sperm. An index <0.80 is seen in males who failed IVF. Its use is limited by the availability of human ova. Since this technique potentially bypasses the step of zona binding, men whose sperm cannot bind may be good candidates for these procedures.

REFERENCE

HEMORRHAGE, POSTOPERATIVE, UROLGIC CONSIDERATIONS

DESCRIPTION
Postoperative hemorrhages can occur after any urologic procedure, but are most common and significant with percutaneous procedures of the kidney. The risk of hemorrhage increases in patients with underlying coagulopathy, aberrant anatomy, multiple needle passages, tract dilatation, or nephrostomy tube placement. Parenchymal bleeding can be persistent, and a large high pressure balloon can be placed through the nephrostomy tube tract to promote tamponade and hemostasis. Not uncommonly, venous lacerations may occur and can be managed by placing a large nephrostomy tube and clamping the tube to allow for tamponade. If arterial bleeding is persistent, selective arterial embolization may be employed. Delayed bleeding can occur soon after surgery, or weeks to months later in the setting of renal pseudoaneurysms or arteriovenous fistulas. If these diagnoses are suspected, evaluation with angiography and treatment with selective embolization can be performed.

REFERENCE

HEMORRHAGE, RETROPERITONEAL AND PERINEPHRIC

DESCRIPTION
Retroperitoneal and perinephric hemorrhage are uncommon in the absence of trauma. Spontaneous retroperitoneal and perinephric hemorrhage is most commonly from the kidney. The most common renal causes are angiolipoma (AML) and renal cell carcinoma (RCC). Vascular diseases such as polyarteritis nodosa (PAN), renal artery aneurysm, infections of kidney such as cortical abscesses, perinephritis, and renal cysts are occasional etiologic factors. Adrenal hemorrhage (AH) is seen with severe stress conditions (lapses, burns, trauma), pheochromocytoma, adrenal carcinomas, myelolipoma, and cortical adrenocortical. Clinical presentation depends on the amount of bleeding ranging from mild flank pain to shock and oliguria. CT scan is considered the gold standard for diagnosis. (See also Section I: “Retroperitoneal Masses, Fluid and Cysts” and Section II: “Retroperitoneal Hematoma.”)

REFERENCE

HEMOSIDERIN, URINARY

DESCRIPTION
Hemosiderin occurs when hemoglobin is reabsorbed by the proximal tubular cells and then catalyzed into heme and hemosiderin. Uremic hemosiderin can occur up to 2 days after an acute hemolytic episode, and is also demonstrated in chronic hemolytic states and hemochromatosis.

REFERENCE

HENCHO–SCHÖNLEIN PURPURA (HSP)

DESCRIPTION
HSP is a form of purpura with an underlying pathologic feature of vasculitis, affecting mainly small blood vessels. The disease is predominantly seen in children. Clinically, the purpuric skin lesions are typically located on the lower extremities. However, the hands, arms, and face can be affected. Joint pain, abdominal pain, and gastrointestinal bleeding may be present. Hematoma denotes a renal lesion, which is usually reversible. HSP is similar to IgA nephropathy, but somewhat more severe, particularly in adults. Progressive renal failure occurs in at least 25%. Kidney biopsy reveals segmental glomerulonephritis with crescents and mesangial deposition of IgA and complement types C3 and C4. Lab tests reveal mild to normal to high protein counts. Clinical involvement is not severe, the disease will subside without sequelae within 6 wk.
HLRCC syndrome is manifested by:

**DESCRIPTION**

- Renal cell carcinoma
- Hereditary leiomyomatosis and renal cell carcinoma syndrome

**TREATMENT**

- Early diagnosis and close follow-up
- Nephrectomy (partial or radical) when indicated

**REFERENCE**


**HEDRATIS PAPILLARY RENAL CELL CARCINOMA (HPVCC)**

**DESCRIPTION**

HPVCC is an autosomal dominant disorder associated with type 1 papillary RCC. Acquired as a proto-oncogene, rather than inactivation of a tumor suppressor gene, is the initiating event. Missense mutations of the c-KIT proto-oncogene on chromosome 4 at 4q11 are the most often described as the relevant genetic locus causing the disorders. A majority of the mutations were isolated on the tyrosine kinase domain of the c-KIT gene. Tumors linked to these mutations are thought to be less aggressive than the sporadic type. (See also Section I: “Renal Cell Carcinoma, General.”)

**REFERENCES**


**HERNIA UTERINE INGUINALE**

**DESCRIPTION**

A cause of male pseudohermaphroditism, thought to be due to an isolated defect in the production of mullerian inhibiting substance or to the response to mullerian inhibiting factor (MI). This is a rare syndrome of mullerian ducts persistence. Affected males are not ambiguous at birth and generally present later, most commonly with an inguinal hernia on 1 side and an irreducible contralateral testis. Hernia sac may extend into the uterus. Karyotype is 46, XY. The involved tissue is exclusively testicular. Both Wolffian and mullerian duct derivatives are present, with a vagina and epididymis alongside an epididymal vesicle, fallopian tube, and upper vagina. Tests have malignant potential. No uterine or vaginal malformation have been reported.

**TREATMENT**

- Sex assignment as male
- Primary or staged orchidopexy
- Müllerian structures do not require removal, as the Mullerian inhibiting substance or the response to Müllerian inhibiting factor may be effective

**REFERENCE**


**HIDRADENITIS SUPPURATIVA (ACNE INVERSA), UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

A chronic suppurative disease of the apocrine gland-bearing areas of the body, such as the axilla, buttok, and groin. Not primarily infectious; caused by plugging of the follicles. Diagnosis is usually accomplished by location and clinical course. Pain, fluctuation, discharge, and sinus tract formation are characteristic. In chronic cases, coalescence of inflamed nodules may cause palpable cordlike bands. The condition may become extensive and disabling. If the pubic and perineal areas are severely involved, walking may be difficult.

**TREATMENT**

- Avoid irritants such as antiperspirants
- Conservative treatment with rest, moist heat, and prolonged antibiotics (tetracycline or erythromycin)
- Oral isotretinoin and intralavital corticosteroids may be effective
- Surgical excision and plastic repair of the affected areas may be necessary

**REFERENCE**


**HINMAN SYNDROME (HINMAN–ALLEN SYNDROME):**

**HINMAN SYNDROME (HINMAN–ALLEN SYNDROME) (NONNEUROGENIC OCCULT NEUROPATHIC BLADDER) (OCCULT NEUROPATHIC BLADDER)**

**DESCRIPTION**

It was described in 1937 by Hinman and Baum, this is a syndrome of vesicovaginal dysfunction (dyssynergic voiding) that is associated with recurrent UTIs, vesical trabeculation, poor emptying, and hypertension with possible progression to renal failure. Hinman syndrome is thought to occur from bladder vesicovaginal dysfunction with no signs of neurologic cause and may begin in the neonate or in the child around the time of bladder training.

**SYNONYM**

Nonurogenic neuropathic bladder

**TREATMENT**

- Clean intermittent catheterization (CIC)
- Catheter vesicostomy

**REFERENCE**

HISPAREUNIA (MALE DYS Pareunia)

REFERENCE

HISPAREUNIA (MALE DYS Pareunia)
DESCRIPTION
Sling erosion/isolation is a recognized complication after suburethral sling (or to treat female stress urinary incontinence [SUI]). Erosion occurs in up to 4% of patients. Female symptoms may include discharge, infections, postcoital bleeding, and alterations of the sexual function. Changes of male sexual function and particularly pain again after sling insertion in their female partner may be due to sling exposure and has been termed “hispareunia.” Sexual interest and drive may be negatively influenced. Male dyspareunia is a complaint that appears to be effectively treated by correcting the sling exposure in the female partner.

REFERENCE

HISTOPLASMOsis, GEnITOURINARY
DESCRIPTION
Histoplasma capsulatum grows in soil entombed by bird guano, with outbreaks reported in caves, construction sites, and on bird farms. Disseminated violent disease is seen in AIDS, children, and immunosuppressed individuals. GI involvement is a manifestation of systemic disease and can result in sloughed papilla, prostatic obstruction, or prostatic abscess. Epiphonitis can resemble sperm granulomas. Up to 1% can experience adrenal insufficiency from adrenal destruction. (See also Section I: “Fungal Infections, Gastrointestinal.”)

TREATMENT
2 g of amphotericin B with maintenance therapy with fluconazole to prevent relapse

REFERENCE

HIV NEPHROPATHY
DESCRIPTION
HIV nephropathy [HIVNA] is the most common cause of chronic renal failure among HIV+ asymptomatic patients. It can occur in both the acute and chronic phase of the illness. Presentation may include nephrotic syndrome, hypertension, hematuria, and renal insufficiency. Pathologically, there is a focal segmental glomerulosclerosis, collapsing nephropathy with podocyte hypertrophy, and hyperplasia. (See also Section I: “HIV/AIDS, Urologic Considerations.”)

TREATMENT
- High-dose antiretroviral therapy
- Steroids
- ACE Inhibitor

REFERENCE

HODGKIN DISEASE, UROLOGIC CONSIDERATIONS
DESCRIPTION
Hodgkin disease is a type of lymphoma differentiated from other lymphomas partially on the basis of the presence of Reed–Stemmer cells. It has become 1 of the most curable forms of malignancy. It has many urologic associations, and an association with a higher incidence in RCC patients has been proposed. Treatment with radiation for Hodgkin may predispose to bladder cancer. The kidney and bladder have been reported to be primary sites of Hodgkin disease. Extensive retroperitoneal lymphadenopathy may cause ureteral obstruction. Renal radiation-induced arterial stenosis can be a treatment effect. (See also Section II: “Symptoma, Urologic Considerations.”)

REFERENCE

HODGKSON TYPES I, II, III HYPOSPADIAS REPAIR
DESCRIPTION
Type I: Chordee is repaired. A longitudinal slit along the urethral axis is formed on the inner surface of the prepuce, which is then transferred to the ventrum through a buttonhole incision at the base of the tube. The proximal neourethra is anastomosed to the proximal native urethra, and the distal neourethral tube is used to create the meatus. Type II: Hodgkin modified type I for the very distal hypospadias where no chordee exists, and the native urethral plate remains intact. The inner surface of the prepuce is again transferred to the ventrum via a buttonhole at the base. In this repair, the proximal flap is sutured onto the urethral plate. Type III: This is modified for the more proximal hypospadias repair. Here, the buttonhole is created at the base of the penis, and a longer tubular neourethra is created, based on preputial and shaft skin.

REFERENCE

HONEYMOON CYSTITIS
DESCRIPTION
Urinary tract infection which affects young sexually active women. It accounts for 4% of UTIs and for 75–90% of episodes in young sexually active women. The pathogenesis of this condition is caused by fusion of the female's urethra to bladder cancer. The kidney and bladder have been reported to be primary sites of Hodgkin disease. Extensive retroperitoneal lymphadenopathy may cause ureteral obstruction. Renal radiation-induced arterial stenosis can be a treatment effect. (See also Section II: “Symptoma, Urologic Considerations.”)

REFERENCE

TREATMENT
• High fluid intake
• Postcoital voiding (controversial if useful)
• Identify any triggers (Spermicide, positioning during sexual activity, etc.)
• Consider single dose of antibiotic before or after intercourse if ≤ 3 symptomatic UTIs/yr (eg, trimethoprim/sulfamethoxazole, trimethoprim, nitrofurantoin, cephalaxin, ciprofloxacin, others)

REFERENCE

HORSESHOE KIDNEY
DESCRIPTION
The most common fusion anomaly, present in 1 in 400 births, with a male predominance. Usually, this represents a true fusion of the lower poles, which may be composed of thick functioning parenchyma or merely a fibrous band. Associated anomalies are seen in 1/3 of patients and include multisystem disturbances of the skeletal and cardiovascular systems and GI tract, as well as GI abnormalities, such as an increased frequency of ureteral duplication, reflux, and dysplasia. Usually asymptomatic, a horseshoe kidney may be associated with urolithiasis and UO infection. Radiographic diagnosis can be made with IVP or CT, which reveals deviation of the axis of the kidney. Renal scan may be helpful in surgical decision making. If necessary, the condition is caused by fusion of poles during ascent of the kidneys. (See also Section 1: “Renal Fusion Anomalies.”)

TREATMENT
• Postcoital voiding (controversial if useful)
• Identify any triggers (Spermicide, positioning during sexual activity, etc.)
• Consider single dose of antibiotic before or after intercourse if ≤ 3 symptomatic UTIs/yr (eg, trimethoprim/sulfamethoxazole, trimethoprim, nitrofurantoin, cephalaxin, ciprofloxacin, others)

REFERENCE

HORTON-DENVEN “FLIP-FLAP” HYPOSPADIAS REPAIR
DESCRIPTION
The distal ventral skin over the urethral meatus, and the distal urethra is also mobilized. Parallel incisions are made in the glans to mobilize. The proximal flap is sutured over and onto the urethral plate. The wings of the glans are then approximated over this distal repair.

REFERENCE

HOUSNFIELD UNITS
DESCRIPTION
Named after Sir Godfrey Newbold Hounsfeld, the inventor of the CT scanner. It is an arbitrary scale created to compare density of different substances seen on CT. Water is represented by 0 HU. Air is –1,000 HU. Bone is 1,000 HU. Fat is in the range of...
**REFERENCES**


**REFERENCES**


**REFERENCES**


**REFERENCES**


**REFERENCES**


**REFERENCES**


Hypercalciuria is the most

**DESCRIPTION**


**REFERENCES**

Cystitis, Hemorrhagic [Infectious, Noninfectious, Cystitis. (See also Section I: “Fournier gangrene”; Section II: “Cystitis: Radiation.”)


**HYPERCALCEMIA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

In urology, hypercalciuria is generally the result of metastatic lesions to bone, hydrochlorothiazide therapy, hyperparathyroidism, or chronic renal failure. Symptoms include anorexia, weakness, constipation, polyuria, and coma. This condition may also occur as a paraneoplastic syndrome from RCC and can lead to hypercalcemia, which can increase chances of urolithiasis.

**TREATMENT**

- Initial therapy involves diuresis by nonthiazide diuretics and IV saline.
- Inorganic phosphate and EDTA may be used for an emergency.
- Mitomycin, strontium, and etidronate disodium have also been used.

**REFERENCE**


**HYPERCALCIURIA (ABSORPTIVE, RENAL, AND RESORPTIVE)**

**DESCRIPTION**

Hypercalciuria is the most commonly associated metabolic abnormality in patients with calcium nephrolithiasis. Defined as urinary excretion of ≥275–300 mg of calcium per day in men or ≥250 mg of calcium per day in women on a regular unrestricted diet. An alternative definition in patients on a calcium-restricted diet (400 mg calcium, 100 mg calcium) is a urinary calcium level of ≤8 mg/L and a urine level of ≥200 mg of calcium,ermen.

**REVIEW**


**HYPERCALCIA DURING LAPAROSCOPY**

**DESCRIPTION**

CO2 is the most abundantly used insufflant in the United States for laparoscopic surgery. CO2 has the ability to diffuse easily into body tissues and out of the peritoneum during surgery. This can lead to increases in blood levels or hypercalciuria that can stimulate the sympathetic nervous system, leading to increases in vascular resistance, tachycardia, and impaired cardiac contractility. Patients who have pulmonary compromise (ie, COPD, fibrosis) may have difficulty compensating for the increased CO2 levels. Rarely a CO2 gas embolism may occur.

**REFERENCE**


<table>
<thead>
<tr>
<th>HYPERCALCIURIA Type</th>
<th>Urinary Calcium on 400 mg Calcium Diet (Normal = &lt;200 mg/24 h)</th>
<th>Renal calcium leak (Normal = &lt;0.11)</th>
<th>Postural load Calcium (Normal = &lt;0.20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Absorptive type I</td>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Absorptive type II</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Absorptive type III (renal phosphate leak)</td>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Renal calcium leak</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Resorptive (hyperparathyroidism)</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>


Unlike primary hyperparathyroidism, serum calcium is normal and the hyperparathyroidism is secondary.

**Absorptive hypercalciuria,** The hypercalcemia is due to primary hyperparathyroidism with excessive reabsorption of bone resulting from hypercortisolism of PTH. Intestinal absorption of calcium is frequently elevated because of the PTH-dependent stimulation of the renal synthesis of 1,25–(OH)2D.

As a guide to testing for hypercalciuria, calcium load usually consists of 1 g of oral calcium gluconate.

**TREATMENT**

- General recommendations include increased urine volume to ≥2 L/d; do not use calcium-restricted diet, but avoid excessive intake of dairy products, salty foods, and red meat protein. (Note: A low calcium intake increases intestinal oxalate absorption, with a subsequent increase in urinary oxalate stone formation.) Patients may be at risk for osteoporosis and osteodensity.
- Absorptive hypercalciuria: Thiazide is not a selective therapy for absorptive hypercalciuria, since it does not decrease intestinal calcium absorption. However, this drug is used because of its hypocalcic action and the high cost and inconvenience of alternative therapy (sodium citrate phosphate).
- Absorptive hypercalciuria type I: Thiazide does not correct the basic, underlying physiologic defect in absorptive hypercalciuria.
- Potassium supplementation (as potassium citrate), to prevent hypokalemia and hypocitraturia (eg, potassium chloride 50 mg/d, or indapamide 2.5–5 mg/d). Potassium supplementation (≥40 mg/d) is required to prevent hypokalemia and attendant hypercalcemia. Potassium chloride has been shown to be effective in preventing hypercalcemia and in increasing urinary citrate when administered to patients with calcium nephrolithiasis taking thiazides.
- Thiazide in combination with thiazide may be more effective than thiazide alone in reducing calcium excretion.
- Potassium supplementation should be used with caution in patients taking amiodole: Thiazides may lose their hypocalcic effect over time and cause hypokalemia, hypercalcemia, and increased urine acid.
- Recent data suggest bisphosphonates (eg, alendronate [Fosamax], risedronate [Actonel], and ibandronate [Boniva]) increase bone deposition of calcium and reduce urinary calcium levels.
- Absorptive hypercalciuria type II: No specific drug treatment may be necessary since the physiologic defect is not as severe as an absorptive hyperparathyroidism. Low calcium intake (400–600 mg) and high fluid intake (sufficient for a minimum urine output ≥2 L/d) is helpful. Normo-calcia can be restored by dietary calcium restriction alone, and increased urine volume has been shown to reduce urinary saturation of calcium.
- Absorptive hypercalciuria type III (renal phosphate leak) is treated with slow-release neutral potassium phosphate (Neutral-Phos P) that corrects the hyperphosphatemic.
- Renal hypercalcemia:
  - Thiazide diuretics augment calcium reabsorption in the distal tubule, causes extracellular volume depletion, and stimulates proximal tubule reabsorption of calcium. Agents include hydrochlorothiazide 50 mg BD, chlorthalidone 50 mg/d, or indapamide 1.25–2.5 mg/d. Potassium supplementation (≥40 mg/d) is required to prevent hypokalemia and attendant hypercalcemia. Potassium chloride has been shown to be effective in preventing hypercalcemia and in increasing urinary citrate when administered to patients with calcium nephrolithiasis taking thiazides.
  - Thiazide is contraindicated because of the risk of transtran renal stone formation.
- Resorptive hypercalciuria: Parathyroidectomy is the optimum treatment.

**REFERENCE**


of the geroinvasive tract (Fournier gangrene) have been described. Hyperparathyroid has also been reported in the treatment of meninistion cystitis. (See also Section I: “Fournier gangrene”; “Cystitis, Hemorrhagic [Infectious, Noninfectious, Radiation.”) and Section II: “Cystitis: Radiation.”)
**HYPERCONTINENCE**

**DESCRIPTION** A condition described in the literature referring to the increased likelihood that females are more likely to require intermittent catheterization than females following a cystectomy or urinary diversion such as orthotopic neobladder.


**HYPERKALEMIA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION** Hyperkalemia usually occurs in urologic patients as a result of renal insufficiency, Addisonian crisis, trauma, shock, and diabetic acidosis. It can also be a consequence of small bowel substitution used in urinary diversion. ECG changes are characteristic, including prolonged T waves, long QT interval, long QRS complex, and absent P wave.

**TREATMENT**

1. Monitor patient on ECG if symptomatic or if K+ > 6.5 mEq/L, discontinue all K+ intake, including IV fluids; order a repeat stat K+
2. Pseudohyperkalemia should be ruled out. If doubt is present.
3. Rapid correction: These steps only protect the heart and are not adequate for other organ systems.
   - Sodium polystyrene sulfonate (Kayexalate) 20–60 g PO with 100–200 mL of sorbitol or 40 g of milk of magnesia in a heparinized tube; order a repeat stat K+
4. Combined sodium and water losses (hypovolemic hypernatremia): Water loss in excess of Na+
5. Hypervolemic hypernatremia: Avoid medications that contain excessive Na+
6. Enteric hyperoxaluria: Accounts for a relatively small number of cases of hyperoxaluria (5%). Caused by chronic diarrhea and malabsorption (cortis or jejunal bypass). Through the reduced GI calcium availability to bind oxalate and keep it from being absorbed systemically.
7. Diabetic hyperkalemia: Caused by increased intake of foods high in oxalates (i.e., nuts, chocolate, tea, spinach, rhubarb, beets, wheat bran, strawberries, and other plant products). Reduced dietary calcium intake can also result in hyperkalemia due to reduced intestinal binding of oxalate and increased oxalate absorption.
8. Idiopathic: The most common cause; may be due to increased dietary absorption or due to increased intrinsic production of oxalate, with some suggestions of a genetic predisposition.


**HYPEROXALURIA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION** Hyperoxaluria in the urologic patient can result from iatrogenic causes and various disease states. Classified according to the mechanisms described below, the symptoms depend on the absolute level and also how rapidly the Na+ level has changed. Symptoms may include confusion, irritability, lethargy, stupor, coma, muscle twitching, and seizures. Signs can include hyperreflexia and mental status changes.

- Combined sodium and water losses (hypovolemic hypernatremia): Water loss in excess of Na+ causes intracellular K+ to shift. If serum Na+ remains normal, but total body water is decreased. Caused by diabetic insipidus (DI) (central and nephrogenic), excess skin losses, respiratory loss, others.
- Excess sodium (hypernatremic hyperkalemia): Total body Na+ increased. Caused by iatrogenic Na+-administration (i.e., hypertonic dialysis), hypernatremic saline enemas, Na-containing medications) or other excessive sources (massive ingestion, salt tablets) or adrenal hyperfunction (Cushing syndrome, hyperaldosteronism).

**TREATMENT**

- Check the serum Na+ levels frequently while attempting to correct hypernatremia.
- Hyperoxaluria: Hyperoxaluria is usually present in patients who have nephrocalcinosis with kidney failure common in childhood. Most patients die before 30 yr. The condition often presents with stone disease producing ureteral obstruction in childhood. Type 1 can be associated with ESRD secondary to stones and interstitial deposits of calcium oxide.
- Primary hyperoxaluria type I: Less common than type I hyperoxaluria, this entity is caused by deficiencies of the hepatic glyoxylate carboligase that causes the conversion of glyoxylate to oxalate. Type I and II primary hyperoxaluria result in about the same degree of hyperoxaluria, with renal failure slightly less common in patients with type II disease. Pyridoxine is generally not effective in type II primary hyperoxaluria.

HYPERPARATHYROIDISM, UROLOGIC CONSIDERATIONS

**HYPERPARATHYROIDISM**

**DESCRIPTION**

Hyperparathyroidism can cause a variety of urologically related conditions and problems, including nephrolithiasis, hypercalciuria, nephrocalcinosis, chronic renal insufficiency, and abnormalities in renal tubular function (decreased concentrating ability). Also associated in the NEN syndrome. About 5% of new stone formers have hyperparathyroidism, whereas up to 20% of patients with hyperparathyroidism will have stones (most common calcium oxalate). These patients usually exhibit elevated serum and urine calcium with an inappropriately normal or elevated serum PTH level and elevated calcium level. Treatment is through parathyroidectomy and works for NPH when appropriate. (See also Section I: “Hyperparathyroidism and Multiple Endocrine Neoplasia.”)

**REFERENCE**


**HYPERPHOSPHATEMIA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

Hyperphosphatemia (↑↑↑↑) can result from hyperparathyroidism, osteomalacia, medications, and chronic renal failure. Signs include muscle cramps, tetany, perioral numbness, renal osteodystrophy, and secondary hyperparathyroidism.

**TREATMENT**

Dietary restriction, stopping medications that include phosphates, and binding agents are the mainstays of therapy.

**REFERENCE**

Pate D, Beck L, Urena P, et al. Recent findings in phosphate, and binding agents are the mainstays of treatment. (See also Section I: “Hyperparathyroidism and Multiple Endocrine Neoplasia.”)

**HYPERURICOSURIA**

**DESCRIPTION**

Hyperuricosuria refers to the uric acid excretion in the urine of >860 mg/d in men and >750 mg/d in women. Uric acid, the end product of purine metabolism, is relatively insoluble in water and can lead to the formation of uric acid calculus. Overproduction and over-excretion of uric acid can be due to excess dietary intake of purine-rich foods and in patients with maladies such as (lymphoma, leukemia, hypoproliferative disease) especially after chemo or radiation induces rapid cell lysis (tumor lysis syndrome). Inherited enzyme defects can also lead to hyperuricosuria and hyperuricemia such as hypoxanthine-guanine phosphoribosyltransferase deficiency (Lesch–Nyhan syndrome) and glucose-6-phosphatase deficiency (glycogen storage disease, type I). Hyperuricosuria can be associated with hyperuricemia. The term “gouty diathesis” refers to the formation of urinary stones in persons with gout. These patients may present with other manifestations of gout such as “gouty arthritis.” These high levels of uric acid can predispose to uric acid stones that can be uric acid, calcium or a combination of both. Uric acid stones are more likely with a low urine pH (pH <6) where the solubility of uric acid is low. Allopurinol and febuxostat reduce urinary levels of uric acid, a drug metabolized via the liver and excreted in the urine of <35%.

**REFERENCE**


**HYPERKALEMIA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

Primary hyperkalemia is the most common form of this disease, but when significant findings on evaluation are present or if the hyperkalemia is sufficiently severe to require multiple-drug therapy or requires hospitalization, a secondary cause should be sought. Common urolithiasis considerations are primary aldosteronism, congenital adrenal hyperplasia (CAH), Cushing syndrome, pheochromocytoma, and renovascular disease. Workup entails physical exam, endocrinologic workup, and imaging.

**REFERENCE**


**HYPOCALCIURIA**

**DESCRIPTION**

Calcium excretion in the urine is low. Hypocalciuria can be seen in states of low calcium intake, dietary malabsorption, or low renal calcium reabsorption. Low calcium intake is the most common cause of hypocalciuria. In the postmenopausal woman, low calcium intake may contribute to the formation of urinary stones in persons with low-renin hypertension and osteoporosis. (See also Section I: “Hypercalciuria.”)

**REFERENCE**


**HYPOGONADISM, SOCIETY DEFINITIONS**

**DESCRIPTION**

The lab diagnosis of testosterone deficiency is a challenge. The Endocrine Society defines male hypogonadism as a clinical syndrome that results from failure of the testis to produce physiologic levels of testosterone (androgen deficiency) and the normal number of spermatids caused by disruption of 1 or more levels of the hypothalamic–pituitary–gonadal (HPG) axis. Unfortunately, there is no consensus among specialists (endocrinologists, urologists, pathologist) as to what lab values defines a “low” testosterone level. Serum testosterone levels are subject to many variables including diurnal, seasonal, and age-related variations. Illness and medications (opioids, glucocorticoids), may impact testosterone levels. In addition testosterone levels impacted by alterations in sex hormone binding protein (SHBG). Further there are a variety of tests that differ in their measurement of testosterone levels leading to a wide variety of normal ranges

**Society Definitions of Hypogonadism Based on Serum Testosterone Total Testosterone**

<table>
<thead>
<tr>
<th>ng/dl</th>
<th>mg/dl</th>
<th>nmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;340</td>
<td>&lt;3.40</td>
<td>&lt;11.8</td>
</tr>
<tr>
<td>340–400</td>
<td>3.40–4.00</td>
<td>11.8–17.0</td>
</tr>
<tr>
<td>&gt;400</td>
<td>&gt;4.00</td>
<td>&gt;17.0</td>
</tr>
</tbody>
</table>

European Academy of Andrology (EAA), International Society of Andrology (ISA), International Society for the Study of the Aging Male (ISSAM)

European Association of Urology (EAU), American Society of Andrology (ASA), International Society for Sexual Medicine (ISSM)

Endocrine Society (ES)

American Association of Clinical Endocrinologists (AACE)


**HYPOPHOSPHATEMIA**

**DESCRIPTION**

Hypophosphatemia is a poorly studied condition characterized by an excessive volume of phosphate defined in studies as <3.5–6.5 μmol/L (μmol/L). Hypophosphatemia is generally defined as a total phosphate of <1.5 mg/dL (See also Section II: “Serum Analysis, Abnormal Findings and Terminology.” and Reference II: “Serum Analysis, Technique and Normal Values.”)
Hypokalemia

Hypokalemia (K+ < 3.6 mEq/L) can result from excessive urinary losses, diarrheal disease, vomiting, diuretic therapy, or mineralocorticoid excess. Potassium intake, malabsorption, chronic diarrhea, and tubular acidosis may cause hypokalemia. Mental confusion, muscle weakness, carpopedal spasm, muscle tetany, abdominal pain, and diarrhea may occur. Hypokalemia can also result from pseudo-hypokalemia (elevated protein or lipids) or hypertonic hyponatremia (hyperglycemia). A serum K+ level of 2 mEq/L probably signifies hypokalemia.

TREATMENT

- Treat underlying cause.
- Potassium supplementation either with PO or IV therapy is recommended. Therapy is based on determination of volume status. Evaluate volume status by physical exam: HR and BP, edema, and skin turgor. Edema and skin turgor are not sensitive determinants of volume.
- Parenteral therapy: Mild 1 g IM q6h or 2 g q24h
- Severe: IV (KCl 0.25 mEq/kg/h or 20 mEq/h; IM or IV KCl 0.5 g–1 g) Tidal, IV KCI can be painful
- Slow correction: Give KCl PO: 3–4 mEq/L (mmol/L) in a 70-kg adult.

Hypomagnesemia

Hypomagnesemia (Mg < 1.5 mEq/L) results from inadequate intake, malabsorption, alcohol abuse, and hypogonadism. It may manifest as muscle weakness, or mental status changes. More severe states can produce problems at the osmotic level leading to white blood cell dysfunction or anemia.

TREATMENT

Potassium supplementation is the treatment of choice. Potassium should be administered IV in severe situations, or PO for patients with milder symptoms or hemodynamically stable states.

Hypophosphatemia

Hypophosphatemia (P < 0.7 mEq/L, mmol/L) can result from inadequate magnesium intake, malabsorption, chronic diarrhea, stress, alcoholism, and medications such as diuretics. Symptoms of hypophosphatemia include weakness, muscle cramps, muscle tetany, confusion, hallucinations, hypertension, and arrhythmias. Often accompanied by hypokalemia.

TREATMENT

- Replace with PO or IV: 10–20 mg/kg or 0.1–0.2 mEq/kg/h.
- Oral treatment: 300 mg PO or 150 mg PO q4h for patients with minimal bone disease and 2.5 g PO q4h for those with moderate/severe bone disease.

Hypophosphatemia, Urologic Considerations

Hypophosphatemia is a sodium/Na+ level of < 136 mEq/L (mmol/L). Many causes exist, but an acute cause in urology is a result of excessive nonelectrolyte irrigant absorption during endourologic procedures. As the fluid is absorbed, volume expansion and dilutional hyponatremia occur. Known as transient renal reaction (TUR) syndrome, nausea, mental confusion, and sensory disturbances are seen, and, if allowed to progress, blindness, convulsions, hypotension, coma, oliguria, and death can occur. Other causes include nephrotic syndrome, renal failure, SIADH, adrenal insufficiency, diuretics, renal tubular acidosis (RTA), GI losses, and mineralocorticoid insufficiency.

REFERENCES

Zhao M, Li Y, Tang Y, et al. Two-stage repair with Y-shaped neo-urethra. Glansplasty and shaft skin closure and running is used to complete a 2-layer closure. A dartos incision allows for easier tubularization of the tissue and creates less scarring. The dartos incision is made with the glans incised, without entering the glans. This incision allows for easier tubularization of the tissue and creates less tension on the ventral reconstruction. Urethral plate tubulization is then performed from the end of the plate to a round urethral mound. Subepithelial running is used to complete a 2-layer layer incision. A dartos flap is then created and rotated ventrally to cover the neo-urethra. Graft is then sutured to shaft skin closure and
HYPOSADIAS, 2-STAGE REPAIR

DESCRIPTION

The basic tenet of the 2-stage hypospadias repair is to create a new urethral plate with a graft of alternative tissue in the 1st stage and then tubulize this tissue to create a neo-urethra in the 2nd stage. The main grafts for the 1st stage repair can be categorized into the following:

- Buie’s flap—paddled flaps of the dorsal hood transposed medially
- Mesh free skin graft in an onlay fashion
- Buccal mucosa free graft in an onlay fashion
- Bracka graft—a free partial thickness skin graft

The choice of graft depends on a multitude of factors including surgeon experience or preference, availability of proper skin, and history of previous surgeries.

During the 1st stage, an orthoplasty is performed and a chosen graft is placed on the ventral penis. The next stage is generally performed 6 mo or more after completion of the 1st stage where the main goal is to create a neo-urethra that corrects the hypospadias. Tubulization of local skin proceeds in a Thiersch-Duplay fashion. This step is followed by reapproximation of the glans over the newly formed urethra and 2nd layer coverage with local subcutaneous tissue or a tunica vaginalis flap. Finally, daily meatal dilation for 6 mo is recommended to completion of the 1st stage where the main goal is to create a new urethral plate that corrects the hypospadias. Tubulization of local skin proceeds in a Thiersch-Duplay fashion. This step is followed by reapproximation of the glans over the newly formed urethra and 2nd layer coverage with local subcutaneous tissue or a tunica vaginalis flap. Finally, daily meatal dilation for 6 mo is recommended to complete the procedure.

REFERENCE


HYPOSADIAS, 2-STAGE REPAIR

DESCRIPTION

The basic tenet of the 2-stage hypospadias repair is to create a new urethral plate with a graft of alternative tissue in the 1st stage and then tubulize this tissue to create a neo-urethra in the 2nd stage. The main grafts for the 1st stage repair can be categorized into the following:

- Buie’s flap—paddled flaps of the dorsal hood transposed medially
- Mesh free skin graft in an onlay fashion
- Buccal mucosa free graft in an onlay fashion
- Bracka graft—a free partial thickness skin graft

The choice of graft depends on a multitude of factors including surgeon experience or preference, availability of proper skin, and history of previous surgeries.

During the 1st stage, an orthoplasty is performed and a chosen graft is placed on the ventral penis. The next stage is generally performed 6 mo or more after completion of the 1st stage where the main goal is to create a neo-urethra that corrects the hypospadias. Tubulization of local skin proceeds in a Thiersch-Duplay fashion. This step is followed by reapproximation of the glans over the newly formed urethra and 2nd layer coverage with local subcutaneous tissue or a tunica vaginalis flap. Finally, daily meatal dilation for 6 mo is recommended to complete the procedure.

REFERENCE


HYPOSADIAS, URETHRAL ADVANCEMENT FOR SUBGONADAL MIDSHAFT DEFECTS

DESCRIPTION

The urethral advancement and glanuloplasty (incorporated MAGPI) procedure was first described by Delclos in 1981 as an option for patients with a glanular or subcoronal hypospadias. A dorsal meatusotomy with glanuloplasty is performed to advance the neo-urethra distally. This was later modified by Zanez in 1989 for patients with a coronal or glanular hypospadias with a deep glanular groove and a fish mouth meatus as the graft approximation or “GAP procedure.” For midshaft defects, rolled mid-line tube techniques based on the initial reports of Thiersch-Duplay in the 1800s have gained renewed popularity. The Sindgraff in situ tube procedure (SITP), a variant of the Thiersch-Duplay technique, is now one of the most popular methods of hypospadias repair. Other techniques include meatal based flap procedures (eg, Mathieu) and on-lay flap repairs with native tissue or free grafts.

REFERENCE


HYSTEROCTOMY, UROLOGIC

HYPOSPADIAS, URETHRAL

DESCRIPTION

Hysterectomy is among the most common complications from TVP urethroplasty is fistula formation, which can be low as 2% in the hands of an experienced surgeon. It has proven to be a versatile procedure used in both distal and midshaft hypospadias repairs.

REFERENCE


ICE WATER TEST

DESCRIPTION

Historically performed after standard cystometry, this test may aid in differentiation of upper and lower motor neuron lesions. Ice water is rapidly instilled into the bladder and left for 1 min. If the water is ejected or the bladder pressure rapidly rises, the test is positive. Most patients with upper motor neuron/spinal lesions (eg, Parkinson, MS, CVT) have a positive test. Patients with lower motor neuron lesions almost never have a positive test.

REFERENCE


ICIQ-MULTS (INTERNATIONAL CONSULTATION ON INCONTINENCE QUESTIONNAIRE-MALE LOWER URINARY TRACT SYMPTOMS)

DESCRIPTION

The ICIQ-MULTS is a patient questionnaire used to evaluate men with LUTS and impact on quality of life. The original questionnaire comprised of 22 items and was shortened to 11 items in 2 distinct factors of voiding and incontinence. Unlike other questionnaires, such as the American Urological Association symptom score, the ICIQ-MULTS contains separate subscales for the domains of incontinence and voiding with separate consideration of frequency, nocturia, and impact on quality of life. It has been validated and reliable instrument for evaluating men with LUTS.

REFERENCE


IEF (INTERNATIONAL INDEX OF ERECTILE FUNCTION)

DESCRIPTION

The IIEF is a validated self-administered patient questionnaire used in the assessment of male sexual dysfunction. A score of 0–5 is given to each of 15 questions in 4 main sexual function domains: Erectile function, organic function, sexual desire, and intercourse satisfaction. The IIEF questionnaire is limited by a superficial assessment of psychosocial issues and other partner relationship factors which can both impact male sexual dysfunction. The abbreviated 5-item version was subsequently developed to specifically diagnose the presence and severity of erectile dysfunction.

REFERENCES


**IMMUNOHISTOCHEMICAL STAINING, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**

This table lists common markers and patterns of immunohistochemical (IHC) staining that are useful in urologic pathology. Individual labs and pathologists may use their own individual panel testing with selective stains.

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>IHC Stains Positive</th>
<th>IHC Stains Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate adenocarcinoma</td>
<td>AMACR (P504S), PSA, PSAP, PSMA, ERG, NK3.1</td>
<td></td>
</tr>
<tr>
<td>Prostate small-cell carcinoma</td>
<td>Chromogranin, serotonin, Cg506, NSE, FTT1, AMACR, CK7, AE1/AE3</td>
<td></td>
</tr>
<tr>
<td>RCC, clear cell</td>
<td>RCC, CD10, vimentin, EMA, AE1/AE3, CAM5.2, CK7, PRAX, CAIX, PSA, PSAP, CAM5.2</td>
<td></td>
</tr>
<tr>
<td>RCC, papillary and papillary adenoma</td>
<td>CK7, vimentin, AMACR, EMA, AE1/AE3, AE1/AE3, AE1/AE3</td>
<td></td>
</tr>
<tr>
<td>RCC, chondroepithelia</td>
<td>CK7, vimentin, ACE1, EMA, CAM5.2, AE1/AE3</td>
<td></td>
</tr>
<tr>
<td>Renal oncocyctoma</td>
<td>CK7, AE1/AE3, vimentin, EMA, CAM5.2, AE1/AE3</td>
<td></td>
</tr>
<tr>
<td>Renal metanephric adenoma</td>
<td>TFEB, TFEB, CD10, RCC, AMACR (TFEB tumor suppressor = MITF)</td>
<td></td>
</tr>
<tr>
<td>Renal MITF/TFE family translocation-associated carcinoma</td>
<td>TFEB, CD10, RCC, AMACR (TFEB tumor suppressor = MITF, β-HCG, EMA)</td>
<td></td>
</tr>
<tr>
<td>Renal angiomyolipoma</td>
<td>HMB45, Melan-A, OCT, CK20, HMB45, p63, p63, unsp, thrombomodulin, GATA-3</td>
<td></td>
</tr>
<tr>
<td>Urothelial carcinoma</td>
<td>AE1/AE3, CK7, vimentin, EMA, CAM5.2, AE1/AE3, CK7, PRAX, CAM5.2, VIMENTIN</td>
<td></td>
</tr>
<tr>
<td>Testis, seminoma</td>
<td>PLAP, CK1, OCT4, CK20, AE1/AE3, CAM5.2, OCT4, PRAX, CAM5.2, AE1/AE3</td>
<td></td>
</tr>
<tr>
<td>Testis, yolk sac</td>
<td>PLAP, AR, AE1/AE3, CAM5.2, OCT4, AE1/AE3, PRAX, CAM5.2, p53, C-Kit, INHIBIN, CEA</td>
<td></td>
</tr>
<tr>
<td>Testis, Leydig cell tumor</td>
<td>INHIBIN, C099, CAM5.2, S100, CAM5.2, AE1/AE3, CEA</td>
<td></td>
</tr>
<tr>
<td>Testis, Sertoli cell tumor</td>
<td>INHIBIN, C099, EMA, CAM5.2, PSAP, PSMA, AE1/AE3, FETOPROTEIN</td>
<td></td>
</tr>
</tbody>
</table>

**REFERENCES**


**IMPERFORATE HYMEN**

**DESCRIPTION**

The hymen is composed of endoderm from the urogenital sinus epithelium and is located between the vaginal canal and vestibule. Normally, it opens during embryonic development. If it does not open, the hymen is called imperforate. Patients may present with hydroceles or hydropsalpinx that may obstruct the urinary tract. At puberty, females often present with primary amenorrhea and cyclic abdominal pain. Treatment is surgical if it causes symptoms.

**REFERENCES**


**IN VITRO FERTILIZATION (IVF) AND EMBRYO TRANSFER**

**DESCRIPTION**

Currently, IVF is used for women with nonremitting endometriosis, ovarian endometriosis, and in couples with male factor infertility or unexplained infertility. In most clinics, the female patient undergoes ovulation hyperstimulation with hormonal agents to increase the number of oocytes for follicle aspiration. The oocyte retrieval is performed by aspiration through the vagina with US guidance of needle placement. After aspiration of the oocytes, the eggs are incubated and placed in culture media. SpERM from the male is then integrated into the culture media and allowed to fertilize the eggs after being separated from the semen. After about 48–96 hr, 1–4 splitting embryos are placed in the uterus via transcervical injection. (See also Section II: “Assisted Reproductive Techniques (ARTs).”)

**REFERENCES**


**INCONTINENCE IMPACT QUESTIONNAIRE (IQ-7)**

**DESCRIPTION**

The underlying pathophysiology of male incontinence is related to either detrusor overactivity or external sphincter weakness, or a combination of the 2. Incontinence clamps are external devices that are used to treat male incontinence by recruiting buttow strength. They are applied externally to the penis to exert nonsurgical compression of the urethra, thereby preventing leakage of urine. The safety, efficacy, comfort, and patient satisfaction with 3 types of commercially available penile incontinence clamps (C3, U-Tex Male Adjustable Tension Band, and Cunningham clamp) has been studied in a small 12-patient trial. Results indicated that the Cunningham clamp was the most efficacious and most accepted by users. There was a concern over reduced distal blood flow velocity. None of the devices completely eliminated urine leakage when applied at a comfortable pressure. Complications of penile clamps can include edema, pain, urethral erosion, and destruction. Penile clamps should not be used for more than 4 hr at a time. (See also Section II: “Incontinence: Urinary, Anal” and Section III: “Catheter Bladders.”)

**REFERENCES**


**INCONTINENCE IMPACT QUESTIONNAIRE (IQ-7)**

**DESCRIPTION**

Short version of the IQ-7 (Incontinence Impact Questionnaire). A 7-question validated questionnaire to assess the impact of female urinary incontinence on activities of daily living. Commonly used in a prospective setting for patients undergoing anti-incontinence procedures and for research purposes.

**REFERENCES**

INCONTINENCE (URINARY) WITH ORGASM (CLIMACTURIA)

INCONTINENCE (URINARY) WITH ORGASM (CLIMACTURIA)

DESCRIPTION: Urinary incontinence can be divided into 2 forms: Incontinence at penetration and incontinence during orgasm. Incontinence during orgasm has been associated with detrusor overactivity (DO), whereas female incontinence during penetration has been associated with stress incontinence. The term climacturia is used mostly when referring to male who has incontinence associated with orgasm; this condition is seen mostly after radical prostatectomy.


INDEUDS URGENCY SEVERITY SCALE (IUSS)

DESCRIPTION: A validated patient-reported questionnaire for the report of urgency severity associated with overactive bladder. This scale has been validated to capture the urgency severity per toilet void. This scale, when combined with a 24-hr diary of frequency and urge incontinence episodes, creates the Overactive Bladder Symptom Composite Score (OAB-SCS).


INFERRENTIAL ANDGMALE SYMBOLOGY


INFLAMMATORY BOWEL DISEASE, UROLOGIC CONSIDERATIONS

DESCRIPTION: Crohn disease and ulcerative colitis are inflammatory diseases of the GI tract. The inflammatory response in ulcerative colitis is mostly confined to the mucosa and submucosa, as opposed to Crohn disease, which can be transmural. These diseases can give rise to a number of urologic manifestations including fistula to the urinary tract, malabsorption syndromes leading to nephrolithiasis, and pyelonephritis gangrenous of the kidney (Image 1).


INFLAMMATORY PSEUDOTUMOR (PSEUDOSARCOMATOUS FIBROMYXOID TUMOR)

DESCRIPTION: An benign mesenchymal tumor of the bladder also referred to by many other names. Postoperative pseudosarcomatous response or lesion, spindle cell neoplasm, pseudosarcomatous or atypical fibromyxoid tumor, atypical myxofibroblastic tumor, plasma cell granuloma, nodular fasciitis, and pseudosarcomatous myxofibroblastic proliferation. The differential diagnosis of benign inflammatory pseudotumors primarily includes the spindle variant of carcinoma and sarcoma. Immunohistochemical stains are used to distinguish spindle variants of carcinoma from benign inflammatory pseudotumors. These can be seen etiologically in postpartum nonparalytic intussusception lesions or as difficult to identify submucosal lesions. These are more common in female. Management is by complete transurethral resection as inflammatory pseudotumors are benign lesions that grow slowly and do not metastasize or undergo malignant transformation.


INFUNDIBULOPELVIC DYSGENESIS

DESCRIPTION: This is an obstructive process secondary to narrowing of the infundibulopelvic system that produces various congenital anomalies such as hydrocolpos, vaginal atresia, ureteropelvic junction stenosis, and malrotation of the kidney.


INGUINAL HERNIA, ADULT UROLOGIC CONSIDERATIONS

DESCRIPTION: A direct hernia is the most common inguinal hernia in adults. It occurs when there is a protrusion of intra-abdominal contents in an area called the Hesselbach triangle (formed by the rectus abdominis muscle, inferior epigastric artery, and inguinal ligament). Unilateral bladder outlet obstruction can lead to recurrent hernia. In addition, urinary retention can occur after hernia repair. In cases of a large inguinal hernia, a portion of a distended bladder can herniate into the groin. Indirect inguinal hernias are more common in infants and children and are caused by patent processus vuvularis.


INGUINAL HERNIA, PEDIATRIC, UROLOGIC CONSIDERATIONS

DESCRIPTION: Typically, an indirect inguinal hernia is the most common type of inguinal hernia in the pediatric population. During embryologic development, the spermatic cord and testes descend through the anterior abdominal wall to the inguinal canal through the projection of the process vuvularis. If the process vuvularis persists, an indirect inguinal hernia may form and is always associated with a hydrocele.

INJECTION THERapy FOR VICESICuREtAL REFUX

DESCRIPTION
Endoscopic treatment of vesicoureteral reflux disease was first described in 1981 by Matuschek using polytetrafluoroethylene (PTFE) paste at the ureteral orifice. The primary principle behind injection therapy is to endoscopically inject a bulking agent beneath the ureteral orifice, which then helps to counter the dilating effect of voiding. The technique involves placement of the needle approximately 2 mm distal to the 6 o’clock position of the ureteral orifice. The objective is to create a “valve” like mound appearance of the ureteral orifice. Agents used for endoscopic correction of ureteral reflux should be nontoxic, cause minimal local inflammation, not migrate to other organs, and should be easy to inject. Broadly they can be categorized into two main categories: Nonoxynol and autologous. PTFE (Teflon), bovine collagen, deoxantrix hyaluronic copolymer (Deflux), and silicone are all examples of nontoxic materials. Chondrocytes, fat, collagen, and muscles are some of the autologous materials that have been used (Image Q).

REFERENCE

INSECT BITE, PENIS AND SCROTUM

DESCRIPTION
Insect bites and stings are typically acute processes with rapid onset of various symptomatologies, including pain, pruritus, signs of ecchymosis, and edema preceding exfoliating dermatitis. While this is a benign process requiring only analgesics and antihistamines for its treatment, it is important to rule out pathologic entities such as testicular torsion or cancer.

REFERENCE

INTERMITTENT HORMONAL THERAPY (IHT/INTERMITTENT ANDROGEN DEPRIVATION (IAD))

DESCRIPTION
The role of testosterone and prostate cancer has been well established; the role of androgen deprivation therapy (ADT) is to achieve serum testosterone levels similar to that induced by surgical castration. The impact of ADT in patient survival is not well known and the ideal serum testosterone level is debated. Intermittent ADT is an alternative to continuous ADT. ADT is continued until PSA reaches a nadir level. ADT is then stopped and restarted when PSA rises to pre-treatment levels. In general, intermittent ADT is better tolerated and improves overall quality of life when compared to standard ADT. There is fair evidence to recommend use of IAD instead of continuous androgen deprivation (CAD) for the treatment of men with relapsing, locally advanced, or metastatic prostate cancer who achieve a good initial response to androgen deprivation. This recommendation is based on evidence against superiority of either strategy for time-to-event outcomes and substantial decrease with IAD in exposure to androgen deprivation, resulting in less cost, inconvenience, and potential toxicity.

REFERENCES

International Germ Cell Cancer Collaborative Group: Classification: A prognostic factor based staging system for
INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)

DESCRIPTION: A patient self-scoring instrument used for assessment of symptom severity in men with LUTS. The symptoms are scored from 0 (0–7), moderate (8–19), to severe (20–35); the score can also be used to measure treatment response. The I-PSS uses the same 7 questions as the AUA Symptom Index for BPH with the addition of the disease-specific QoL question (known as the bother score), scored on a scale from 0–6 points (delighted to terrible). (See Section VII: “AUAA Symptom Index for BPH” and “The I-PSS Appendix.”)


INTERSTITIAL NEPHRITIS

DESCRIPTION: Acute interstitial nephritis is most commonly caused by drugs, but autoimmune diseases (eg, lupus or sarcoidosis), Steroids are medication or treating the underlying infection or symptoms. Treatment involves stopping the offending drug or class of drugs. Nonspecific symptoms and medications such as analgesics, anticonvulsants, and antibiotics are typically caused by long-term exposure to medications such as analgesics, anticonvulsants, and Chinese herbal medications; heavy metal exposure; chronic interstitial nephritis is typically caused by chronic urinary infection or condition (eg, lupus or sarcoidosis). Steroids are controversial in treating acute interstitial nephritis but they may benefit chronic interstitial nephritis; most cases resolve spontaneously, although persistent renal dysfunction may remain.


INTRACYTOPLASMIC SPERM INJECTION (ICSI)

DESCRIPTION: An assisted reproduction technique (ART) in which a single spermatozoon is injected into the cytoplasm of an oocyte. This technique is typically utilized in males with severe oligospermia or azoospermia, as the cost is high. (See also Section D: “Assisted Reproductive Techniques (ART).”)


INTRAOPERATIVE FLOPPY IRIS SYNDROME (IFIS)

DESCRIPTION: The term of intraoperative observations of fibril iris struma that undulates and billows in response to ordinary intraocular fluid currents, a propensity for the floppy iris to prolapse toward the phacochromatization (tip and incision, and progressive intraoperative pupil constriction. This syndrome has been associated with a dislocated therapy in men with BPH, especially tamoxifen and is due to relaxation of the dilator muscle. Discontinuation of tamoxifen appears to be unpredictable and may not reliably reduce the severity. To mitigate the intraoperative problems, pharmacologic and mechanical strategies are used.

REFERENCE: Friedman AB. Tamoxifen and the intraoperative floppy iris syndrome. JAMA. 2009;301(1):244–245.

INTRAUTERINE INSEMINATION (IUI)

DESCRIPTION: An ART in which the placement of spermatozoa that have been separated from the seminal fluid are placed into the endometrial cavity through a small catheter. Typically used to treat male factor infertility caused by oligospermia and abnormalities of semen volume or viscosity. Also used with cervical stenosis or as fertility cervical tumors in femalae. (See also Section D: “Assisted Reproductive Techniques (ART).”)


INTRINSIC SPHINCTER DEFICIENCY (ISD)

DESCRIPTION: ISD is one of many components that contribute to stress urinary incontinence (SUI) and is defined as the loss of coaptation and compression of the urethra in its length. Its etiology is usually multifactorial. ISD in women may occur simultaneously with urothelial hypermobility, but should be differentiated, as the latter is an anatomic cause of SUI and not synonymous with ISD. After radical prostatectomy, ISD caused by ISD in most cases, the clinical parameters for ISD are loosely defined as a Valvular leak point pressure < 20 cm H2O or a maximal urethral closure pressure < 20 cm H2O, consensus is lacking.

CAUSES:
- Complete loss of urethral tone (catheter trauma, surgical trauma)
- Pudendal nerve dysfunction and denervation of the mid-urethral complex (external sphincter)
- Erogenic deficiency (resulting in mucosal changes effecting coaptation)
- Skene’s (anterior) dysfunction and nonsteroid skeletal muscle
- Rectal (puborectalis) and pelvic floor dysfunction
- Symmetrical injury during RP or other transurethral procedure
- Traumatic injury (pelvic fracture

TREATMENT:
- Conservative management including Kegel exercises and biofeedback
- Pelvicalyceal and needles suspension; periurethral bulking agents; synthetic (mesh) urethral sling; fascial urethral sling; artificial urinary sphincter
- Male: Male urethral artificial urinary sphincter


INVERTED PAPILLOMA, BLADDER

DESCRIPTION: An uncommon tumor of the urinary tract characterized by proliferating urothelium arranged as inverting and rests with an intact overlying urothelium. Inverted papillomas is thought to be a benign lesion but because of reports of multiplicity, recurrence, and associated TCC have been seen in the literature. Its management has been controversial (Image 1).


INVERTED PAPILLOMA, ÜRETEN RENAL PELVIS

DESCRIPTION: Consisted by most researchers to be benign, this lesion can coexist with malignant tumors. These rare, benign lesions have a presentation similar to that of other upper tract papillomas. Papillary fronds project opposite into the mucosa, appearing as smooth-surfaced, pedunculated, or sessile lesions of the urethra. There is a strong male predominance (91%). The lesions are typically small (< 3 cm), pedunculated, and project. Muscular invasion is not seen microscopically. Inverting conds and rests of urothelial cells continuous with the urothelium is a typical finding. The etiology is unknown, but probably generated by reaction to inflammation. Although benign, the lesions have a high association with urothelial carcinoma (TCC). Staging is by unnecessary for direct visualization and biopsy. Treatment has been nephroureterectomy; however, local excision is possible, but careful follow-up for other sites of cancer along the urinary tract is essential.

JOINT REPLACEMENT, UROLOGIC CONSIDERATIONS

DESCRIPTION

Originaly observed by Jarisch in 1895 and later by Herxheimer and Kraus, this reaction occurs after patients are given mercury for the treatment of syphilis. The reaction is now associated with the antimicrobial treatment of syphilitic infections such as leptospirosis, Lyme disease, tick-borne relapsing fever, and also syphilis. The reaction mostly occurs within 12–24 hr after treatment, and presents with symptoms such as rigors, malaise, headache, hypertension, and sweating. The reaction may be caused by a release of endotoxins or a transient elevation of cytokines, and it may be prevented with TNF-α antibodies or vaccine.

REFERENCE


Increased Risk of Hematogenous Total Joint Infection

Patients during the 1st 2 yr after prosthetic joint replacement

Increased Risk of Bacteremia Associated with Urologic Procedures

Any stone manipulation (includes shock-wave lithotripsy)

Any procedure with tranavascular access into urinary tract (does not include简单的 excision or percutaneous drainage procedure)

Any endoscopic procedures of upper tract (jeter and kidney)

Any procedure that includes bowel segment or transternal prostate biopsy

Any procedure with entry into the urinary tract (except for urethral catheterization) in individuals with higher risk of bacterial colonization

Indwelling catheter or indwerrant catheterization

Indwelling urethral stent

Urinary retention

History of recent recurrent urinary tract infection or prostatitis

Urinary diversion

Recommended antimicrobial regimens:

- A single-system level dose of a quinolone (eg, ciprofloxacin, 500 mg; levofloxacin, 500 mg; ofloxacin, 400 mg PO 1–2 hr preoperatively).
- Ampicillin 2 g IV (or vancomycin 1 g IV over 1–2 hr)
- A single systemic level dose of a quinolone (eg, ciprofloxacin, 400 mg; levofloxacin, 400 mg; moxifloxacin, 400 mg PO 1–2 hr preoperatively)
- Ampicillin 2 g IV (or vancomycin 1 g IV over 1–2 hr for patients allergic to ampicillin)

Recommended prophylactic agents for patients at risk for bacteremia:

- Antibiotic prophylaxis may be indicated to reduce the risk of hematogenous joint infection in patients who fit the criteria for increased risk of total joint infection and who have an increased risk of bacteremia and who meet the [7070] criteria of bacteremia.
- Antibiotic prophylaxis may be indicated to reduce the risk of other infections. Based on AUA Guidelines: Best Practice Policy Statement on Urologic Antimicrobial Prophylaxis

Increased Risk of Urinary Infection

Any procedure with entry into the urinary tract

Recommended prophylactic agents for patients at risk for urinary infection:

- Antibiotic prophylaxis may be indicated to reduce the risk of urinary infection in patients who fit the criteria for increased risk of urinary tract infection and who have an increased risk of bacteremia and who meet the [7070] criteria of bacteremia.
- Antibiotic prophylaxis may be indicated to reduce the risk of other infections. Based on AUA Guidelines: Best Practice Policy Statement on Urologic Antimicrobial Prophylaxis

TREATMENT

Recommended antimicrobial regimens:

- A single-system level dose of a quinolone (eg, ciprofloxacin, 500 mg; levofloxacin, 500 mg; ofloxacin, 400 mg PO 1–2 hr preoperatively).
- Ampicillin 2 g IV (or vancomycin 1 g IV over 1–2 hr for patients allergic to ampicillin)
- A single systemic level dose of a quinolone (eg, ciprofloxacin, 400 mg; levofloxacin, 400 mg; moxifloxacin, 400 mg PO 1–2 hr preoperatively)
- Ampicillin 2 g IV (or vancomycin 1 g IV over 1–2 hr for patients allergic to ampicillin)

For some procedures, additional or alternative agents may be considered for prophylaxis against specific organisms and/or other infections.
JUVENILE GANGRENOUS VASCULITIS, SCROTAL (PYODERMA GANGEROSUM)

DESCRIPTION


Microphallic, cryptorchidism, blindness, and deafness are also associated conditions. Testes are typically hypogonadal with anosmia, hypogonadotropic hypogonadism with anosmia, caused by failure of Kallmann syndrome.

Also called primary ciliary dyskinesia syndrome, this syndrome is characterized by situs inversus, chronic sinusitis, otitis media, airway disease, and immotile spermatozoa leading to infertility. The absence of the inner and outer sperm axoneme of cilia is the primary pathology. Most men have live but immotile spermatozoa and are infertile, whereas some have motile spermatozoa but immotile cilia. Women have decreased fertility, with <50% completing pregnancy. This is the most common of a group of inherited ciliary defects that lead to respiratory disorders called primary ciliary dyskinesias. ICSI may be used for reproduction, but genetic counseling should be offered.

Also known as hyponadism with anosmia, caused by failure of GnRH secretion by the hypothalamus, leading to testicular failure. KAL1, encoding the extracellular subunit of the GnRH receptor, is responsible for the X-linked recessive form of the disease. It is a cause of male infertility due to the defect in the short arm of the X chromosome, and has variable inheritance and penetrance. Anosmia, cleft palate, renal anomalies, microphthalmus, cryptorchidism, blindness, and deafness are also associated conditions. Notes are typically small. Delayed puberty is often an initial presenting sign.


REVIEWS


A classification system developed by Kelami to define the severity of penile curvature. The system consists of a grading system from 1–3; Grade 1, curvature of ≤90°; grade 2, curvature of 90–45°; and grade 3, >45° curvature. (See also Section I: “Penile, Curvature and/or Pain.”)

The incidence of testicular cancer is generally used as a dissociative anesthetic compound by licensed anesthesiologists. When used recreationally, it can cause hallucinations, delirium, and thought
disorders. It has been seen in increase in use in young adults. Ketamine abuse can cause urinary tract changes. These include findings of bladder trabeculation by urodynamic studies.

**REFERENCE**


**KUBRICK TEST**

**DESCRIPTION** A test designed to evaluate circulating immune factors, as an aid to diagnosing causes of infertility. Solutions of serum from both partners are combined with semen samples in a medium with an agglutinating protein. Agglutination will occur if antibodies in the serum are reactive against the sperm. Controls are usually also run with the samples to prevent errors.


**KIDNEY, METASTASIS TO**

**DESCRIPTION** Kidney metastases may present as a renal mass and grossly appear as a renal primary neoplasm. Occurs most often at autopsy, with an incidence of about 7%. They are frequently asymptomatic, but flank pain, hematuria, or hemorrhage may occur. Common primary tumors are lung (bronchogenic carcinoma most common), ovary, bowel, breast, and lymphoma. Virtually any origin is possible.


**KIDNEY, SUPERNUMERARY**

**DESCRIPTION** One of the least common genitourinary anomalies, this mass of renal tissue has no parenchymatous connection with the definitive kidney (unlike a horseshoe kidney). The supernumerary kidney is usually in a caudal position relative to the normal kidney and is rarely in a more cephalad position. The kidney is usually smaller or hypoplastic than a normal kidney and can function normally or not function at all. The ureter can insert into a normal ureter or bladder. It is usually associated with other GU anomalies, such as duplicated renal pelvis, vesicoureteral reflux, and duplicated female urethra. Treatment is unnecessary unless disease is present. (See also Section I: Renal Ectopia and Renal Ureteral Anomalies.)


**KLINFEHLER SYNDROME**

**DESCRIPTION** A syndrome characterized by small, firm testes, gynecomastia, and elevated urinary gonadotropins. It is present in 1 in 600 male births. Usually presents as incomplete virilization, infertility, or rarely as male pseudohyphardrophtyndrom. Menstrual irregularity and low bone mineral density (BMD) are associated. A testicular biopsy usually shows sclerosis of tubules. The condition is caused by a nondisjunction of the melotic chromosome, resulting in XXY karyotype and its variants. FSH is markedly elevated. Azoospermia is traditionally described on semen analysis, but recent series indicate that sperm can be found in over 50% of men with Klinefelter syndrome; thus, these men are not always sterile. Recent evidence suggests that children with Klinefelter syndrome are born with spermatogonia and lose large numbers of germ cells during puberty. No treatment can improve spermatogenesis. (See also Section II: “XY Syndrome.”)


**KLIPPEL–TRENAUNAY–WEBER SYNDROME**

**DESCRIPTION** Klippel–Trenaunay–Weber syndrome was first described by French physicians in 1900. It consists of cutaneous vascular malformations in combination with soft tissue and bone hypertrophy. The defects are present at birth and most commonly involve the lower extremities. The vascular lesions may develop before or after birth. A study of 214 patients by Hussain et al., 30% had genital cutaneous involvement. Of these patients, 36% developed intractable bleeding. Surgical excision of these vascular malformations was associated with significant blood loss.


**KOYLE STENT**

**DESCRIPTION** The Koyle stent (Cook Medical Inc., Bloomington, IN, USA) is used for stenting the urethra after hypospadias repair. It has an 8 Fr circumference in the fossa navicularis to minimize distal meatal or urethral ischemia while providing excess tubing externally to allow drainage into a 2nd or outside stent while keeping the inside stent dry to allow healing.


**KRUGER STRICT SPERM MORPHOLOGY**

**DESCRIPTION** Some fertility experts use the test to decide between intrauterine insemination (IUI) and in vitro fertilization (IVF) although the test is controversial. This test examines sperm morphology more in-depth than the standard WHO method. Finally sediment sperm are smeared on a slide and stained. Sperm are judged as normal based on the following criteria:

- Head must be oval in shape with smooth contours, 4.5–6 μm in length and 2.5–3.5 μm wide with the acrosome taking up 40–70% of the head.
- Neck and mid-piece must have no abnormalities and a cytoplasmic droplet (a remnant from sperm production) if present must not be larger than 1/2 the size of the head.
- Tail must not be coiled or bent and should not have a droplet at the end.

After 200 individual sperm are counted at 1,000 X, the percent normal forms are calculated. The Kruger prognosis is based on the following scale:

- ≤15% normal
- 15–14% normal
- Normal range: Good prognosis
- Sub optimal range: Prognosis is fair to good, however, the lower the percent normal the lower the chance of successful fertilization
- 0–4% normal
- Poor prognosis: IVF usually needed

LABIAL ADHESIONS AND FUSION

DESCRIPTION
Complete (fusion) or partial adhesion of labia minora. Low estrogen levels contribute to a thin atrophic lining, which is easily denuded and later heals with adhesions. The condition is acquired, not born at birth, and occurs in prepubertal girls and postmenopausal women. focal coiling as age, trauma, hormones, and sexual abuse may be inciting factors. It may cause voiding dysfunction in some cases, with resulting hydronephroplasty.

SYNONYMS
Acquired postinflammatory cohesion of the labia minora
Vulvar fusion
Synchiae of the vulva

TREATMENT
- Conjoined labial frenum locally applied
- Surgical treatment for severe cases

REFERENCE

LACTATE DEHYDROGENASE (LDH), UROLOGIC CONSIDERATIONS
DESCRIPTION
LDH is a cellular enzyme useful in monitoring the treatment of GCT. It tends to have low specificity (further impaired in smokers), and therefore must be correlated with other clinical markers in the evaluation of male germ cell tumors.

CONSIDERATIONS
LAPIDES CLASSIFICATION OF VOIDING DYSFUNCTION
DESCRIPTION
A historical system for categorizing neurogenic voiding dysfunction into 5 areas:
- Sensory neurogenic bladder: Intermittent altered sensation during bladder filling; delayed bladder sensation on voiding
- Motor neurogenic bladder: Destruction of parasympathetic motor innervation to the bladder results in painful overdistension initially and inability to initiate and maintain micturition. Common processes include diabetes mellitus, tobin disorders, and perineum anemia.
- Parasympathetic bladder: Intravesical and interstitial cystitis: can be present neonatally in up to 25% of males.
- Reflex neurogenic bladder: Complete interruption of sensory and motor pathways between the sacral spinal cord and brainstorm leads to lack of bladder sensation and inability to voluntarily micturate. Common processes include trauma and transverse myelitis.
- Autonomous neurogenic bladder: Complete motor and sensory separation from the sacral spinal cord leads to inability to voluntarily micturate and lack of reflex bladder activity and bladder sensation.

REFERENCE

LASER TECHNOLOGIES AND UROLOGIC APPLICATIONS
DESCRIPTION
The use of laser (short for “light amplification by stimulated emission of radiation”) in urology has gained widespread acceptance. The primary mechanism of laser operating systems is based on the process of stimulated emission of radiation where excited electrons rapidly decay and emit photon energy, which leaves a resonator cavity as a coherent laser beam. Lasers impart 4 different effects: Thermal, mechanical, photomechanical, and tissue welding effects. The thermal effect is most commonly employed. The laser light energy is absorbed and transformed into heat. The heat denatures proteins at 42–45°C, shrinks arteries and veins at 70–90°C, and coagulates the tissue at 100°C. After water has evaporated from the tissue, the temperature rapidly rises, with carbonization at 250°C, and vaporization occurs at 300°C. Mechanical effects are used to create a plasma bubble that expands rapidly to disrupt stones. Photomechanical effects involve laser activation of specific drugs or compounds taken up by the tissue and tissue welding relies upon collagen cross-linking with materials activated by lasers of specific wavelength.

CONDITIONS such as nephrolithiasis, benign prostatic obstruction (BPO), bladder cancer, kidney cancer, urethral cancer, and stricture disease have all been treated by laser therapy. Some modern laser systems include potassium titanyl phosphate (KTP), holmium:yttrium-aluminum-garnet (Ho:YAG), and semiconductor diode lasers. The frequency-doubled, short-pulse Nd:YAG (FREDDY) laser is a double-pulse Nd:YAG, Ho:YAG, KTP:YAG, semiconductor diode, or CO2.

The laser operating systems are based on the process of stimulated emission of radiation: “Stimulated emission of radiation” is derived from the Greek word “stima,” meaning “to excite.” The laser operating systems is based on the process of stimulated emission of radiation: “Stimulated emission of radiation” is derived from the Greek word “stima,” meaning “to excite.” The thermal effect is most commonly employed. The laser light energy is absorbed and transformed into heat. The heat denatures proteins at 42–45°C, shrinks arteries and veins at 70–90°C, and coagulates the tissue at 100°C. After water has evaporated from the tissue, the temperature rapidly rises, with carbonization at 250°C, and vaporization occurs at 300°C. Mechanical effects are used to create a plasma bubble that expands rapidly to disrupt stones. Photomechanical effects involve laser activation of specific drugs or compounds taken up by the tissue and tissue welding relies upon collagen cross-linking with materials activated by lasers of specific wavelength.

LAURENCE–MOON–BARDET–BIEDL SYNDROME
DESCRIPTION
This autosomal recessive disease was initially described in 1860 by Laurence–Moon and received a more exact description in 1920 by Bardet–Biedl. A wide variety of manifestations include retinal pigmentary dystrophy (previously termed retinitis pigmentosa), postnatal polydactyly, obesity, mental retardation, and hypogonadism. More recently, renal abnormalities have been described, including chronic glomerulonephritis, characteristic cystic tubular disease, lower urinary tract malformations, and defects of tubular concentrating ability. Renal failure is the major cause of morbidity and early mortality. Underdiagnosed or overlooked cases can be present neutronally in 1 to 2% of males.

SYNONYMS
- Laurence–Moon syndrome: More general, including all of the above description
- Laurence–Moon–Bardet–Biedl syndrome: Much rarer; differs with the above description, including progressive spastic paraparesis and distal muscle weakness but without proptosis

REFERENCES
Bakal A, Winter AR, H terms. A wide variety of manifestations include retinal pigmentary dystrophy (previously termed retinitis pigmentosa), postnatal polydactyly, mental retardation, and hypogonadism. More recently, renal abnormalities have been described, including chronic glomerulonephritis, characteristic cystic tubular disease, lower urinary tract malformations, and defects of tubular concentrating ability. Renal failure is the major cause of morbidity and early mortality. Underdiagnosed or overlooked cases can be present neutronally in 1 to 2% of males.

LAZY BLADDER SYNDROME (NURSE’S BLADDER)
DESCRIPTION
First described by Spawin in 1962, this condition occurs when children exhibit hold behavior and void infrequently. Thought to be caused by the continued voluntary suppression of the normal desire to void, it is more common in girls. Patients are prone to develop UTIs due to urinary stasis and often have problems with constipation. Some patients have overflow or stress incontinence. The VCGU shows a large smooth-walled bladder, and US of the upper tract is usually normal. Voiding studies show large bladders with decreased sensation during bladder filling, low pressures, and long postvoid residuals. Timed voiding studies, antibiotic suppression,
LeBAG NEobladder

**DESCRIPTION** This is a modification of the classic orthotopic neobladder, which uses only 1 ileal limb instead of 2. The detubularized colon and a single segment of ileum can be joined using metal staples to create a broad intestinal plate, which is then converted into a pouch with a ureterointestinal and urethral anastomosis.


**LeDuc Ureteral Anastomosis**

**DESCRIPTION** The end of the small bowel segment is opened 4–5 cm and a longitudinal incision is made in the mucosa, which is then raised. At the distal end of this incision, a hole is made through the wall of the ureter. The ureter is pulled through this opening and laid in the mucosal incision. The mucosa is then sutured to the side of the ureter.


**LEIGYOMATOSIS, HEREDITARY**

**DESCRIPTION** Familial cancer syndrome of a urothelial tract and skin. The syndrome may result from BEjemmal syndrome, a germline or somatic event that leads to loss of function of the FBEM2 gene. Familial cancer syndrome of the urothelial tract includes a renal tumor, skin lesions, and dysplasia of the eye, skin, and testis. Lesions are usually seen in women 20–35 yo. Given their aggressive nature, the prompt surgical resection of renal tumors is recommended. (See also Section II: “Renal Neoplasms.”)


**LEOPARD SYNDROME**

**DESCRIPTION** An autosomal dominant condition similar to Noonan syndrome, except for multiple lentigines (melanin pigment accumulation within the dermis and epidermis). LEOPARD syndrome is the mnemonic for lentigines, eye anomalies, cardiac anomalies, pericardial effusions, adenopathy, renal anomalies, and dental abnormalities. Prominent lentigines in children, including a small penis and small, often undescended testicles, is the most common association. Hypoplastic and delayed puberty may also be found.

**SYNONYMS**

- Multiple lentigines
- Progressive cardiomyopathy

**TREATMENT** Orthoptics, repair of hypoplastic


**LERICHE SYNDROME**

**DESCRIPTION** Described in 1923 as symptoms characteristic of thrombotic occlusion of the terminal aorta, this syndrome is caused by atherosclerosis of the arterial wall, with thrombus and gradual occlusion. Symptoms include fatigue of both lower limbs, symmetrical atrophy of lower extremities, pallor of legs, and an inability to maintain a stable position due to inadequate arterial flow to the penis (hypogastric arterial obstruction). Gradual occlusion allows for collateral circulation; therefore, acute symptoms are unlikely.

**SYNONYM** Gradual thrombotic obliteration of the abdominal aorta and iliac arteries

**TREATMENT** Bypass graft from the aorta to iliac or common femoral arteries

LEUKOPLAKIA, PENIS

TREATMENT
- If the lesion is the isolated site of relapse, local irradiation (up to 20 Gy) to both testes and reinstitution of systemic chemotherapy can be curative.
- Therapy can cause irreversible damage to seminiferous tubules and Leydig cells.
- Patients can develop hypergonadotropic hypogonadism and low testosterone with azoospermia.

REFERENCES

LEUKOPLAKIA, PENIS

DESCRIPTION
Saffory or whitish plaques with hyperkeratosis, papulexerosis, and hypertrophy of the squamous intra-epithelium, with edema and papillary proliferation. The condition often involves the penile mucosa and has been associated with in situ squamous cell carcinoma (SCC) and verrucous carcinoma.

TREATMENT
- Eliminate chronic irritation
- Circumcision
- Surgical excision with periodic biopsy of incompletely excised lesions

REFERENCES

LEUKORRHEA

DESCRIPTION
Generally refers to nonspecific, mucous, white, or yellowish vaginal discharge in the absence of any pathological cause. The quantity and quality vary among individuals, and mild irritative symptoms can be common. Leukorrhea is also seen during infancy secondary to maternal estrogens, as well as during puberty secondary to estrogen surge. Leukorrhea is at all that is necessary if the cervical and vaginal exam is normal, vaginal pH is normal (<4.5), and there are normal findings on microscopic and a negative amine test. (See also Section II: “Vaginosis”; Section III: “Normal findings on microscopy and a negative amine test.”)

REFERENCES

LICHEN NITIDUS, PENIS

DESCRIPTION
An uncommon chronic inflammation appearing as flesh-colored papules with sharp demarcations and flat, shiny, and slightly elevated surfaces. The etiology is unknown, but it is believed to be a variant of lichen planus. Histologically, lichenoides, histiocytes, and melanophages form a ball-like structure covered by epidermis with a characteristic claw-like projection of the rete ridges. The condition is usually asymptomatic.

TREATMENT
- • Step healing is common
- Oral histamines
- Topical antivirals and topical corticosteroids may be helpful

REFERENCE

LICHEN PLANUS, PENIS

DESCRIPTION
An uncommon pruritic lichenoid dermatologic eruption that occurs almost exclusively on the penile glans, but may also involve the shaft, scrotum, and inner surfaces of the thighs. It is characterized by patches of violaceous, flat-topped papules. Histologically, there can be degeneration of the basal cell layer keratinocytes and dense infiltration of lymphocytes in the upper dermis hugging the epidermis. Multiple lesions occur and can ulcerate. Differential diagnoses include secondary syphilis, bowel disease, psoriasis, lichen sclerosus et atrophicus, and squamous cell carcinoma (SCC). There is no specific treatment; symptomatic relief is obtained through antihistamines, zastatic, and topical lotions.

REFERENCES

LICHEN SCLEROSIS ET ATROPHICUS

DESCRIPTION
An uncommon cutaneous disorder with a female predominance. Early lesions are characterized as white macules, which may coalesce into patches, or flat, white, or pink-depressed papules and plaques. Confluence of the papules and marked hyperkeratosis and atrophy may develop. Extra-genital areas (eg, arms, shoulders, trunk, neck, and face) are less commonly affected in men. Dysuria, pruritus, and pain are associated with the disease process. Squamous cell carcinoma (SCC) has been reported to occur.

SYNONYMS
- Lichen sclerosus
- Lichen sclerosus et atrophicus
- The late stage evolves into balanitis xerotica obliterans

TREATMENT
- Circumcision
- Topical treatments for nongenital areas

REFERENCES

LICHEN SIMPLEX CHRONICUS

DESCRIPTION
Localized chronic pruritus with patches of dermographism, resulting from chronic scratching/scratching. Common sites are the periumen, thigh, scrotum, and vulva. The lesions appear as multiple oval plaques that become thickened and scaly. There is a whitish gray discoloration caused by lichenification and hyperkeratosis. The skin may become more susceptible to secondary infection and allergic contact dermatitis. Etiologies include irritants (irritant and allergic), infection, and underlying dermatitis. Microscopically, the lesions resemble chronic dermatitis with hyperkeratosis and parakeratosis. Diagnosis is usually clinical, but biopsy may be necessary.

SYNONYM
Circumscibed neurodermatitis

TREATMENT
- • Break the scratch itch cycle
- Stop all irritants
- Sit baths or soaks
- Open wet compresses to affected areas
- Systemic antihistamines and/or sedating medications may be necessary to lessen the itching
- Topical and occasionally systemic steroids are necessary

REFERENCES

LICHEN–GREGOIR URETERAL REIMPLANTATION

DESCRIPTION
This extravesical, less invasive repair does not disrupt the ureteral trigone continuity. A 4–5 cm trough is created by dissecting the mucosa of the mucosa, and the mobilized ureter is placed in the trough with the detrusor closed over it.

REFERENCE

LIDDLE’S SYNDROME

DESCRIPTION
Liddle’s syndrome is an autosomal dominant disorder of the sodium channels of the collecting duct. Mutations in the epithelial sodium channels in the kidney result in increased activity and severe hypertension is typically the result. Features of hypokalemia and metabolic alkalosis can also occur mimicking primary hyperaldosteronism. Treatment generally focuses on a low salt diet in conjunction with a potassium sparing diuretic.

REFERENCES
LIFE EXPECTANCY, UROLOGIC CONSIDERATIONS

DESCRIPTION: Life expectancy is commonly used by urologists when determining therapy for localized prostate cancer, as age may influence choice of treatment.

<table>
<thead>
<tr>
<th>Current Age</th>
<th>Life Expectancy (yr) Male</th>
<th>Life Expectancy (yr) Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>17.19</td>
<td>19.89</td>
</tr>
<tr>
<td>66</td>
<td>16.48</td>
<td>19.10</td>
</tr>
<tr>
<td>67</td>
<td>15.77</td>
<td>18.32</td>
</tr>
<tr>
<td>68</td>
<td>15.08</td>
<td>17.55</td>
</tr>
<tr>
<td>69</td>
<td>14.40</td>
<td>16.79</td>
</tr>
<tr>
<td>70</td>
<td>13.73</td>
<td>16.05</td>
</tr>
<tr>
<td>71</td>
<td>13.08</td>
<td>15.32</td>
</tr>
<tr>
<td>72</td>
<td>12.44</td>
<td>14.61</td>
</tr>
<tr>
<td>73</td>
<td>11.82</td>
<td>13.91</td>
</tr>
<tr>
<td>74</td>
<td>11.21</td>
<td>13.22</td>
</tr>
<tr>
<td>75</td>
<td>10.62</td>
<td>12.55</td>
</tr>
<tr>
<td>76</td>
<td>10.04</td>
<td>11.90</td>
</tr>
<tr>
<td>77</td>
<td>9.48</td>
<td>11.26</td>
</tr>
<tr>
<td>78</td>
<td>8.94</td>
<td>10.83</td>
</tr>
<tr>
<td>79</td>
<td>8.41</td>
<td>10.03</td>
</tr>
<tr>
<td>80</td>
<td>7.90</td>
<td>9.49</td>
</tr>
<tr>
<td>81</td>
<td>7.41</td>
<td>8.86</td>
</tr>
<tr>
<td>82</td>
<td>6.94</td>
<td>8.31</td>
</tr>
<tr>
<td>83</td>
<td>6.49</td>
<td>7.77</td>
</tr>
<tr>
<td>84</td>
<td>6.06</td>
<td>7.26</td>
</tr>
<tr>
<td>85</td>
<td>5.65</td>
<td>6.77</td>
</tr>
<tr>
<td>86</td>
<td>5.26</td>
<td>6.31</td>
</tr>
<tr>
<td>87</td>
<td>4.88</td>
<td>5.87</td>
</tr>
<tr>
<td>88</td>
<td>4.55</td>
<td>5.45</td>
</tr>
<tr>
<td>89</td>
<td>4.23</td>
<td>5.06</td>
</tr>
<tr>
<td>90</td>
<td>3.92</td>
<td>4.69</td>
</tr>
</tbody>
</table>

REFERENCE

LIPOMA, BLADDER

DESCRIPTION: Bladder lipoma is a rare entity. It can be associated with a pelvic lipoma, and has been reported to cause bladder outlet obstruction. A capsule surrounds the homogenous, sharply margined fat, if it is benign and must be distinguished from liposarcoma, angiolipoma, and cystic teratoma, usually by CT. Treatment is by surveillance, unless otherwise abnormal in children.

REFERENCE

LIPOMA, SPERMATIC CORD

DESCRIPTION: Foreign infiltrated preperitoneal fat that can project down the cord. Accounts for up to 90% of spermatic cord tumors and is most commonly seen in adults. Histologically, it contains adipose, fibroadipose, fibromyxoid, myxoid liposarcoma, and myxoid liposarcoma. The lesion can present as a mass, and must be distinguished from adenomatosus tumor, leiomyoma, fibroma, lipoma, leiomyosarcoma, and fibrosarcoma.

See also Section I: “Spermatic Cord Mass.” Complete excision at time of surgery is recommended.

REFERENCE

LIPOMATOSIS, PELVIC

DESCRIPTION: Pelvic lipomatosis was first described in 1939 as an outgrowth of fat in the perineal and perirectal regions that can cause compression of the lower urinary tract and lead to urgency. Rare disease found primarily in men in the 3rd-6th decades of life. Approximately 2/3 of patients are African American, with an 18:1 male to female ratio. Lipomatous tissue is composed of mature adipose and may be associated with inflammation. Histopathologically, it is found to be dense, vascular, unencapsulated lipomatous tissue that commonly envelops the pelvic viscera. It differs from a simple lipoma by the fact that it does not arise from a single focus, is not encapsulated, and does not expand centrifugally. Clinical features vary from urinary frequency to constipation. Pelvic lipomatosis has been associated with a higher incidence of hypertension. On a plain abdominal r-ray, it presents with radiolucency of the pelvic perivisceral area. Other radiographic signs include an elongation and elevation of the bladder, and the rectum and sigmoid colon. There is widening of the rectovesical space and increased lucency of the pelvic sidewalls. On computed tomography, a full bladder has an abnormal shape (banana shape) and position (superiorly as well as anteriorly). Cystoscopy should be performed, as there are reports of associated cystitis glandularis. Surgical removal of the lipomatosis may be feasible in selected few patients. For those patients with obstructive uropathy, treatment options include ureteral stenting, nephrostomy tubes, ureteral reimplantation, or urinary diversion. Pelvic lipomatosis is done with caution as the normal anatomic planes are disrupted by the infiltrating fat.

REFERENCE

LIPOMENINGOCELE, UROLOGIC CONSIDERATIONS

DESCRIPTION: A meningocele associated with an underlying lipoma. This condition belongs to the family of occult spinal lipomas in which the formation of the spinal column is affected but does not result in an open vertebral canal. Outward signs and symptoms may be subtle, and the neurologic exam may be normal. As children get older, they may present with dryness, recurrent UTIs, or fecal soiling. In children incontinence (incontinence after initial period of normal. As children get older, they may present with features vary from urinary frequency to constipation. Pelvic lipomatosis has been associated with a higher incidence of hypertension. On a plain abdominal r-ray, it presents with radiolucency of the pelvic perivisceral area. Other radiographic signs include an elongation and elevation of the bladder, and the rectum and sigmoid colon. There is widening of the rectovesical space and increased lucency of the pelvic sidewalls. On computed tomography, a full bladder has an abnormal shape (banana shape) and position (superiorly as well as anteriorly). Cystoscopy should be performed, as there are reports of associated cystitis glandularis. Surgical removal of the lipomatosis may be feasible in selected few patients. For those patients with obstructive uropathy, treatment options include ureteral stenting, nephrostomy tubes, ureteral reimplantation, or urinary diversion. Pelvic lipomatosis is done with caution as the normal anatomic planes are disrupted by the infiltrating fat.

REFERENCE

LIPOMENINGOCELE, UROLOGIC CONSIDERATIONS

DESCRIPTION: A meningocele associated with an underlying lipoma. This condition belongs to the family of occult spinal lipomas in which the formation of the spinal column is affected but does not result in an open vertebral canal. Outward signs and symptoms may be subtle, and the neurologic exam may be normal. As children get older, they may present with dryness, recurrent UTIs, or fecal soiling. In children incontinence (incontinence after initial period of normal. As children get older, they may present with dryness, recurrent UTIs, or fecal soiling. In children incontinence (incontinence after initial period of normal. As children get older, they may present with features vary from urinary frequency to constipation. Pelvic lipomatosis has been associated with a higher incidence of hypertension. On a plain abdominal r-ray, it presents with radiolucency of the pelvic perivisceral area. Other radiographic signs include an elongation and elevation of the bladder, and the rectum and sigmoid colon. There is widening of the rectovesical space and increased lucency of the pelvic sidewalls. On computed tomography, a full bladder has an abnormal shape (banana shape) and position (superiorly as well as anteriorly). Cystoscopy should be performed, as there are reports of associated cystitis glandularis. Surgical removal of the lipomatosis may be feasible in selected few patients. For those patients with obstructive uropathy, treatment options include ureteral stenting, nephrostomy tubes, ureteral reimplantation, or urinary diversion. Pelvic lipomatosis is done with caution as the normal anatomic planes are disrupted by the infiltrating fat.

REFERENCE

LIVER METASTASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION: The liver is a primary site for many malignant neoplasms, including those arising in the G1 tract. Stomachal carcinoma (TCC), renal cell carcinoma (RCC) and testicular carcinoma may spread to the liver, but metastasis is most commonly seen in prostate cancer. In addition to bone pain and spinal cord compression, liver metastasis can be very painful. A liver lesion itself should not affect the urinary tract, but extensive disease may be reflected in increased bilirubin and abnormal liver function studies on urine analysis.

TREATMENT
• Evaluate and treat primary tumor.
• Segmental resection or lobar ablative therapies may be appropriate (Image 9).

REFERENCE

LOBAR NEPHRONIA

DESCRIPTION: A renal mass caused by acute focal infection without liquefaction. Clinical characteristics most frequently encountered are fever, flank pain, or back pain. Uroradiographic findings in this condition can mimic a renal abscess or neoplasm. Bacterial infection (e.g., K. pneumoniae, Proteus, Pseudomonas) and Candida albicans are common causes. Appropriate medical treatment will cause the infected mass to disappear, but scarring may occur. (See also Section I: “Pyelonephritis, Acute, AAM.”)

SYNONYMS
Acute focal bacterial nephritis.

TREATMENT
• IV antibiotics
• Radiologic surveillance: CT or US

REFERENCE

LORD PROCEDURE (HYDROCELECTOMY)

DESCRIPTION: During the Lord procedure for hydrocelectomy, radical sutures are used to gather the sac around the posterior aspect of the testis and epididymis. It was initially developed in 1964 to reduce the size of postoperative hematoxia formation after hydrocelectomy. This technique does not require dissection of the hydrocele sac and therefore can be relatively bloodless. Generally this technique is recommended for thin-walled hydroceles.

REFERENCE

719
LOWE SYNDROME

DESCRIPTION Lowencephalencephalodysplasia is a rare autosomal recessive condition characterized by mental retardation, microcephaly, and a characteristic facial appearance. It is caused by mutations in the P Tillion gene on chromosome 11q23.3.

SYNONYMS P Tillion syndrome, Lowe syndrome


LYMPHANGIOMA, BLADDER

DESCRIPTION Bladder lymphangioma is a rare, benign, lymphatic malformation that presents as a solitary, encapsulated mass. It is often associated with urothelial abnormalities and may cause symptoms such as hematuria or urinary tract infections.


LYMPHANGIOGRAM, PEDAL

DESCRIPTION Pedal lymphangiogram is a radiographic examination used to visualize the lymphatic system. It involves the injection of contrast material into the lymphatic system and imaging the resulting lymphatic vessels to assess their function and structure.


LYMPHANGIOGRAM, SCROTAL

DESCRIPTION Scrotal lymphangiogram is a diagnostic procedure used to evaluate the lymphatic vessels in the scrotum. It involves injecting contrast material into the scrotal lymphatic vessels and imaging the resulting changes to assess for abnormalities.


LYMPHATIC ASCITES

DESCRIPTION Lymphatic ascites is a rare complication of lymphatic obstruction, typically seen in patients with lymphatic malformations or lymphedema. It is characterized by the accumulation of lymphatic fluid in the peritoneal cavity, leading to ascites.


LYMPHOPHAGNIOLUINOMA VENEREUM

DESCRIPTION Lymphogranuloma venereum (LGV) is a sexually transmitted infection caused by Treponema pallidum subspecies pallidum. It is typically transmitted through sexual intercourse and affects the genital tract, anus, rectum, and lymph nodes.


LYMPHOPHAGNIOLUINOMA, RETROPÉRITONEAL

DESCRIPTION Retroperitoneal lymphangioma is a rare, benign lymphatic malformation that can occur anywhere in the retroperitoneal space. It is typically asymptomatic but can cause symptoms such as pain, swelling, or palpable masses.

including HIV should be considered. Fluctuant buboes can be aspirated to reduce morbidity.

**TREATMENT**
- Doxycycline is the treatment of choice and can be aspirated to reduce morbidity.
- Alternatives and should be used for at least 3 wk.
- They involve chemotherapy for primary lesions combined with local low-dose radiation.

**REFERENCE**

---

**LYMPHOMA, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**
- Lymphoma can involve any part of the urinary tract, but is more commonly seen in the testicle and kidney.
- Lymphoma is often a cause of testicular cancer in older men. It may be a local tumor growth or a late manifestation of widespread disease.

**TREATMENT**
- Primary bladder lymphoma occurs almost exclusively in hemophiles. Lesions may be sessile or pedunculated and should be differentiated from chronic inflammatory bladder inflammation, small cell carcinoma, and a rare entity called lymphoma-like carcinoma.
- Prostate lymphoma typically presents in older men, with symptoms of bladder outlet obstruction. PSA is rarely elevated. This is usually a manifestation of systemic disease, with primary prostate disease rare.
- The differential diagnosis includes chronic inflammatory bladder inflammation, small cell carcinoma, and a rare entity called lymphoma-like carcinoma.
- Treatment: The differential diagnosis includes chronic inflammatory bladder inflammation, small cell carcinoma, and a rare entity called lymphoma-like carcinoma.

**REFERENCE**

---

**LYMPHORETICULAR MALIGNANT NEOPLASM, PENIS**

**DESCRIPTION**
- Rarely, lymphoreticular malignancies (eg, leukemia) may infiltrate the penis. Primary disease is rare, and a search for systemic disease is mandatory. The most common presentation is priapism, a painful prolonged erection. Treatment involves chemotherapy for primary lesions with focal low-dose radiation.

**REFERENCE**

---

**LYMPHOVASCULAR INVASION (LV), UROLOGIC CONSIDERATIONS**

**DESCRIPTION**
LV1 describes an important feature for many aspects of urologic oncology, because it is an adverse prognostic indicator in urothelial carcinoma of the bladder and upper tracts, prostate cancer, and testicular cancer. In upper tract UCC, it has been found to be an independent prognostic factor for disease-specific survival. In noninvasive bladder cancer, it is a relative indication for early cystectomy. In testicular cancer, it is a risk factor for reinterventional and/or systemic failure.

**REFERENCE**

---

**LYNCH SYNDROME**

**DESCRIPTION**
An autosomal dominant genetic syndrome caused by mutations in mismatch repair enzymes, most commonly MSH2 and MLH1. This creates DNA MSI (microsatellite instability) and increases the risk of colon and endometrial malignancy. An increased risk of upper tract urothelial carcinoma (UTUC) is also observed and these cases can be successfully managed with ureteroscopic treatment/surveillance. In addition, these patients are at increased risk of developing bladder lesions as well.

**SYNONYMS**
- Nevoid polyposis colorectal cancer
- Nevoid site-specific colon cancer

**TREATMENT**
- Screening for mutation can be performed via genetic testing.
- If screening is positive, surveillance colonoscopy is recommended.
- Netherlands Surveillance Protocol for specific individuals (includes regimented colonoscopies, urine cytology, upper endoscopy, and US of the endometrium).

**REFERENCE**

---

**MACRO-ORCHIDISM (MO)**

**DESCRIPTION**
Macro-orchidism (MO) is an increase of testicular volume, up to 25 mL, seen in the adult male. It is frequently associated with mental retardation with fragile X-chromosome. MO has also been described in association with bilateral testicular tumors, idiopathic precocious puberty, juvenile hypothyroidism, and, more rarely, with congenital testicular cysts (cystic testicular dysplasia). Management of MO must be conservative in all cases, and testicular biopsy must only be performed to diagnose leukemic infiltrate, carcinoma in situ, or as part of a fertility workup. MO may be related pathogenetically to some hormonal regulation mechanism or to higher seminiferous tubule sensitivity to FSH.

**REFERENCE**

---

**MAG 3 RENAL SCAN**

**DESCRIPTION**
A nuclear medicine scan is used to evaluate renal function and the presence of obstruction. MAG3 (technetium-99m mercaptoacetyltriglycine) is a renal isotope secreted by the renal tubules. Multiple images are taken over time to give anatomic details, including scanning and function of the kidney. A split differential function between the 2 kidneys is obtained. Commonly, isosulfan blue is administered to induce diuresis, and the time for the kidney to clear 1/2 of the tracer is calculated (t1/2). A 1-2 of 0–10 min indicates nonobstructive drainage, >10 min is indeterminate, and >20 min is consistent with obstruction.

**REFERENCE**

---

**MACRO HYPOSPADIAS REPAIR**

**DESCRIPTION**
The median advancement and glansplasty procedure (MAG) was first described by Budzik in 1981. After a circumferential subcoronal incision, the bridge of tissue immediately distal and dorsal to the meatus is split in a vertical fashion and...
closed in a horizontal orientation (Heineke–Mikulicz closure). The ventral edge of the new meatal opening is pulled up, and the flap is reapproximated ventrally which, in effect, advances the meatus.

**REFERENCE**

**MAINZ I, II, III POUCH URINARY DIVERSION**
**DESCRIPTION**
The MAINZ pouch (coelocystoanal) is an orthotopic pouch created by opening theoreum and 2 limbs of distal ileum, the Wigs are then sutured to create a broad intestinal plate. After a tunneled enterococcal anastomosis is made, the orificial portion of the plate is anastomosed to the male urethral stump and the plate is closed into a sphere. The MAINZ II (urogenital pouch) is an augmented valved intestine created by making a 10–12 cm rectosigmoid opening. The orificial column is configured into a U shape, and the medial plate is closed. Urines are implanted through submucosal tunnels. After securing the apex of the pouch to the sacral promontory, the remaining plate is closed. The MAINZ III is a continent cutaneous diversion created by making a 10–12 cm rectosigmoid opening. The orificial column is a transverse-descending colon pouch (transverse ascending color pouch or transverse-descending color pouch) with the pelvis. The different segment created from a transposed bowel segment embedded in the pouch wall.

**REFERENCE**

**MALACOPLAKIA, GENITOURINARY**
**DESCRIPTION**
Malacoplakia, derived from the Greek term for soft plaque, is a chronic inflammatory disease, the etiology of which remains obscure. It appears related to an underlying infectious process. It has a very low incidence and affects primarily the GU tract. The diagnosis is made by biopsy. The pathologic specimens typical of malacoplakia consist of large histiocytes known as von Hansemann cells and intracytoplasmic inclusions known as Michaelis–Gutmann bodies. The goal of treatment is to stabilize the disease process by controlling UTI. (Image 40).

**REFERENCES**

**MALARIA (BLACK WATER FEVER), UROLOGIC CONSIDERATIONS**
**DESCRIPTION**
The preclinical Plasmodium parasitism in the parotid responsible for malaria. From a urologic perspective, malaria can cause hemorrhagic gastroenteritis. Treatment includes full-dose antimalarials with supportive care. Acute renal tubular necrosis can occur if the infection is left untreated and some patients with chronic malaria develop nephritic syndrome. (See Section II: “Black Water Fever.”)

**REFERENCE**

**MALE SEXUAL FUNCTION SCALE**
**DESCRIPTION**
An 8-question sexual health inventory completed by the patient, which assesses core components of male sexual function including desire, erection, ejaculation, and satisfaction. The scale is meant to screen for sexual health in both the primary care and urogynecologic practice settings.

**REFERENCE**

**MALE SEXUAL HEALTH QUESTIONNAIRE (MSHQ) AND THE MSHQ SHORT FORM**
**DESCRIPTION**
A patient self-administered test developed in 2004, the MSHQ is a 25-question questionnaire that evaluates sexual function and satisfaction in older men with LUTS. It provides more in-depth assessment of ejaculatory functioning than previous measures of sexual dysfunction, namely the International Index of Erectile Function (IIEF). A 4-item version is called the MSHQ short form, and both forms can be used in research settings as well as in clinical practice to assess ejaculatory dysfunction. (See Section VII: “Reference Tables: Male sexual health questionnaire, Short Form.”)

**REFERENCE**

**MALROTATED KIDNEY/RENAL MALROTATION**
**DESCRIPTION**
Malrotated kidney occurs when the kidney does not rotate 90° medially during fetal development. As a result, the renal pelvis, which normally lies medial to the parenchyma, is located anterior to the parenchyma. Often a malrotated kidney is an incidental finding. Malrotation makes the kidney more susceptible to trauma, and is also commonly observed in ectopic kidneys. (See also Section I: “Renal Ectopia.”) (Image 45)

**REFERENCE**

**MARSHALL–MARCHETTI–KRANTZ (MMK) CYSTOURETHEROPEXY**
**DESCRIPTION**
A historical procedure used to repair urinary-vaginal fistulae. The flap is a well-vascularized fat pad from the labia majora and receives its blood supply from the branches of the pudendal artery. It is tunneled beneath the labia minora into the vaginal lumen, where it is used as a peritoneal graft fixated with the site of the fistula repair. It serves as a well-vascularized barrier between two bariatric layers to prevent recurrent fistula formation.

**SYNONYMS**
- Martius labial pedicle graft
- Martius labial fat pad
- Martius flap

**REFERENCE**

**MATHIEU HYPOSPADIAS REPAIR**
**DESCRIPTION**
A ventral flap is mobilized based on the dorsal blood supply, and it is transposed over the urethral plate to advance the meatus. The lateral wings of the flaps are reapproximated over the repair.

**REFERENCE**

**MATURATION ARREST**
**DESCRIPTION**
The term maturation arrest has been used to describe testicular biopsies in cases of infertility. A 2-forms of maturation arrest have been described: Spermatogenic arrest and spermatocytic (meliotic) arrest. The arrest is most frequently observed at the primary spermatocyte level. Reversible arrest at this level can be due to heat, infections, and hormonal and nutritional factors. Irreversible arrest at this level occurs at the primary spermatocyte or spermatid level and has a genetic origin due to chromosomal anomalies. The dysfunction occurs in somatic and germ cells.

**REFERENCE**
**MAXIMUM ANDROGEN BLOCKADE (MAB)/COMBINED HORMONAL THERAPY (CHT)**

**DESCRIPTION**

The main concept behind maximum androgen blockade (MAB), sometimes referred to as combined hormonal therapy (CHT) or total androgen blockade is that by adding an antiandrogen in conjunction with surgical castration or LHRH agonist therapy, urologists can minimize the effects of any extragonadal sources of androgen production similar to what is observed in the prepubertal child. This strategy was traditionally noted to be the adrenal gland. Studies in both being conflicting with some showing prolonged survival in patients treated with MAB with advanced prostate cancer and others demonstrating no significant difference. In a large meta-analysis published by the Prostate Cancer Trialists’ Collaborative group, a nonsignificant 1.8% 5-yr survival was found in the MAB group. This study included 27 randomized trials and over 8,200 patients.

Short-term MAB (1–2 wk) is generally agreed to in men with newly diagnosed metastatic disease when starting androgen deprivation with an LHRH analog to block the so-called “false” reaction. Most RDS trials that combine radiation therapy and external beam radiation therapy for intermediate- and high-risk disease are performed using MAB (9–10 mo to 2–3 yr based on the risk and protocol).

**REFERENCES**


**MAYOR–ROKITANSKY–KUSTER–HAUSER SYNDROME (ROKITANSKY–KUSTER–HAUSER SYNDROME)**

**DESCRIPTION**

A congenital absence of the vagina. The uterus is either absent or absent. The diagnosis is usually made when amenorrhea is noted in a normal pubertal XX person with a female phenotype. Renal and skeletal anomalies are a common association. The defect involves mesodermal development and the mesecephalic kidney, the latter resulting in abnormalities in the paramesonephric (uterus and vagina) and in the metanephric kidney.

**REFERENCES**


**MAYO CLINIC GRADING SYSTEM FOR PROSTATE CANCER**

**DESCRIPTION**

A grading system for prostate cancer that uses not only assessment of glandular architecture similar to Gleason’s grading system, but also histologic criteria. Grading is done on a scale of 1–4, with 4 having the worst prognosis. Cellular morphology, mitotic activity, and tumor invasiveness, are all used to assign grade.

**REFERENCES**


**MC-CUNE–ALBRIGHT SYNDROME**

**DESCRIPTION**

A syndrome characterized by a classic triad of fibrous dysplasia (cystic bone lesions), gonadotropin-independent precocious puberty, and cutaneous pigmentation with cafe-au-lait spots. It is caused by a mutation of chromosome 20q13, coding for the α-subunit of G-protein coupled receptors that are involved with many hormone receptor signaling pathways.

**SYNONYMS**

- Polysystic fibrous dysplasia
- Distal fibrous cystoscopy

**TREATMENT**

Treatment is targeted at the specific endocrinopathy and may include:

- Hypothalamic surgery
- Adrenalectomy
- Aromatase inhibitors, anti-estrogens, and anti-androgens

**REFERENCES**


**ME-GUIRE URINAL**

**DESCRIPTION**

An external male urine collection device consisting of a malleable latex urinary catheter that is either self-contained or attached directly to a leg bag. It is often supported by fabric suspensions in a joey-strap type fashion.

**REFERENCE**


**MEATL STENOSIS, URETHRAL, MALE**

**DESCRIPTION**

Most commonly seen after neonatal circumcision, this acquired condition is theorized to follow a postsurgical inflammatory reaction at the glans, resulting in an extremely narrow urethra. Meatal stenosis is usually not apparent until the child is toilet trained. Strength and direction of stream can be affected. Dysuria, frequency, incontinence, and hematuria are symptoms that have been associated with this condition. Meatal stenosis rarely causes obstructive changes in the urinary tract. Meataloplasty is the corrective procedure for these requiring surgical correction. (See also Section II: “Catheter, Mucus and Urethra.”)

**REFERENCES**


**MECKEL–GRUBER SYNDROME (MECKEL SYNDROME)**

**DESCRIPTION**

Meckel–Gruber syndrome is a rare, lethal, autosomal recessive disorder with major characteristic features consisting of the triad of occipital encephalocele, polydactyly, and bilateral polycystic kidneys. Prenatal sonographic exam has been demonstrated to be of valuable diagnostic accuracy. For this reason, appropriate prenatal counseling is advocated for those at high risk.

**REFERENCE**


**MEDIAN BAR**

**DESCRIPTION**

Median bar refers to prostatic posterior commissural hyperplasia, an abnormal hyperplasia involving the posterior bladder base that produces a wide bar. Patients suffering enlargement of the middle lobe or posterior commissure are more likely to develop obstructive symptoms due to the tissue location, which easily obstructs the bladder neck. This explains the correlation between the size of the gland and the degree of obstruction.

**REFERENCE**

Randal A. Surgical Pathology of Prostatic Obstruction. Baltimore, MD: Williams & Wilkins; 1931.

**MEDIAN RAPHE CYST**

**DESCRIPTION**

Median raphe cysts are uncommon congenital lesions of the male genitalia. Theories proposing its origin include the development of embryologic outgrowths of epithelium after primary closure of urethral folds, or that they arise from epithelial remnants caused by incomplete closure of the folds. Cysts can be found anywhere from the distal penis to anus at the midline. They are usually
**MEDICATIONS THAT CAN IMPACT VOIDING FUNCTION**

### Medications That Can Impact Voiding Function

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect on Voiding Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Frequency, urgency, sedation, delirium, immobility</td>
</tr>
<tr>
<td>Adrenergic-converting enzyme inhibitors</td>
<td>Associated cough, worsened stress and possibly urge leakage in persons with impaired sphincter function</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Urge incontinence</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Urge incontinence</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>Urge incontinence</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Impaired detrusor contractility and retention; the dihydropyridine agents can cause pedal edema, leading to nocturnal polyuria</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Pedal edema: causing nocturia and nighttime incontinence</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Women’s stress and mixed leakage in women</td>
</tr>
<tr>
<td>GABAergic agents (gabapentin, pregabalin)</td>
<td>Pedal edema: causing nocturia and nighttime incontinence</td>
</tr>
<tr>
<td>Ketamine 1 receptor antagonists</td>
<td>Confusion</td>
</tr>
<tr>
<td>Latanoprost</td>
<td>Unexplained urgency</td>
</tr>
<tr>
<td>Lithium</td>
<td>Polyuria</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>Polyuria, frequency, urgency</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>Pedal edema: causing nocturnal polyuria</td>
</tr>
<tr>
<td>Opioid analogics</td>
<td>Sedation, anticholinergic effects</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Stress, urge, and mixed incontinence</td>
</tr>
<tr>
<td>Sedative hypnotics</td>
<td>Sedation, delirium, immobility</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Pedal edema: causing nocturnal polyuria</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Anticholinergic effects, sedation</td>
</tr>
<tr>
<td>α-Adrenergic agonists</td>
<td>Outlet obstruction (men)</td>
</tr>
<tr>
<td>α-Adrenergic blockers</td>
<td>Stress leakage (women)</td>
</tr>
</tbody>
</table>

### MEDULLARY CYSTIC KIDNEY

**DESCRIPTION**

A nonobstructive enlargement of the calyces due to a congenital malformation of the renal papilla. There is no dilatation of the renal pelvis, and no evidence of UPJ obstruction. Found almost exclusively in males (6:1), it often presents in children due to a UTI workup or in adults with menuriasis and renal calculus. The clinician must differentiate between hypersphincterism and UPJ obstruction.

**TREATMENT**

Not necessary. A diuretic renogram should fail to demonstrate any obstruction.

**REFERENCE**


### MEGACYSTIS, CONGENITAL

**DESCRIPTION**

A distal, thin-walled bladder with a wide and poorly developed trigone. Because of the widenly displaced ureters, vesicoureteral reflux is commonly seen. Bladder contractility is normal, but most urine refluxes retrograde into the collecting system. Connection of the reflux often results normal bladder dynamics. It is most often diagnosed on prenatal US. It is associated with megacysto- microcystic-renal polycystic syndrome, a rare congenital disorder characterized by a dilated, nonobstructive urinary bladder and hyperostosis of the skull.

**TREATMENT**

Correction of vesicoureteral reflux after 6 mo of age.

**REFERENCE**

Megalourethra is an extremely rare congenital deficiency of the mesodermal tissues of the phallicus. It can be best described as a urothelial diverticulum that affects the entire penile urethra. 2 types have been described, scaphoid and fusiform. Scaphoid megalourethra are more common and have an absence of corpus spongiosum whereas fusiform megalourethra lack both spongiosum and corpus cavernosum. Often associated with lethal congenital anomalies, fusiform megalourethra are present in some stillborns. Transient obstruction during early development may be responsible for the fusiform type. With the scaphoid type, a failure of development of erectile tissue is present, a meandroidal defect similar to the pathophysiologic of prune belly syndrome (MPS). Many other conditions are associated, such as MPS, renal agenesis, hypopigmentation, cryptorchidism, and others. For MPS, urothroms may be needed secondary to bladder outlet dysfunction and renal failure. In surgical repair of the scaphoid type, longitudinal reduction urethroplasty over a catheter to decrease urethral caliber or plication techniques can be used. For the fusiform variant, each case is managed based on the amount of tissue present and the severity of disease (Image q).

MEGALOURETHRA

DESCRIPTION Megalourethra is an extremely rare congenital deficiency of the mesodermal tissues of the phallicus. It can be best described as a urothelial diverticulum that affects the entire penile urethra. 2 types have been described, scaphoid and fusiform. Scaphoid megalourethra are more common and have an absence of corpus spongiosum whereas fusiform megalourethra lack both spongiosum and corpus cavernosum. Often associated with lethal congenital anomalies, fusiform megalourethra are present in some stillborns. Transient obstruction during early development may be responsible for the fusiform type. With the scaphoid type, a failure of development of erectile tissue is present, a meandroidal defect similar to the pathophysiologic of prune belly syndrome (MPS). Many other conditions are associated, such as MPS, renal agenesis, hypopigmentation, cryptorchidism, and others. For MPS, urothroms may be needed secondary to bladder outlet dysfunction and renal failure. In surgical repair of the scaphoid type, longitudinal reduction urethroplasty over a catheter to decrease urethral caliber or plication techniques can be used. For the fusiform variant, each case is managed based on the amount of tissue present and the severity of disease (Image q).

MELANOMA, ABDOMINAL/PELVIC


MELANOMA, GENITOURINARY

DESCRIPTION Malignant melanoma of the GU tract is rarely seen. However, lesions of the penis, scrotum, and urothra can present as primary sites of disease. Secondary melanoma metastatic to the GU tract is a common autopsy finding. The majority of patients whose secondary melanoma is discovered clinically have metastatic disease within 2 yr.


MELANOMA, URETHRAL

DESCRIPTION A malignant degeneration of melanocytes and nerve cells, primary malignant melanomas are rare. The urethra is the preferred site of the urinary tract and accounts for ~4% of urothelial cancers. A urethral melanoma is more likely to be primary compared with cases in the bladder or kidney. It is 3 times more common in women, more frequent in the white population, and most commonly affects the distal urethra. Presentation is similar to that of other urothelial tumors, but melanoma is sometimes seen. It may be confused with urethral polyps, caruncles, mucosal prolapse, or more common urothelial tumors. It is most malignant melanoma of the adventitial plane. A rarer variant, deep dermal melanoma, crops up in the bladder of young, black women. In the local setting, it is the most common primary melanoma of the urinary tract. Carcinoma, General Considerations.”

TREATMENT

- Limited data are available; most are treated with radical surgery and frequently bilateral lymph node dissection.
- Chemotherapy, immunotherapy, and radiotherapy may be used at the discretion of the principal investigator; both are experimental.


MENOPAUSE, UROLOGIC CONSIDERATIONS

DESCRIPTION Menopause is the cessation of the menstrual cycle and is caused by reduced secretion of the ovarian hormones estrogen and progesterone. This causes a variety of symptoms, including those that affect the GU tract. Vaginal side effects such as dryness (40%), itching, and vaginal dryness (50–55%) occur secondary to reduced estrogens and androgenic hormones. A change in the pH of vaginal fluid from acidic to neutral that increases urinary infections. Decreased estrogen contributes to collagen loss and subsequent pelvic organ prolapse and urinary symptoms. Urinary incontinence and irritative bladder symptoms occur in 20–40% of perimenopausal and postmenopausal women.

TREATMENT

- Topical estrogen therapy has been shown to decrease the incidence of urinary infections, increase bladder control with reduction in urge and irritative symptoms, and improve vaginal dryness and atrophy. It has no effect on stress urinary incontinence (SUI).
- The use of hormone therapy is generally on a short-term basis and only for symptomatic individuals. Although it has been shown to possibly have cardioprotective effects, an increase in breast cancer risk is also seen.


MENKES SYNDROME (MENKES KINKY HAIR DISEASE)

DESCRIPTION A rare congenital disorder of copper metabolism with an X-linked recessive inheritance. Symptoms appear in the neonatal period and include hypothermia, poor feeding, and impaired weight gain. Neuropathic function progressively deteriorates. A colorless and friable hair is characteristically found. There tends to be a high incidence of GU conditions, including bladder diverticula, UTI, IP: obstruction, vesicoureteral reflux, and cryptorchidism.

Patients with urolithiasis should undergo metabolic stone evaluation to identify risk factors for future stone formation. This evaluation may diagnose uncommon, but potentially serious, stone-forming diseases:

- Metabolic syndrome
- Urolithiasis
- Hyperparathyroidism
- Hypercalcemia
- Diabetic nephropathy
- Hypertension
- Hypothyroidism
- Cystinuria
- Idiopathic hypercalciuria
- Hyperuricemia

This evaluation includes:

- A 24-hour urine collection
- A fasting blood sample
- A physical examination

The results help guide treatment and prevent future stone formation.

**REFERENCE**

**SYNONYMS**
- Hypercalciuria
- Hyperuricemia
- Cystinuria
- Idiopathic hypercalciuria
- Hyperuricosuria

**TREATMENT**
- Lifestyle modifications to reduce stone formation
- Medications to prevent stone recurrence
- Surgery for large stones

**MESOTHELIOMA, MALIGNANT, TESTICULAR TUNIC**

**DESCRIPTION**
Mesothelioma is a rare tumor arising from the mesothelial lining of the parietal or visceral peritoneum. It affects men more frequently than women and is more common in smokers. The peritoneum is the serous membrane that lines the abdominal cavity and covers the abdominal organs. Peritoneal surface mesothelioma is the most common type.

**TREATMENT**
Surgical resection is considered for localized tumors, whereas chemotherapy and radiation are used for disseminated disease. Adjuvant therapy is occasionally recommended.

**REFERENCE**

**METABOLIC STONE EVALUATION (24-HR URINE STUDIES)**

**DESCRIPTION**
Patients with urolithiasis should be encouraged to retrieve stones or stones removed surgically should be submitted for stone analysis. The evaluation’s extent depends on the patient’s history and physical examination.

**REFERENCE**

**Cystine screening** is performed on an optional basis and is not part of standard metabolic stone evaluation unless following patients with cystinuria.

**REFERENCE**

**METABOLIC SYNDROME, UROLOGIC CONSIDERATIONS**

**DESCRIPTION**
An increasingly more prevalent disease affecting ~22% of American adults, metabolic syndrome is characterized by having any of the following: abdominal waist circumference, hypertension, low HDL, hypertriglyceridemia, low HDL, hypertension, or abdominal fasting glucose parameters. Sexual dysfunction can occur, including hypogonadism and erectile dysfunction (ED). Many patients have a low urinary pH, thus increasing the risk of uric acid stones.

**SYNONYMS**
- Syndrome X
- Insulin resistance syndrome
- Obesity dyslipidemia syndrome

**TREATMENT**
- Lifestyle modifications with dietary changes, increased physical activity, and smoking cessation
metanephric adenoma (Image from RCC on imaging studies. WT1 and CD57 metastases were reported. It cannot be differentiated from a benign neoplasm but in 1 case lymph node metastases were reported in 12% of the cases that resolves after nephrectomy, but all have been treated with Wilms tumor chemotherapy. There has been 1 case described with nodal metastases of the papillary RCC component of their tumor.

REFERENCE

METANEPHRIC ADENOFIBROMA, KIDNEY (NEPHROGENIC ADENOFIBROMA)

DESCRIPTION A peduncular renal tumor with stromal features resembling congenital mesoblastic nephroma. The epithelial component has varying levels of activity ranging from inactive metanephric adenoma to Wilms tumor. Some masses contain areas identical to papillary RCC. Lesions with a Wilms tumor component occur at a young age (mean of 12 mo). No tumors have recurred after nephrectomy, but all have been treated with Wilms tumor chemotherapy. There has been 1 case described with nodal metastases of the papillary RCC component of their tumor.

REFERENCE

METANEPHRIC ADENOMA

DESCRIPTION A recently recognized renal tumor originally described in 1980; it shows a cytologic resemblance to early metanephric tubular differentiation and to the metanephric hamartomatous element of nephroblastomatosis. Fewer than 100 cases have been reported, with a 2:1 female to male predominance. Most cases present in the 1st-4th decades of life, and the lesion is often discovered incidentally. An association with polycythemia has been reported in 12% of the cases that resolves after surgical resection. These adenomas appear unremarkable, rarely multifocal. The majority are either unencapsulated or have only a limited and discontinuous pseudocapsule. It is largely regarded as a benign neoplasm but in 1 case lymph node metastases were reported. It cannot be differentiated from RCC on imaging studies. WT1 and CD99 immunohistochesizing stains in the diagnosis of metanephric adenoma (Image 9).

REFERENCE

METAPYRONE TEST

DESCRIPTION Cushing syndrome describes the symptom complex caused by excess circulating glucocorticoids. Metapyrone is a blocking agent used to reduce the secretion of cortisol peripherally, thereby lessenig the severity of symptoms. Metapyrone blocks the conversion of 11-deoxycortisol to cortisol. It is a diagnostical test for hypothalamic–pituitary ACTH function.

Day 1: Control period: Collect 24-hr urine to measure 17-hydroxy cortisol or 17-ketosteroids.
Day 2: ACTH test: 50 units ACTH infused over 8 hr and measure 24-hr urinary steroids. Days 3–4: Rest period.
Day 5: Administer metapyrone with milk or snacks. (Adult: 750 mg PO q6h for 6 doses; Pediatric: 15 mg/kg q6h for 6 doses [min 250 mg dose]).
Day 6: Determine 24-hr urinary steroids.
Normal 24-hr urine 17-OHCS is 3–12 mg; following ACTH, it increases to 15–45 mg/24-hr; normal response to metapyrone is a 2–4-fold increase in 17-OHCS excretory drug interactions with phenytin, cyclophosphamide, and steroids may lead to subnormal response.

REFERENCE

MEYER–WEGGART LAW

DESCRIPTION In cases in which separate ureteric buds on the same mesonephric duct form a completely duplicated collecting system, separate investigators (Higgin and then Meyers) noted that there exists a consistent relationship between the upper and lower pole orifices as they relate to 1 another on the trigone. The caudal, or distally placed, orifice actually drains the upper pole moiety, whereas the cranial, or suprasciopic orifice drains the lower pole moiety. The distal orifice is more medial on the trigone, as opposed to the laterally placed cranial orifice. This is a reliable rule for cases of ureteral duplication.

REFERENCE

MIBG SCAN

DESCRIPTION A form of molecular imaging using metaiodobenzylguanidine (MIBG), an analog of guanethidine. MIBG accumulates into cells via norepinephrine transporters and is collected into secretory granules. It is useful in identifying primary and metastatic pheochromocytoma, paraganglioma, and neuroblastoma.

REFERENCE

MICHAELIS–GUTMANN BODIES

DESCRIPTION Michaelis–Gutmann bodies are the pathognomonic finding in the benign inflammatory process known as malakoplakia. Low light microscopy demonstrates a granulomatous inflammatory process, characterized by the accumulation of large mononuclear cells with abundant granular cytoplasm and PAS-positive calcium immunoprecipitate inclusions (so-called Michaelis–Gutmann bodies). On electron microscopy, such inclusions appear as concentric lamellated structures with a mineralized core (Image 3).

REFERENCE

MICROCYSTIC/NESTED VARIANT UROTHELIAL CARCINOMA

DESCRIPTION Microcystic and nested variant urothelial carcinomas are rare histologic subtypes of bladder cancer that appear similar to benign conditions of the bladder, however demonstrate aggressive behavior. Microcystic urothelial carcinoma has an ill-defined growth pattern that resembles cystitis cystica. It has been identified in bladder, upper tract, and prostate urothelial carcinoma. Microcystic variant urothelial carcinoma is usually mistaken for reactive or athermatic. Studies have shown that in patients with microcystic variant urothelial carcinoma has a better prognosis than conventional urothelial carcinoma.

REFERENCE

MICRORHISLATHIA, TESTIS

DESCRIPTION Testicular microthelia is an uncommon condition characterized by the presence of collections within degenerating seminiferous tubules. It is a soft indurated tubule that shows providers of between 2 and 8% of males. Microthelia is often found in conjunction with other testicular pathologies, with testicular malignancy being the most concerning, however, there are conflicting reports. Currently, no guidelines exist for follow-up of patients diagnosed with microthelia of the testis. Recommendations range from no follow-up to a staging workup for testicular cancer. At a minimum, testicular self-exams are important and annual physical exam by a physician is recommended. Some authors suggest annual exam by a urologist in conjunction with annual ultrasound for patients with risk factors for testicular cancer (Image 8).

REFERENCE

MICROPAPILLARY BLADDER CANCER

DESCRIPTION A variant of bladder cancer first described in 1984. The histologic features closely resemble papillary versus carcinoma of the neck. It accounts for 0.7–2.3% of all bladder tumors and is nearly always associated with an advanced stage of...
MICTURITION SYNOCOPE

DESCRIPTION: Syncope episodes occurring during voiding are known as micturition syncope. This was originally thought to be a disorder of young healthy men, however, additional studies have found micturition syncope in spous ages and genders. Several mechanisms have been suggested in the literature. 1 is that decompression of the bladder results in a decreased intra-abdominal pressure therefore decreasing blood return and causing a sudden decrease in cerebral blood flow. Another is that increased vagal tone during voiding results in a syncopal episode. Finally, micturition syncope could be an orthostatic event as a result of waking from sleep that occurs during the 1st void of the day immediately after awakening. Rarely, micturition syncope can be a symptom of a pheochromocytoma/pheanglioma of the bladder. Further investigation with urinalysis and cystoscopy are warranted in addition to workup of a cardiovascular source of syncope.


MILK ALKALI SYNDROME

DESCRIPTION: Hypercalcemia and alkalosis associated with the ingestion of large amounts of milk and antacids containing calcium and absorbable alkali. Patients can develop nephrocalcinosis and renal insufficiency, but typically do not have hypercalcemia. The associated vomiting and dehydration can produce further volume contraction and alkalosis. (See also Section I: “Nephrocalcinosis, Adult.”)

TREATMENT: Withdrawal of milk and alkali, with gentle hydration to lower serum calcium. Vomitus can result in rebound hypercalcemia due to the chronic suppression of the parathyroid glands.


Mixed Epithelial Stromal Tumor of the Kidney (MEST)

DESCRIPTION: MEST is a subset of benign renal tumors composed mainly of smooth muscle cells in which epithelial structures are embedded. It is usually found in middle-aged and perimenopausal women. Grossly, MEST is well-circumscribed but unencapsulated, and cystic or a cut surface. Microscopically, it is composed both of epithelial structures similar to renal tubules and stroma comprising non-specific spindle cells. The differential diagnosis for these tumors is focus cystic nephroma and cystically differentiated nephroblastoma.


Milk-Alkali Syndrome

MILK–ALKALI SYNDROME

DESCRIPTION: Hypercalcemia and alkalosis associated with the ingestion of large amounts of milk and antacids containing calcium and absorbable alkali. Patients can develop nephrocalcinosis and renal insufficiency, but typically do not have hypercalcemia. The associated vomiting and dehydration can produce further volume contraction and alkalosis. (See also Section I: “Nephrocalcinosis, Adult.”)

TREATMENT: Withdrawal of milk and alkali, with gentle hydration to lower serum calcium. Vomitus can result in rebound hypercalcemia due to the chronic suppression of the parathyroid glands.


MINTROFANOFF PRINCIPLE

DESCRIPTION: A surgical procedure, originally described by Mitrofanoff, in which the appendix is excised with a button of cecum, reversed, and tunneled to create a catheterizable channel with a reported continence rate of 93–100%. Stomal stenosis is an early complication affecting 7–24% within 3 yr in published series.


MIXED EPITHELIAL STROMAL TUMOR OF THE KIDNEY (MEST)

DESCRIPTION: MEST is a subset of benign renal tumors composed mainly of smooth muscle cells in which epithelial structures are embedded. It is usually found in middle-aged and perimenopausal women. Grossly, MEST is well-circumscribed but unencapsulated, and cystic or a cut surface. Microscopically, it is composed both of epithelial structures similar to renal tubules and stroma comprising non-specific spindle cells. The differential diagnosis for these tumors is focus cystic nephroma and cystically differentiated nephroblastoma.


MOLLUSCUM CONTAGIOSUM

DESCRIPTION: A benign, self-limited skin tumor or papular eruption caused by a virus. Infection occurs after breakage of the skin and characteristically begins as a small pimple. When mature, it is a discrete 2–5 mm smooth, dome-shaped, pearly or flesh-colored nodule that is often umbilicated. Single to hundreds of lesions may track alone the line of a scratch. In adults, they occur on the trunk, thigh, and public areas. Lesions usually disappear by themselves within 6–12 mo, although this may take up to 4 yr with impaired cell mediated immunity. Diagnosis is usually clinical, but brick-shaped vesicles can sometimes be seen under negative-stain electron microscopy. Henderson-Paterson bodies are characteristic. Often seen on pathology. (See also Section I: “Genital Warts.”)

TREATMENT: Observation is reasonable for nongenital lesions. Caustic is useful for treating a few lesions; scraping may develop.


MONDOIR DISEASE

DESCRIPTION: Mondor disease is superficial thrombophlebitis of the dorsal vein of the penis. It is typically diagnosed in young males after excessive sexual activity and can be diagnosed in older males due to venous obstruction secondary to bladder disinterest. Physical exam typically reveals a tender palpable cord on the dorsal surface of the penis as well as distal penile edema. Treatment is conservative with abstinence of sexual activity until completely resolved. Anticoagulation and antiphlogistics medications have not been shown to be beneficial. Vein stripping surgery is indicated for patients with associated cellulitis.


MONOFORT TECHNIQUE

DESCRIPTION: A type of abdominal wall reconstruction in patients with prune belly syndrome. This technique utilizes an abdominal incision that preserves the umbilicus and thickens and strengthens the anterior abdominal wall. Full-thickness resection of the parietal peritoneum is performed, and the anterior wall is sutured in a double-breasted fashion preserving vascularity and the umbilicus. This technique offers excellent exposure for concomitant intra-abdominal surgery.


MONTI PROCEDURE

DESCRIPTION: Also known as the Monti procedure, this technique most often used in children to create a continent catheterizable stoma. A short segment of bowel (2–3 cm of ileum) is included...
along the antimesenteric border and then closed transversely to create a uniform tube that can be tunneled into the bladder and out through the abdominal wall. This allows preservation of the appendix for the Malone antegrade continent enema (MACE) procedure. A review of 199 patients undergoing Monti ileovesicostomy at a single institution reported a revision rate of 8.5% and a continence rate of 96.5% with mean follow-up of 28 mo.

- **REFERENCE**
  

**MOHRIS SYNDROME**

**DESCRIPTION**

An intense disorder that affects 1 in 20,000 live male births; it is caused by a mutation in the androgen receptor gene located on the long arm of the X chromosome. This prevents appropriate androgen binding and/or function. If complete androgen insensitivity occurs, the child will appear to have a normal female phenotype and the testes are located internally. Many children are diagnosed at the time of hernia repair as infants or not diagnosed until puberty during an evaluation for primary amenorrhea. **SYNONYMS**

- **Testicular feminization syndrome**
- **In-class of male pseudohermaphroditism**

- **REFERENCE**


**MOSTOFI (WHO) GRADING SYSTEM**

**DESCRIPTION**

- **Grade I:** Well-differentiated, with slight nuclear anaplasia
- **Grade II:** Moderately differentiated, with moderate nuclear anaplasia
- **Grade III:** Poorly differentiated, with marked nuclear anaplasia, and/or differentiated carcinoma

- **SYNONYM**

  World Health Organization Grading System

- **REFERENCE**


**MOWAT-WILSON SYNDROME**

**DESCRIPTION**

A syndrome of multiple congenital anomalies due to a heterozygous mutations or deletions in ZEB2, or Zinc finger E-box-binding homeobox 2 gene. It is generally discussed on genetic workup for Hirschsprung disease. Patients present with a distinct facial phenotype, mental retardation, lipoatrophy, agenesis of corpus callosum, and congenital heart defects. Roughly 50% of patients have genitourinary anomalies with hypoplasia being the most prominent (52%). Another common anomaly is cryptorchidism (39%). Rhinitis, scrotophelial reflux and misunderstood are rare but have been reported.

- **REFERENCE**


**MUCORMYOSIS, GENITOURINARY**

**DESCRIPTION**

A fungal infection that usually affects immunocompromised patients. Patients receiving hemodialysis and diabetics are at particular risk for disseminated disease. The kidneys are the organs most often involved in the GU system, but penile involvement has also been reported. The course is usually fatal. (See also Section I: “Fungal infections, Genitourinary.”)

- **TREATMENT**

  Amphotericin B systemically; nephrectomy for involved kidney

- **REFERENCE**


**MULBERRY STONES**

**DESCRIPTION**

A term that refers to the surface appearance of irregular calcium oxalate dihydrate stones often seen in the bladder. Based on their less well-developed spikes than seen on pectinate; the spikes possess more of a mammillated appearance.

- **REFERENCE**


**MULCAHY PROTOCOL**

**DESCRIPTION**

Infection of a penile prosthesis is suspected when there is local pain and erythema, fever and listlessness of the prostheses components. In this situation there are 2 main options. The 1st is to remove the prosthesis and reinser it at least 6–8 mo later. This repeat surgery can be difficult due to formation of scar tissue in the corpora. Another option is to remove the prosthesis, perform a corporos antibiotic washout of the corpora cavernosa with an antibiotic solution, then place a “tutor” cylinder inside the corpora to prevent shrinking and scarring.

Another approach to the management of an infected penile prosthesis is the Mulcahy protocol. This involves complete removal of the infected part of the prosthesis and all other components followed by the use of the specific Mulcahy salvage procedure outlined below with reinser tion of a new penile prosthesis in the same sitting with a reported success rate of 85%. (See also Section I: “Penile Prosthesis Problems.”)

**MULTIPLICATION**

**REFERENCE**

- Administer oral antibiotics for 1 month
- Change gowns, gloves, surgical drapes, and all other components followed by the use of the specific Mulcahy salvage procedure outlined below with reinser tion of a new penile prosthesis in the same sitting with a reported success rate of 85%. (See also Section I: “Penile Prosthesis Problems.”)
- Remove all prosthetic parts and foreign material
- Irrigate wounds using 5 antiseptic solutions: – Antibiotic solution (1 g vancomycin and 80 mg gentamicin in 1 L of normal saline) – 1/2 strength Povidone-iodine (Betadine or similar) – Pressure washing with 1 g vancomycin and 80 mg gentamicin in 5 L irrigation – 1/2 strength Povidone-iodine (Betadine or similar) – Antibiotic solution rinse
- Change gowns, gloves, surgical drapes, and instruments immediately before prosthesis insertion
- Insert new prosthesis
- Close wounds with no drains or catheters
- Administer oral antibiotics for 1 month

**REFERENCES**

- Mulcahy KD, Oukhors AO. Mucin-producing tumors of the sebaceous gland or keratoacanthoma associated with ≥1 visceral malignancies including renal, endometrial, prostatic, and upper GI. Usually considered a subtype of hereditary nonpolyposis colorectal cancer syndrome—25% of the visceral cancers are associated with the most common of which are urachal carcinoma.

  - Reference

MÜLLERIAN DUCT REMNANTS AND SYNDROME (PMDS)

DESCRIPTION: Refers to the persistence of the müllerian duct structures (ovary, fallopian tubes) in the genotypically and phenotypically normal male. The remnants period due to the absence of müllerian inhibiting substance. It is an autosomal recessive inherited disorder. Patients present with cryptorchidism and hernia, and the persistent müllerian structure are found within the hernia sac. Increasing evidence is mounting that persistent müllerian structures are at risk for malignant transformation. 11 cases of malignancy have been reported in the literature out of 200 reported cases of persistent müllerian duct syndrome (PMDS).

SYNONYMS: • Prostatic stricture cyst • Müllerian duct cyst (Image 4)


MULTILOCULAR CYSTIC NEPHROMA (CYSTIC NEPHROMA, MULTILOCULAR CYST)

DESCRIPTION: Around, well-encapsulated multilocular cystic mass whose septae are composed of well-differentiated tissues, without blastic elements. The current thinking is that multilocular cystic nephroma is at the benign end of a spectrum that includes cystic partially differentiated nephroblastoma (CPDN) and cystic nephroma at the malignant end. Usually, multilocular cystic nephroma and CPDN look identical. The contents of the cysts consist of either yellow fluid or thick myxomatous gel. The lesion is usually solitary but rarely can be multiple. Cystic nephroma presents in a bimodal age distribution of 2–6 years (male-50% female-50%) and in adulthood (81% female-9%). Children usually present with a palpable mass and adults with pain; hematuria, or infection. Imaging cannot distinguish between cystic nephroma and CPDN. The lesion often is close to the renal pelvis, and herniation of the renal pelvis is a pathognomonic finding on US, CT, or MRI. The nephromas separate the cysts. On US, multiple anechoic spaces representing the cysts may be seen. The septa are thin, variable in thickness, and are not uniformly thick. The septa are not calcified and cannot be distinguished from thin vessels. Imaging cannot reliably separate CPDN from nephroma that extends beyond the normal renal outline. Children usually present with a palpable mass and adults with pain, hematuria, or infection. Imaging cannot distinguish between cystic nephroma and CPDN. On US, CT, or MRI, the lesions are usually solitary but rarely can be multiple. Cystic nephroma presents in a bimodal age distribution of 2–6 years (male-50% female-50%) and in adulthood (81% female-9%). Children usually present with a palpable mass and adults with pain; hematuria, or infection. Imaging cannot distinguish between cystic nephroma and CPDN. The lesion often is close to the renal pelvis, and herniation of the renal pelvis is a pathognomonic finding on US, CT, or MRI. The nephromas separate the cysts. On US, multiple anechoic spaces representing the cysts may be seen. The septa are thin, variable in thickness, and are not uniformly thick. The septa are not calcified and cannot be distinguished from thin vessels. Imaging cannot reliably separate CPDN from nephroma that extends beyond the normal renal outline.


MULTIPLE ENDOCRINE NEOPLASIA (MEN I, MEN II)

DESCRIPTION: A group of inherited syndromes primarily consisting of endocrine tumors of both benign and malignant nature. MEN syndrome lesions are of unilgic interest because of the possibility of adrenal involvement, hyperparathyroidism, renal stones, and hypercalcemia.

• MEN I (Werner’s syndrome): Autosomal dominant condition with neuroendocrine parathyroid, pancreas, duodenal, and pharyngeal lesions. Cutaneous tumors also may be seen (angiofibromas, others). Hyperparathyroidism is the most common presentation of this syndrome, but overall this is a rare cause of hyperparathyroidism in the general population. Primary lesions may cause hyperplasia and ACTH-producing lesions.

• MEN II (ipple syndrome): Autosomal dominant: Type IA: Pheochromocytoma, medullary carcinoma of the thyroid, parathyroid adenoma Type IB: Phaeochromocytoma, medullary carcinoma of the thyroid (but not parathyroid hyperplasia) with mucosal neuromas, intestinal ganglioneuromas, and occasionally marfanoid habitus. Some literature refers to this as MEN III (mucosal neuromuscular syndrome).


MULTIPLE MYELOMA, UROLOGIC CONSIDERATIONS

DESCRIPTION: A malignant proliferation of plasma cells derived from a single clone. The classic triad involves marrow plasmacytosis, light bone lesions, and a serum and/or urine M component. Renal failure occurs in 25% of patients. Hypercalcemia is the most common cause, but hyperuricemia is also present and a rarely cause. Tumor lysis syndrome is uncommon with multiple myeloma. There may be tubular precipitation of light chain proteins (myeloma kidney), urinary obstruction due to uric acid or calcium-containing stones, or recurrent pyelonephritis. Gliomblastoma, tubule, and interstitial involvement can cause renal insufficiency. The development of a myeloma kidney can lead to adult Fanconi syndrome, which is a type II proximal renal tubular acidosis. NSAIDs are to be avoided. Renal failure is rare but has been reported after the use of contrast agents in patients with multiple myeloma.


MUMPS ORCHITIS

DESCRIPTION: Mumps is a single-stranded RNA virus (paramyxovirus) viral. After the prodromal period, 1 or both parotid glands begin to enlarge. Mumps orchitis follows the development of parotitis by 4–7 days, with about 25% of males developing orchitis (10% bilateral and 80–90% unilateral). It has been reported following mumps vaccination. The presentation is high fever, testicular pain, and swelling. The management of mumps orchitis is supportive (bedrest, social support, analgesics) with resolution in about 7 days. Unilateral testicular atrophy occurs in 60%. Impaired fertility can affect up to 15%, but fertility is rare. (See also Section II: “Obstetrical General.”)


MURCS ASSOCIATION (MÜLLERIAN DUCT, RENAL, AND CERVICAL VERTEBRAL DEFECTS)

DESCRIPTION: MURCS association consists of a novel association of müllerian duct aplasia, renal aplasia/agenesis, and cervicothoracic somite dysplasia. The incidence of cervicothoracic-vertebral defects, especially from C5–T1, is 80%. Other abnormalities may include spinoglenoid defects, upper limb defects, and moderately frequent rib anomalies. It is the 2nd most frequent cause of primary amniarhoea after Turner syndrome.


MUSCLE FLAP TYPES, UROLOGIC CONSIDERATIONS

DESCRIPTION: Muscle flaps are a reconstructive technique using local or distant muscle donor sites to provide tissue coverage in complex reconstructive procedures. The most simple muscle flaps are local and regional flaps where blood supply of the muscle is not interrupted when the flap is repositioned to its new location. Pedicle and micro-skin free flaps are more complicated forms of tissue transfer that are finding new indications in reconstructive urologic procedures. Tissue transfer has become increasingly used in centers for complex repair of fistula disease following radiation. In addition, clinical study has shown latissimus dorsi transferred to acraliminate the rectus abdominies has restored voluntary voiding in patients with detrusor anuria.


MUSTARDÉ HYPOSPADIAS REPAIR

DESCRIPTION: A more extensive Mustarde technique in which the ventral flap is mobilized to form a neourethra and then transposed distally. The glans wings are often approximated over the neourethra.


MULTIPLE CYSTIC NEPHROMA (CYSTIC NEPHROMA, MULTILOCULAR CYST)

DESCRIPTION: Around, well-encapsulated multilocular cystic mass whose septae are composed of well-differentiated tissues, without blastic elements. The current thinking is that multilocular cystic nephroma is at the benign end of a spectrum that includes cystic partially differentiated nephroblastoma (CPDN) and cystic nephroma at the malignant end. Usually, multilocular cystic nephroma and CPDN look identical. The contents of the cysts consist of either yellow fluid or thick myxomatous gel. The lesion is usually solitary but rarely can be multiple. Cystic nephroma presents in a bimodal age distribution of 2–6 years (male-50% female-50%) and in adulthood (81% female-9%). Children usually present with a palpable mass and adults with pain; hematuria, or infection. Imaging cannot distinguish between cystic nephroma and CPDN. The lesion often is close to the renal pelvis, and herniation of the renal pelvis is a pathognomonic finding on US, CT, or MRI. The nephromas separate the cysts. On US, multiple anechoic spaces are seen, separated by hyperchoic septa. CT reveals a well-marginated, rounded, or polycystic cortical mass that extends beyond the normal renal outline. Enhancement of the septa may be seen due to the presence of thin vessels, imaging cannot reliably predict malignant potential.

SYNONYMS: • Cystic kidney, cystic nephroma • Local polycystic kidney • Multilocular or cystic adenoma

TREATMENT: • Partial nephrectomy or radical nephrectomy is indicated. • Follow-up is required because of local recurrence (Image a).


730
Mycoplasma hominis

**DESCRIPTION**


Mycoplasma hominis is a common organism that resides in the genital tracts of both men and women. However, it may be a cause of choriocytotropism in men or vaginal infections in women. Identifying and culturing this organism is difficult. Initial treatment includes doxycycline 100 mg BID for 2 wk or azithromycin 1 g in a single dose.

REFERENCES


Mycoplasmal pain, urogenital conditions

**DESCRIPTION**

Gracilis flap: The origin of the gracilis muscle is the medial tibia. The gracilis muscle is a branch of the obturator nerve, which provides full anterior thigh sensation. The gracilis muscle is a branch of the lateral femoral circumflex artery, and its blood supply is a single artery from the profunda femoris system.

Tension fascia lata flap: The tension fascia lata flap can be harvested from the lateral aspect of the upper leg. The vascular pedicle is comprised of the descending lateral circumflex femoral artery, and the sensory supply is the lateral femoral cutaneous nerve of the thigh, which originates from T12.

REFERENCES


Myocutaneous flaps

**DESCRIPTION**

Myocutaneous flaps, such as the rectus abdominis flap and the gracilis muscle flap, can be utilized during urogenital reconstructive surgery. Common applications for skin coverage during inguinal node dissections for penile cancer, closure of urinary fistula, and reconstruction afterourean surgery.


NAGAMATSU INCISION

**DESCRIPTION**

A dorsolateral incision is made over either the 11th or 12th rib, which is resected. After rib removal, the diaphragm and pleura are opened over either the 11th or 12th rib, which is resected. The diaphragm and pleura are opened over either the 11th or 12th rib, which is resected.

REFERENCES


Myoglobinuria

**DESCRIPTION**

Myoglobinuria is described by Fleischer in 1881. Myoglobinuria refers to the presence of excessive amounts of myoglobin, a protein found in muscle, in the urine. Myoglobinuria occurs when serum levels exceed the renal threshold. Myoglobin is released into the serum following massive muscle necrosis (rhabdomyolysis) from crush, compartment syndrome, electrical injury, burns, malignant hyperthermia, and other causes, and imparts a cola-like color to the urine. Diagnosis is made by electrophoresis separation and radioimmunooassay of urinary myoglobin. Serum creatinine kinase is elevated, and there is an absence of red cells in the urine. (See also Section I: “Rhabdomyolysis”; Section II: “Myoglobin Nephrotoxicity.”)

CAUSES

- Diabetic acidosis
- Fluid/electrolyte imbalance
- Infections myocutaneous
- Ischemia
- Malignant hyperthermia
- Neuromuscular malignant syndrome
- Rhabdomyolysis or compartment syndrome
- Trauma
- Trauma

TREATMENT

- Remove the causative agent.
- Protect against renal failure through correction of electrolyte imbalance, alkalization of urine with sodium bicarbonate, hydration, and diuretics.

REFERENCES


NAGAMATSU INCISION

**DESCRIPTION**

Myoglobinuria refers to the presence of excessive amounts of myoglobin, a protein found in muscle, in the urine. Myoglobinuria occurs when serum levels exceed the renal threshold. Myoglobin is released into the serum following massive muscle necrosis (rhabdomyolysis) from crush, compartment syndrome, electrical injury, burns, malignant hyperthermia, and other causes, and imparts a cola-like color to the urine. Diagnosis is made by electrophoresis separation and radioimmunooassay of urinary myoglobin. Serum creatinine kinase is elevated, and there is an absence of red cells in the urine. (See also Section I: “Rhabdomyolysis”; Section II: “Myoglobin Nephrotoxicity.”)

CAUSES

- Diabetic acidosis
- Fluid/electrolyte imbalance
- Infections myocutaneous
- Ischemia
- Malignant hyperthermia
- Neuromuscular malignant syndrome
- Rhabdomyolysis or compartment syndrome
- Trauma
- Trauma

TREATMENT

- Remove the causative agent.
- Protect against renal failure through correction of electrolyte imbalance, alkalization of urine with sodium bicarbonate, hydration, and diuretics.

REFERENCES

The development of pituitary mass enlargement on MRI are diagnostic.


Nephrocalcinosis, Neonatal

Nephrocalcinosis with or without nephrocalcinosis are commonly observed in both term and premature infants who have had difficult neonatal courses. Neonates with prolonged illness are at particular risk, especially those who still require oxygen at 28 days. While multifactoral, such as high calcium and phosphorous intake, loop diuretics appear to be the major cause in this group of patients. Loop diuretic use (furosemide most commonly used) predisposes to nephrocalcinosis by increasing urinary calcium excretion. Other factors such as immaturity renal function and physiologic hypercalciuria that occurs between 32 and 42 weeks of gestation contribute. Nephrocalcinosis in infants with a birth weight <1,500 g may be as high as 64% and may be independent of diuretic use. In infants born <32 wk gestation, 27% had nephrocalcinosis with 70% having been treated with a loop diuretic. Other causes of neonatal nephrocalcinosis include William syndrome (supravalvular aortic stenosis and hypercalcemia), neonatal primary hyperparathyroidism and distal type (1) renal tubular acidosis. The loop diuretic-induced hypercalciuria can be diminished and radiologic appearance of renal calcifications diminished by administering a thiazide diuretic in place of or alternating with a loop diuretic. The long-term impact of nephrocalcinosis on renal outcome is unclear because data are limited and inconsistent. Long-term follow-up is recommended.

REFERENCE


Nephrogenic adenoma (NA) and metaplasia

Description: A rare lesion occurring in the urinary tract that was once thought to be a metastatic reaction to chronic irritation and has now been shown to originate from unstimulated and implanted renal epithelial cells. It is named for its histologic similarity to renal tubules and can cause hematuria, dysuria, and urgency. On cytology nephrogenic adenoma can appear papillary, nodular, or sessile and is very friable. It is typically unifocal. It is considered a benign lesion, however malignant transformation has been reported and therefore complex resection and long-term follow-up is recommended.

REFERENCE


Nephrogenic adenoma (NA) and metaplasia

Description: A rare lesion occurring in the urinary tract that was once thought to be a metastatic reaction to chronic irritation and has now been shown to originate from unstimulated and implanted renal epithelial cells. It is named for its histologic similarity to renal tubules and can cause hematuria, dysuria, and urgency. On cytology nephrogenic adenoma can appear papillary, nodular, or sessile and is very friable. It is typically unifocal. It is considered a benign lesion, however malignant transformation has been reported and therefore complex resection and long-term follow-up is recommended.

REFERENCE


Prophylactic percutaneous radiotherapy (shown to reduce the incidence of Nelson syndrome by 50%)

REFERENCE


Nephrocalcinosis, with or without nephrocalcinosis are commonly observed in both term and premature infants who have had difficult neonatal courses. Neonates with prolonged illness are at particular risk, especially those who still require oxygen at 28 days. While multifactoral, such as high calcium and phosphorous intake, loop diuretics appear to be the major cause in this group of patients. Loop diuretic use (furosemide most commonly used) predisposes to nephrocalcinosis by increasing urinary calcium excretion. Other factors such as immaturity renal function and physiologic hypercalciuria that occurs between 32 and 42 weeks of gestation contribute. Nephrocalcinosis in infants with a birth weight <1,500 g may be as high as 64% and may be independent of diuretic use. In infants born <32 wk gestation, 27% had nephrocalcinosis with 70% having been treated with a loop diuretic. Other causes of neonatal nephrocalcinosis include William syndrome (supravalvular aortic stenosis and hypercalcemia), neonatal primary hyperparathyroidism and distal type (1) renal tubular acidosis. The loop diuretic-induced hypercalciuria can be diminished and radiologic appearance of renal calcifications diminished by administering a thiazide diuretic in place of or alternating with a loop diuretic. The long-term impact of nephrocalcinosis on renal outcome is unclear because data are limited and inconsistent. Long-term follow-up is recommended.

REFERENCE

NEPHROPATHY, URATE (URATE NEPHROPATHY)

DESCRIPTION
A disorder in which an abrupt tubular deposition of urate and uric acid crystals. Their chronic use leads to recurrent papillary necrosis with impaired concentrating ability, sterile pyuria, and renal insufficiency. Removal of phenacetin from OTC pain medications has drastically reduced the incidence of this condition. During periods of acute necrosis, patients may have flank pain, pyuria, hematuria, and acute ureteral obstruction from passage of sloughed, necrotic papillary tissue. H/P shows the ring sign, which refers to the contrast agent surrounding sloughed papilla, although the current use of H/P is limited due to contrast load. Renal US shows small kidneys, with irregular thinning of the renal cortex. Renal biopsy shows interstitial inflammation and fibrosis. Noncontrast CT shows bilateral reduced renal size, humpy renal cortex, and papillary calcifications (ie, small, indented, and calcified kidneys). The mechanism of injury is believed to be a combination of injury from the production of toxic metabolites and medullary ischemia. These patients are at increased risk of developing TCC of the urinary tract. Cessation of drug use can lead to stabilization of renal function.

REFERENCE

NEPHROPATHY, ISCHEMIC

DESCRIPTION
Ischemic nephropathy is described as a deterioration of renal function due to a reduction in renal blood flow, commonly caused by atherosclerotic renovascular disease or renal artery stenosis. The disease progresses with worsening renal failure and decreased overall survival. It can present as hypertension (HTN) with unexplained renal insufficiency, worsening azotemia with HTN, azotemia in the setting of coronary artery disease or peripheral vascular disease, ACE inhibitor-induced ARF, or flash pulmonary edema. Numerous tests are used to define the presence, site, and function of the kidneys, as well as to establish the presence of a vascular lesion and its clinical significance, including CT or MR angiography, conventional angiography, Doppler US, ACE I renography or renal vein renin measurements. Controversy still exists on the appropriate management of renal artery stenosis. Options include medical therapy, percutaneous transluminal angioplasty with or without stent placement, as well as surgical revascularization or nephrectomy. (See also Section I: “Renal Artery Stenosis/Renovascular Hypertension”.)

REFERENCE

NEPHROPATHY, MINIMAL CHANGE

DESCRIPTION
Minimal change nephropathy is the most common cause of idiopathic nephrotic syndrome, most often affecting children but can account for up to 15% of adult nephrotic syndrome. Sometimes called minimal change disease, this condition manifests as nephrotic syndrome, with massive proteinuria and anasarca without hyperension. NCS in the urine are a common finding; histologic evaluation shows essentially no changes on light microscopy. Electron microscopy shows epithelial foot process fusion. The pathogenesis is unknown, but T-cell dysfunction is theorized. The nephropathy can be primary or secondary to medications, neoplasms, infection, allergy, or other renal glomerular diseases; it frequently undergoes spontaneous remission, is responsive to corticosteroid therapy, and rarely progresses to chronic renal failure. (See also Section I: “Nephrotic Syndrome.”)

REFERENCE

NEPHROPATHY, OBSTRUCTIVE

DESCRIPTION
Obstructive nephropathy occurs when renal obstruction is due to obstruction of the urinary system. The point of obstruction can be in the upper or lower urinary tract. Congenital, inflammatory, neoplastic, and anatomic etiologies of urinary obstruction are all common. Obstruction of the outflow from the kidney results in several changes that lead to renal failure. The tubular injury in obstructive nephropathy is caused initially by the increased intratubular pressure and later by atrophy induced by reduced perfusion pressure, ischemia. The recovery of renal function after relief of the obstruction is determined by the duration of the obstruction, baseline renal function, patient age, and degree of obstruction. The total obstruction of the ureter, relatively complete recovery of GFR can be achieved within 1 wk, whereas after 12 wk, little or no recovery is seen. (See also Section I: “Hydronephrosis.”)

REFERENCE

NEPHROPATHY, URATE (URATE NEPHROPATHY)

DESCRIPTION
A disorder in which an abrupt deterioration in renal function occurs due to the renal tubular damage caused by uric acid crystals. Chronic renal injury from uric acid deposition is most often associated with gout and is uncommon today.

REFERENCE
Nephrotic Syndrome

2 forms are recognized, acute and chronic. Acute renal nephropathy occurs almost exclusively in the setting of malignancies, such as leukemia and lymphomas, with rapid cell turnover leading to increased purine metabolism and loss of nucleotides in the plasma. This is further enhanced by added acceleration of cell lysis, which occurs with chemotherapy and radiation used in these patients, producing the so-called tumor lysis syndrome. Nucleotides are converted to urate by xanthine oxidase, resulting in hyperuricemia with levels of 25–90 mg/dL at the time of onset of renal dysfunction. Diagnosis requires the appropriate clinical setting of increased cell lysis (usually with chemotherapy), oliguria, marked hyperuricemia, and hyperuricosuria. A urinary uric acid-to-creatinine ratio >1 distinguishes this from other catabolic states with hyperuricosuria. A urinary uric acid-to-creatinine ratio >1 distinguishes this from other catabolic states with increased serum urate levels and renal failure, such as trauma with rhabdomyolysis. (See also Section I: “Dietl Crisis.”)

TREATMENT
- Prevention is the key, using xanthine oxidase inhibitors with allopurinol and aldehyde dehydrogenase prior to initiation of chemotherapy.
- Alkalization of urine in the acute tumor lysis syndrome is not possible in the setting of renal diabetes.
- Rhabdovac (Esic) is recombinant urate oxidase that converts uric acid to water-soluble allantoin.
- Occasionally, dialysis is required to correct azotemia and reduce urate levels.

REFERENCE

NEPHROPTOSIS

DESCRIPTION
A largely historic classification system for describing the level of tumor thrombus associated with a renal mass. The categories are renal vein, vena cava, aorta, and confluence. The primary clinical application of nephropexy in renal cell carcinoma with tumor thrombus extension within the inferior vena cava, hepatic veins, and vena cava right atrial junction. The proportion of renal cell carcinoma patients with tumor thrombus in the inferior vena cava is approximately 5%.[2] This proportion is likely higher if patients demonstrating a more favorable prognosis for surgical resection are excluded. The role of nephropexy with respect to the management of renal cell carcinoma with tumor thrombus is to provide better surgical access, facilitate a potential cure, and improve patient survival. Nephropexy is performed when the tumor is too distant from the hilus for adequate surgical resection without additional morbidity. Nephropexy may be indicated in patients with high-risk tumors or when the tumor is too large to be removed safely. Nephropexy is performed by transperitoneal or retroperitoneal approaches. The transperitoneal approach is associated with a lower rate of complications, but the retroperitoneal approach allows for better visualization of the tumor and surrounding structures. The retroperitoneal approach is preferred for tumors involving the inferior vena cava, hepatic veins, and vena cava right atrial junction. The retroperitoneal approach is also associated with a lower rate of complications. Nephropexy should be performed by experienced surgeons with expertise in open and laparoscopic surgery.

REFERENCE

NEUROENDOCRINE TUMORS, GENITOURINARY

DESCRIPTION
A group of tumors that share a characteristic morphology, often being composed of clusters and trabecular sheets of round blue cells, granular chromatin, and an attenuated rim of poorly demarcated cytoplasm. Neuroendocrine tumors include carcinoids, small (blast) cell carcinomas, medullary carcinoma of the thyroid, Merkel cell tumor, cutaneous neuroendocrine carcinoma, pancreatic islet cell tumors, and pheochromocytoma. Small (blast) cell carcinomas have been described most often in the prostate and bladder. Prostate cancer with neuroendocrine differentiation is considered a variant of Gleason’s adenocarcinoma of the prostate. Undifferentiated carcinomas of the urinary bladder and prostate should be analyzed not only by means of hematoxylin and eosin but also by immunohistochemical staining for chromogranin A (Chr A) and synaptophysin (SNP), to demonstrate a neuroendocrine origin. Because the prognosis of small cell neuroendocrine cancers is very poor, aggressive multimodal therapy is often employed. (See also Section II: “Neuroendocrine Tumors,” Section III: “Multiple Endocrine Nodules (MEN I, MEN II),” “Prostate Cancer, Small Cell.”)

REFERENCE

NEUROFIBROMATOSIS, UROLOGIC CONSIDERATIONS

DESCRIPTION
A hereditary disorder characterized by cafe-au-lait spots, cutaneous fibromas, and neurofibromas. It is associated with renovascular lesions and pheochromocytomas. Vascular lesions are characterized by endothelial proliferation, with or without aneurysmal formation and cellular nodules in the vessel walls. The aorta is frequently involved, and the renal arteries may demonstrate large areas of stenosis that are generally best treated with revascularization rather than angioplasty. In addition, a 20-fold increase in the incidence of neurofibromatosis in patients with Wilms tumor has been reported.

REFERENCE

NEUROGENIC DETURS OVERACTIVITY (NDO)

DESCRIPTION
NDO patients are a heterogeneous group with both storage and voiding dysfunction. The NDD symptoms include urinary frequency, urgency, and incontinence. Neurogenic conditions associated with NDO include multiple sclerosis (MS), spinal cord injury (SCI) Parkinson disease, cerebral palsy, and myelomeningocele. Neurogenic bladder dysfunction is present in 80.8% of individuals with MS, 95% with myelodysplasia, virtually all SCI patients with persistent neurologic deficits and 70% of ambulatory SCI patients. NDO impacts quality of life and can also result in risk of UTI and upper urinary tract damage. Anticholinergic therapies such as oxybutynin are primarily used for patients with DO and poor compliance. CIC may be best for those who have poor bladder emptying. Although not FDA approved neuromodulation via sacral nerve stimulation is useful in patients who have failed anticholinergics. Intramuscular injection of onabotulinumtoxin A is FDA approved in the management of NDO in patients refractory or intolerant of anticholinergics. In selected individuals, a chronic indwelling catheter may be the best management therapy. Surgical intervention (bladder augmentation, urinary diversion, continent urinary diversion, and ileovesicostomy) may be indicated for protection of the upper urinary tract in high-risk patients or to achieve continence. (See also Section I: “Neurogenic Bladder, General Considerations.”)

REFERENCE

NEURONMODULATION, UROLOGIC CONSIDERATIONS

DESCRIPTION
Neuromodulation involves the use of electrical current to alter physiologic properties. This technology has been applied to lower urinary tract dysfunction for the past decade by stimulation of the sacral nerve roots. Sacral neuromodulation was approved in patients with overactive bladder refractory to medical and behavioral therapy by the FDA in 1997. A recent multi-institutional clinical trial shows success rates as high as 68% for urge incontinence, 56% for urgency-frequency, and 71% with obstructive urinary retention at 5 yr after implantation. Posterior tibial nerve stimulation is also being used. (See also Section II: “Posterior Tibial Nerve Stimulation: Urgent PC [PTN].”)

REFERENCE

NEVES–ZINCKE CLASSIFICATION

DESCRIPTION
A legacy of anatomic classification system for describing the level of tumor thrombus associated with a renal mass. The categories are renal vein, vena cava, aorta, and confluence. The primary clinical application of nephropexy in renal cell carcinoma with tumor thrombus extension within the inferior vena cava, hepatic veins, and vena cava right atrial junction. The proportion of renal cell carcinoma patients with tumor thrombus in the inferior vena cava is approximately 5%.[2] This proportion is likely higher if patients demonstrating a more favorable prognosis for surgical resection are excluded. Nephropexy should be performed by experienced surgeons with expertise in open and laparoscopic surgery.

REFERENCE
**NMP-22 TESTING**

Description: NMP-22 has been found to serve as a urinary marker for TCC. The NMP-22 test (Marinechip, Inv. Alpha, NA) is a quantitative immunassay that measures NMP-22. The addition of NMP-22 testing to cytology may increase the sensitivity for recurrent detection in patients with superficial transitional cell bladder cancer. Patients with positive NMP-22 findings develop significantly more recurrences compared with those with negative NMP-22 findings in several studies.


**NOCTURNAL ERECTIONS, NORMAL AND ABNORMAL**

Description: Nocturnal erections occur at night during REM sleep. The number of erections peaks during puberty. Various criteria exist for what is considered normal nocturnal activity at night, but normal is usually 4–5 erections per night with a mean duration >30 min and an increase in circumference of >3 cm at the base and >2 cm at the tip, as well as maximal rigidity above 75% at both base and tips. (See also Section II: “Nocturnal Penile Tumescence Testing.”)


**NOCTURNAL PENILE TUMESCENCE (NPT) TESTING**

Description: NPT refers to a recurring cycle of penile erections associated with rapid eye movement sleep. The primary goal of NPT testing is to distinguish between psychogenic and organic causes of impotence; nocturnal monitoring devices measure the number of erectile episodes, maximal penile rigidity, tumescence, and duration of erections. This testing assumes that the mechanism for nocturnal erections is the same as that for sexually induced erections. (See also Section II: “Nocturnal Erections, Normal and Abnormal.”)


**NOCTURNAL POLYURIA (NP) TESTING**

Description: NP is a condition in which the rate of urine output is excessive only at night, and total 24-hr output is within normal limits. NP is defined as the production of >13 of total 24-hr urine output between midnight and 8 AM (normal physiologic response is reduced urine output at night).


**NONARTERITIC ANTIEROSIONIC OCULAR NEUROPATHY (NAION)**

Description: NAION describes the acute, painless loss of vision in 1 eye associated with optic disc edema (crowded optic disk). It is a common cause of acute optic neuropathy in adults. Associations have been found between NAION and the phosphodiesterase inhibitors sildenafil, vardenafil, and others.


**NONSACRAL NEUROMODULATION**

Description: Neuromodulation involves the use of electrical current to alter physiologic properties. This technology has been applied to lower urinary tract dysfunction for the past decade by stimulation of the sacral nerve roots. There has been recent interest into stimulation of more distal branches of the same nerve roots as well, including the pudendal, dorsal genital, and posterior tibial nerves. (See also Section II: “Neurostimulation, Urologic Considerations.”)


**NOONAN SYNDROME**

Description: This autosomal dominant syndrome consists of multiple congenital anomalies, including characteristic facial features, short stature, and heart defect. Over 1/2 of males with Noonan syndrome have unilateral or bilateral cryptorchidism. Females can have delayed sexual maturation, but normal development is expected. Renal anomalies occur in 10% of children. Because congenital cardiac anomalies are found in 1/2 of the patients, all patients with this syndrome should have cardiac evaluation and slow follow-up. Growth hormone replacement may have value in treating short stature.


**N-TELOPEPTIDE, URINARY**

(NTX)

**DESCRIPTION**

NTX is a product of type I collagen breakdown that can be measured in the urine. Several studies suggest its utility as a marker for bone turnover in osteoporosis, and for response to treatment of bone metastases and bisphosphonate therapy. Typical reference ranges are (bone collagen equivalent) BCE(24 h): 26–124 nM BCE/mM creatinine; adult female premenopausal: 17–84 nM BCE/mM creatinine; postmenopausal: 26–124 BCE/mM creatinine. A decrease of 30–40% from the NTX baseline after 3 yrs of therapy is typical for treatment with bisphosphonate.

**REFERENCE**


**NUTCRACKER SYNDROME**

**DESCRIPTION**

This syndrome occurs secondary to compression of the left renal vein by the superior mesenteric artery and the aorta. Patients are usually young and previously healthy. Presentation classically is due to gross hematuria caused by left renal vein hypertension. Pelvic pain may be present. Various modalities, including nephrotomies, autotransplantation, renal neophlebitis, and nephrectomy have been employed. Gom-Test graft renal vein interposition and anterior nephropexy have been successful (Image 9).

**REFERENCE**

The obturator nerve, which is made to trim both segments sharply. In the event of a nerve is frayed and grossly devitalized, efforts can be repair when applied to the new anastomosis. If the approximation. An absorbable collagen implant nerve be made to align the nerve fibers prior to edges with four 6–0 to 10–nylon or Prolene epineural surgical repair may be done by end-to-end intraoperative obturator nerve injury is not well helpful in making the diagnosis. Symptoms include hypertension, diabetes, and vascular disease.

Likewise, this aromatization of androgens leads to conversion of testosterone to estradiol in adipocytes. Obese men is postulated to result, at least partially, by adverse pathology. Renal cell carcinoma (RCC) is also associated with obesity. The increased incidence in prostate cancer in obese men is postulated to result, at least partially, by treatment involves the removal of potentially bladder tumors located on the posterolateral wall, or laparoscopic pelvic lymph-node dissection) can cause unexpected adduction of the thigh. Surgeons must be aware of this response so as not to cause inadvertent injury, such as perforation of the bladder. This response can usually be prevented by muscle-paralyzing anesthetic agents.

O’Leary MP, Sant GR, Fowler FJ Jr, et. al. The O’Leray–Sant Interstitial Cystitis Symptom Index (ICSI) DESCRIPTION The ICSI is a validated questionnaire that documents and scores patient’s questionnaire that documents and scores patient’s symptoms of urinary urgency, frequency, nocturia, and dysuria/pain over a 30-day period. It has been found useful as a tool to follow symptoms of but not the diagnosis of interstitial cystitis.


**REFERENCE**

**DESCRIPTION**
OPITZ-FRIAS SYNDROME
**DESCRIPTION**
Also called the OIF syndrome (named for 1 of the first patients), this condition is due to a defect of midline development, characterized by numerous congenital abnormalities of the face. Many patients have hypertelorism and posteriorly rotated ears, hypogonadism is almost always present. Other manifestations include cleft lip and palate, high trigeminal and facial paralysis, upper extremity syndactyly, microcephaly, anorectal malformations, long hypoplastic, and cardiac abnormalities. Inheritance is autosomal dominant with incomplete penetrance. Carries show minimal abnormalities. It is more common in males, and perinatal mortality is around 30%.

**REFERENCE**
Conklin BJ, O’Dwyer TH. The G syndrome, Opitz

**DESCRIPTION**
Briefly, the OPI syndrome (named for 1 of the first patients), this condition is due to a defect of midline development, characterized by numerous congenital abnormalities of the face. Many patients have hypertelorism and posteriorly rotated ears, hypogonadism is almost always present. Other manifestations include cleft lip and palate, high trigeminal and facial paralysis, upper extremity syndactyly, microcephaly, anorectal malformations, long hypoplastic, and cardiac abnormalities. Inheritance is autosomal dominant with incomplete penetrance. Carries show minimal abnormalities. It is more common in males, and perinatal mortality is around 30%.

**REFERENCE**
Conklin BJ, O’Dwyer TH. The G syndrome, Opitz

**DESCRIPTION**
OPITZ-FRIAS SYNDROME
**REFERENCE**

**DESCRIPTION**
ORTHO-PHTHALALDEHYDE
**DESCRIPTION**
OPA 0.55% is a chemical disinfectant. It can irritate eyes, skin, rose, and other tissues. OPA is FDA approved as a high level disinfectant (2 min at 20°C and 5 min at 25°C). Ortho-Pthalaldehyde has been reported in patients with a history of bladder cancer who underwent repeated cystoscopy with scopes sterilized with OPA. OPA is contraindicated in patients with a history of bladder cancer but can be used in manual or automated repacking protocols.

**REFERENCE**

**DESCRIPTION**
OSTEONECROSIS OF THE JAW (ONJ), UROLOGIC CONSIDERATIONS
**DESCRIPTION**
Osteonecrosis is a newly recognized complication of long-term therapy with bone strengthening agents in patients with metastatic cancer to the bone such as prostate, breast and renal cell cancer and in multiple myeloma. Bisphosphonates and denosumab decrease cancer-induced bone resorption thereby reducing SREs, pain, and improving quality of life. Initially identified as an exposure-necrosis multifocal bone for >9 wk in patients treated with bisphosphonates or denosumab who have not had radiation to the jaws. The exposed bone becomes infected with oral flora, resulting in significant pain and need for surgery. A new term is bisphosphonate-related osteonecrosis of the jaws (BRONJ). Symptoms include pain, swelling, redness, or other signs of infection in the gums, ears or cheeks that don’t heal after dental work, loose teeth and numbness or a heavy feeling in the jaw. The risk of developing ONJ is related to the potency of the antiresorptive, the duration of exposure, and demineralized trauma. Prospective studies of patients taking bisphosphonates for metastatic prostate cancer that include regular exam by dentist estimate an incidence as high as 20% which is much higher than retrospective studies that suggested an incidence of 3-4%. Dental clearance before initiating therapy is recommended as well as avoiding extensive dental work while on therapy.

**REFERENCE**
DESCRIPTION
Ovarian cancer is the leading cause of death from gynecologic cancer and is usually of epithelial origin. These tumors can often involve adjacent structures or cause extrinsic compression of the urinary tract, including the bladder and ureters, with the resultant need for urologic intervention.

REFERENCE

OVARIAN REMNANT SYNDROME
DESCRIPTION
This condition is a rare complication of bilateral oophorectomy and occurs when remnants of ovarian cortex are inadvertently left behind. The remaining ovarian tissue becomes functional and cystic. Typically, patients present with pelvic pain that can be chronic or intermittent and a pelvic mass. Symptoms may begin weeks to 5 yr postoperatively. Unusual obstruction has been reported. Excision of the ovarian remnant is the most widely accepted treatment method. Prespective ovarian stimulation can help reproductive identification of retained tissue. Surgery is associated with an 8–10% recurrence rate.

REFERENCES

OVARIAN VEIN SYNDROME
DESCRIPTION
Unilateral obstruction, usually rightsided, occurring secondary to occlusion or dilated ovarian veins. The ovarian veins lie adjacent to the ureters, and dilatation of these veins, especially during pregnancy, is thought to occur in uterine obstruction. The obstruction is usually seen around the L3–L4 vertebral level. Symptoms include chronic flank pain, but uterine pain has also been found. The symptoms can also begin several days prior to menarche and then regress. Diagnosis can be made by IV urogram, retrograde ureteropyelography, and simultaneous angiography. Untreated and ovarian vein exclusion can be performed using open or laparoscopic techniques.

REFERENCES

OVARIAN CANCER, UROLOGIC CONSIDERATIONS
DESCRIPTION
Ovarian cancer is the leading cause of death from gynecologic cancer and is usually of epithelial origin. These tumors can often involve adjacent structures or cause extrinsic compression of the urinary tract, including the bladder and ureters, with the resultant need for urologic intervention.

TREATMENT
• Caution: 1,200 mg/d; it is recommended most calcium come from foods (dairy, green leafy vegetables).
• Vitamin D: at least 800–1,000 IU (daily preferable from foods [forty for and intake, liver, raw milk]) with sun exposure of 30 min or supplements.
• Exercise to include weight bearing.
• Stop smoking, limit alcohol and caffeine intake.
• Calcium carbonate: 1–2 g PO Q 4–6 h.

CONSIDER-Biphosphonates:
• Alendronate (Fosamax, Fosamax Plus D) approved for treatment of men with osteoporosis and treatment/prevention of osteoporosis in men taking glucocorticoids.
• Risedronate (Acteon, Alar) approved for treatment of men with osteoporosis and treatment/prevention of osteoporosis in men taking glucocorticoids.
• Pamidronate (Areda) for men with Paget disease, hyperparathyroidism, malignancy, malignant myeloma.
• Zoledronic acid (Zometa): 4 mg intravenously IV approved for bone metastasis but not male osteoporosis.
• Denosumab: (Xgeva) 120 mg SC Q every 4 wk (for osteoporosis).

REFERENCES

REFERENCE

Oxalate, Dietary
DESCRIPTION
An excessive intake of oxalate-rich foods should be limited or avoided to prevent an oxalate load. This includes fruits and vegetables rich in oxalate such as bean sprouts, kidney beans, and spinach. Some studies have shown that a daily intake of up to 4 g might be allowed without risk. However, a recent study demonstrated an increased risk in stone formation for men taking 1 g/d or more of vitamin C vs. < 0.9 g/d. It is therefore seems justified to advise calcium-oxalate stone formers to avoid excessive intake of vitamin C. (See also Section I: “Urolithiasis, Calcium Oxalate/Phosphate.”) The following products have high oxalate content:
• Rhubarb, 530 mg oxalate/100 g
• Spinach, 570 mg oxalate/100 g
• Cocoa, 625 mg oxalate/100 g
• Tea leaves, 375–1,450 mg oxalate/100 g
• Nuts, 200–450 mg oxalate/100 g

REFERENCES

Oxalate-Associated Renal Disease
DESCRIPTION
Hypersudrosis is associated with calcium oxalate nephrolithiasis. An increased oxalate production or absorption, or an idiopathic form, might be responsible for the disease. In cases of primary hyperoxaluria, stone formation usually starts during childhood, with eventual tubulointerstitial nephropathy and chronic renal failure. Oxalate deposition in heart, joints, and other tissues (oxalosis) may occur. (See Section II: “Hypersudrosis,” for the causes of increased urinary oxalate.)

TREATMENT
• Piroxicam supplements (200–400 mg/d) for primary hyperoxaluria
• Oral hydration; low oxalate, low-fat diet for enteric hyperoxaluria
• Pyridoxine (thiamine) for idiopathic hyperoxaluria

REFERENCES

Oxalate-AssOCIATED RenAL DisEASE
DESCRIPTION
The p53 gene produces a nuclear phosphoprotein that has a tumor-suppression function. Loss of wild-type p53 is the most common genetic abnormality associated with UC. Its presence is associated with high grade, late stage, and relices. Potentially, it may be useful in grading tumors. In prostate cancer, p53 is associated with an increased probability of biochemical relapse and is found in a higher percentage of hormone-refractory cancers.

REFERENCES

Pad Testing
DESCRIPTION
Used as a clinical tool to assess the severity of urinary incontinence, often in association with a urodynamic study. The pad test provides a gross/semi-quantitative measurement of urine loss over a given period of time. Several types have been described, but none has met with widespread approval. 1 technique has a patient take...

Osteotomy, Urologic Considerations
DESCRIPTION
Osteotomy is the surgical technique of cutting bone to its shape, length, or alignment. This becomes of particular necessity in surgical repair of bladder exstrophy to correct a wide pubic diastasis. Advantages of pelvic osteotomy include decreased bladder dehiscence, improved continence, and less late pelvic organ prolapse in females.

REFERENCE

REFERENCES

P53, Urologic Considerations
DESCRIPTION
The p53 gene produces a nuclear phosphoprotein that has a tumor-suppression function. Loss of wild-type p53 is the most common genetic abnormality associated with UC. Its presence is associated with high grade, late stage, and relapse. Potentially, it may be useful in grading tumors. In prostate cancer, p53 is associated with an increased probability of biochemical relapse and is found in a higher percentage of hormone-refractory cancers.

REFERENCE

Pad Testing
DESCRIPTION
Used as a clinical tool to assess the severity of urinary incontinence, often in association with a urodynamic study. The pad test provides a gross/semi-quantitative measurement of urine loss over a given period of time. Several types have been described, but none has met with widespread approval. 1 technique has a patient take...
Pyridium 200 mg TID and then change pads every 6 hr for a 24-hr period. The amount of staining is an estimate of hemorrhage. Another approach is to weigh the pads (1 g = 1 mL urine).

REFERENCE

**PAGANO URETERAL ANASTOMOSIS**
DESCRIPTION
A 4–5-cm linear incision is made through the skin of the colon, and the muscularis is dissected from the submucosa to the level of the mesentry. The ureters are pulled through the lateral muscular wall and implanted directly into the mucosa. The ureters are then reapproximated while incorporating muscosa in the midline.

REFERENCE

**PAGE KIDNEY**
DESCRIPTION
This condition was first described in 1909, after hypertension was created by wrapping cellophane around a canine kidney. Applied clinically, this term was given to hypertension secondary to subcapsular or perirenal compression resulting in renal ischemia. Elevated serum creatinine from the compromised kidney and decreased renal production from the contralateral renal unit result. Diagnosis can be made with CT, IV, or MRA, demonstrating a surrounding heterogeneous capsule. Clinical causes include blunt trauma, closed renal biopsy, anticoagulation, or tumor bleed. Treatment is directed at the primary cause. Further therapy may include ACE inhibitors, open or percutaneous drainage, or nephrectomy. Spontaneous resolution can occur secondary to resumption of the hematoma.

REFERENCE

**PAGET DISEASE, ANOGENITAL/EXTRAMAMMARY**
DESCRIPTION
Lymphoplasmacytic leukemia in the epimysium can affect many areas in the body, the mammary gland areas of the body, the mammary glands and may also result from extraneous adenocarcinoma that spread into the epimysium. Evacution of skin lesion and evaluation for underlying malignancy should be performed.

REFERENCE

**PAGET DISEASE, BONE**
DESCRIPTION
This condition affects up to 10% of elderly individuals, with a 3:1 male-to-female ratio. Bone pain is the most common presenting symptom. Paget disease of the spine may also be a cause of low back pain. The disorder is due to increased bone remodeling, bone hypertrophy, and bone deformity of uncertain origin. Paget disease, also called osteitis deformans, is characterized by an initial phase of intense osteoclastic resorption, followed by an increase in bone formation, but the new skeletal tissues are deformed and prone to inducing pain and fracture. Approximately 1/5 of Paget disease cases have monocytic disease, with pelvic involvement in 72%. In these cases, the lumbar spine is involved in 58%, the thoracic spine in 45%, and the femur and skull in 55% and 42%, respectively. Patients’ elevated alkaline phosphatase or bone pain may be due to Paget disease or other diseases, such as liver disease, renal disease, or metastatic prostate cancer. Radiographically, the localized enlargement of bone is a characteristic feature. Areas of lytic due to osteoclastic resorption can also be present. It can be confused with metastatic prostate cancer to bone. Suspect Paget disease over metastatic prostate cancer when there is widening of the bone, thickening of the cortex, and a prominent tubular pattern. MRI of the bone may help in differentiating the processes.

TREATMENT
Pain reduction and decreasing long-term complications are the main goals.
- Inhibitors of osteoclastic bone resorption, such as bisphosphonates (zoledronic acid, risedronate, alendronate) are now the treatment of choice. (See Section II: “Osteoporosis and Osteopenia, Urologic Considerations.”) Calcitonin is reserved for those intolerant of bisphosphonates.

REFERENCE

**PAINFUL BLADDER SYNDROME (PBS)**
DESCRIPTION
The ICS defines PBS as suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and night-time frequency, in the absence of proven urinary infection or other obvious pathology. According to the ICS, PBS differs from interstitial cystitis in that the latter has cystoscopic and histologic findings. Treatment begins with conservative measures including dietary modification, behavioral changes, and nonprescription medications, followed by intravesical therapy and prescription medications. Patients who fail these therapies may resort to more invasive therapies including hydrodistention, neuromodulation, and finally urinary diversion or augmentation.

REFERENCE

**PALLIATIVE RADIATION, UROLOGIC CONSIDERATIONS**
DESCRIPTION
The symptoms of advanced urologic malignancies are often treated with palliative radiation. Approximately 1/2 of prescribed radiation is given for palliation of symptoms from incurable cancer. For example, 90% of patients with symptomatic bone metastases, commonly seen in metastatic prostate cancer, obtain some pain relief with a low-dose, brief course of palliative radiation. Bone metastases can also result in erosion of cortical bone and tumor invasion into the extraspinal space, which affects either within the spinal cord and compression of the neurologic structures. The degree of edema within the cord is directly related to the neurologic impairment. Spinal cord compression from malignancy requires early diagnosis and treatment with emergency surgery to prevent irreversible neurologic injury. Radiation therapy has also been shown to relieve clinical symptoms in 75–90% of patients with bone metastases, sometimes seen in patients with metastatic RCC.

REFERENCE

**PANCREATITIS, AUTOIMMUNE UROLOGIC CONSIDERATIONS**
DESCRIPTION
Autoimmune pancreatitis (AIP) has been referred to by a variety of names including sclerosing pancreatitis, tumorlike pancreatitis, and nonalcoholic obstructive pancreatitis. It is recognized to be an idiopathic, chronic, inflammatory disorder of the pancreas (IgG4-RD). IgG4-related kidney disease can include tubulointerstitial nephritis and membranous glomerulonephritis.

REFERENCE

**PANETH CELL-LIKE CHANGE, PROSTATE**
DESCRIPTION
Paneth cell metaplasia of the prostatic epithelium, due to the presence of PSA and PAP on immunohistochemistry. These changes have been described in normal, hyperplastic, dysplastic, and malignant prostate tissue, and must be differentiated from other pathology.
Prostatic intraepithelial neoplasia including secretory vessels, induration, CIN-like areas, or viral-like particles.

REFERENCE

PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL (PUNLMP)

DESCRIPTION
The World Health Organization defines PUNLMP as a papillary urothelial tumor that resembles an exophytic urothelial papilloma, but shows increased cellular proliferation exceeding the thickness of normal urothelium. They are typically small (1–2 cm) and have little or no, cystic atypia. Treatment and follow-up are the same as for low-grade noninvasive urothelial carcinoma. (See also Section II: “WHO/ISUP Classification of Urothelial Neoplasms” [1998 and 2004].) (Image 90)

REFERENCE

PAPILLORENAL SYNDROME

DESCRIPTION
Also called renal condrum, this is an autonomic dominant disorder characterized by bilateral congenital optic disc anomalies and hypoplastic kidneys. It is associated with mutations in the PK2X gene. Many patients suffer from renal failure due to renal hypoplasia or chronic pyelonephritis from urothelial reflux.

REFERENCE

PAQUIN URETERAL REIMPLANTATION

DESCRIPTION
This repair is done using combined extravesical ureteral mobilization and intravesical implantation. A submucosal plane is developed extravesically ureteral mobilization and intravesical implantation. A submucosal plane is developed

REFERENCE

PARAPHILIAS, UROLOGIC CONSIDERATIONS

DESCRIPTION
Paraphilias are psychosocial concerns related to abnormal sexual behavior. These may be encountered in daily urologic practice and are often referred for psychological intervention. Different kinds of paraphilias, based on the Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Text Revision (DSM-IV-TR) classification are noted in the accompanying table.

SYNONYM
Sexual Deviation

Paraphilia Designation Description
Exhibitionism Exposure of genital to unsuspecting strangers (not considered the same as public nudity).
Fetishism Use of nonliving objects as repeatedly preferred or exclusive method of sexual excitement (eg, leather goods, clothing, undergarments, fabrics, shoes). Of female clothing is used in cross-dressing or devices are used for genital stimulation (eg, vibrator) this is not considered as fetishism.
Frottiration Touching and rubbing against a nonconsenting person.
Pedophilua Children are the sexual target (perpetrator is ≥16 yo and ≤5 than 5 years older than the prepubescent child).
Sexual masochism Perpetrator receives the humiliation/suffering can lead to death, especially during “hypoxyphilia” or sexual arousal during hypnosis.
Sexual sadism Perpetrator inflicts the humiliation/suffering on another.
Transvestic fetishism Wearing clothing of the other sex for sexual arousal.
Voyeurism Observing sexual activity or naked/dressing individuals.
Paraphilias: Not Otherwise Specified

REFERENCE

PARASTOMAL HERNA

DESCRIPTION
A parastomal hernia is an incisional hernia related to an abdominal wall stoma. In urologic surgery, parastomal hernias occur infrequently (<1–3% of cases) and are more likely to arise in low-type stoma than in end-type stoma. To prevent parastomal herniation, it is recommended that the stoma be placed through the rectus muscle and that the opening in the abdominal wall not be too large. In addition, some have placed mesh at the time of stoma creation to prevent hernia formation. Repair of a parastomal hernia follows the same principles as treating other types of incisional hernias and can be completed in an open or laparoscopic fashion, with or
without mesh. (See also Section I: "Urostomy Problems.")

REFERENCE


PARATESTICULAR RHABDOMYOSARCOMA

DESCRIPTION

Rhabdomyosarcoma is the most common sporadic childhood cancer, arising from the mesenchymal elements of the paratesticular tissues and representing 40% of all paratesticular malignancies and 5% of all testicular and paratesticular malignancies. There is a bimodal age distribution, peaks at 3–4 mo and 16 yr. Patients present with a painless firm mass which can be a wide range of sizes. Roughly 40% have metastases at presentation. Ultrasound reveals a heterogeneous mass. CT scan of the abdomen and pelvis, liver function tests, bone scans, and chest x-ray are required for staging. Several histologic patterns are described, with almost all being embryonal. After treatment, cross-sectional imaging and liver function tests are needed every 2–3 mo. (See also Section I: "Urothelial Paratesticular Tumors and Cysts."

TREATMENT

• Radical orchectomy.
• Boys 10 yr or older with evidence of retroperitoneal disease should undergo retroperitoneal lymph node dissection (RPLND).
• Those with evidence of lymph node spread undergo adjuvant therapy and multigland chemotherapy.

REFERENCE


PARAURETHRAL AND VAGINAL WALL MASSES

DESCRIPTION

Paraurethral masses can be benign (urothelial caruncles, Simee’s gland abscesses, vesical prolapse, acdotic watermelon, urethral diverticulum, vaginal wall cyst, Gartner’s duct cyst, leiomyoma, hamartoma or malignant) (adenocarcinoma, SCC, TCC, histiocytoma, and melanoma), and can be classified according to the location of the lesion. The most common paraurethral mass is the urethral diverticulum, followed by the leiomyoma and the vaginal wall cyst. Masses may be asymptomatic or particularly for masses causing voiding dysfunction. Physical exam may help distinguish benign from malignant lesions. Paraurethral malignancies do not normally present as paraurethral masses, but more commonly with complaints of bleeding and discharge.

REFERENCE


PARTN TABLES

DESCRIPTION

Nomograms for patients with biopsy-proven prostate cancer, developed by Dr. Partin and associates at Johns Hopkins University, these charts incorporate PSA, TMM stage, and Gleason score. They are used to predict rate of lymph node and distant spread or whether patients have organ-confined cancer, and to aid in making accurate treatment decisions. The tables have been updated several times, using larger patient cohorts. Information is available online: http://urology.jhu.edu/prostate/partintables.php. Accessed March 3, 2014.

REFERENCE


PATAU SYNDROME

DESCRIPTION

This rare syndrome is associated with trisomy 13 and has a median survival of 3 mo. The incidence is 1 in 6,000 live births and is associated with multiple cardiac, neurologic, and renal abnormalities. Renal anomalies occur in about 80% of children. Unilateral renal agenesis, renal duplication, hydrouphrosis, and polycystic kidneys have been associated with Patau syndrome.

REFERENCE


PATIENT PERCEPTION OF BLADDER CONDITION (PPBC)

DESCRIPTION

The Patient Perception of Bladder Condition (PPBC) is a questionnaire that attempts to obtain a global assessment of the patient’s bladder condition. It has been validated and shown to be responsive to changes. It has been translated into many languages and is widely available for use.

Which of the following statements describes your bladder condition best at the moment? Please mark X in 1 box only.

- My bladder condition does not cause me any problems. (0 pt)
- My bladder condition causes me some minor problems. (1 pt)
- My bladder condition causes me some moderate problems. (2 pt)
- My bladder condition causes me some severe problems. (3 pt)
- My bladder condition causes me (some) severe problems. (4 pt)
- My bladder condition causes me (none) moderate problems. (5 pt)
- My bladder condition causes me severe problems. (6 pt)

REFERENCE


PATENT PERCEPTION OF INTENSITY OF URGENCY SCALE (PPUIS)

DESCRIPTION

A simple question tool to assess the patient’s perception of the degree of urgency. PPUIS as a reliable measure of urgency in both clinical trials and real life settings. The question is as follows:

Patient Perception of Intensity of Urgency Scale

0. No urgency. I felt no need to empty my bladder but did so for other reasons.
1. Mild urgency. I could postpone voiding as long as necessary without fear of wetting myself.
2. Moderate urgency. I could postpone voiding for a short while without fear of wetting myself.
3. Severe urgency. I could not postpone voiding but had to rush to the toilet in order not to wet myself.

REFERENCE


PC2A (PROSTATE CANCER GENE 3 URINE ASSAY)

DESCRIPTION

Prostate cancer antigen 3 (PCA2) is a gene that expresses a noncoding RNA. PCA2 is over expressed in 95% of prostate cancers and is upregulated 64-fold in cancerous tissue as compared to normal tissue. No other human tissues have yet been shown to produce PCA2. While serum PSA levels are known to be influenced by volume of BPH tissue, age, inflammation, trauma, and use of 5α-reductase inhibitors (finasteride, dutasteride), preliminary data indicate that these factors do not appear to influence PCA2 scores. Urine samples are collected after an “attention” digital rectal exam (5 swipes on each side of the prostate), 1st voided urine is then collected and sent to labs for analysis. PCA2 and PSA can be detected in the urine utilizing reverse transcriptase PCR techniques on the collected cells. PCA2 expression is detected against a background of prostate specific genetic material, a PCA2 score (a ratio of PCA2 to PSA mRNA). Studies have shown excellent specificity and sensitivity in men undergoing confirmatory prostate biopsy, and its role in the diagnosis of prostate cancer is currently evolving. A useful role of the new marker appears to be in men with persistently elevated serum PSA levels, but a negative initial biopsy.

REFERENCE

Martin T. ASCO. 2013;111(1):5 For analysis.

PC2A/PSA mRNA Ratio vs Serum PSA in Men with Previous Negative Biopsy

<table>
<thead>
<tr>
<th>Serum PSA</th>
<th>PCA2 Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0 ng/mL</td>
<td>0.25 × 10^{-1}</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>83%</td>
</tr>
<tr>
<td>Specificity</td>
<td>74%</td>
</tr>
<tr>
<td>Odds Ratio of</td>
<td>1.2</td>
</tr>
<tr>
<td>Positive likelihood</td>
<td>3.6</td>
</tr>
</tbody>
</table>
PELARY PAPERIES OF PENIS

DESCRIPTION

These are normal anatomic structures located on the proral genital penis or corona. They appear as minute, dome-shaped, flesh-colored papules. The incidence is 1%–10%. These lesions are asymptomatic and can be confused with genital warts. Histologically, these papules are angio-architecture, his treatment is usually needed. Although these lesions represent a bane condition, psychological and social consequences often prompt patients to seek therapeutic removal. Multiple therapeutic modalities have been reported; however, removal of CO2 laser has proven to be the most effective to date.

REFERENCE


PELARY PAPERIES OF PENIS (PELLARY PAPULIES OF PENIS)

DESCRIPTION

Acute kidney injury (AKI) is defined as a decrease in GFR, manifested by an elevated or rising creatinine. However, serum creatinine is a delayed and insensitive test as it reflects GFR in individuals at steady state with stable kidney function, and may not estimate the GFR in a patient whose renal function is changing. Recognizing a need for a criteria definition of AKI called the RIFLE classification of AKI based on changes in creatinine and urine output were developed. The RIFLE criteria consists of 3 graded levels of injury (Risk, Injury, and Failure) based upon either the magnitude of elevation in serum creatinine or urine output, and 2 outcome measures (loss and End-stage renal disease). This is a pediatric modification of the adult RIFLE classification (see table). The urine of RIFLE has been strongly advocated as a research and clinical tool. AKI defined by the RIFLE criteria has been shown to be an independent risk factor for mortality and morbidity. (See also Section I: “Acute Kidney Injury, Pediatric”).

REFERENCE


Pediatric Rife (rifLE) Classification of Acute Kidney Injury

<table>
<thead>
<tr>
<th>pRIFLE Stage</th>
<th>Estimated Creatinine Clearance (cCr)</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>eCr &lt; 60 ml/min</td>
<td>&lt; 0.5 mL/kg/h</td>
</tr>
<tr>
<td>I</td>
<td>eCr &lt; 50 ml/min</td>
<td>&lt; 0.5 mL/kg/h</td>
</tr>
<tr>
<td>F</td>
<td>eCr &lt; 30 ml/min</td>
<td>&lt; 10 mL/kg/h</td>
</tr>
<tr>
<td>L</td>
<td>eCr &lt; 15 ml/min</td>
<td>Persistent failure</td>
</tr>
<tr>
<td>F</td>
<td>eCr &lt; 15 ml/min</td>
<td>Persistent failure</td>
</tr>
</tbody>
</table>

PEDIOLYSIS PUBIS (CRAB LICE/PUbic LICE)

DESCRIPTION

Ectoparasitic infection (Phthirus pubis), marked by severe pruritus and tending to have an incubation period of 4 wk. Signs include observation of the lice, 1–2 mm long gray-brown organisms, on the skin or on the hair shaft or the presence of “nits” (egg stage) on the hair shaft. The recommended regimens should not be applied to the eyes. Pediculosis of the eyelashes should be treated by applying occlusive ophthalmic ointment to the eyelid margins twice a day for 10 days. Bedding and clothing should be decontaminated (i.e., dry cleaning or machine-washed and dried using the heat cycle) or removed from body contact for at least 72 hr. Fumigation of living areas is not necessary. Nits need to be mechanically removed with a fine-toothed comb. Patients with pcsiolysis pubis should be evaluated for other STIs/TDs. Patients should be evaluated after 1 wk if symptoms persist. Prevention might be necessary if the host are found or if eggs are observed at the hair skin junction. Patients who do not respond to 1 of the recommended regimens should be retreated with an alternative regimen. Sex partners that have had sexual contact with the patient within the previous month should be treated. (See also Section II: “Sexually Transmitted Infections (STI)” Sexually Transmitted Diseases (STD), general.”)

TREATMENT

CDC-recommended regimens: Permethrin 1% cream rinse applied to affected areas and washed off after 10 min OR Pyrethrins with piperonyl butoxide applied to the affected area and washed off after 10 min

CDC Alternative Regimens: Malathion 0.5% lotion applied for 8–12 hr and washed off OR Ivermectin 250 μL/kg orally, repeated in 7 wk

REFERENCE

Wolters Kluwer. 2013. Published online 26 September 2013.

PELVIC FLOOR DYSFUNCTION

DESCRIPTION

Pelvic floor dysfunction represents a constellation of symptoms that include lower urinary tract, bowel, sexual, and other local symptoms, including pelvic organ prolapse. These conditions are all associated with damage to the pelvic floor through disruption of the connective tissue or by primary or secondary neuropathy and hypotrophy. Many predisposing, initiating, and promoting factors can lead to pelvic floor dysfunction. Treatments range from conservative/biologic therapies, to medications and surgical considerations.

REFERENCE


PELVIC FRACTURE, UROLOGIC CONSIDERATIONS

DESCRIPTION

Pelvic fractures can result in bladder and urethral injury. The length and tethered anatomy of the male urethra makes it more vulnerable to injury. Blood at the urethral meatus is the cardinal sign of urethral injury. For patients suspected of having a urethral injury, a retrograde urethrogram should be performed prior to insertion of a Foley catheter. This should be followed by a cystogram. Depending on the location and extent of trauma, several options exist for treatment including drainage of the bladder with a Foley catheter or suprapubic cystostomy, primary repair of the injury, or delayed repair after stabilization. (See also Section I: “Urinary Trauma (Anterior AND Posterior).”)

REFERENCE


PELVIC LIPOSARCOMA

DESCRIPTION

Pelvic liposarcoma can present as a tumor of the spermatic cord or as a parasacral tumor. Treatment includes ipsilateral orchidectomy with high ligation of the cord, adjunct treatment is controversial but could include postoperative
PELVIC PAIN, MALE

DESCRIPTION

Bacterial prostatitis or prostatitis syndrome (BPH) is a chronic inflammatory condition of the prostate gland.

REFERENCES


PELVIC ORGAN PROLAPSE QUANTIFICATION SYSTEM (POP-Q)

DESCRIPTION

A quantitative description of pelvic support using the hymenal ring as the reference point. Negative numbers are assigned to structures that have prolapsed beyond the hymen, and positive numbers to those that are protruding. Three reference points are defined anteriorly and 3 points posteriorly. Once the measurements are complete, the patient is assigned to 1 of 4 stages as noted below.

Stage

0

No prolapse demonstrated

I

The most distal portion of the prolapse is > 1 cm above the level of the hymen

II

The most distal portion of the prolapse is ≤1 cm proximal or distal to the hymenal plane

III

The most distal portion of the prolapse protrudes > 1 cm below the hymen but protrudes no further than 2 cm less than the total vaginal length

IV

Complete vaginal eversion

REFERENCE


PELVIC PAIN AND URGENCY/FREQUENCY (PUF)

PATIENT SYMPTOM SCALE

DESCRIPTION

Instrument for the evaluation and treatment of patients with interstitial cystitis (IC)/Painful Bladder syndrome (PBS). See also Section I: "Pelvic Organ Prolapse/Enterocele."

REFERENCES


PELVIS, BIFID, RENAL

DESCRIPTION

A normal variant seen in ~10% of patients in which the renal pelvis is divided into 2 major calyces just inside the kidney. See Pelvis, bifid, renal (Image E)

REFERENCE


PELVIS, EXTRARENAL

DESCRIPTION

Most often a normal anatomic variant that can be mistaken for a pathologic condition (hydronephrosis, parapelvic cyst, or renal cyst, etc.). Calyces are normally appearing on imaging with an unstructured extrarenal pelvis but will be blended with the extrarenal pelvis. The extrarenal pelvis can also be associated with conditions such as renal visualization or ectopic kidney and rarely may cause urinary stasis and difficulties with infection and stones.

REFERENCE


PELVIC BRACHIAL PRESSURE INDEX (PBI)

DESCRIPTION

The PBI can be defined as the pelvic systolic BP divided by the brachial systolic BP. A pelvic-brachial index of ≤0.7 has been suggested to indicate arteriogenic impotence. However, due to several limitations, this test is considered an unreliable tool to exclude arteriogenic impotence.

REFERENCE


PELVIC DOPPLER ULTRASOUND INDICATIONS AND PARAMETERS

DESCRIPTION

This type of minimally invasive urologic imaging is used for men with ED who have a potentially surgically treatable cause (eg, young men who may have suffered traumatic perineal injuries and do not respond to oral or intracavernous therapy). Pelvic Doppler US is used for evaluation of pelvic blood flow and requires intravesical potassium sensitivity. Peak systolic velocity (PSV) in healthy individuals varies from 35–47 cm/s. A PSV <25 cm/s has a sensitivity of 100% and specificity of 95% in patients with abnormal functional arteriopathy. Patients with severe ED will have a cavernous artery luminal diameter ≤0.7 mm and an increase of >75% in diameter post-injection. Patients with evo-occlusive dysfunction will exhibit good PSV (>25 cm/s) and have persistent end diastolic flow velocity of <5 cm/s with quick detumescence after stimulation. A resistive index calculation (RI = EDV – ESV/PSV) >0.9 (where EDV is end-diastolic velocity) usually indicates no evidence of evo-occlusive dysfunction, whereas an RI of <0.75 was associated with venous leakage in 95% of cases.

REFERENCE


PELVIC ENHANCEMENT AND LENGTHENING

DESCRIPTION

Penile lengthening can be accomplished by release of the suspensory ligament of the penis and the use of penile weights. Increased girth can be obtained by the use of circumferential dermal fat grafts. There are reports of significant complications from lengthening and girth procedures including scarring, skin deformities, irregular fat deposits, chronic enlargement of the penis, and ED.

REFERENCE

Penile Prosthesis

DESCRIPTION

Penile prosthesis is considered for men whose erectile function is nonresponsive to medical or psychological aids and is seriously disabling. Various models are available with the majority used inflatable units. They are in 3 categories: Semi-rigid, 2-piece, and 3-piece inflatable (see table) (Image 1). The earliest attempts of implantable devices began in the 1930s with the 1st successful prosthesis in 1955. Prosthetic devices have been improved in design and materials over the years to aid erectile function recovery after RP.

REFERENCE

Baranowski AP, Abrams P, Fall M. Erectile dysfunction (ED) following radical prostatectomy: the evolutionary concept in the management of erectile dysfunction. BJU Int. 2013 Apr;112(7):998–1008. doi: 10.1111/bju.12228.

Penile Prosthesis, Models and Descriptions

<table>
<thead>
<tr>
<th>Prosthesis Type</th>
<th>American Medical Systems</th>
<th>Mentor Corporation</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semi-rigid</td>
<td>AMS Malleable 600</td>
<td>AcuForm</td>
<td>Malleable core rods that can be bent up and down 2 cylinders connected to a small scrotal pump</td>
<td>Low mechanical failure rate, easy to insert</td>
<td>Constant penile rigidity, increased risk of penile erosion, increased risk of mechanical failure</td>
</tr>
<tr>
<td></td>
<td>AMS Malleable 650</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-piece inflatable</td>
<td>AMS Malleable 650</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-piece inflatable</td>
<td>AMS 700 CX</td>
<td>Titan</td>
<td>2 cylinders, large abdominal fluid reservoir, and scrotal pump</td>
<td>Penile girth and rigidity most similar to normal erectile length</td>
<td>Highest risk of mechanical failure, technically more difficult, risk of autoinflation with physical activity</td>
</tr>
<tr>
<td></td>
<td>AMS 700 CM</td>
<td>Titan Narrow Base</td>
<td></td>
<td>As above, increased penile length</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AMS 700 COR (65 mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>AMS 700 Ultrex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Commonly used systems as of March 2014.

Penile Prosthesis, Models and Descriptions

REFERENCE


Penile Shortening

DESCRIPTION

Penile shortening may occur congenitally in patients with bladder exstrophy and more commonly after radical prostatectomy (RP) and penile revascularization surgery. Patients with bladder exstrophy have penile shortening because of diastasis of the pubic symphysis and short corporal lengths (<40% the size of controls). More commonly, patients may have shortening of the penis following RP because of unopposed sympathetic stimulation of the penis, fibrosis resulting from hypogonadism (as a consequence of denervation), or possibly as a result of revascularization of the penile structures into the pelvic. Treatment of Peyronie disease may result in minor penile shortening. Amelioration of this side effect by revascularization surgery for vascular ED may result in penile shortening in 20% of patients as a result of scar formation. In a prospective study of stretched flaccid penile length changes after RP, there was evidence of stretched flaccid penile length loss at 2 mo, but not at 6 mo after RP. PDE5 inhibitors increase stretched flaccid penile length loss, with patients who regularly used PDE5 inhibitors having no loss in stretched flaccid penile length.

REFERENCE

PENIS, AGNATHOSARCOMA

DESCRIPTION Approximately 12 cases of penile angiosarcoma have been reported. No site of predilection is demonstrated, and the tumor may be well-margined or ill-defined. Deaths may occur 1 wk to 5 yr after presentation (mean = 1.1 yr). The application of immunoperoxidase staining for factor VIII, present in normal endothelial cells, aids in diagnosis.

TREATMENT
- Local excision with lymph node dissection
- Radiation therapy
- Systemic chemotherapy with more widespread disease

REFERENCE

PENIS, ANGIOSARCOMA

DESCRIPTION Tumors are vascular neoplasms, followed by tumors of soft tissue. These tumors can be classified as benign or malignant, most have been reported as isolated case reports. The management varies considerably. (See also Section II: Soft tissue tumors of the penis: a review.)

REFERENCE

PENIS, ARTIFICIAL NODULES (TANCHO NODULES, BULLETS, FANG MUK, CHAGAN BALLS)

DESCRIPTION Sarcoïd nodules are spherical foreign objects, in the form of beads, implanted in the subcutaneous tissue of the shaft of the penis proximal to the glans. They are placed to allegedly enhance the sexual pleasure of females during sexual intercourse. It is a practice common in southeast Asia, especially Thailand. However, non-Asian groups in Romania, Russia, and Middle East have adopted this practice as well. The incidence and severity of early or delayed complications are unknown but are probably underestimated.

REFERENCES

PENIS, BASAL CELL CARCINOMA

DESCRIPTION Basal cell carcinoma is a common cutaneous malignancy, but it is very rare at the penis. Ultraviolet radiation is an important risk factor. Basal cell carcinoma of the penis most likely presents in the 5th–7th decades of life. The natural history is that of a slowly growing tumor with little propensity to local destruction, including superficial excision, laser surgery, and use of topical retinoid acid, podophyllin resin, and topical 5-fluorouracil. The recurrence rate is 20%.

REFERENCES

PENIS, BOWENOID PAPULOSIS

DESCRIPTION Bowenoid papulosis of the penis is a benign lesion that appears as rounded, reddish, single, or multiple papules on the glans or shaft of penile skin, although they can occur anywhere on the external genitalia or perianal regions of both males and females. These papules typically occur in sexually active women who are 25–35 yr of age. They are caused by HPV and maybe confused with carcinoma in situ (CIS) of the penis. Histologically, these lesions show parakeratosis and acanthosis in squamous epithelium with disorganization of the epithelial cells.

REFERENCES

PENIS, BURIED (CONCEALED/ HIDDEN/ TRAPPED)

DESCRIPTION This condition must be differentiated from an abnormally small penis. A buried or concealed penis refers to a normal-sized penis that is hidden because of the prepuce fat pad. Congenital causes or obesity can hide the penile shaft. The penis can usually be exposed by retracting skin lateral to the penile shaft. The intraurethral hidden penis after circumcision is more properly called a trapped penis. Children who undergo circumcision with testosterone swelling or with a hernia or a webbed penis are at risk for excess penile shaft skin loss and a trapped penis. Congenital buried penis is a spectrum characterized by a longer inner prepuce and may include in addition; short penile shaft; abnormal attachment of hamular, and suspensory ligaments; and excess supra-pubic fat. Congenital mega prepuce (OMAP) is a variant. Theoretically, obese adults who undergo circumcision are also at risk for removal of excess shaft skin. Symptoms can sometimes be associated (baldness, LUT, painful inguinal, ballooning of the foreskin, and urinary retention) with the condition.

SYNONYM
Inconspicuous penis (general term for buried, trapped, or webbed penis)

TREATMENT
- Surgery is the treatment of choice in patients with symptoms or complications.
- Laser therapy has been successful in some cases.

REFERENCES

PENIS, CUTANEOUS HORN

DESCRIPTION Cutaneous horn is a clinical diagnosis referring to a conical projection above the skin that resembles a miniature horn. The lesions usually arise in sun-exposed skin and are benign. Penile cutaneous horn is rare and is characterized by overgrowth of epithelium above a lesion that may be a wart, nodule, or tumor. It is important to note that the incidence of SCC is 33% when penile horn is present.
**PENIS, CYSTS**

- **Penile hemangiomas** are rare, occurring in 1% of all patients with hemangiomas. They should be differentiated from cutaneous hemangiomas, which are more common and tend to involute with time. By contrast, penile hemangiomas tend to become larger and may require surgical intervention. The physical exam often does not reveal the extent of the lesion, and ultrasound or angiography should be performed to delineate the anatomic. Treatment is surgical excision or laser ablation.

**SYNONYMS**
- Cutaneous hemangiomas
- Subcutaneous hemangiomas
- Penile hemangiomas

**TREATMENT**
- Surgical excision or laser ablation.

**REFERENCE**

**PENIS, HEMANGIOMA (CAVERNOUS HEMANGIOMA)**

**DESCRIPTION**
Penile hemangiomas are rare, occurring in 1% of all patients with hemangiomas. They should be differentiated from cutaneous hemangiomas, which are more common and tend to involute with time. By contrast, penile hemangiomas tend to become larger and may require surgical intervention. The physical exam often does not reveal the extent of the lesion, and ultrasound or angiography should be performed to delineate the anatomic. Treatment is surgical excision or laser ablation.

**SYNONYMS**
- Cutaneous hemangiomas
- Subcutaneous hemangiomas
- Penile hemangiomas

**TREATMENT**
- Surgical excision or laser ablation.

**REFERENCE**

**PENIS, HIRSUTE PAPILLOMA (PEARLY PENILE PAPULES, CORONAL PAPILAE)**

**DESCRIPTION**
Hirsute papillomas of the penis, more commonly known as pearly penile papules, are asymptomatic acral angiofibromas, typically distributed circumferentially on the corona and sulcus of the glans penis. The lesion is often confused with 151/155 D, and persists through life, gradually becoming less noticeable with increased age. Treatment is not required, but sometimes offered for cosmetic reasons. CO2 laser is effective.

**REFERENCE**

**PENIS, HYPOPLASIA**

**DESCRIPTION**
A small or hypoplastic penis may be the result of genital tract deficiency, hypoplasia, or epispadias. (See Section I: “Micro penis.”)

**REFERENCE**

**PENIS, KAPOSI SARCOMA**

**DESCRIPTION**
Kaposi sarcoma of the penis is rare, with only 37 cases reported in literature. Amongst those most are associated with HIV, cases do not have been described in immunocompetent patients. It is clinically identified by painless, red-violaceous nodules, as well as pearly plaques, and wart-like pedunculated lesions. The lesions are most commonly found on the glans, although the foreskin, urogenital meatus, and scrotum can also be affected. Treatments described include local surgery, radiotherapy, electroscaupulation, laser, and injection of interferon-α into the lesion. (See also Section I: “Penis, Lesion, General.”)

**REFERENCE**

**PENIS, LEIOMYOMA**

**DESCRIPTION**
Penile leiomyoma is a rare benign tumor of smooth muscle that commonly involves the shaft, with glans penis involvement being less frequent. The lesions tend to be small (1 cm in diameter), well-circumscribed, rubbery in consistency, with light yellow to white cut surface. Electron microscopy and immunohistochemistry should be used to confirm diagnosis. Multiple recurrences are rare. Primary excision of the tumor is the treatment of choice.

**REFERENCE**

**PENIS, LEIOMYOSARCOMA**

**DESCRIPTION**
Penile leiomyosarcoma is a very rare malignant smooth muscle tumor that usually occur on the fifth to seventh decades. Superficial lesions commonly arise from the dermis of the shaft or the smooth muscle of the glans penis and usually form subcutaneous nodules. Deep leiomyosarcoma is less common, arising from the smooth muscle of the corpora cavernosa, and tends to invade the urothelium and metastasize early. These tumors are firm, gray-white, lobulated, and poorly circumscribed, and can range in size from 3–8 cm. Electron microscopy and immunohistochemistry should be used to confirm diagnosis.

**TREATMENT**
- Primary excision of the tumor is the treatment of choice in low-grade (superficial) tumors; however, the tumor tends to recur locally.
- In high-grade (deep) malignancies, the treatment depends on the age of the patient, size, location of the tumor and the degree of invasiveness.

**REFERENCE**

**PENIS, LENGTH, NORMAL**

**DESCRIPTION**
Data on pediatric penile length considerations are discussed in Section I: “Micro penis (Micro penis).” At birth, dimensions of the normal term infant phallic are 3.5 ± 0.7 cm in stretched length and 1.1 ± 0.2 cm in diameter. In adults, concerns over phallic size can direct some men to seek penile augmentation. There is no real delineation between normal and abnormal, since many variables (fat pad, erect vs. flaccid length) are present. For example, a large fat pad can cause a penis to become buried and give a shorter appearance. (See Section II: “Penis, Buried (Concealed).”)

**REFERENCE**
PENIS, STRANGULATION

DESCRIPTION A malignant nerve sheath tumor arising from Schwann cells that very rarely occurs on the penis. These tumors most commonly occur on the dorsal aspect of the penis, near the dorsal nerve. Paraffinomas result from injection of paraffin, petroleum jelly, bear grease, or other materials into penile shaft, in an attempt to increase penile girth. Injections of oil-based substances may also be performed for therapeutic or cosmetic purposes, but these procedures are usually performed by the patient or an untrained person practicing medicine fraudulently. Complications usually occur, including penile deformity, skin necrosis, ED, and painful intercourse (Image 49).

TREATMENT
- Complete excision
- Careful follow-up for recurrence
- Recurrent schwannomas may require total penectomy

REFERENCE

PENIS, SCLEROSING LYMPHANGITIS

DESCRIPTION Sometimes referred to as Mondor phlebitis of the penis, these are thin and often asymptomatic subcutaneous cordlike swellings along the dorsal shaft of the penis or around the coronal sulcus. They can be confused with lymphangitis circumscriptum, a uncommon tumor of the lymphatic channels. The lesion is caused by thickening or thrombosis of the superficial veins of the penis, probably secondary to trauma. Treatment is not usually necessary, and the condition usually resolves in several weeks. Avoid vigorous sexual activity. Failure to resolve in a timely manner may require biopsy.

REFERENCE

PENIS, SCLEROSING NONVENEREAL LYPHANGITIS

DESCRIPTION Penile stricture is caused by attachment of and encircling by a foreign object around the penis, which leads to entrapment and distal ischemia. These efforts are usually associated with an attempt to maintain a longer erection and sexual interest. Foreign objects used include iron rings, rubber bands, steel washers, and strings. Wearing constraining rings on the flaccid penis often result in the impossibility of their removal after erection, leading to vascular complications usually within a few
PENIS, SYRINGOMA

Description: Syringomas are benign apocrine tumors that normally occur in adolescents on the face, neck, axillae, or abdomen. They are extremely rare on the penis; only 6 cases have been reported in the literature to date. On exam, a cordlike structure is palpated. Doppler US can demonstrate a noncompressible portion of the lesion. Therefore, it is crucial to perform a punch biopsy to determine whether the lesion is a syringoma or an appendageal tumor. A punch biopsy can be obtained to relieve patient hours of discomfort and to avoid the need for a transabdominal exposure. Through a transvaginal incision, the bladder neck and perirectal tissue are exposed. The syringoma is passed through a suprapubic stab incision and, under digital guidance, delivered through the perineal tissue. The bladder neck is then suspended with absorbable suture.


PERINEAL GROOVES

Description: Perineal groove is a rare congenital malformation characterized by a wet sulcus lined by mucous membranes, extending from the posterior fourchette to the anterior edge of the anus. There are 2 reasons for surgical correction: cosmetic reasons and the groove mucosa is often infected due to colonization by rectal germ. Patients present with inflammatory aspects of the groove mucosa, infection of the external genitalia, and urinary tract infection. Considering that infectious complications occur in about 50% of patients, surgical excision is often recommended. Generally, the tissue defect is closed by interrupted sutures and some advocate the use of surgical glue over the suture line to help prevent infection/movement of the skin edges and, therefore, the development of subsequent delamination.


PERINEAL MASS

Description: Perineal masses are classified as either benign in malignant and can arise from the perineum directly or from pelvic extension of gastrointestinal, genitourinary, or gynecologic structures. Benign conditions include soft tissue masses, traumatic, or iatrogenic, and infections leading to abscess formation, various fibrosis, genitourinary masses, vaginal and anorectal fistulae. Benign masses are generally limited in size and do not cause symptoms. Malignant tumors that present as a perineal mass include squamous cell carcinoma as well as malignancies of the prostate, urethra, anus, vagina, and metastases from other pelvic structures.

DESCRIPTION
According to the ICS, function (image choice with the aim of negative resection margins form of wide local excision, is often the treatment of origin, extent, and radiologic features of the lesion. Cross-sectional imaging, with CT scan or MRI, is usually required to further define the anatomic origin, extent, and radiologic features of the lesion. Aggressive surgical treatment of mass lesions, in the form of wide local excisions, is often the treatment of choice with the aim of negative resection margins without causing disturbances to urinary or anorectal function (Image 10).

REFERENCES

PERINEAL PAIN, DIFFERENTIAL DIAGNOSIS
DESCRIPTION
According to the ICS, perineal pain syndrome is the occurrence of persistent or recurrent episodic perineal pain which is either related to the micturition cycle or associated with symptoms suggestive of urinary tract or sexual dysfunction. Perineal pain is felt in the female, between the posterior fourchette (posterior lip of the introitus) and the anus. There is no proven infection or other obvious pathology. The ICS suggests that in men, the term prostatodynia (prostate-pain) should not be used as it pathologic. The ICS suggests that in men, the term prostatodynia (prostate-pain) should not be used as it pathologic.
PERIURETERITIS

DESCRIPTION
Most cases of periureteritis, or inflammatory changes surrounding the ureters, are secondary to infection from microorganisms that cause infections elsewhere in the genitourinary tract. Any associated anatomic abnormality of the ureters, including strictures, megareter, and ureterocolic, predisposes an individual to ureteritis. Urinary obstruction, trauma, and adenomucinous obstruction are other causes for periureteral inflammation. The 1st step in treatment of periureteritis is treating the underlying etiology, including the treatment of infection, stricture, stone, or tumor. This step is not used in most cases of periureteral inflammation.

REFERENCE

PERITONEAL ABSCESES

DESCRIPTION
A life-threatening infection of the peritoneum and peritoneal tissues that can spread rapidly to the adjacent soft tissues. It most commonly presents with peritoneal irritation (94%), fever (70%), urinary retention (39%), a draining abscess (11%), dysuria, and urethral discharge. Peritoneal abscesses have often been associated with gonococcal urethritis infections, urethral strictures, perineal bulking agent injections, and urethral diverticulitis. Drainage and broad spectrum antibiotics are the mainstay of treatment.

REFERENCE

PERLMAN SYNDROME

DESCRIPTION
An overgrowth syndrome characterized by fetal gigantism, visceromegaly, distinct facial features, and nephropathosis. Similar overgrowth syndromes include Beckwith–Wiedemann, Sotos, and the Simpson–Golabi–Behemel syndromes. Neonatal mortality is extremely high. The kidneys are often dysplastic, with numerous cysts and nephroblastomatosis. The cause is unknown, and the diagnosis is based entirely on the phenotypic description.

REFERENCE

PHIMOSIS, CLITORAL

DESCRIPTION
Phimosis should be suspected in women with clinical pain, itching, or burning. A physical exam may reveal a mild, moderate, or severe degree of an inability to visualize the entire clitoris. Initial conservative treatment involves testosterone and estrogen cream to improve the elasticity of the prepuce and potentially antifungal agents such as nystatin or fluconazole. Rarely, when phimosis may result in a white scarring of the clitoris, prepuce, and perineum. Treatment with distal clitoral skin can improve symptoms. Women with respiratory symptoms may require a dural slit.

REFERENCE

PHOSPHATE NEPHROPATHY, ACUTE

DESCRIPTION
Acute phosphate nephropathy is characterized by acute and subsequent chronic renal failure following exposure to oral sodium phosphate (OSP) bowel purgatives. Renal biopsy demonstrates acute and chronic tubular injury with prominent tubular and interstitial calcium phosphate deposits. Risk factors include older age, female gender, hypertension (HTN), chronic kidney disease (CKD) and treatment with angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and diuretics. The pathologic mechanism of action involves hypercalciuria-induced proximal salt and water reabsorption, delivery of a large phosphate load to the distal nephron, and precipitation of calcium phosphate in the distal tubule and collecting duct. Prevention of acute phosphate nephropathy is best achieved by avoiding sodium phosphate purgatives in high risk patients, aggressive hydration, minimizing the dose, and maintaining a minimum of 12 hr between administrations.

REFERENCE

PINWORMS, UROLOGIC CONSIDERATIONS

DESCRIPTION
Approximately 209 million people are infected with intestinal pinworms (Enterobius vermicularis) worldwide. They most commonly reside in the large intestine, and females lays by ∼15,000 eggs nightly on the perineum, causing intense perineal itching and sleep disturbances. Occasionally, worms may ascend the vagina and enter the urinary bladder through the fallopian tubes, where they may lay eggs causing an intense inflammatory response resulting in fever, abdominal pain, adhesions, and granulomas. Involvement of the urinary tract is rare, and only 1 report exists of E. vermicularis in the bladder.

TREATMENT
- Mebendazole 100 mg PO once (1st-line) or pyrantel pamoate 11 mg/kg up to 1g PO once (2nd-line)
- Nonsteroidal anti-inflammatory drugs
- Clean bedsheets and bedding

REFERENCE

PIECE OF STEEL URETHRA

DESCRIPTION
A rare form of intussusception, deficiency of urothelium caused by a fixed, open, and nonfunctioning urethra. This is usually the result of prior pelvic surgery, irradiation, or longstanding indwelling catheter drainage. Patients typically have a high bladder neck on cystoscopic exam and severe urinary incontinence.

TREATMENT
- Mid-urethral sling
- Urethroplasty
- Artificial urinary sphincter

REFERENCE

PI-RADS PROSTATE MRI SCORING SYSTEM

DESCRIPTION
The European Society of Urogenital Radiology (ESUR) developed a scoring system to present multi-parametric prostate MRI data in a simple but meaningful way in the diagnosis of prostate cancer. The system is similar to that used by breast radiologists (BI-RADS) for breast mammography, breast ultrasound, and MRI. Multiple parameters for each lesion are scored on a 5-point scale and the overall score predicts the chance of the lesion being a clinically significant cancer.

- Score 1: Clinically significant disease is highly unlikely to be present.
- Score 2: Clinically significant cancer is unlikely to be present.
- Score 3: Clinically significant cancer is equivocal.
- Score 4: Clinically significant cancer is likely to be present.
- Score 5: Clinically significant cancer is highly likely to be present.

REFERENCE
POLYARTERITIS NODOSA (PAN), UROLGIC CONSIDERATIONS

PLAP (PLACENTAL ALKALINE PHOSPHATASE)
DESCRIPTION PLAP is a fetal isoenzyme that has a different source than the adult alkaline phosphatase. It is 1 of many tumor markers used for the diagnosis, staging, and monitoring of treatment response in patients with GC, and it may be useful as a prognostic index. Although the individual sensitivity of PLAP is low, when combined with gamma-glutamyl transpeptidase, simultaneous determinations have shown elevations in 1% or both in 90% of patients with active disease.
REFERENCE

PLASMACYTOMA UROTHELIAL CARCINOMA
DESCRIPTION Plasma cytomai urothelial carcinoma (PUC) is a rare and recently described histologic variant of urothelial cancer (TCC). Tumor tissue is predominantly manifested by infiltrating tumor cells, with characteristics of plasmacytoid morphology. Cells appear medium-sized and desmoplastic with abundant eosinophilic cytoplasm, small hyperchromatic nuclei, and frequent mitotic features. In addition, immunohistochemical staining play an important role in the diagnosis of PUC. The most common presenting symptom is hematuria, generally accompanied by, lightly hematuria usually of low output. However, early diagnosis cannot be made due to the absence of hematuria until the later stages of disease. Due to the highly metastatic potential and poor prognosis of this variant of urothelial carcinoma (TCC), treatment options include deep TURBT for initial diagnosis, followed by radical cystectomy with adjuvant therapy.
REFERENCE

PLASMACYTOMA, BLADDER
DESCRIPTION This tumor is characterized by a monotonous proliferation of plasma cells at variable stages of differentiation, with predominance of the immature variety. 5 cases have been reported in the literature, with a mean age of 54 yr, none of which had multiple myeloma at the time of diagnosis. Local suprapubic recurrences and regional lymph node metastasis may occur. Survival up to 12 yr after diagnosis has been reported.
TREATMENT
• Subtotal cystectomy
• Radiation and chemotherapy
REFERENCE

PLASMACYTOMA, TESTICULAR
DESCRIPTION Neoplastic collections of plasma cells occurring in the testes. Plasmaocytes are most commonly found in the head and neck region. These are very rare tumors, with an incidence of 1 in 1,000 testicular tumors. They are most commonly associated with a previous or concurrent diagnosis of multiple myeloma and are generally not believed to occur as primary tumors. Presentation is a painless, tender testicular mass. Treatment is radical orchectomy and monitoring or management of multiple myeloma.
REFERENCE

PLASMACYTOMA, BLADDER CANCER
DESCRIPTION Ploidcy is the chromosomal content of cells, which can be measured using flow cytometry. Ploidcy analysis, when considered as an independent variable, is a fair predictor of clinical outcome. Tumor stage and grade are considered to be the most important predictors of survival. Although ploidcy may be more significant in predicting survival than grade, the addition of ploidy to the known stage and grade of a bladder tumor usually does not drastically alter the clinical management of a patient.
REFERENCE

PLOIDY ANALYSIS, BLADDER CANCER
DESCRIPTION Ploidcy is a variation in the number of chromosomes in a cell. Aneuploidcy is a variation in the number of chromosomes in a cell that is other than a single multiple of the number of chromosomes. In a prostate specimen, flow cytometry is used to measure the DNA content of the cells. DNA ploidy in addition to the histologic grading may improve the ability to predict the pathologic stage and ultimately the prognosis of any given lesion. The frequency of aneuploidy increases with advancing tumor stage. Inherent problems with ploidcy analysis include heterogeneity of DNA cell sampling, as well as whether it will change clinical management.
REFERENCE

PLOIDY ANALYSIS, PROSTATE CANCER
DESCRIPTION Ploidcy is a variation in the number of chromosomes in a cell. Aneuploidcy is a variation in the number of chromosomes in a cell that is other than a single multiple of the number of chromosomes. In a prostate specimen, flow cytometry is used to measure the DNA content of the cells. DNA ploidy in addition to the histologic grading may improve the ability to predict the pathologic stage and ultimately the prognosis of any given lesion. The frequency of aneuploidy increases with advancing tumor stage. Inherent problems with ploidcy analysis include heterogeneity of DNA cell sampling, as well as whether it will change clinical management.
REFERENCE

PNEUMOSCROTUM
DESCRIPTION Pneumoscrotum, the presence of air within the scrotum, can result from both pathologic and iatrogenic etiologies. This term includes both scrotal emphysema, which is subcutaneous air palpated as crepitis, and pneumatocele, where air is present within the tunica vaginalis and not directly palpable. Air may come from extraperitoneal (lytic pneumatocele, intraperitoneal (perforated viscus), or local self-producing (microorganisms) sources. The underlying cause must be recognized early, as certain conditions may be life-threatening (pneumothorax, fourner gangrene, intestinal perforation) and treatment of the underlying cause allows the pneumoscorpoum to resolve. Today, pneumoscorpoum is sometimes seen after laparoscopic or robotic peritoneal or extraperitoneal procedures and resolves spontaneously.
REFERENCES

PNEUMOTRIPOLITUNEOMA
DESCRIPTION Pneumotriporitoneum, the presence of air or gas within the peritoneum, can result from both pathologic and iatrogenic etiologies. This term includes both scrotal emphysema, which is subcutaneous air palpated as crepitis, and pneumatocele, where air is present within the tunica vaginalis and not directly palpable. Air may come from extraperitoneal (lytic pneumatocele, intraperitoneal (perforated viscus), or local self-producing (microorganisms) sources. The underlying cause must be recognized early, as certain conditions may be life-threatening (pneumothorax, fourner gangrene, intestinal perforation) and treatment of the underlying cause allows the pneumotripolituneum to resolve. Today, pneumotriporitoneum is sometimes seen after laparoscopic or robotic peritoneal or extraperitoneal procedures and resolves spontaneously.
REFERENCES

POLYARTERITIS NODOSA (PAN), UROLGIC CONSIDERATIONS

PNEUMOSCROTUM
DESCRIPTION Air may affect many organ systems. It usually presents with a systemic illness characterized by malaise, weight loss, myalgia, arthralgia and signs of end-organ damage. PAN is not well understood, but is believed to be caused by the deposition of immune complexes on the walls of primarily medium-sized arteries, causing inflammatory changes in these walls. This may lead to thickening and neointimal changes, causing acute renal hemorhage and often leading to chronic renal failure. When left untreated, the 5-yr survival rate of PAN is 13% with some renal features being associated with poor prognosis: Renal insufficiency (serum creatinine > 1.58 mg/dL and proteinuria > 1 g/dL).
REFERENCES

POLYARTERITIS NODOSA (PAN), UROLGIC CONSIDERATIONS
DESCRIPTION PAN can affect many organ systems. It usually presents with a systemic illness characterized by malaise, weight loss, myalgia, arthralgia and signs of end-organ damage. PAN is not well understood, but is believed to be caused by the deposition of immune complexes on the walls of primarily medium-sized arteries, causing inflammatory changes in these walls. This may lead to thickening and neointimal changes, causing acute renal hemorhage and often leading to chronic renal failure. When left untreated, the 5-yr survival rate of PAN is 13% with some renal features being associated with poor prognosis: Renal insufficiency (serum creatinine > 1.58 mg/dL and proteinuria > 1 g/dL). Corticosteroids and azathioprine are used in the treatment of PAN. The majority of patients with PAN have renal involvement. Flank pain is sometimes present and splenomegaly (ischemic changes, and renal atery vasculitis can cause renal failure) (a small percentage of patients may require dialysis), hypertension, or both. Infrequently patients may develop pain over the testicular or ovarian area with testicular infarction reported. Renal spontaneous renal hemorrhage is also reported. Steroids with or without cyclophosphamide is the standard treatment.
REFERENCE

PNEUMOTRIPOLITUNEOMA
DESCRIPTION Pneumotriporitoneum, the presence of air or gas within the peritoneum, can result from both pathologic and iatrogenic etiologies. This term includes both scrotal emphysema, which is subcutaneous air palpated as crepitis, and pneumatocele, where air is present within the tunica vaginalis and not directly palpable. Air may come from extraperitoneal (lytic pneumatocele, intraperitoneal (perforated viscus), or local self-producing (microorganisms) sources. The underlying cause must be recognized early, as certain conditions may be life-threatening (pneumothorax, fourner gangrene, intestinal perforation) and treatment of the underlying cause allows the pneumotriporitoneum to resolve. Today, pneumotriporitoneum is sometimes seen after laparoscopic or robotic peritoneal or extraperitoneal procedures and resolves spontaneously.
REFERENCES
POLYEMBRYOMA

DESCRIPTION A mixed germ cell tumor (SGT) of the testis, containing embryonal carcinoma and yolk sac tumor. Histologic analysis reveals a distinctive, well-differentiated pattern of endodermal bodies in a mesenchymal stroma, which resembles extraterritorial mesothelioma. Due to the yolk sac component there may be substantial alpha fetoprotein (AFP) elevation. Treatment mirrors that for OCT.


POLYOMA VIRUS (BK, JC), UROLOGIC CONSIDERATIONS

DESCRIPTION The polyoma viruses may cause transplant renal nephropathy, unilateral obstruction or stricture, and hemorrhagic cysts. BK virus may cause transplant renal nephropathy in up to 6% of transplant recipients, and may cause unilateral obstruction secondary to fibrosis. It is also thought to be the causative agent in the majority of patients with hemorrhagic cysts following immunosuppression for bone marrow or solid organ transplantation.BK virus causes clinical disease of the genitourinary tract, due in part to its tropism for genitourinary epithelium. The JC virus causes a similar disease pattern but is less common. BK nephropathy occurs in up to 10% of kidney transplant recipients and causes graft failure in as many as 50% of individuals affected. BK and JC viruses can be diagnosed with PCR of the urine or blood. Urine cytology may demonstrate the so-called “decoy cells.” Most renal transplant programs employ posttransplant screening programs. Decreasing immunosuppressive medications is essential. Additional therapies include agents such as ciprofloxin and ivig. (See also Section I: “Immunocompromised Patients, Urologic Considerations” and Section II: “BK Virus, Urologic Considerations.”)


POLYORCHIDISM

DESCRIPTION This is a very rare condition characterized by multiple (>2) testicles. It may be the result of transverse division of the urogenital ridge. The majority of cases are asymptomatic and associated with inguinal hernia, torsion, or cryptorchidism. It is most often discovered as an asymptomatic swelling in the scrotum; the supernumerary testes usually occur with its own separate epididymis and vas deferens. If a testicular tumor can be ruled out using US or MRI, and if surveillance indicates no other associated disorders, surgical exploration is not necessary.

TREATMENT Surgery, exploration, biopsy, if indicated

A test that evaluates the interaction between sperm and cervical mucus. It determines the adequacy of sperm and the receptivity of cervical mucus. Testing consists of retrieving specimens from the posterior vaginal fornix, excervix, and endocervical canal —6–8 hr after intercourse. The test should be performed close to the time of ovulation, and couples are asked to abstain from sex for 48 hr prior to the test. These specimens are examined to determine the number of motile sperm, with 10 sperm/field considered adequate and excluding the cervical mucus as cause of infertility. When these test results are poor, the specimen may be repeated on another occasion, 1–3 hr after coitus.

SYNONYM
Sims–Frunieri Test

REFERENCE

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER

DESCRIPTION
Posttransplant lymphoproliferative disorder (PTLD) is a heterogeneous disease that may occur in recipients of solid organ transplants and hematopoietic stem cell transplants. The risk of lymphoma is increased 20–100% compared with the general population. Epstein–Barr virus infection at the time of transplantation appears to be a significant risk factor. Based on morphologic, immunophenotypic, and molecular criteria, PTLD is classified into four pathologic categories: Early lesions, polymorphic, monomorphic, and classical Hodgkin lymphoma. A mainstay of therapy is reduction of immune suppression but often single agent rituximab or even combination chemotherapy is needed.

REFERENCE

POSTVOD DRIBBLING

DESCRIPTION
Urine that leaks out or the urethra at the end of micturition. It may be caused by bladder outlet obstruction, an urethral diverticulum, or vesicovaginal reflux of urine. Recent data suggests it may also be seen in the median lobe hypertrophy.

REFERENCE

POTASSIUM SENSITIVITY TESTING

DESCRIPTION

REFERENCE
Precocious puberty

DESCRIPTION

Precocious puberty is sexual development at an earlier age than expected. In general, signs of secondary sexual development in boys <9 and in girls <10 are not precocious. In white girls <7 or in black girls <6 is precocious. Common causes include medications (illegitimate estrogens or testosterone), idiopathic causes, pituitary and CNS tumors (harmatogenous), CSH, adrenal tumors, ovarian cysts and tumors, McCune-Albright syndrome, Leydig cell tumors, HCG-secreting GCT, neuroblastoma, or pseudopseudohyponadism.

REFERENCE


PREGNANCY, BACTERIURIA, PYURIA, AND URINARY TRACT INFECTION

DESCRIPTION

Pregnant women with asymptomatic bacteriuria have a higher likelihood of developing a UTI and should be treated to reduce the incidence of pyelonephritis, sepsis, and fetal complications (low birth weight, prematurity, death). Pyuria in the presence of bacteriuria indicates UTI. Pyuria in the absence of bacteriuria should raise suspicion for nephrolithiasis, TB, or less commonly, malignancy of the urinary tract. Pericystitis and cholelithiasis (FDA category B) are generally agreed to be safe in pregnancy. Drugs with high protein binding (eg, Ceftazidime) may be inappropriate the day before birth as a result of the placental barrier. Because of the likelihood of bilateral displacement and herniation risk, fluoropyrimidines should be avoided in pregnancy. (See also Section II: “Bacteriuria and Pyuria” and “Pregnancy, Obstetrics.”)

TREATMENT

The following regimens have been reported in treating cystitis in pregnancy modified based on urine culture results:

- Nitrofurantoin 100 mg orally every 12 hr for 5 days
- Ceftriaxone: 1 g every 24 hr
- Cefazolin: 1 g orally every 12 hr for 3–7 days
- Fosfuromycin: 3 g orally as a single dose

The following regimens have been reported in treating pyelonephritis in pregnancy modified based on urine culture results:

- Nitrofurantoin 100 mg orally every 12 hr for 5 days
- Ceftriaxone: 1 g every 24 hr
- Cefazolin: 1 g orally every 12 hr for 3–7 days
- Fosfuromycin: 3 g orally as a single dose

The following regimens are reported for mild to moderate pyelonephritis in pregnancy:

- Cephalexin: 500 mg PO every 8 hr
- Amoxicillin: 500 mg PO every 8 hr
- Cefprozil: 250 mg PO every 12 hr

The following regimens are reported for severe pyelonephritis with intra-abdominal and/or incomplete urinary drainage:

- Trimethoprim-sulfamethoxazole: 1.975 g every 6 hr
- Meropenem: 500 mg every 8 hr
- Daptomycin: 600 mg every 8 hr
- Vancomycin: 1 g every 8 hr

The following regimens are reported for severe pyelonephritis with intra-abdominal and/or incomplete urinary drainage:

- Trimethoprim-sulfamethoxazole: 1.975 g every 6 hr
- Meropenem: 500 mg every 8 hr
- Daptomycin: 600 mg every 8 hr
- Vancomycin: 1 g every 8 hr

REFERENCES

PREGNANCY, URINARY DIVERSION

DESCRIPTION Pressure after urinary diversion has not been well studied, and only 210 cases have been reported in the literature thus far. Patients have more difficulty getting pregnant because of their inherent underlying disease process, metabolic changes from urinary diversion, and because of the fixed position of the uterus from prior surgery. These patients have special ureteral considerations from decreased perfusion of the bowel segment from compression of the conduit or neobladder by the uterus, malabsorption of food due to use of the terminal ileum, stoma prolapse from increased intra-abdominal pressure, sternal stenosis from impaired blood flow, difficulty catheterizing continent pouches from stretching of the urethra, and an increased risk of UTI from the presence of bacteria. Unique postpartum issues include adhesions of the small intestine that may complicate cesarean section, increased residual urine volumes from stretching of conduits or neobladders, and an increased risk of pelvic organ prolapse.


PREGNANCY, URINARY TRACT OBSTRUCTION

DESCRIPTION Urinary tract obstruction during pregnancy most commonly occurs from a urinary stone or extrinsic compression from the gravid uterus. Patients will commonly present with flank pain, UI, magnetic resonance urography, or low-dose CT may be used to evaluate for a ureteral stone and evidence of obstruction. Hydronephrosis is a common finding in pregnancy and may be found in 15%, 20%, and 50% of patients in their 1st, 2nd, and 3rd trimesters, respectively. It is more common on the right side, and is commonly thought to occur from progesterone-mediated ureteral dilatation and extrinsic compression. See also Section II: "Pregnancy, Urothology" and Section III: "Pregnancy, Radiologic Considerations."

TREATMENT
- Initially, conservative with IV hydration and analgesic therapy.
- Patients who fail may require stent or nephrostomy tube placement. Stones can rapidly erode due to increased urinary calcium excretion and should be changed in a timely fashion.
- Lithotripsy and laser lithotripsy.


PREGNANCY, UROLOGIC MALIGNANCY

DESCRIPTION Urologic malignancies are rare in pregnancy but often misdiagnosed due to overlapping signs and symptoms with pre eclampsia and eclampsia. The most common tumor is RCC, which may present as flank pain, hematuria, and a palpable mass. It is often identified incidentally on imaging. Pheochromocytomas have been reported to occur in 1 of 50,000 term pregnancies. They present with severe hypertension, headaches, palpitations, vomiting, visual changes, and without proteinuria unlike preeclampsia. Adrenal adenomas may present with Cushing syndrome. Renal angiomyolipomas may present with flank pain, hematuria, and retropitoneal hematuria, although it is sometimes incidentally diagnosed on imaging. Urolithiasis of the upper or lower tracts is rare and presents with hematuria. If urine analysis reveals hematuria and the culture is negative, cystoscopy, and upper tract imaging are warranted.

TREATMENT
- Removal of pheochromocytomas is controversial, but medical therapy may be used until the 3rd trimester or delivery of the fetus.
- The size and type of tumor should dictate management for RCC, and laparoscopic nephrectomy has been shown to be safe in pregnant women.
- Angiomyolipoma (AML) with hematuria may be managed with embolization or partial or total nephrectomy.
- Urolithal cancer should be managed endoscopically given its propensity for aggressive growth and lymphatic invasion. Mitomycin should be avoided, and only 1 case report exists of using RCC.


PREGNANCY, UROLGIC MEDICATIONS

DESCRIPTION Medications in pregnancy have not been well studied or documented. Urologic issues include antibiotics for UTI and anesthesia for surgical procedures. Macrobid is a safe, well-tolerated antibiotic classified as a category B (no evidence of harm to human fetus) drug by the FDA. There is a recommendation against using this in the 3rd trimester because of the risk of hemolytic anemia in patients with G6PD deficiency. Fluoroquinolones are considered category D medications, but multiple studies have failed to demonstrate any evidence of harm. Penicillins are category B drugs, and often the medication of choice in pregnancy. General anesthesia may carry a slightly higher risk of maternal infections and premature labor; this effect is directly related to the complexity and length of the procedure but the overall increased risk is thought to be minimal. See also Section II: "Pregnancy, Urothology, Fyuna, and UI."


PREHN SIGN

DESCRIPTION Prehn sign is a clinical test used to aid in distinguishing epididymitis from testicular torsion although it is not always reliable. The physical lifting of the testicle is said to relieve the pain of epididymitis (positive Prehn sign), but does not relieve the pain of testicular torsion (negative Prehn sign). It is important to note that Prehn sign is not always reliable and Doppler ultrasonography is a valuable tool in confirming the diagnosis.


PRENTISS MANEUVER

DESCRIPTION Additional curl in an orchiopexy operation can be gained by fixing the inguinal floor and lifting the inferior epididymal vessels. The internal ring and transversalis fascia are then closed lateral to the cord.


PREPUTIAL STONES

DESCRIPTION Preputial stones (preputial calculus) are rare occurrences, generally found in adults and associated with poor penile hygiene, low socioeconomic status, and phimosis. Factors in preputial stone formation include obstruction, stress, foreign body, nodule formation, and infection. Removal of stone and elimination of the predisposing condition is the treatment.


PRESSURE-FLOW STUDIES

DESCRIPTION The simultaneous measurement of bladder pressure and urethral flow through the entire voiding cycle. Performed as part of urodynamic study, these studies improve on some of the limitations of uniflowmetry alone. Measurements for this study can include the variables that affect the study. Intravesical pressure, rectal pressure, intrarenal pressure, urothelial electromyogram, and urine flow rates. A small catheter is placed to fill the bladder and measure the flow. All variables are plotted and recorded simultaneously to compare the various readings during various points in the micturition study.


PREGNANCY, STUTTERING (INTERMITTENT PRIAPISM)


PRIMITIVE NEUROECTODERMAL TUMORS (PNET) (EXTRASKELETAL EWING SARCOMA)

TREATMENT
- Hormonal therapy (bupropion, busulamide, bicalutamide)
- Self-injection therapy with phenylephrine

REFERENCE

PRIMITIVE NEUROECTODERMAL TUMORS (PNET) (EXTRASKELETAL EWING SARCOMA)

DESCRIPTION
Primitive neuroectodermal tumors are part of the Ewing family of tumors (EFT) that include Ewing’s sarcoma of the bone. Peripheral PNETs are a very aggressive neoplasm that predominantly affects children and adolescents. Renal PNET is the most reported PNET of the genitourinary tract, however bladder, prostate, ureter, and seminal cord PNETs have also been reported. PNETs are often diagnosed as metastatic disease (20–50%) and the outcome is often poor, with a 5-yr survival rate of 6%.5

TREATMENT
Multimodal therapy including surgical resection, chemotherapy, and radiation.

REFERENCE

PRINCETON III CONSENSUS RECOMMENDATIONS: ERECTILE DYSFUNCTION (ED) AND CARDIOVASCULAR DISEASE

DESCRIPTION
The recommendations of the 3rd Princeton Consensus Conference focus on (1) evaluation and management of cardiovascular risk in men with and/or no known CV disease, (2) reevaluation and modification of the 2nd conference recommendation for evaluation of cardiac risk associated with sexual activity in men with known CV disease, and (3) the role of testosterone replacement therapy (TRT) in ED and CV disease management (Image Q).

REFERENCE

PROLACTIN, SERUM LEVEL

DESCRIPTION
Elevated prolactin levels (>50 ng/mL) suggest a prolactinoma. Renal failure, stress, medications, and hypothyroidism have serum prolactin value <50 ng/mL.

TREATMENT
- Cabergoline
- Bromocriptine
- Surgical resection

REFERENCE

PROLAPSE, STAGING SYSTEMS

DESCRIPTION
Since the early 1960s multiple practitioners including Porge, Baden, Walker, and Beecham have attempted to standardize pelvic organ prolapse. Then in 1996 the American Urogynecologic Society, the Society of Gynecologic Surgeons, and the ICS adopted the Pelvic Organ Prolapse Quantitation (POP-Q) exam. The POP-Q exam, in which 9 specific points of measurement are obtained in relation to the hymenal ring, has been demonstrated to be learned easily and performed quickly with highly reproducible exam findings. The most widely used classification systems used today are the Baden-Walker and POP-Q systems. (See also Section II: “Cystocele Grading: Baden-Walker. Pelvic Organ Prolapse Quantification (POP-Q).”

REFERENCE

PROPRANOTHINE STIMULATION TEST

DESCRIPTION
This test is used when involuntary detrusor contractions are demonstrated during cystometry to predict the outcome of pharmacologic treatment with anticholinergic. Propranolol bromide is an anticholinergic with side effects that include dry mouth and blurred vision. Since involuntary detrusor contractions have been confirmed, 15 mg of propranolol bromide are administered parenterally. Once effects of the drug are noted, cystometry is repeated. A positive response is defined as the complete abolition of involuntary detrusor contractions, or a 20% increase in the bladder volume at which they occur. If the parenteral dosage is effective, a tolerable clinical response to the orally administered dose can be expected in most patients.

REFERENCE

PROPHYLACTIC ANTIBIOTICS, AUA GUIDELINES

DESCRIPTION
Recommendations include limiting antibiotic prophylaxis to a maximum of 24 hr, no prophylaxis solely to prevent infectious endocarditis, and defining characteristics for patients at higher risk. These characteristics include advanced age, prostatic anomalies of the urethral tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, external catheters, colored endogenous/exogenous material, distant cancer infection, and prolonged hospitalization. Recommendations for specific procedures and agents are found in Section VII. “Reference Tables: Antibiotic Prophylaxis: AUA guidelines.”

REFERENCE

PROSTASCINT SCAN

DESCRIPTION
A nuclear medicine imaging study designed to localize prostate cancer cells using a radiolabeled monoclonal antibody to PSMA (prostate-specific membrane antigen) called indium 111 capromab pendetide. Patients are injected, and single photon emission computed tomography is performed immediately after scan and 4–5 days later. This allows for washout of antibody from the blood and bowel. The test was initially designed to identify extraprostatic disease, and current applications include identifying the location of cancer recurrence following definitive therapy for prostate cancer. It has traditionally suffered from poor specificity and interobserver reliability and issues concerning uptake of mid abdominal lymph nodes. Recent data suggest that there may be renewed interest in integrating the Prostascint scan in clinical decision making for deciding between local vs. systemic salvage therapy for PSA recurrence following definitive management of prostate cancer (Image H).

REFERENCE

PROSTATE CANCER SCREENING GUIDELINES

DESCRIPTION
Screening asymptomatic men for prostate cancer is controversial. Concerns about over diagnosis and overtreatment of clinically important cancers are part of this reason. Many professional organizations have developed guidelines concerning prostate cancer screening that are summarized in the table. (See also Section II: “AUA, General Considerations” and Section VII: Reference Tables: Prostate Cancer Screening Guidelines.)

REFERENCES

Several 1st degree relatives diagnosed with PCa at age 50-70 with normal DRE & PSA

American Cancer Society (ACS) 2010

American College of Physicians (2013)

American Urological Association (2013)

National Comprehensive Cancer Network (NCCN)2014

USPSTF (2012)

a African-American or have a 1st degree relative diagnosed with PCA ≤ 65 yr of age

b Several 1st degree relatives diagnosed with PCA ≤ 50 yr of age

DESCRIPTION

As screening for prostate cancer can result in the diagnosis of prostate cancer in many men who are not likely to suffer any consequences or die from the disease. This often results in over-treatment of many men with prostate cancer. Deferred therapy for those with prostate cancer generally involves 2 different approaches although the terms are often used interchangeably. They are not completely identical:

- Active surveillance is a strategy aiming to individualize the management of early prostate cancer by selecting only those men with significant cancers for active therapy. This involves actively monitoring the course of prostate cancer with the intent of intervention with definitive local therapy (eg, radiation therapy, RP) if cancer progression is documented.

- Watchful waiting uses less aggressive follow-up until the patient develops symptomatic disease progression, at which time he is often placed on hormonal treatment. (See also Prostate Cancer, General and “Prostate Cancer, Very Low Risk and Active Surveillance.” Section 8: “Surgical Options.”)

PROSTATE CANCER, BASAL CELL CARCINOMA

DESCRIPTION

A very rare variant of prostate cancer comprising ≤ 0.1% of malignant tumors. Lesions exist in 2 distinct forms, adenoid cystic carcinoma (ACC), and basal cell carcinoma (BCC), that occur clinically separate or as mixed tumors with 1 dominant pattern. Immunohistochemical analysis reveals strongly positive results for both 34 βE12 and p63. OncotypeDX is a more reliable form of prostate cancer current evidence supports the potential for local recurrence and metastasis and therefore suggests radical surgery with life-long follow-up as 1st-line management.

PROSTATE CANCER, CIRCULATING TUMOR CELLS (CTC’S)

DESCRIPTION

Circulating tumor cells (CTC’S) can be detected using molecular techniques such as RT-PCR. An identification assay for actual circulating cells (CellSearch) is commercially available for use in patients with hormone-refractory prostate cancer. In patients with advanced prostate cancer, men with ≥5 CTC’s per 7.5 mL blood prior to chemotherapy had a significantly shorter median survival (10 vs. 21 mo in those with <5 CTC’s). The role of the CTC assay continues to evolve in the management of prostate cancer. It appears to be only valid at present for men with advanced, castrate resistant prostate cancer disease and is not used for earlier stages of disease. (See also Section 8: “PSA, BT-PSA.”

REFERENCES


PROSTATE CANCER, DUCTAL ADENOCARCINOMA

DESCRIPTION

These terms have been replaced by ductal adenocarcinoma of the prostate. It accounts for 1-2% of all prostate adenocarcinomas. Due to its appearance, ductal adenocarcinoma was previously thought to arise from mesothelial remnants and possess unique clinical features related to its origin. While further analyses have shown that these tumors do in fact arise from prostatic tissue. The disease originates from perineural ductal prostate ducts and may grow into an exophytic seminal vesicle around the verumontanum. A mixture of cribriform and papillary structures is seen on microscopy, resembling endometrial adenocarcinoma of the uterus and hence the earlier descriptive terms. Histologically, these tumors are composed of tall columnar cells with clear to eosinophilic cytoplasm and large nuclei. The cells form glands with scant intervening stroma. Prostatic ductal adenocarcinoma cells express PSA. Prostate adenocarcinoma is also present in 17% of cases. Early presentation is hematuria, irritative and obstructive symptoms and it tends to occur in older men (>60-80 yr). Serum PSA levels and DRE at the time of diagnosis tend to underestimate disease.

Cytoscopically it may appear multiple polyloid friable protrusion from near the notch of the prostate. Often these are not as easily endoscopic findings. Sources are conflicting concerning the clinical presentation of ductal adenocarcinoma. Due to the early symptom presentation most are organ confined and others more likely to present with advanced stage cancer. The behavior has been compared to behave similar to adenocarcinoma (4-4-4) prostate adenocarcinoma.

SYNONYMS

- Ductal carcinoma of the prostate
- Endometrioid carcinoma, prostate
- Endometrial carcinoma of the prostate
- Papillary adenocarcinoma of the prostate

TREATMENT

Similar to high-grade urothelial adenocarcinomas of prostate. Most of the literature has been managed by local prostatectomy. Ductal carcinoma of the prostate tends to be hormone sensitive and advanced disease is initially responsive to androgen deprivation. The overall mortality was significantly worse in men with ductal adenocarcinoma, almost 3-fold higher rate of death, as compared to prostate adenocarcinoma.

REFERENCES


757
PROSTATE CANCER, FAMILIAL

DESCRIPTION
The risk of prostate cancer is directly dependent upon the number of affected 1st-degree relatives, the age of the relative when diagnosed, and whether the relative is a father or brother. Risk is also associated with a family history of breast cancer.

REFERENCES

PROSTATE CANCER, LEIOMYSARCOMA, AND OTHER UNCOMMON SARCOMAS

DESCRIPTION
Leiomyosarcoma of the prostate is extremely rare and a highly aggressive neoplasm, accounting for <0.1% of primary prostate malignancies. It is the most common primary prostatic sarcoma of the prostate in adults, and comprises 38–52% of adult prostatic sarcomas. Rhadomyosarcoma is most common in pediatric patients and can be seen in adults. Other less common prostatic sarcomas include MPNST and prostatic chondromalacia. Presentation can include urinary obstruction frequency, urgency, hematuria, pelvic pain, rectal pain, constipation, burning on ejaculation, and frequency, urgency, hematuria, perineal and/or rectal pain, clumping.

REFERENCES

PROSTATE CANCER, PREVENTION (CHEMOPREVENTION)

DESCRIPTION
Numerous medications and nutraceuticals, including selenium, statins, and green tea, have been evaluated for the prevention of prostate cancer, with the most notable being the 5α-reductase inhibitors (5 ARIs) finasteride and dutasteride. The Prostate Cancer Prevention Trial (PCPT) using finasteride demonstrated an almost 25% reduction in the incidence of prostate cancer but a slightly increased incidence of higher Gleason score prostate cancer. Some have hypothesized this may be due to selection inhibition of low-grade cancers along with a smaller prostate size resulting in less sampling error and better detection of higher grade cancers already present. This is supported by whole-mount correlation from RP specimens. The Reduction of Prostate Cancer (REDUCE) trial using dutasteride (a dual 5α-reductase inhibitor) reported a 23% reduction in prostate cancer in high-risk men with a slight increase in high-grade cancers. The large SELECT trial using selenium and vitamin E was stopped prematurely because it did not appear that either agent alone or in combination reduced the risk of prostate cancer. In 2011, updated trial data showed that the men taking vitamin E had a 17% increased risk of prostate cancer compared to men taking placebo. Trial sponsors recommended that men avoid supplementation with these agents.

REFERENCES

PROSTATE CANCER RISK CALCULATORS

DESCRIPTION
Usually in the form of tables or nomograms, these are predictive instruments developed to aid clinicians and patients alike in disease throughout its various stages of diagnosis and treatment. Most calculators are available online, with scores that facilitate their incorporation into clinical practice (see below).

REFERENCES

758
PROSTATE CANCER, RISK STRATIFICATION (D’AMICO CLASSIFICATION)

DESCRIPTION

One challenge presented by prostate cancer is choosing the appropriate therapy based on the risk of disease progression. It is often useful to assign a relative risk to an individual. These risk groups were established from literature and based on known prognostic factors: PSA level, biopsy Gleason score, and 1993 AJCC staging. A typical system, commonly referred to as the D’Amico classification, is described here. Note that this is risk of PSA progression posttherapy and not overall or disease-specific survival:

- Low risk: Stages T1c and T2a, PSA level of ≤10 ng/mL, and biopsy Gleason score of ≤6 (25% PSA progression at 5 yr posttherapy)
- Intermediate risk: PSA levels of 10–20 ng/mL, biopsy Gleason score of 7, or AJCC clinical stage T2b (25–50% PSA progression at 5 yr posttherapy)
- High risk: T2c disease or a PSA level >20 ng/mL or a Biopsy Gleason score of ≥8–10 (50–100% PSA progression at 5 yr posttherapy)

REFERENCE


PROSTATE CANCER, SMALL CELL (NEUROENDOCRINE)

DESCRIPTION

A rare subtype of prostate malignancy that has a rapid fatal course. Considered to be a variant of Gleason's adenocarcinoma of the prostate, it is identical to small cell carcinoma of the lung and has neuroendocrine (small cell, oat cell) differentiation. In 50% of the cases, the tumors are mixed small cell carcinoma with adenocarcinoma. Histopathologically, prostate SCCs of the prostate are part of a spectrum of anaplastic tumors of the prostate and are similar to SCCs of the lung. Neuroendocrine cells are identified by special staining (ie, neuro-specific enolase [NSE] or other markers). It should be noted that the normal prostate does have some neuroendocrine positivity, but it is limited and can only be detected by staining. About 10% of adenocarcinomas of the prostate can have Paneth-like cells (large eosinophilic cells) that are neuroendocrine, and it is recognized that adenocarcinoma of the prostate that is not classified as neuroendocrine can have some pathy cells that stain as neuroendocrine cells. Large numbers of these cells in a prostate sample should prompt a neuroendocrine staining workup of the sample. Tumors can exhibit a spectrum of differentiation, with a carcinoid-like pattern (low-grade neuroendocrine carcinoma) to the small cell undifferentiated type (oat cell), the highest grade of neuroendocrine tumor. Immunohistochemically, these cells can stain for serotonin, calcitonin, ACTH, HCG, and other markers. Most of these small cell tumors do not produce detectable levels of hormones but sometimes can produce detectable levels in the serum. They may also express and stain for PSA and acid phosphatase, but pure small cell carcinoma usually does not stain for PSA. The clinical behavior of small cell prostate carcinoma is characterized by extensive local disease, visceral disease, and low PSA levels despite large metabolic burden. At diagnosis, 70% of patients have metastatic disease, and visceral metastases are common (ie, liver). The average survival is <1 yr. Androgen receptor-positive tumors have a worse prognosis than do tumors that do not express the receptor (median survival 10 mo vs. 30 mo). Diagnosis is made by TRUS biopsy, symptoms associated with metastasis, and elevated LFTs and CEA.

SYNONYMS

- Small cell anaplastic carcinoma of the prostate (SCCP)
- Oat cell carcinoma of the prostate
- Neuroendocrine prostate cancer
- Carcinoid of the prostate

TREATMENT

- These tumors respond poorly to androgen ablation, but this should be attempted.
- Surgery and/or radiation therapy may provide local control.
- Chemotherapy with agents such as VP-16 and cisplatin have some activity.

REFERENCE


PROSTATE CANCER, SQUAMOUS AND ADENOSQUAMOUS

DESCRIPTION

A rare lesion that can arise in patients infected with Schistosoma haematobium. It can be confused with more common conditions, such as squamous metaplasia of the prostate due to infection, radiation, and hormonal therapy. Pure primary SCC of the prostate does not respond to estrogen therapy, and it does not develop elevated serum PSA or NET levels with metastatic disease. Bone metastases are osteolytic instead of osteoblastic. Median survival is about 14 mo.

REFERENCE


PROSTATE HEALTH INDEX (PHI) AND [–2] proPSA

PHI

The Prostate Health Index (PHI) is a mathematical combination of total PSA (tPSA), free PSA (fPSA) and [–2] proPSA (Ostenson et al. 2013). The mathematical equation is: PHI = (tPSA) × (fPSA). The PHI has been shown to have a higher PSA predictivity value than both total PSA and free PSA. The measurement of %[–2] proPSA improves the accuracy of prostate cancer detection in comparison with PSA or fPSA, particularly in the group of prostate cancer patients between 3 μg/L and 10 μg/L. The PHI may also be able to reduce the number of unnecessary biopsies, maintaining a high cancer detection rate. Published results also showed that %–2 proPSA and PHI are related to the aggressiveness of the tumor.

REFERENCES

PROSTATE URETHRAL ANGLE

DESCRIPTION
The prostatic urethral angle is the angle formed between the prostate from the base to the apex, making an anterior angle of ≈35° at the proximal verumontanum. In men with prostate hypertrophy, this angle tends to be >75°. However, men without hypertrophy have a more uniform prostatic urethral angle. A high bladder neck in men without prostatic enlargement, and in preliminary clinical studies, the PUA was inversely associated with the urinary flow rate.

REFERENCE

PROSTATE, BASAL CELL HYPERPLASIA

DESCRIPTION
Basal cell hyperplasia is important in that it is commonly associated with BPH and may sometimes be mistaken for prostate cancer. The prostate epithelium consists of 3 major cell types: epithelial, basal, and neuroendocrine cells. The basal cells are small and round with a scant cytoplasm and dark nuclei. These cells are less differentiated and almost devoid of secretory products; they are located between the secretory cells and rest on the basement membrane. Basal cells are negative for PSA and PAP.

Typical basal cell hyperplasia consists of a proliferation of basal cells ≥2 cell layers thick at the periphery of prostatic glands and acini. Basal cell proliferation in the prostatic gland is highlighted from focal basal cell hyperplasia in the setting of nodular hyperplasia to a florid adenoid basal cell tumor. Many confusing names have been used in the literature. Totallization of prostate, embolial hyperplasia, basal cell tumor, basal cell adenoma, BC adenoid carcinoma. The differential diagnosis includes transitional cell hyperplasia, squamous metaplasia, urothelial carcinoma (TCC) of the prostate, and adenocarcinoma of prostate.

REFERENCE

PROSTATE, BENIGN ENLARGEMENT (BPE)

DESCRIPTION
Benign prostatic enlargement is used when there is gland enlargement and is usually a prescriptive diagnosis based on the size of the prostate. This term differs from BPH which is reserved for the histological pattern it describes. A patient may have LUTS with or without BPE. (See also Section I: “Bladder Outlet Obstruction [BDO].” Prostate, Benign Obstruction [BPO]) and “Section II: “Prostate, Benign Obstruction [BPH].”"

REFERENCE

PROSTATE, BENIGN OBSTRUCTION (BENIGN PROSTATIC OBSTRUCTION [BPO])

DESCRIPTION
BPO is used when obstruction has been proven by pressure-flow studies, or is highly suspected from flow rates and if the gland is enlarged. This is different from bladder outlet obstruction, the generic term for all forms of obstruction to the bladder outlet (e.g., urethral stricture including BPO). (See also Section I: “Bladder Outlet Obstruction (BDO).” Prostate, Benign Hypertrophy/Hyperplasia [BPH]."

REFERENCE

PROSTATE CALCULI

DESCRIPTION
Calculi are more common in older males and are rarely found in children. They usually occur in clusters and are associated with other disease processes. Often found in a dilated prostatic urethre. They are generally asymptomatic but may cause symptoms such as decreased urinary stream, prostatism, and lower back pain; they are a rare source of chronic bacterial prostatitis. Calculi may form secondary to calcification of the corpora amylacea and simple precipitation of prostatic secretions.

TREATMENT
 generally none
• Transurethral resection with laser lithotripsy as needed if markedly symptomatic

REFERENCE

PROSTATE, FEMALE

DESCRIPTION
A cored radiographic expression that refers to an impression at the base of the female bladder seen on cystography or ultrasonography. The impression resembles an enlarged prostate in the male and can be caused by urinary diverticulism, benign and malignant tumors of the anterior vaginal wall, urethral neoplasm, and repair of UI. Anatomically, the paraurethral glands and ducts are considered homologous to the male prostate and immunohistochemical studies demonstrate expression of PSA and prostate-specific acid phosphatase (PSAP) in these paraurethral glands and ducts.

REFERENCE

PROSTATE, HEMATURIA

DESCRIPTION
Hematuria attributed to bleeding from the prostate is a diagnosis of exclusion. Patients should have an appropriate workup according to the guidelines provided by the AUA. Older patients with larger, more vascular prostates are more susceptible and can be managed with finasteride, KIR/MIBI or transurethral resection if bleeding is refractory to medical therapy. Most often urothelial, Kawada can also be iatrogenic after prostate biopsy and endoscopic/evacuated resection or due to locally advanced prostate cancer late manifestation.

TREATMENT
• Prostatectomy (1st line therapy for troublesome benign prostatic hyperplasia bleeding)
• Intravesical alum, silver nitrate, and formalin
• Cold-line therapy
• Transurethral resection or vaporization of the prostate

REFERENCE

PROSTATE, INFARCTION

DESCRIPTION
The etiology of prostatic infarction is still unclear, although it has been linked to prostatic hyperplasia. Histologic findings include infarction of prostatic epithelium, with hemosiderin and neutrophils in the intervening stroma. Recent infarcts generally do not have squamous metaplasia, whereas older ones do. Typically, the infarction is multiple and located in the central and middle zones of the middle 1/3 of the prostate. Prostatic infarction may elevate PSA levels.

REFERENCE

PROSTATE, MASSAGE

DESCRIPTION
Repetitive prostate massage is not a new tool in the urologists’ armamentarium. It can be used to locate lower UTIs or as a therapeutic modality. Once the most popular therapeutic maneuver used to treat prostatitis, it was abandoned as primary therapy almost 30 yr ago. Based on experience reported outside North America and anecdotal experiences of some patients and their physicians, some believe it has a role in certain forms of prostatitis, such as chronic non-bacterial prostatitis or chronic pelvic pain syndrome (CPPS). The prostate is massaged from the lateral border to the medial aspect on each side, from base to apex. Firm pressure is necessary to express prostatic fluid into the urethra. A sterile container should be held by the patient or the measles to capture the expressed prostatic fluid. The test is commonly performed in acute bacterial prostatitis. (See also Section II: “Attentive Digital Rectal Exam (DRE).”"

REFERENCE
“Afferent Digital Rectal Exam (DRE):” Expressed Prostatic Secretions (EPS)."

Stamey Test (Three glass test, Four glass tests, Nilsson-Stamey Test):"
**PHOSPHATASE (PAP)**

**SYNONYMS**

Duct Syndrome [PMDS] and Prostatic Utricle

DESCRIPTION

A type of granulomatous prostatitis. Its activity is much greater in the prostate than in any other tissue. PAP is not prostate-specific, and can be found in other tissues. Historically, PAP was used as a serum marker for the staging and detection of prostatic cancer before the discovery of prostate-specific antigen (PSA). Although enzymatic activity of PAP is associated with advanced prostate cancer, other causes of an elevated PAP are possible, including liver, skeletal, and renal disease. PAP is the primary target for the prostate cancer immunotherapy sipuleucel-t.

**REFERENCES**


**PROSTATIC URETHRAL POLYPS**

DESCRIPTION

Urethral polyps are rare abnormalities in male children who present with hematuria or obstructive symptoms. Strangury (strenuous and painful urination) may be seen, with large lesions on a long stalk. The diagnosis is best confirmed by voiding cystourethrography. These polyps are nearly always in the prostatic fossa, although anterior urethral polyps have been reported. These are benign lesions and are not related to the polypidoma masses of sarcoma botryoids.

**TREATMENT**

Transurethral excision of the polyps

**REFERENCE**


**PROSTATIC URETHRAL ANOMALIES**

**DESCRIPTION**

The prostatic utricle is a small utilelne orifice found at the apex of the verumontanum. The utricle has been considered by most to be a remnant of the fused caudal ends of the mullerian ducts while others propose the origin is from the urogenital sinus. The most common anomaly associated with the prostatic utricle is a prostatic utricle cyst. Can be associated with unilaterial renal agenesis, hypogonadism, and cryptorchidism. Prostatic utricle cysts are within the level of the verumontanum and are always in the midline.

**REFERENCE**


**PROSTATIC UTRICLE CALCIFICATION**

**DESCRIPTION**

The prostatic utricle is a remnant of the mullerian ducts. It is a small indentation located at the apex of the verumontanum. Enlargement of the prostatic utricle (EPU) is a rare anomaly which is associated with hypertrophy and is the result of insufficient androgenic stimulation. The incidence of stones in EPU is unknown. 1 study found stones in 8 patients out of 46(18%). Their size ranged from 3–18 mm and they were all composed of hydroxyapatite (HAP) crystal. Treatment includes transurethral utricle fenestration and stone removal. (See also Section II: “Prostatic Utricle Anomalies” and “Calcification, Prostate.”)

**REFERENCE**


**PROSTATITIS, MYCOTIC (FUNgal PROSTATITIS)**

**DESCRIPTION**

A type of nonbacterial prostatitis that is not associated with any specific symptom but is seen as inflammation on prostate biopsy. No specific treatment is necessary. (See Section II: “Prostatitis: Inflammatory (NIH IV).”)

**REFERENCES**


**PROSTATITIS, MYCOTIC (Fungal PROSTATITIS)**

**DESCRIPTION**

A type of prostatitis its caused by fungi and typically associated with systemic mycosis or immunocompromised hosts. Fungal infections can include blastomycosis, coccidiomycosis, cryptococcosis, histoplasmosis, and candida. Diagnosis is based on prostate histology and culture results. For systemic therapy, see the specific invasive agent. (See Section I: “Fungal Infections.”)

**SYNONYM**

Fungal prostatitis

761
PROSTATITIS, NIH CLASSIFICATION SYSTEM

REFERENCE

PROSTATITIS, NIH CLASSIFICATION SYSTEM
DESCRIPTION
A classification proposed by an NIH working group that clearly defines the different types of prostatitis in order to improve the diagnosis and management of the disease. See Section I: “Prostatitis, Acute, Bacterial (NIH I).” “Prostatitis, Chronic, Bacterial (NIH II).” “Prostatitis, Chronic, Nonbacterial, Inflammatory & Noninflammatory (NIH CVCPPS I & II-B)” and Section II: “Prostatitis, Asymptomatic Inflammatory (NIH III).” For an explanation of EPS (expressed prostatic secretion) and V8 (voided bladder urine) see Section II: Startney Test (Three-glass Test, Four-glass Test, Monti-Startney Test).

• Category I: Acute bacterial prostatitis; acute infection of the prostate gland
• Category II: Chronic bacterial prostatitis; recurrent infection of the prostate
• Category III: Chronic non-bacterial prostatitis/CPPS; no demonstrable infection – Category IIIA: Inflammatory CPPS; WBCs in semen/EPS VB3 and/or semen/EPS VB3
• Category IV: Asymptomatic inflammatory prostatitis; no symptoms.

REFERENCE

PROSTATITIS, STRESS
DESCRIPTION
Classically defined as a subset of chronic abacterial non-inflammatory prostatitis/prostatodynia in which a pattern of excessive tension could be identified as a trigger of the syndrome. Symptoms usually responded to anxiolytic agents or behavioral modifications. No longer considered an appropriate term in the NIH Prostatitis classification system.

REFERENCE

PROSTATITIS, TUBERCULOUS
DESCRIPTION
TB of the prostate is rare, and in many cases, it is diagnosed incidentally after a transurethral resection in the prostate chips. Tuberculous prostatitis results from hematogenous dissemination, with an incidence of 10% with men in TB. Symptoms are nonspecific, and the diagnostic evaluation is usually not definitive. On exam, the prostate may be hard, irregular, and nodule. On labs, urine analysis can demonstrate microscopic hematuria or sterile pyuria. Acid-fast bacilli staining of urine and smear has a sensitivity of only 52%; however, culture can take up to 8 wk. A transrectal ultrasound can demonstrate collections or abscess, and an intravenous urogram (IVU) and/or an intravenous urogram (CTU) can be diagnostic. The incidence of TB in patients with obstructive uropathy is approximately 72% of patients with prostatic TB have renal TB.

TREATMENT
• Hospitalization is usually necessary.
• Transurethral resection of the prostate in patients with obstructive uropathy is reasonable.
• Medication includes a 3-drug regimen of sulfamethoxazole/trimethoprim and either ethambutol or streptomycin.
• In complicated cases, 9–12 mo therapy may be required. A negative prostatic biopsy to document successful treatment is recommended.

REFERENCE

PROSTATODYNIA
DESCRIPTION
Classically described as a syndrome complex of multiple complaints including pain in the perineum, lower back, or upon ejaculation; slow stream; and hysteresis. Patients exhibit no evidence of prostatic inflammation. Dysuria, frequency, and systemic signs are usually absent. This term is no longer currently considered to be appropriate and has been replaced by the designation chronic pelvic pain syndrome or CPPS NIH Category II Chronic Abacterial Prostatitis. (See also Section I: “Prostatitis, Chronic, Bacterial, Inflammatory & Noninflammatory (NIH CVCPPS I & II-B).”)

REFERENCE

PROSTITIS, INFECTED PENILE
DESCRIPTION
A dreaded complication of penile prosthesis implantation. Rates of infection range from 1–8%; risk factors include spinal cord injury (SCI), diabetes mellitus especially (if poorly controlled with insulin—<11.5%), history of UTI, and multiple sensitizers must be eliminated and cleansing and toilet habits should be addressed. Treatment of the specific sensitizers is essential. A short course of a cephalosporin is recommended.

REFERENCE

TREATMENT
• Surgical removal
• Irrigation and antibiotic treatment
• Immediate salvage procedures with surgical removal
• Without and immediate replacement have reported good results: Vynnyk intraoperative irrigation with 4 different solutions, including vancomycin,

immediate reimplantation of a new inflatable penile prosthesis, and postoperative outpatient antibiotics, with oral discontinuation or IV vancomycin or oralised.

REFERENCE

PRURITUS, EXTERNAL GENITAILA, MALE
DESCRIPTION
The anogenital area is a common location for pruritic complaints in men and women. Itching can precede the appearance of a rash or other lesion. When the itching results in red, weeping skin with crusts, it is often called “eczematous dermatitis.” Pruritus scroti is a historic term for scrotal itching. The differential diagnosis of itching of the male external genitalia includes:
• Allergic reactions (algae; dermatitis)
• Cancer: Perineal, scrotal, extra-mammary Paget disease (metaplastic adenocarcinoma, found in areas with apocrine sweat glands).
• Candid infection
• Chemical irritants; Detergents, fabric softeners, soaps, creams, ointments, and sexual lubricants
• Dermatologic conditions: Seborrheic dermatitis, psoriasis, eczema (atopic dermatitis), lichen simplex chronicus (LSC)
• Fixed drug reaction
• HIV: Pruritus is 1 of the most frequent symptoms encountered in HIV infection and can even be the 1st clinical symptom
• Infections; Pubic lice (“lice”), scabies
• Nutritional deficiencies; Malnutrition, vitamin deficiencies
• Red scrotum syndrome possibly due to steroid abuse
• Sexually transmitted infections: Genital herpes
• Sunburn/toxicity
• Systemic illnesses: Diabetes mellitus, renal failure
• Testa crisis: Also known as “ringworm of the groin”
• Fixed drug reaction

Some patients manifest itching with or without a demonstrable rash. The skin may appear normal or demonstrate excoriation (lichenification skin thickening) from rubbing, or both. The skin may be subject to mechanical trauma (drying of the skin, scratching, any rubbing of the skin). Sealing antihistamines may limit night symptoms. Some patients may require psychiatric agents for adequate sedation. Antidepressants may be required in patients refractory to standard treatment or those who are experiencing psychiatric disorders. (See also Section II: “Scabies, Urologic Considerations.”)

REFERENCES

762
DESCRIPTION

- Active PSA can also enter the bloodstream where it is rapidly bound and inactivated (completely by prostate inhibitory alpha-1-antichymotrypsin (ACT) and alpha-2-macroglobulin). Most of the PSA in serum exists as a complex with ACT.

- With prostate cancer the disrupted basal membrane allows proPSA and several truncated PSA isoforms direct access to the circulation. This PSA "leaking" into the blood has a larger fraction of the PSA produced by malignant tissue escaping proteolytic processing (ie, activation of proPSA to active PSA and degradation of active PSA to inactive PSA).

- In men with a normal prostate (no cancer or infection), the majority of free PSA in the serum reflects protein inactivated by internal proteolytic cleavage. In contrast, the cleaved fraction is relatively decreased in prostate cancer. Thus, the percentage of free or unbound PSA is lower in the serum of men with prostate cancer (and, conversely, the amount of complexed PSA is higher) compared with those without cancer.

- These observations have resulted in the use of the ratio of free to total PSA and complexed PSA (cPSA) as a means of distinguishing prostate cancer and BPH.

- PSA Collection: The PSA blood sample should be centrifuged, and the serum separated in 2–3 hr. If the assay is not performed within the next 2–3 hr, the serum should be frozen.

- PSA Basic Clinical Considerations: There is a vast amount of clinical data available to guide the clinicians in the use of PSA in patient care. This section highlights some of the published PSA clinical data in a highly annotated form.

- Routine PSA blood testing refers to Total PSA and accounts for increases in prostate volume with age.

- Positive bone scan and PSA: 2.3% PSA bounce (SEE SECTION II, “PSA, GENERAL CONSIDERATIONS”)

- PSA, AGE-ADJUSTED (SEE SECTION II, “PSA, GENERAL CONSIDERATIONS”)
PSA, GENERAL CONSIDERATIONS AND PSA DERIVATIVES

- If measured during external beam radiation therapy for prostate cancer, PSA shows a progressive decline.
- Since prostatic glandular tissue remains after radiation, PSA levels are unlikely to fall to undetectable following radiation therapy unless androgen ablation is also followed. The PSA increases are generally small (0.8 ng/mL) but can sometimes reach 10 ng/mL and may last 6–18 mo. Ironically, bounces may predict a good outcome.
- PSA should fall to a low level after high intensity focused ultrasound (HIFU) and cryotherapy and should not rise on successive occasions. Data is limited using other.
- Salvage radiation following RP, especially those with positive surgical margins receiving treatment when the PSA is low (2.0–1.5 ng/mL) and slowly rising, appear to have best outcomes.
- With metastatic disease or androgen depletion, failure to radiate PSA >4.0 ng/mL. 7 mo after initiation of therapy is associated with a poor prognosis. Median survival >1 yr. With PSA nadir of <0.2 ng/mL, median survival is 6 yr. PSA increase after RP is no radiologic evidence of metastases, a PSA nadir of <0.75 ng/mL/yr in the year prior to diagnosis: Associated with an increased risk of prostate cancer death after RP or radiation. Very high PSA V (≥3.0 ng/mL/yr) is often associated with prostate infiltration as the cause of the elevated PSA.

- PSA doubling time (PSA-DO)
- PSA bounce:
- PSA should fall to an undetectable following radiation therapy unless androgen ablation is also followed. The PSA increases are generally small (0.8 ng/mL) but can sometimes reach 10 ng/mL and may last 6–18 months. Ironically, bounces may predict a good outcome.
- PSA doubling time (PSA-DO):
- PSA bounce:
- PSAV < 2.0–3.9 ng/mL 18.7%
- PSAV > 2.0–3.9 ng/mL 21.3%
- PSAV < 6–7.9 ng/mL 28.6%
- PSAV > 6–7.9 ng/mL 31.7%
- PSAV > 10.0 ng/mL 56.5%
PSA ABCCESS, UROLOGIC CONSIDERATIONS

• Based on the following data there is some support for 1.5 ng/mL being the new “normal” PSA in mid-life.
• In one longitudinal PSA biopsy study baseline PSA level >1.5 ng/mL, the risk of developing prostate cancer increased from 12.3–78.4% at 7 yr.
• PSA >1.5 ng/mL between the ages of 45 and 49 yr accounted for nearly 1/2 of the prostate cancer deaths over the next 30 yr.
• PSA level at age 44–50 yr was very strongly associated with the likelihood of developing prostate cancer during the 20 yr study, the odds ratio for a PCA diagnosis:
  - PSA <0.50 ng/mL, (population average = Odds Ratio 1.0)
  - PSA 0.51–1.0 ng/mL, Odds ratio 2.57
  - PSA 1.0–1.5 ng/mL, Odds ratio 7.02
  - PSA 2.01–3.0 ng/mL, Odds ratio 9.01

REFERENCES

Catriona WJ, Parvin AM, Sanda MG, et al. Multicenter study of Uro-Pro PSA combined with PSA and free PSA for prostate cancer detection in the 2.0 to 10.0 ng/mL PSA range. J Urol 2011;185:1695

PSA, RACE-ADJUSTED (SEE SECTION II “PSA, GENERAL CONSIDERATIONS AND PSA DERIVATIVES”) PSA, RT-PCR

DESCRIPTION: First clinically reported in 1982, RT-PCR is used to amplify mRNA transcripts of PSA. These tiny crib-like species should theoretically only be present in prostate tissues. Extraprostatic tissue of patients with biopsy-proven cancer tissue is tested, including peripheral blood, lymph nodes, and bone marrow, to detect PSA mRNA transcripts and presumably prostate cells in extraprostatic sites. It is being investigated as an assay to detect micrometastasis of prostate cancer before clinical presentation or evidence of disease spread (molecular staging). Its clinical utility as a diagnostic assay remains uncertain and is generally replaced by CTC assays.

REFERENCE


PSA VELOCITY (PSAV) AND PSA DOUBLING TIME (PSADT) (SEE SECTION II “PSA, GENERAL CONSIDERATIONS AND PSA DERIVATIVES”) PSEUDODYSSYNERGIA (HINMAN SYNDROME) DESCRIPTION: A form of detrusor external sphincter dyssynergia in which voluntary contraction of external sphincter occurs during detrusor contraction. It produces the functional voiding dysfunction seen in children with intractable voiding symptoms, men with chronic prostatitis or prostatodynia, and women with urethral syndrome. It may sometimes be a cause of urinary incontinence. This condition is thought to be a learned behavioral abnormality, possibly an uncorrected compensatory mechanism. Diagnosis is based on urodynamic evidence of increased or uncoordinated external sphincter activity during detrusor contraction, usually with simultaneous elevation of intra-abdominal pressure indicating voluntary nature of contraction, without clinical evidence of neurologic deficit. (See also Section II: “Hinman Syndrome” [Hinman–Allen Syndrome, Nonneurogenic Neurogenic Bladder; Ousch Neurogenic Bladder]”)

SYNONYM:
Nonneurogenic neurogenic bladder
Hinman syndrome/Hinman–Allen syndrome in children
Dysfunctional voiding syndrome
Ousch Neuropathic Bladder

TREATMENT:
Children must be motivated to participate in the therapy.
Teach how to void and defer properly.
Timed voiding, voiding diary, double voiding, psychotherapy, and biofeedback may all be appropriate in select children.
Anticholinergics may correct instability.
α-adrenergics may improve outlet resistance.
Psychotherapy, with a change in parental attitude, can greatly improve the situation.
Intermittent catheterization may be necessary in more difficult cases (e.g., with upper tract changes, failure to respond to less invasive measures).
Rhabdovirus

REFERENCE


PSUEDOMYXOMA OVARI-LIKE POSTTHERAPEUTIC ALTERATION IN PROSTATE ADENOCARCINOMA DESCRIPTION: Pseudomyxoma ovarii-like posttherapeutic alteration in prostate adenocarcinoma refers to histologic alterations observed in prostate cancer foci after exposure to total androgen blockade. Changes in neoplastic glands exposed to total androgen blockade characteristically display disorganized acinar atrophy, basal cell hyperplasia, squamous or transitional cell metaplasia, and stromal hypercellularity. Conversely, tumor glands may shrink in size and exhibit mucin. This extravasated mucin resembles pseudomyxoma ovarii. This is an important distinction, as this appearance can be easily confused with mucinous carcinoma. It is important to recognize these posttreatment effects, as they may be the sole histologic evidence of therapeutic response and may guide definitive treatment after neoadjuvant hormone deprivation.

REFERENCE


PSMA (PROSTATE-SPECIFIC MEMBRANE ANTIGEN) DESCRIPTION: A protein with intracellular, transmembrane, and extracellular components of prostatic epithelial cells. PSMA levels are reported to be elevated in hormone refractory prostate cancer and with metastatic disease. Its use as a tumor marker is not as useful in screening as PSA. PSMA is highly sensitive and specific immunomarker for the detection of metastatic prostate carcinoma; however, cells of the small intestine, prostatic renal tubules, and salivary glands also can express PSMA. PSMA may be an in vivo target for imaging utilizing radiolabeled mAb 7E11 (C7T356, capozolid), the Prostate Stem. PSMA is currently being targeted as a therapeutic intervention for advanced prostate cancer including novel AB-directed therapy (PSMA- Specific Membrane Antigen Antibody Drug Conjugate (PSMA ADC)), radiolabeled and anti PSMA vaccines and other immunotherapies.

REFERENCE


PSA ABCCESS, UROLOGIC CONSIDERATIONS

DESCRIPTION: A psa abscess is a discrete abscess or phlegmon in the retroperitoneum, adjacent to the prostate muscle. Usually the consequence of direct spread of infection from an adjacent structure; primary psa abscesses are rare and are a result of hemorrhagic spread. A wide variety of etiologies are reported in the literature, including perirectal abscess; pyelonephritis; postoperative infection following renal, ureteral, or bladder surgery; complications from EIVAS, and urethral carcinoma.
PSOAS HITCH PROCEDURE

metastasis. Clinical presentation includes fever, lower abdominal or back pain, referred lower extremity pain, dyspnea, delirium, altered mental status, and frank hoarseness, and a psoas sign. Rarely, a psoas abscess can directly obstruct the psoas muscle or cause a retroperitoneal inflammatory response. Treatment can initially be medical using antibiotic therapy; however, failure to resolve requires drainage. (See also Section I “Retroperitoneal Abscess, Retroperitoneal Masses and Cysts.”) (Image 0)

REFERENCE

PSOAS HITCH PROCEDURE
DESCRIPTION
A surgical procedure used to replace short segments of distal ureteral loss or in combination with a ureteral reimplantation to provide a fixed posterior bladder wall. The bladder is mobilized and stretched superiorly along the axis of the ureteral defect. The stretched bladder is then sutured to the fascia of the ilio-psoas muscle (Image 0).

REFERENCE

PSORIASIS, EXTERNAL GENITALIA
DESCRIPTION
A chronic papulosquamous skin disease frequently affecting external genitalia, more commonly in males. Generalized involvement is rare. 25–40% of patients with psoriasis. The lesions characteristically are sharply demarcated plaques with silvery, scaly patches. Psoriasis most frequently involves the penis in males and the mons pubis, labia majora, and inguinal crease in females. It is reported to increase the risk of squamous cell carcinoma (SCC) genitale. Treatment includes topical steroids, carprofen and maintaining good hygiene. (See also Section II: “Pruritus, External Genitalia.”)

REFERENCES

PSYCHOGENIC POLYDIPSIA
DESCRIPTION
Psychogenic polydipsia (PPD) is a clinical disorder characterized by polyphagia and polyuria, and is a common occurrence in patients with psychiatric disorders. The underlying pathophysiology of this syndrome is unclear, but multiple factors have been implicated, including a hypothalamic defect and adverse medication effects. Workup for PPD includes a comprehensive evaluation for other medical causes of polydipsia, polyuria, hyponatremia, and the syndrome of inappropriate secretion of antidiuretic hormone. Workup should include plasma and urine osmolality and plasma and urine sodium. Other tests may include a complete metabolic panel, urinary osm, unen, chest x-ray, and CT scan of the head.

TREATMENT
- Treatment for hypovolemia: Fluid restriction, furosemide (diuretics), intravenous normal saline, or hypertonic saline
- Behavioral Treatments: Fluid restriction, therapy, including cognitive techniques
- Drug treatments: Tricyclic antidepressants, chlophedian, risperidone, olanzapine, quetiapine, demerol/lotec, clonidine, ACE inhibitors, conivaptan

REFERENCE

PURPLE URINE BAG SYNDROME
DESCRIPTION
Purple urine bag syndrome (PUBS) is an uncommon disorder in which the urine bags of catheterized patients turn purple or blue. Most patients are bedridden, cognitively impaired, and constipated. The disposition is attributed to indigo and indirubin pigments, which appear purple when combined. The pigments are created when infected tryptophan is exposed to intestinal flora in patients with altered gut motility. PUBS is usually associated with organisms that have indoxyl phosphatase/putrefactive activity (Klebsiella pneumonia, Providencia stuartii, Enterobacter, Proteus mirabilis, Morganella morganii, and E. coli).

TREATMENT
- Antibiotics to treat urinary tract infection
- Catheter change

REFERENCE

PYELITIS CYSTICA
DESCRIPTION
Hypertrophy of urothelial cells into the lamina propria with subsequent fibrosis, giving a cystic appearance. Identical to cystic dysplasia, this lesion occurs in the renal pelvis and calyces. It is a rare condition, usually associated with chronic infection, and is more common in females, usually >50 yr of age. Presenting symptoms are variable, including infections, including fever, dysuria, hematuria, and flank pain. Identified on radiographic studies as multiple small cysts up to 10 mm in diameter in the renal pelvis and calyces, and confirmed by endoscopic biopsy. Not thought to be a premalignant condition, but rare neoplastic conditions. See also Section I “Filling Defect, Upper Urinary Tract [Renal Pelvis and Ureter].”

REFERENCE

PYELITIS GLANDULARIS
DESCRIPTION
In this condition, combined urothelial hyperplasia and metabolic changes of the renal pelvis occur and characteristic glandular structures are seen haphazardly arranged within the lamina propria. These glands are lined by mucin-secreting columnar epithelial cells, which differentiate them from other forms of urothelial hyperplasia such as Von Brunn nests and pyelitis.

766
Cystitis. It is not uncommon to see late hyperplastic changes and pyloric glandularis in a single specimen. Intermittent and luminal mucin can be demonstrated by mucicarmine stain. Most commonly, the overlying surface epithelium remains of the transitional cell type, although metaplastic squamous epithelium or mucous secreting columnar cells may be seen. Pyloric glandularis is commonly focal. Extensive lesions with columnar cell metaplasia of the surface urothelium bear a high resemblance to colonic mucosa. However, the absence of muscularis mucosa helps distinguish these 2 entities. (See also Section I: “Filling Defect, the absence of muscularis mucosa helps distinguish these 2 entities. (See also Section I: “Filling Defect, "Filling Defect, Upper Urinary Tract [Renal Pelvis and Ureter").")

**REFERENCE**


**PYELOGENIC CYST**

**DESCRIPTION** A pyeogenic cyst is a smooth intrarenal diverticulum that communicates directly with the renal pelvis through a calyx or infundibulum. Pyeogenic cysts are lined with transitional cell epithelium. Diagnosis is best made by CT urography or delayed phase or retrograde pyelography showing contrast pooling in the cyst. Asymptomatic pyeogenic cysts do not require treatment. Pain, persistent or recurrent infections, stones, and milk of calcium warrant surgical intervention through uroendoscopic, percutaneous, laparoscopic, or open surgical techniques.

**REFERENCE**


**PYOCYSTIS**

**DESCRIPTION** Pyocystis is a severe UTI of the bladder associated with a nonfunctioning bladder or in patients with chronic colonic anemia. Also called vesical enpermia. Commonly seen (20–30%) in patients with a neurogenic bladder treated with urotherapy. Pyocystis should be suspected in patients with a nonfunctioning bladder or in those who are oligo- or amenorrheic with persistent signs of infection. Bladder catheterization should be performed and the urine cultured. A positive culture is diagnostic; however, imaging studies such as CT may reveal diagnostic signs such as bladder wall thickening. Conservative medical therapy is often adequate, comprised of specific antibiotics and bladder drainage. Some advocate periodic bladder irrigations and instillations with antibiotic solutions therapy are directed by the specific organisms isolated. Bladder irrigation with either saline or an antibiotic solution benefit is not clear. Cystectomy is reserved for refractory pyocystis.

**REFERENCE**


**PYONEPHROSIS**

**DESCRIPTION** Infected, obstructed collecting system with grossly purulent drainage and suppurative necrosis of renal parenchyma. This can be a chronic, indolent infection, but it usually presents acutely with sepsis, flank pain, and ipsilateral loss of renal function. Immediate aspiration with retrograde or percutaneous puncture is essential.

**REFERENCE**


**PYOSPERMIA**

**DESCRIPTION** The World Health Organization defines pyospermia as >1 x 10^9 WBCs/cell (either peroxidase or by immunohistologic methods). Pyospermia (also referred to as leukospermia) has multifactorial causes, including infection, inflammation, and autoimmunity, and is considered to be 1 of the causes of male infertility. The short half-life of polymorphonuclear neutrophils (PMNs) in semen makes them a major source for factors that can be harmful to sperm. The differential diagnosis of symptomatic pyospermia includes infection, autoimmune disease, and inflammation of the accessory sex glands and lower male urogenital tract. Urogenital infections include acute and chronic prostatitis, seminal vesiculitis, epididymitis, orchitis, urethritis, urethral strictures, stone disease, foreign bodies, upper UTI, retrograde ejaculation, localized sepsis of the adjacent lower UT tract, and asymptomatic bacteriuria. The chronic infections that may result in pyospermia include fungal, mycobacterial, and conjunctival lesions causing infection of the urogenital tract. Autoimmune diseases that affect the urogenital tract include Behçet syndrome and Reiter syndrome (Reactive arthritis/mucocutaneous arthritis triad). There is no defined medical management of pyospermia once the specific cause cannot be reliably identified. Options include antibiotic treatment (doxycycline, trimethoprim-sulfamethoxazole, ciprofloxacin) and other medications such as calcium dibromide, propylidione, n-acetyl-c-cysteine, glutathione, and vitamins C and E. Removal of cause and primary predisposing factors include the correction of any congenital or acquired defect in the GU tract, harboring infection and inflammation, se颠覆ous reflux, prostatitis obstructive and infection, retrograde ejaculation, and urethral valves. Although antibiotics are a commonly used empiric therapy, studies have not confirmed their benefit, and a high risk of spontaneous resolution occurs without specific therapy. (See also Section II: “Semen Analysis, Abnormal Findings and Technology.” "Semen Leukocytes.")

**REFERENCE**


**Q-TIP TEST**

**DESCRIPTION** The Q-tip test is useful to evaluate the vesical neck and evidence of hypermobility in the evaluation of urinary incontinence in the female. A cotton-tipped applicator is advanced per urethra to the level of the bladder neck and observed for changes in angle during straining maneuvers. Hypermobility suggests that a bladder neck suspension may restore continence.

**REFERENCE**


**QUAKEL CORPUSAL SHUNT**

**DESCRIPTION** Used for the treatment of priapism. Through a crural-perineal approach, a longitudinal incision is made in the corpus spongiosum urethrae (making sure not to completely traverse and injure the urethra), and a parallel incision is made in the corporal body. After irrigating stagnant corporal blood, these 2 incisions are anastomosed.

**REFERENCE**


**RADIATION EXPOSURE GUIDELINES**

**DESCRIPTION** The National Council on Radiation Protection and Measurements has recommended maximum permissible dose limits for occupational exposure to members of the public, which apply to the sum of the effective doses from external radiation and the committed effective doses from internal exposures. Occupational exposure

- The individual worker’s Lifetime effective dose should not exceed 0.5 mSv in any 1 yr.
- An annual effective dose limit of 50 mSv.
- An annual dose limit of 150 mSv for the lens of the eye.
- An annual dose limit of 500 mSv for localized areas of the skin and the hands and feet.
- A monthly dose limit of 0.5 mSv to the fetus once a pregnancy is declared.
- No occupational exposures should be permitted until age 18 yr.

Public exposure

- An annual effective dose limit of 1 mSv for continuous exposure and 5 mSv for infrequent exposure.
- An annual dose limit of 50 mSv for the hands and feet and localized areas of the skin and 15 mSv for the lens of the eye.
- For educational and training purposes involving people aged >18 yr, an annual effective dose limit of 1 mSv.

**REFERENCE**

Radiation Proctitis, Urologic Considerations

Radiation proctitis refers to radiation-induced injury to the rectal mucosa beginning 3 mo after treatment has ended. The incidence varies from 5–20%. Predisposing factors include prior lower abdominal surgery, diabetes, hypertension and possibly chemotherapy. Symptoms of radiation proctitis include tenesmus, bleeding, low-volume diarrhea, rectal pain, and loss of continence. Treatment is made with sigmoidostomy.

**TREATMENT**
- Correction of fistula
- Sacrouterine enemas
- Argon laser
- Bipolar electrocoagulation
- Sucralfate enemas
- Corticosteroids
- Surgery

**REFERENCE**

**Radiation, Renal and Retroperitoneal, Urologic Considerations**

**DESCRIPTION**
Radiation therapy (RT) for RCC as primary therapy is ineffective, but it is useful for palliation of bone metastases. It can be utilized for renal carcinomas or lymphoma. Retroperitoneal radiation is used for seminoma but not for nonseminomatous tumors. Nonseminomatous germ cell tumors (NSGCT) are generally less radiosensitive, and RT is typically not used. Side effects of renal and retroperitoneal RT include retroperitoneal fibrosis, ureteral stricture or obstruction, hydronephrosis, enteritis, cardiovascular complications, and secondary malignancy.

**REFERENCE**

**Radioisotopes, Urologic Considerations (Strontium-90, Samarium-153, Radium-223)**

**DESCRIPTION**
Strontium-90 and Samarium-153 are ε-emitters which can emit high linear energy transfer; may be halted by an aluminum plate. 100-1000 hits to kill cells; single strand breaks that are more easily repaired.

**REFERENCES**

**Rapid Plasma Reagin (RPR) Blood Test**

**DESCRIPTION**
The RPR test is a screening test for syphilis (T. pallidum infection). RPR detects serum antibodies to substances released by cells damaged by T. pallidum. It is 78%, 100%, and 95% sensitive in screening for primary, secondary, and tertiary syphilis, respectively. If a patient tests positive, a confirmatory treponemal antibody test should be ordered. False positives can be seen in viral infections, and HIV can cause a false negative reaction.

**REFERENCES**

**Raz Bladder Neck Suspension (Urethroplasty)**

**DESCRIPTION**
This is 1 of many surgical bladder neck suspension techniques aiming to fix the vesicourethral junction in a physiologic position to correct genuine stress incontinence in females. It is a modification of the Pereyra needle suspension. Through an inverted U-shaped incision in the anterior vaginal wall, the operator performs (1) retropubic urethropexy, (2) fundopexy guidance of a double- stranded suture carrier placed through a suprapubic opening, and (3) placement of helical reabsorbable sutures through the urethropexic ligament, otherwise known as the endopelvic fascia. Cystoscopy is performed after the sutures are placed. Best suited for patients with urethral and bladder neck hypermobility and no cystocele.

**REFERENCE**

**Raz Vaginal Wall Slung**

**DESCRIPTION**
Technique to treat urinary incontinence due to intrinsic sphincter dysfunction or anatomic incontinence, this is a modification of the original Raz bladder neck suspension. This technique provides support for both the bladder neck and mid-urethra. In addition to the principal maneuvers described in the Raz urethrolysis, the author incorporates a patch of anterior vaginal wall with the suspension sutures at the level of the bladder neck, which, in effect, creates a hammock that supports a backboard to the bladder neck and mid-urethra.

**REFERENCE**

**Reactive Arthritis/ Reactive Arthritis Triad (Formerly Reiter Syndrome)**

**DESCRIPTION**
The preferred term today is reactive arthritis, a classic triad of polyarthritides, conjunctivitis, and nongonococcal urethritis; in women, cervicitis. Anterior uveitis and skin or genital rash may be seen. Thought to be a systemic inflammatory response triggered by microbial infection in the GI or GU tracts, the condition is a member of the spondyloarthritic family of disorders. The arthritis is usually asymmetric, with predominately lower extremity involvement. Joint aspiration is typically sterile. Association with HLA-B27 is noted, and may confer susceptibility. 2 forms exist: Sexually transmitted, in which symptoms emerge 10-14 days after exposure. Causes include C. trachomatis, Ureaplasma urealyticum. The overall prognosis is good, with spontaneous remission or relapse following NSAID therapy within 6-9 mos of onset. A small proportion have chronic persistent arthritis, a few will develop ankylosing spondylitis more frequent if HLA-B27 positive. Clinical treatment includes supportive care, NSAIDs, intra-articular or systemic corticosteroids for polyarthritides. Antibiotic treatment is initiated for identified organisms, if possible, such as C. trachomatis doxycycline 100 mg PO bid for 7-14 days. (Note: The name change from Reiter syndrome to reactive arthritis is based in part on allegations that Dr. Reiter was an un-convicted war criminal.)

**REFERENCE**
RENOLOGY, NORMAL RADILOGRAPHIC FINDINGS (SIZES, CALYCES)

RECTOCELE, UROLOGIC CONSIDERATIONS

DESCRIPTION Recesses generally presents as a posterior bulge in the perineum in the setting of proteus. It can present with urological symptoms including sexual dysfunction and voiding symptoms, as well as constipation. If a patient presents with voiding dysfunction, a urodynami study should be performed with the recessed redundant to confirm the patient’s underlying urodynamic parameters. Prior to repair, it is important to determine if there is a deviation of enterocoe or cystal, to determine the appropriate reconstructive procedure. Treatment can be conservative using a vaginal pessary or surgical fixing of 1 or several techniques, including open or laparoscopic, transvaginal, or endoscopic. (See reference “Pelvic Organ Prolapse (Cystocoele and Entocoele”).)

REFERENCE Hall GM, Shanmugan S, Nobel T, et al. Symptomatic muscle tumors and renal cell cancer as a result of the mutations in the fumarate hydratase gene. The term muscle tumors (leiomyomas) in the skin and uterus increased predisposition to develop benign smooth leiomyomatosis, also known as Reed syndrome, is an initial with gabapentin a 2nd-line therapy. (See also Section II: “Scrotal Skin Lesion.”)

RED SCROTUM SYNDROME

DESCRIPTION The external genitalia can be affected by many inflammatory processes such as atopic and irritant dermatitis, psoriasis, or syphilis. A common disease Red Scrotum Syndrome (RSS) affects makes in their 2nd half of life and typically runs a chronic course. It may represent a localized phenotypical expression of erythromelalgia. RSS is characterized by persistent redness of the anterior 1/2 of the scrotum and may also involve the base of the penis. Symptoms include itching, burning, and pain sensations. It can develop after prolonged use of topical corticosteroids. It is often mistaken for eczema but itching is not common in RSS. Burning and hyperesthesia are typical in RSS and are not usual with eczema. The pain is aggravated by warmth, relieved by cold. Differential diagnosis includes atopic dermatitis, contact dermatitis, psoriasis, lichen simplex, and Langerhans cell histiocytosis among others. Oral dicyclomine is used initially with gabapentin a 2nd-line therapy. (See reference “Rectocele: Urologic Considerations.”)


REED SYNDROME

DESCRIPTION Multiple cutaneous and uterine leiomyomas, also known as Reed’s syndrome, is an autosomal dominant condition. Individuals have an increased predisposition to develop benign smooth muscle tumors (leiomyomas) in the skin and uterus. Survivors of these patients are at risk for renal cell cancer and have been determined to have mutations in the Fumarate hydratase gene. The term hereditary leiomyomatosis and renal cell cancer refers to tumors with an increased prevalence of smooth muscle tumors and renal cell cancer as a result of the fumarate hydratase genetic defect. (See also Section II: “Uterine Leiomyomas, Hereditary” and “Renal Cell Carcinoma, Familial.”)


REFLUX NEPHROPATHY

DESCRIPTION Racial scarring secondary to reflux of urine or infected urine from the bladder to the kidneys. Girls are at increased risk of developing reflux nephropathy because of the increased incidence of UTIs. Most cases are associated with vesicoureteral reflux, and children are usually asymptomatic or may present with infection, hypertension, or renal failure in cases of severe scarring. Usually a radiographic diagnosis, US and voiding cystourethrography identify the reflux, and renal scarring is detected radiographically by a conical imaging agent such as DMSA technetium99m (dimercaptosuccinic-acid). Treatment is directed at the cause (such as vesicoureteral reflux antibiotic suppression or surgical correction). (See also Section I: “Vesicoureteral Reflux,” and Image 60.)


REIFENSTEIN SYNDROME

DESCRIPTION A form of incomplete male pseudohernphroditism, usually presenting with penoscrotal hypoplasia and frequently cryptorchidism at birth, azoospermia and incomplete virilization at puberty, and infertility and gynecomastia at or after puberty. Causation by mutations in the SFRS5 binding domain of androgen receptor, with varying degrees of androgen receptor dysfunction. Patients are usually assigned to male sex at birth, and they exhibit elevated levels of testosterone and inhibin B. Surgical repair of hypospadias and cryptorchidism as the treatment and supplemental testosterone is not beneficial. (See also Section II: “Androgen Insensitivity Syndrome (AIS or Androgen Resistance Syndrome), Complete and Partial.”)


SYNONYMS

- Isolated Mildly-Deferens Syndrome
- Type 1 incomplete male pseudohernphroditism


REINKE CRYSTALS

DESCRIPTION Cryotopically crystallized inclusions found in human leydig cells. The crystals are large, distinctive, and easily visible under light microscopy. It has been noted that their numbers increase with age, their function or significance is unknown.


RENAL ANATOMY, NORMAL RADILOGRAPHIC FINDINGS (SIZES, CALYCES)

REFERENCE The most common renal epithelial neoplasms and found in 1.6–7% of autopsies. Controversial if these are small adenocarcinomas. Stenosis diagnostic criterion include papillary, sclerotic, or tubulopapillary architecture, <5 mm and no resemblance to any renal malignancy.


REFERENCE This condition is defined by the cephalic absence of 1 or both kidneys.

REFERENCES

- Bilateral renal agenesis. Incompatible with life as kidney function in utero is necessary in development of the lungs, infants born with bilateral agenesis have hypoplastic lungs, oligohydramnios, anuria, and renal failure, as well as a well-described group of physical findings such as a flattened nose, low-set ears, bowed knees, and a small chest collectively referred to as Potter syndrome. Bilateral agenesis is reported in 1 in 3,000 births but the actual incidence is unknown since many fetuses are believed to spontaneously abort without a diagnosis.

- Unilateral renal agenesis. In contrast, unilateral agenesis is usually asymptomatic and is often undiagnosed throughout life. It occurs in 1 in 1,100 births, and is more common in males (1.8:1); the left kidney is more commonly missing. Commonly associated with mullerian duct, Wolffian duct, and urogenital system anomalies. The most common anomalies are uterine anomalies, renal anomalies (cystic kidneys, horseshoe kidney), and female sex reversal. Bilateral renal agenesis is also associated with anomalies of other systems (such as cardiovascular in 30% valvular or septal cardiac anomalies, GO in 20%, imperforate anus or absence of anus or esophagus, and vertebro or pharyngeal anomalies. If diagnosed, some clinicians propose yearly screening of BP and urinary protein levels because of the risk of hypertension, renal insufficiency, and proteinuria found in some adult studies. (See also Section I: “Potter Syndrome/Potter Facies.” and Image 29.)


REFERENCE The kidney can be imaged by plain film, US, CT, MRI, radionuclide scanning, or angiography, either by venography, arteriography, or retrograde. A normal adult kidney should measure 10–15 cm vertically, 5–7 cm transversely, and 3 cm vertically.
**RENAL ARTERY ANEURYSM**

DESCRIPTION: A renal artery aneurysm is defined as a dilated segment of renal artery that exceeds twice the diameter of a normal renal artery. Although rare, the diagnosis and incidence of this entity have been steadily increasing due to the routine use of cross-sectional imaging. Incidence ranges from 0.3–1.0% on radiographic studies, accounting for 1% of all arterial aneurysms and 10% of renal aneurysms. They are commonly bilateral or multiple and occur typically in the 5th–6th decades of life, slightly more frequently on the right. They are associated with hypertension, HTN, flank pain, hematuria, or an incidental finding on imaging. Presentation is usually secondary to occlusion of aneurysmal segments is reserved for high-risk surgical candidates. Occlusion of aneurysmal segments is reserved for high-risk surgical candidates. Occlusion of aneurysmal segments is reserved for high-risk surgical candidates. Occlusion of aneurysmal segments is reserved for high-risk surgical candidates.

**TREATMENT**
- Microsurgical repair or percutaneous embolization is recommended for repair of renal artery aneurysms (RAAs) >2 cm. Spontaneous rupture, or asymptomatic rupture in high-risk patients is not recommended.
- Aneurysms associated with pheochromocytoma, ectopic adrenocortical neoplasia, paraganglionic, renal pelvic clear cell RCC or testicular germ cell neoplasia may be more aggressive.
- Unruptured aneurysms greater than 2 cm can be observed if symptomatic.
- Angioplasty and stenting for aneurysms greater than 4 mm in size should be considered for high-flow lesions.
- Aneurysms >5 mm in diameter require surgical intervention.
- Intrarenal aneurysms: Surgical intervention.
- REFERENCES

**RENTAL ARTERY FIBROMUSCULAR DYSPLASIA**

DESCRIPTION: Fibromuscular diseases of the renal arteries account for 1/3 of cases of renovascular hypertension. Treatment consists of antihypertensive therapy for asymptomatic individuals and percutaneous balloon angioplasty for patients with indications for intervention. Patients with macroaneurysms should be treated with either a covered stent or surgery. BP control with ACE inhibitor or angiotensin II receptor blocker. 4 pathologic entities have been described:
- Intimal fibroplasia
- Medial fibroplasia
- Perimedial fibroplasia
- Intimal hyperplasia

- Angioplasty is the treatment of choice.
- Spontaneous rupture is rare, but risk is increased during pregnancy.
- Prompt repair is advised because of the progressive nature of the disease.

**TREATMENT**
- Repair includes primary repair with excision of the aneurysmal segment, or aortorenal bypass with autologous or bypass with a bypass.
- Aneurysms >2 cm can be observed if symptomatic.
- Angioplasty is the treatment of choice.
- REFERENCES

**RENAL CANCERINOID TUMOR**

DESCRIPTION: Rare tumor derived from enterochromaffin or atrial precursor uptake and decarboxylation (APUD) cells, occurring most commonly in the GI tract and lung, but also in ovaries, testes, thyroids, parotis, and hepatobiliary system. Primary renal lesions are extremely rare, with only 32 cases reported. The lesions are thought to originate in renal collecting cells undergoing intestinal metaplasia or from renomedullary epithelial cells within the kidney. Hormones (62) are secreted and may have a markedly elevated risk of carcinoid tumor, although still very rare, and may have a more benign course.

**TREATMENT**
- Primary renal lesions are extremely rare, with only 32 cases reported. The lesions are thought to originate in renal collecting cells undergoing intestinal metaplasia or from renomedullary epithelial cells within the kidney. Hormones (62) are secreted and may have a markedly elevated risk of carcinoid tumor, although still very rare, and may have a more benign course.
- REFERENCES
  - REFERENCES

**RENAL CELL CARCINOMA, CLEAR CELL**

DESCRIPTION: This represents up to 85% of renal tumors. It is thought to arise from the proximal renal tubule unit and is characterized by a lipid content in over 90% of cases. It has a better prognosis than other RCC histologies. Chromophobe RCC is difficult to distinguish from oncocytoma on biopsy, making definitive diagnostic difficult without a complete pathologic exam. C-kit and epithelial-related antigen (MOC31) may be helpful in the distinction between chromophobe RCC and renal oncocytoma. (See also Section “Renal Cell Carcinoma, General” and Image 42.)

**SYNONYMS**
- Hypernephroma (once thought to be adrenal origin)
- Grawitz tumor

**REFERENCES**

**RENAL CELL CARCINOMA, FAMILIAL**

DESCRIPTION: Approximately 2% of renal cell carcinomas (RCC’s) can be inherited. Familial renal cancers are characterized by an early onset compared with sporadic cases and frequently comprise bilateral and multifocal tumors. Moreover, extrarenal features suggestive of a described familial renal cancer syndrome might be present. See table for common renal familial syndromes. (See also Section “Renal Cell Carcinoma, General.”)

**SYNONYMS**
- Hereditary cancer syndrome

**REFERENCES**

**REFERENCES**
- Molecular data suggests that many of these patients with RAs >2 cm can be observed if symptomatic.
- Angioplasty and stenting for aneurysms greater than 4 mm in size should be considered for high-flow lesions.
- Aneurysms >5 mm in diameter require surgical intervention.
- Intrarenal aneurysms: Surgical intervention.

**REFERENCES**
RENAL CHELSTEROL EMBOLISM SYNDROME

DESCRIPTION: The syndromic features of cholesterol embolism are usually the result of severe hypertension. It is increasingly associated with thrombolytic therapy. Clinical findings include severe hypertension, digital gangrene, livedo reticularis, cerebrovascular accidents, GI hemorrhage or infarction, bowel perforation, retinal ischemia, and mental retardation.


RENAL CHELSTEROL EMBOLISM SYNDROME

DESCRIPTION: Cholesterol microembolism (also called choleterol embol and cholesterol crystal embol of the kidney) is an uncommon cause of hypertensive emergencies, affecting primarily elderly men with atherosclerotic vascular disease. It is increasingly associated with thrombolytic therapy. Clinical findings include severe hypertension, digital gangrene, livedo reticularis, cerebrovascular accidents, GI hemorrhage or infarction, bowel perforation, retinal ischemia, and mental retardation. Diagnosis is most often made from clinical history, physical exam, labs findings, and imaging studies.

DESCRIPTION
These benign vascular neoplasms are most frequently affected. Treatment is supportive and preventative with management of hypertension and albuminuria through control of the underlying pathology.

CAUSES
- Angiographic manipulation
- Anticoagulant medications
- Cardiovascular surgery
- Traumatic
- Spontaneous

REFERENCE

REPRESENTATIVE IMAGE

RENAL LEIOMYOSARCOMA
See Section "1. Renal Sarcomas, Adult and Pediatric."

REPRESENTATIVE IMAGE

REPRESENTATIVE IMAGE

REPRESENTATIVE IMAGE

REPRESENTATIVE IMAGE

REPRESENTATIVE IMAGE
Utility of Radiologic Procedures in Evaluation of Indeterminate Renal Mass

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT abdomen without and with contrast</td>
<td>9</td>
<td>Either CT or MRI is appropriate. See statement regarding contrast in text under “Anticipated Exceptions.”</td>
</tr>
<tr>
<td>MRI abdomen without and with contrast</td>
<td>9</td>
<td>Either CT or MRI is appropriate. See statement regarding contrast in text under “Anticipated Exceptions.”</td>
</tr>
<tr>
<td>US kidney retroperitoneal with Doppler</td>
<td>8</td>
<td>To clarify mass that is probably a hyperdense or simple cyst.</td>
</tr>
<tr>
<td>Biopsy and aspiration kidney</td>
<td>5</td>
<td>Depends on clinical scenario—the appearance and size of mass. US, CT, or MRI may be used for image guidance.</td>
</tr>
<tr>
<td>MRI abdomen without contract</td>
<td>3</td>
<td>Can be used to characterize simple cysts.</td>
</tr>
<tr>
<td>Tr-99m DMSA scan</td>
<td>1</td>
<td>May be useful to rule out pseudolesions of functioning renal tissue.</td>
</tr>
<tr>
<td>Arteriography kidney</td>
<td>1</td>
<td>To rule out arteriovenous malformation, arteriovenous fistula, or renal artery aneurysm.</td>
</tr>
<tr>
<td>US, CT, MRI with or without contrast</td>
<td>1</td>
<td>May be helpful to differentiate parenchymal masses from collecting system masses.</td>
</tr>
</tbody>
</table>

Rating Scale: 1, 2, 3, usually not appropriate; 4, 5, 6, may be appropriate; 7, 8, 9, usually appropriate.

REFERENCE

RENALE MEDULLARY CARCINOMA

DESCRIPTION
This is an aggressive renal malignancy limited almost exclusively to young black patients with sickle cell trait and, less commonly, sickle cell disease. Typical age of presentation is 21–24 yr of age with a peak prevalence of 75% occurring in the right kidney. Genetic testing has suggested a potential association with various chromosomal anomalies. It is considered a variant of collecting duct carcinoma. Patients usually present with gross hematuria, flank pain, an abdominal mass, and/or weight loss. Metastases in the central nodes to brain are often the initial finding. Therapy in the senior population should prompt evaluation for renal medullary carcinoma. Excludes an abdominal mass at a centrally located infrarenal lesion resembling the renal sinus with peripheral calcifications. tumor ranges from 4–12 cm (averaging 7 cm) and usually associated with hemorrhage and necrosis. Metastatic disease is commonly present at diagnosis. Surgical resection is not usually curative. There is a limited experience in the treatment of metastatic disease. Survival after diagnosis is usually 6–12 mo (Image No. 94).

REFERENCE

RENALE OSTEODYSTROPHY

DESCRIPTION
Renal osteodystrophy is defined by the National Kidney Foundation as bone morphology abnormalities observed in chronic kidney disease. Several changes can occur, including osteitis fibrosa cystica due to secondary hyperparathyroidism, osteomalacia, or low bone turnover. The most common presenting symptoms are bone fracture and pain, and usually occurring once lower is on dialysis. Treatment may include treating hyperparathyroidism, calcitriol, vitamin D analogs, calcimimetics, or parathyroidectomy.

REFERENCE

RENALE PSEUDOTUMOR

DESCRIPTION
A bizarre condition of the kidney mimicking a renal neoplasm on radiographic studies. Most commonly a hyperintense column of Adenoma hypertrophy (adenoma) a prominent medullary column usually located between the upper and middle pole calyces that can appear as a renal mass but is homogeneous with surrounding renal parenchyma, with normal appearing calyces. Other conditions giving appearance of renal tumor include persistent fetal lobulation, medullary dysplasia, and renal dysplasia. Metastases in the central nodes to brain are often the initial finding. Therapy in the senior population should prompt evaluation for renal medullary carcinoma. Excludes an abdominal mass at a centrally located infrarenal lesion resembling the renal sinus with peripheral calcifications. tumor ranges from 4–12 cm (averaging 7 cm) and usually associated with hemorrhage and necrosis. Metastatic disease is commonly present at diagnosis. Surgical resection is not usually curative. There is a limited experience in the treatment of metastatic disease. Survival after diagnosis is usually 6–12 mo (Image No. 94).

REFERENCE

RENALE SINUS ABNORMALITIES

DESCRIPTION
The renal sinus is a central space usually located in the renal pelvis. It is usually filled with adipose tissue, lymphatic channels, nerve fibers, and fibrous tissue. Lesions that may develop in the sinus could be benign, including parapelic simple cysts, lipomatosis, cysts, urinomas, and various lesions such as renal artery aneurysm or AV fistula. Malignant tumors originating in renal pelvis or pararenchyma, such as TCC and RCC, may develop in the renal sinus. Primary tumors, such as hemangioma, fibroma, kystoma, and MRH are rare but may develop in the space.

REFERENCE

RENALE TRANSPLANT TYPES (STANDARD/EXTENDED/ DONOR AFTER DEATH)

DESCRIPTION
Renal transplant donors can be by living donors or deceased donors. Decreased donors are individuals who meet the criteria for brain death, but whose organs are being perfused by life support methods, allowing adequate time for procurement. Donor after cardiac death is an expanded criteria donor. Nonheart beating donor (NHBD) death is characterized by irreversible absence of circulation. NHBDs are less than ideal because organ function is impaired because organ function is impaired during prolonged periods of circulatory arrest. Nearly 70% of all renal transplants are from deceased donors. Living donors can be either related or unrelated. On prospective evaluation, normal renal function after donation is the goal. In line with this, the better functioning kidney is left with the donor. RAH-identical siblings have the highest graft survival rates followed by 1-haplogene siblings. In paired donor exchange, also known as kidney swap, 2 kidney recipients exchange willing donors whom they are willing to receive. This allows the donors to provide 2 recipients with grafts where previously no transplant would have been possible. Overall, living donor grafts have higher survival rates, with 80% surviving at the 5-yr mark compared to 67% of deceased-donor grafts (Image 49).

REFERENCE

RENALE TRANSPLANTATION AND NEOPLASIA

DESCRIPTION
The transplant recipient has an elevated risk of cancer. There is a very small risk of primary malignancy harbored in the graft being transplanted to the recipient. The most common malignancies that form after transplantation are de novo malignancies. They are thought to occur secondary to chronic use of immunosuppressive drugs. After 10 yr of immunosuppressive therapy, kidney transplant recipients have a cumulative incidence of cancer as high as 20%. The most common are Kaposi’s sarcoma

773
P1: OSO/OVY

P2: OSO/OVY

LWBK1391-Section-II-P2

QC: OSO/OVY

LWBK1391-Gomella

T1: OSO
uro˙short-topics-r.xml

September 18, 2014

19:55

RENAL TUMORS, WHO 2004 CLASSIFICATION

REFERENCE

and non-Hodgkin lymphoma. Compared to age and
sex matched general population, kidney cancer
recipients are 3–5-fold increased risk of developing
skin cancers and urologic malignancies. Recipients
who have been on hemodialysis are also at a higher
risk of acquired cystic disease and subsequent primary
renal malignancy.

Eble JN, et al. Pathology and Genetics. Tumors of the
urinary system and male genital organs. Lyon: IARC

RENAL VEIN,
LEIOMYOSARCOMA

REFERENCE

DESCRIPTION A rare tumor arising from the

Piselli P, Serraino D, Segoloni GP, et al. Risk of
de novo cancers after transplantation: Results from
a cohort of 7217 kidney transplant recipients, Italy

smooth muscle element of the renal vein, occurring
most commonly on the left side. The highest incidence
is seen in 60–69 year olds and is twice as common in
women. Only 32 cases of renal vein leiomyosarcoma
have been reported in the literature. The renal vein is
the most common site of venous leiomyosarcoma
outside of the vena cava. Presenting symptoms include
flank or abdominal pain, weight loss, and a palpable
abdominal mass. 3-dimensional abdominal imaging
imaging reveals a homogeneous, well-circumscribed
mass at or near the renal hilum, commonly encasing
the renal vein. Mean survival is 28 mo, with an
aggressive malignant pattern to distant sites, including
lung, liver, bone, skin and soft tissue, and brain.

RENAL TUMORS, WHO 2004
CLASSIFICATION
DESCRIPTION The 2004 World Health
Organization (WHO) classification of the adult renal
epithelial neoplasms replaced the previous 1998 WHO
classification. It incorporates other classifications
(Mainz, Heidelberg) and describes entities based on
both pathologic and genetic analyses. (See table)

WHO (2004) Classification of All Renal Tumors
Renal cell tumors
Clear cell renal cell carcinoma
Multilocular clear cell renal cell carcinoma
Papillary renal cell carcinoma
Chromophobe renal cell carcinoma
Carcinoma of the collecting ducts of Bellini
Renal medullary carcinoma
Xp11 translocation carcinomas
Carcinoma associated with neuroblastoma
Mucinous tubular and spindle cell carcinoma
Renal cell carcinoma, unclassified
Papillary adenoma
Oncocytoma
Metanephric tumors
Metanephric adenoma
Metanephric adenofibroma
Metanephric stromal tumor
Nephroblastic tumors
Nephrogenic rests
Nephroblastoma
Cystic partially differentiated nephroblastoma
Mesenchymal tumors
Occurring Mainly in Children
Clear cell sarcoma
Rhabdoid tumor
Congenital mesoblastic nephroma
Ossifying renal tumor of infants
Mesenchymal tumors
Occurring Mainly in Adults
Leiomyosarcoma (including renal vein)
Angiosarcoma

Rhabdomyosarcoma
Malignant fibrous histiocytoma
Hemangiopericytoma
Osteosarcoma
Angiomyolipoma
Epithelioid angiomyolipoma
Leiomyoma
Hemangioma
Lymphangioma
Juxtaglomerular cell tumor
Renomedullary interstitial cell tumor
Schwannoma
Solitary fibrous tumor
Mixed mesenchymal and epithelial tumors
Cystic nephroma
Mixed epithelial and stromal tumor
Synovial sarcoma
Neuroendocrine tumors
Carcinoid
Neuroendocrine carcinoma
Primitive neuroectodermal tumor
Neuroblastoma
Pheochromocytoma
Hematopoietic and lymphoid tumors
Lymphoma
Leukemia
Plasmacytoma
Germ cell tumors
Teratoma
Choriocarcinoma
Metastatic tumors

WHO Histologic Classification of Benign Renal Neoplasms
Renal Cell Tumors

Metanephric Tumors

Oncocytoma
Papillary adenoma

Metanephric adenoma
Metanephric adenofibroma
Metanephric stromal tumor

774

Mesenchymal
Tumors

Mixed Epithelial and
Mesenchymal Tumors

Angiomyolipoma
Leiomyoma
Hemangioma
Lymphangioma
Reninoma
Fibroma
Schwannoma

Cystic nephroma
Mixed epithelial and stromal tumor

TREATMENT

r Aggressive surgical resection with nephrectomy and
en-bloc resection
r Nonsurgical treatment with XRT and chemotherapy
can be instituted but the efficacy is limited.

REFERENCE
venous leiomyosarcomas: a review of the literature.

RENAL–RETINAL SYNDROME
DESCRIPTION Also called juvenile
nephronophthisis with retinal disease or Senior-Loken
syndrome (SLS) it is a subtype of juvenile
nephronophthisis. (See Section II: “Juvenile
Nephronophthisis.”) It is an autosomal recessive
disease characterized by development of retinitis
pigmentosa- or Leber congenital amaurosis-like retinal
dystrophy and a medullary cystic kidney disease. These
patients have concomitant retinitis pigmentosa, which
is slowly progressive and bilateral, with retinal
degeneration. Rods are affected, leading to defective
night vision that becomes symptomatic in early
childhood. The disc may look yellow and waxy.
Treatment is supportive, with renal replacement
therapy as needed.

SYNONYMS

r Juvenile nephronophthisis with retinal disease
r Senior–Loken syndrome

REFERENCE
Ronguillo CC, Bernstein PS, Baehr W. Senior-Loken
syndrome: A syndromic form of retinal dystrophy
associated with nephronophthisis. Vision Res.

RENIN, PLASMA AND RENAL
VEIN
DESCRIPTION In suspected renovascular

hypertension, an elevated renin level of >50% in the
renal vein compared to the renal artery plasma level
(estimated from the IVC renin level) of the affected
kidney is diagnostic. Individual renal veins can be
sampled to isolate ischemic individual renal segments
using this same technique. Normal, morning plasma
renin activity for seated subjects ranges from about
1– 4 ng/mL/h (0.8–3.0 nmol/L/h). Corresponding
active renin concentrations are 8–35 mU/L. Renin is
increased with diuretics (including spironolactone),
dihydropyridine calcium channel blockers, angiotensin
converting enzyme inhibitors and angiotensin receptor
antagonists. Levels are decreased by β-blockers,
clonidine, or α-methyldopa (all of which reduce
β-sympathetic stimulation of renin release), or
nonsteroidal anti-inflammatory agents (which promote
salt retention and also inhibit renal prostaglandin
production).
r Normal renin: Secondary adrenal insufficiency (ie,
hypopituitarism or isolated ACTH deficiency);
Cushing syndrome, but they can be low when there
is a marked degree of hypercortisolism.
r Low renin: Primary aldosteronism; with
11β-hydroxylase or 17α-hydroxylase deficiency (due
to mutations in CYP11B1 and CYP17, respectively),
which are hypertensive forms of CAH; primary
glucocorticoid resistance; DOC-producing adrenal
tumors; ectopic ACTH syndrome.


REFERENCES

RENO-ALIMENTARY FISTULA
DESCRIPTION
A broad group of nonanatomic communications between the upper urinary collecting system and the alimentary canal, with nephrocolic and nephrobronchial fistulas being the most common presentations. Symptoms vary from GI symptoms such as nausea, vomiting, and diarrhea, to recurrent UTIs with flank pain and fever. Retrograde ureterography is generally needed to visualize the fistula. (See also Section II: “Fistula, Enterovesical.”)

CAUSES
• Renal inflammatory disease (acute or chronic)
• Malposition of other intestinal or visceral organs
• Iatrogenic (eg, percutaneous surgery)
• Trauma
• Urol disease

TREATMENT
• Conservative: Stenting or nephrostomy tube
• Nephrectomy with removal of fistula tract and bowel resection

REFERENCE

RENO-BRONCHIAL FISTULA
DESCRIPTION
Fistulas communicating between pleural cavity and kidney, associated with pyelonephritics and perirenal abscesses. Usually presents with flank or abdominal pain with an (isolated) pneumonia. Patients commonly have a history of pyelonephritis or abdominal abscess. Fistulas involving the kidney are most commonly caused by iatrogenic trauma. These may include perirenal nephrostomy or nephrothoracostomy tract placement. Renobronchial fistulas usually develop from an upper pole approach to the kidney, where the pleural cavity may be traversed. It can involve pleural space alone or one into lung parenchyma and bronchial tree. Diagnosis is made with CT.

SYNONYMS
• Nephrobronchial fistula
• Renal, bronchopulmonary fistula

CAUSES
• Pyelonephritis with peripheric abscess
• Xanthogranulomatous pyelonephritis
• Most common pathogens: E. coli and Proteus sp account for 1/3 of cases
• Tubercular infections also reported
• Urinogenital trauma: Perrenostasis nephrostomy, nephrotomy tract placement

TREATMENT
• Percutaneous or open drainage and antibiotic therapy usually required

REFERENCE

RENO-MEDULLARY INTERSTITIAL CELL TUMOR
(ADENOCARCINOMA)
DESCRIPTION
Also referred to as medullary fibroma and renal hamartoma, this is a benign renal interstitial cell neoplasm. Rarely they are large and symptomatic. It is a common incidental finding in as many as 5% of adults at autopsy. Renomedullary interstitial cell tumor arises from interstitial cells of the medulla. They do not appear to have any effect on blood pressure. At gross exam, medullary fibromas are white or gray nodules within the renal pyramids. At histologic exam, this tumor is characterized by variable-sized spindle cells in the background of a lymphocytic stroma. It can be seen on CT as a well demarcated noncalcified hypoattenuating cold mass within the renal medulla. Although it is a benign tumor, it is difficult to differentiate this lesion from other malignancies of the kidney on radiologic basis and heroic many patients undergo radical nephrectomy (Stuart OS).

REFERENCES

REPERFUSION INJURY, RENAL (RENAL ISCHEMIA AND REPERFUSION INJURY)
DESCRIPTION
Ischemic acute kidney injury (AKI) is a syndrome that develops following a transient drop in total renal blood flow to the kidney. Although reperfusion is essential for the survival of ischemic tissue, there is evidence that reperfusion itself causes additional cellular injury after a period of ischemia. Therefore, strategies that can provide protection against ischemic injury may be beneficial to such patients. Studies comparing partial nephrectomy with and without clamping show that ischemia is associated with an increase in proteinuria and albuminuria in patients with ischemia. However, advanced protection and reperfusion strategies have proven beneficial. Clamping decreases the incidence of renal failure by decreasing the amount of renal ischemia. Although a minority of patients may experience serious complications from clamping, many patients also experience relatively mild complications, such as hypertension, hypotension, and tachycardia. Therefore, clamping may be a useful tool in managing AKI.

REFERENCES

RETE TESTIS, ADENOCARCINOMA
DESCRIPTION
Adenocarcinoma arising from the rete testis is an extremely rare tumor, typically occurring in older men. The majority of patients present with a painless mass in the testis, often mistaken for a spermatic cord cyst or epididymal cyst. On rare occasions, a patient may present with a testicular mass and an elevated hCG level. The tumor most commonly affects the rete testis, which is the epididymal portion of the testis. It is a highly malignant tumor arising from the rete testis, which is composed of a network of capillaries and lymphatics that drain the testis. It is also known as testicular adenocarcinoma. The tumor is typically unilateral and may present with symptoms such as pain, swelling, and a mass. It is important to note that rete testis adenocarcinoma has a more aggressive behavior compared to other testicular tumors. It is important to diagnose and treat this tumor promptly to improve the outcome for the patient.
commonly presents with a painless scrotal mass or symptoms related to metastasis. Pathology reveals papillary adenocarcinoma in the rete testis, commonly with local invasion. May be associated with maldeveloped testes or adenomatous hyperplasia of the rete testis. Prognosis is poor, with ~10% survival at 5 yr. Malignant carcinoid include retroperitoneal lymph nodes, lungs, bone, and liver. The diagnostic criteria include:

- Tumor in mediastinum separate from the body of testis
- Transition in rete testis from normal gynadenium to neoplastic cells
- No evidence of teratoma
- No primary tumor elsewhere
- Intact pial arterial tumor

**TREATMENT**
- Radical orchectomy is the mainstay of treatment.
- XRT and chemotherapy have limited efficacy for metastatic disease.
- Retroperitoneal lymph node dissection may have a role in the absence of metastasis.

**REFERENCE**

---

**RETROCEVAL/CIRCUMCEVAL URETER**

**DESCRIPTION**
A rare congenital anomaly in which the intrapelvic ureters (IVU) are derived from the right subarcuate or preaortic vein, anterior to the vena cava. The term circumcaval ureter refers to the ureter emerging medial to IV, after running behind it. While the term retroceval applies to those ureters that only belong to the IV (but re-erune normally. Nodules are affected at times more often than are females. Not all retroceval/circumcaval ureters are obstructed, but if obstruction exists, surgical repair is typically warranted. CT is the best imaging modality for identification. Despite its congenital origin, symptoms are usually absent in childhood and present later in life. Less commonly, patients present with hematuria or UI.

**REFERENCE**

---

**RETROGRADE URETHROGRAM (RUG), TECHNIQUE**

**DESCRIPTION**
RUG is used to radiographically evaluate the urethra. It is most commonly used to evaluate urethral stricture disease or trauma. It is commonly performed by inserting a Foley catheter or Broden’s clamp into the Fossa Navicularis. The balloon is inflated with a few milliliters of water to create a seal. Then 50 cc of contrast solution is injected into the urethra under low pressures while obtaining a series of x-rays. An oblique view allows best visualization of the entire urethra (Image 1).

**REFERENCE**

---

**RETROPERITONEAL NEPHROMATOSIS**

**DESCRIPTION**
A retroperitoneal hematoma is hemorrhage contained within the retroperitoneum. Etiologies include disruption of the kidney or renal pedicle from trauma, postoperative hemorrhage, spontaneous hemorrhage of a renal mass typically angiomylipoma (or RCC), or abdominopelvic visceral hemorrhage. Echocardiomy may be observed around the umbilicus (Lumen sign) or flank (Loin-Turner sign). Management is primarily conservative, including frequent hemoglobin levels, resuscitation, and transfusion, as necessary. However, if the patient is hemodynamically unstable and the bleeding is from a renal source, and they have an expanding pelvic hematoma, or renal hematoma cannot be stopped with selective embolization, then surgical exploration is indicated. Further evaluation of the underlying pathology and follow-up imaging for resolution is warranted. (See also Section I. Renal Angiomyolipoma; “Retroperitoneal Abcess,” “Retroperitoneal Masses and Cysts,” and Image 2.)

**REFERENCE**

---

**RETROPERITONEAL LIPOSARCOMA**

**DESCRIPTION**
Retroperitoneal liposarcoma is the most common retroperitoneal sarcoma arising from adipose tissue. However retroperitoneal sarcomas are rare, with just 2-3 new cases per 1 million persons reported annually. They are usually identified incidentally or at a locally advanced stage when they cause symptoms from adjacent tissue invasion or compression. Compression of ureters can cause obstructive uropathy. Metastatic disease includes bone, lung, skin, and liver. If the mass is visualized on CT or MRI, abdominal mass containing variable amount of fat (<20 Hounsfield units) and soft tissue components. A germ cell tumor (GCT) must be ruled out by tumor markers, and a biopsy is necessary if there is diagnostic uncertainty. Complete resection is the only curative treatment. Radiotherapy can be used preoperatively for local control. (See also Section I. “Retroperitoneal Masses and Cysts,” and Image 2.)

**REFERENCE**

---

**RETROPERITONEAL LIPOMATOSIS**

**DESCRIPTION**
Lymphoma involving retroperitoneal lymph nodes: it can be the primary site of involvement or a site of metastasis. The lesion can cause extrinsic compression of ureters with obstructive uropathy. Positive diagnosis is made when a mass is visualized on CT or MRI. Differential diagnosis may include retroperitoneal fibrosis, retroperitoneal fat necrosis, lipoblastoma, sarcocoma, metastasis from other tumors such as prostate, or bladder or germ cell tumor metastasis. (See also Section I. “Retroperitoneal Masses and Cysts,” and Image 2.)

**TREATMENT**
- CHOP chemotherapy (cyclophosphamide, Adriamycin, vincristine, prednisone) and radiation therapy
- Obstructive uropathy may require ureteral stenting or percutaneous decompression prior to chemotherapy

**REFERENCE**

---

**RETROPERITONEAL RHEUMATOID NODULES**

**DESCRIPTION**
Rheumatoid nodules (necrobiotic granulomas) are a common extra-articular manifestation of rheumatoid arthritis, usually found in subcutaneous tissue. They have been reported in numerous other locations, including blood vessels, skin, eye, and extraspinal space. GU involvement is rare and can include renal tumor and bladder. Retroperitoneal occurrence has been reported and can cause extrinsic compression or obstruction requiring ureterolysis and repair. (See also Section I. “Retroperitoneal Masses and Cysts.”)
The most lethal renal neoplasm, Ewing’s sarcoma, comprises 2% of all renal tumors and primarily affects children under the age of 15. The incidence has increased from 1976 to 1996, Volume 3, Journal of Cancer Control.

**RETROPERITONEAL SARCMA**

DESCRIPTION Retroperitoneal sarcomas are mesenchymal neoplasms. Approximately 1/2 of retroperitoneal sarcomas are high-grade tumors, with the most common type being liposarcoma, followed by leiomyosarcoma. Median age at presentation is 50, although they can occur at any age. At the time of diagnosis, more than 50% are ≥ 2 cm in size. They are typically incidentally diagnosed but when patients do present with symptoms they are abdominal or back pain and increased abdominal girth. Differential diagnosis of a retroperitoneal mass includes neoplasm from a retroperitoneal viscerial structure, lymphoma, or a metastatic lesion. Retroperitoneal sarcomas carry a worse prognosis than extrarenal sarcomas due to the difficulty of complete resection, involvement of critical structures, and delay of diagnosis. CT is the imaging modality of choice. In patients with systemic therapy; or radiation therapy should be based on optimizing the patient for surgical resection. (See also Section 1: "Retroperitoneal Masses and Cysts.)" REFERENCES Mullins R, Zager JS, Gonzalez RJ. Current diagnosis and management of retroperitoneal sarcoma. Cancer Control. 2011;18(3):177–187.

**RETROPERITONEAL FAT NECROSIS**

DESCRIPTION Retroperitoneal fat necrosis is a pathology syndrome characterized by the histologic hallmarks of coalescence of fat cells into fat cysts bordered by foreign body giant cell granulomas. Local injury to fat cells from trauma appears to be the initiating event of fat necrosis in the retroperitoneum. In addition, an inflammatory trigger such as acute pancreatitis can result in the inflammatory syndrome. In patients with systemic therapy; or radiation therapy should be based on optimizing the patient for surgical resection. (See also Section 1: "Retroperitoneal Masses and Cysts.)" REFERENCES Ross JS, Plotz MR. Retroperitoneal fat necrosis producing severe obstruction. J Urol. 1974;113(5):524–529.

**RHABDOMYOID TUMOR, MALIGNANT**

DESCRIPTION The most lethal renal neoplasm, termed a “tumor of Wilms,” is comprised of 2% of all renal tumors and primarily affects children under the age of 15. The incidence has increased from 0.1 per million in 1986 to 1.4 per million in 2005. It has a tendency to early metastatic spread. The most common presentation is an abdominal mass detected in these young patients. Extrarenal sites include central nervous system (35%), liver, and gastrointestinal tract. Presence of mutations in the HOX11 gene on chromosome 12 is the hallmark. The lack of staining of the RKI gene product is diagnostic. Younger patients have a worse prognosis compared with older patients. Radiation therapy is an essential part of multimodality therapy. REFERENCES Zhuge Y, Cheung MC, Yang R, et al. Pediatric rhabdomyosarcoma: update on etiology, pathology, and management of rhabdomyosarcoma. J Surg Res. 2010;163(2):257–269.

**RIEGER SYNDROME**

DESCRIPTION Also known as the Axenfeld-Rieger Syndrome, this is an autosomal dominant syndrome affecting multiple organ systems. It is manifested by ocular anomalies such as glaucoma, cardiovascular defects, and malformations of craniofacial structures, which can result in severe endodermal stenosis. Genitourinary anomalies occur in the form of hypoplasia. In most cases, there has been identified as FTOX2 and FOXC1 on chromosome 25. REFERENCES Chang HC, Simmons CG, Schimmenti LA, et al. Axenfeld-Rieger syndrome: new perspectives. Br J Ophthalmol. 2012;96(3):318–322.

**RIFLE CRITERION FOR ACUTE RENAL INJURY**

DESCRIPTION Also referred to as the RIFLE Classification system for AKI, it assesses levels of renal injury (Risk, Injury, and Failure) based on the degree of elevation in serum creatinine or urine output, and 2 outcome measures (Loss and End stage renal disease):• Risk: 1.5× increase in creatinine or 25% GFR decrease by 25% or urine output <0.5 mL/kg/h for 6 hr• Injury: 2× increase in creatinine or 50% GFR decrease or urine output <0.5 mL/kg/h for 12 hr• Failure: 3× increase in creatinine or 75% GFR decrease or urine output <0.25 mL/kg/h for 12 hr or urine output <0.5 mL/kg/h for 4 hr or anuria for 12 hr• Loss: Complete loss of kidney function (eg, renal replacement therapy necessary) for >4 wk• End stage renal disease (ESRD): Complete loss of kidney function (eg, renal replacement therapy necessary) for >3 moThe RIFLE criteria correlate with prognosis, with a stepwise increase in the risk of death in patients who meet the RIFLE criteria for various stages of AKI. Compared to patients without AKI, patients in the RIFLE stages of risk, injury, and failure had increased mortality risks of 2.4, 4.13, and 6.37, respectively. (See also Section 1: “Acute Kidney Injury, Adrenal (Renal Failure, Acute)."


**RIM SIGN (RIM NEPHROGRAM)**


**ROBINOW SYNDROME**

DESCRIPTION A skeletal dysplasia with both autosomal dominant and recessive inheritance pattern. It is characterized by short stature, limbs shortening, genital hypoplasia (micropenis), and craniofacial abnormalities. The more phenotypically severe autosomal recessive form has been associated with mutations in the ROR2 gene on the long arm of chromosome 10. REFERENCES Penson AD, Beiraghi S, Sieben CM, et al. WNT3A mutations in patients with autolosomal dominant Robinow syndrome. Dev Dyn. 2010;239(1):327–337.

**ROBSON STAGING SYSTEM**

DESCRIPTION Robson’s modification of Flocks and Kadow’s staging system for renal cell carcinoma (RCC) was the most commonly used in the United States. The fact that long-term evaluation of patients with stage IIIA lesions, without disease extension into perinephric fat and lymph nodes, has shown survival comparable to those at stage II and III, has currently led many investigators to prefer the TNM system proposed by UICC. (See Section 2: “Renal Cell Carcinoma, General”; Section VII: “Tumors.”) Stage I: Tumor is confined within the kidney parenchyma (no involvement of perinephric fat, renal vein, or regional nodes). Stage II: Tumor involves the perinephric fat but is confined within Gerota fascia (including adrenal). Stage III: Tumor involves the renal vein or inferior vena cava. Stage IV: Tumor involves regional lymph nodes. Stage IVB: Tumor involves both local vessels and regional lymph nodes. Stage IVc: Tumor involves adjacent organs other than the adrenals (colon, pancreas, etc.). Stage IVf: Distant metastases. REFERENCES Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. Trans Am Assoc Genitourin Surg. 1968;90:122–129.
ROKITSKY–KUSTER–HAUSER SYNDROME

DESCRIPTION Pathologic condition characterized by the presence of ovaries and infertility and by a congenital aplasia of the uterus and upper 2/3 of the vagina. Also referred to in the literature as Mayer–Rokitansky–Kuster–Hauser Syndrome. The condition is usually discovered during evaluation of a normal-appearing girl who presents with failure of menstruation at the time of expected puberty. They have a normal female karyotype 46, XX and do not develop normal secondary sexual characteristics. The syndrome may be caused by the lack of development of the Müllerian ducts between the 5th and 6th wk of gestation. In some patients, cyclic abdominal pain suggestive of some functional endometriosis is noted. Vaginal reconstruction with bowel or skin grafting is performed. It can also be associated with renal and skeletal abnormalities.


ROSEWATER SYNDROME

DESCRIPTION Rosewater syndrome is an infertility disorder associated with germ cell aplasia. On histologic biopsy, the seminiferous tubules contain only Sertoli cells. This is considered irreversible and precludes germ cell restoration. Not infrequently, tubular and peritubular fibrosis is associated with germ cell aplasia.


ROVING POLYCYSTIC KIDNEY OPERATION

DESCRIPTION A historically important surgical procedure that entails unroofing multiple renal cysts. The procedure of implantation occurs in usually 2 stages. Stage I consists of percutaneous placement of temporary wire leads into the 53 tumor. It can either be performed in the office or in the operating room. A 1–2 wk trial period occurs with the leads in place and voiding symptoms are monitored. If >50% improvement in symptoms occur, the patient moves on to Stage II which is always performed in the operating room. Permanent leads are placed as well an implantable pulse generator. The most commonly used device is the implantable® (Medtronic, Minneapolis, Minnesota) (FDA-approved since 1997 for urge incontinence and since 1999 for urinary retention and significant symptoms of urge-frequency) (Stage I).


SANI SCORE

DESCRIPTION The Sani Score (Survival after Nephrectomy and Immunotherapy) score is a tool for predicting survival for patients with metastatic RCC in response to the multimodality treatment of aggressive surgical resection and systemic immunotherapy. The regional lymph node status, the presence or absence of constitutional symptoms, the location of metastases, the presence or absence of sarcomatoid pathologic features, and TSH levels are incorporated into the scoring algorithm. Patients are stratified based on predicted survival into low-risk, intermediate-risk, and high-risk groups for appropriate treatment regimens and for prospective trials of new therapies.


SCABIES, UROLOGIC CONSIDERATIONS

DESCRIPTION An intensely pruritic parasitic infection that affects superficial areas of the body, including the genitalia, anus, legs, hands, umbilicus, and axilla. Diagnosis can be made by identifying the mite (Sarcoptes scabiei), expressed from the papular (FDA-approved since 1997 for urge incontinence and decrease in available sex hormone-binding globulin) or papule. In females, the presence or absence of sarcomatoid pathologic features, and TSH levels are incorporated into the scoring algorithm. Patients are stratified based on predicted survival into low-risk, intermediate-risk, and high-risk groups for appropriate treatment regimens and for prospective trials of new therapies.

SCROTAL SKIN LESIONS

SCROMISTOSOMIASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION A parasitic infection by the blood fluke Schistosoma haematobium. This condition has a broad spectrum of urologic manifestations due to the parasite’s life cycle. Infection across the skin-hematuria migration to pelvis/vesical venous plexus, transmural migration into bladder, and shedding into urine. Typically, patients will exhibit polypoid urethral mucosal lesions (active infection) or “sandy patch” flat, tan lesions (inactive infectious). Significant upper urinary tract obstruction is possible with chronic disease. Classic symptoms are hematuria and terminal dysuria. Infection has been linked to bladder cancer, occurring earlier in life (40–50 yr); this is most common squamous cell carcinoma (SCC) (80–90%) and adenocarcinoma (5–15%). The presence of fluke eggs in urinary sediment is diagnostic of schistosomiasis. (See also Section 1: “Bladder Cancer, Squamous Cell Carcinoma” and Image 90.)

TREATMENT

Medical management: Metrifonate and praziquantel

SCHWANNOMA, RENAL

DESCRIPTION Also called neurinoma or neurolemmoma, a tumor arising from Schwann cell neural elements of the kidney. Schwannomas of renal origin are very rare with only 20 reported cases in the literature. They present in middle-aged patients with a male-to-female ratio of 2:1. They typically appear as spherical, solid, and well-circumscribed encapsulated lesions. The vast majority are benign, and the malignant degeneration is very rare. Partial or radical nephrectomy (open or laparoscopic technique) is the treatment of choice as there are no reliable preoperative diagnostic methods.

REFERENCES


SCROTAL PEARLS (SCRUTOLITHS)

DESCRIPTION Benign calcifications within the scrotum, usually non-fungating. Usually diagnosed by ultrasound, these are described as a hypoechoic density in the scrotal wall that demonstrates acoustic shadowing. Scrotal pearls can occur from infection or trauma and themselves are rarely symptomatic. They may also be noted as artifacts after torsion of the scrotum.

REFERENCES


SCROTAL SKIN LESIONS

DESCRIPTION Scrotal skin lesions may be localized or a manifestation of more systemic diseases.

- Benign
  - Amyloidosis (rare)
  - Angiokeratoma of Fordyce: Small, 1–2 mm red, vascular elevations seen predominantly in male non-smokers
  - Atopic dermatitis: Involves the scrotum or scratch cycle with lichenification with or without excoriation. The posterior scrotum is a common site.
- Calcinosis, idiopathic scrotal
SCROTAL TONGUE

- Contact dermatitis: Allergic or irritant. Pruritus, burning, and itching.
- Eczema: frequently affects the genital region, particularly the scrotum. Patients present with intense, itchy, erythematous plaques on the lateral scrotum. The eruption may develop into Lichen simplex chronicus (LSC) (also referred to as “Neurodermatitis”) characterized by extensive lichenification and hyper trophy of the affected skin due to excessive scratching and rubbing.
- Epithelioid hemangioendothelioma, penis, and scrotum
- Fixed drug eruption: Erythematous, well-demarcated “bump-like” area, may evolve from erythema to vesicles or blisters.
- Folliculitis: Usually caused by Staphylococcus aureus.
- Gential lichen: Hyperpigmented macules that may be confused with melanoma.
- Gental warts (condyloma): Uncommon on the scrotum
- Ichthyosis: excessive amounts of dry surface scales; inherited or acquired.
- Insect bite
- Kaposi sarcoma: A purple, papular, plaque-like, or ulcerated lesion.
- Lichen simplex chronicus (LSC): Reaction to irritants, particularly the scrotum. Patients present with lichenified erythematous plaques on the lateral scrotum, which drain the testis that can be palpated through the scrotal skin. Overall, they are present in 15% of the male population. Varicocele is the most common etiology of male factor infertility, being present in 35% of males with primary infertility and 81% with secondary infertility. They most commonly occur on the left scrotum and the testis. If the gonad is dysplastic and associated with other GU anomalies (upper tract), this is termed scrotal tongue, with the condition representing a spectrum of penoscrotal transposition abnormalities. Surgical repair is recommended management. (See Section II: “Scrotum, Engulfment (Penscrotal Transposition),” and Image 6).

REFERENCES


SCROTAL TONGUE

DESCRIPTION

Scrotal tongue is not a urticarial condition. It refers to a deeply fissured tongue.

TREATMENT

- If the varicocele is not associated with infertility, decreases testicular volume or pain, it is considered subclinical and surgical correction is not indicated.
- The scrotum is repositioned around the scrotal skin and the base of the penis. This allows placement of the scrotal flaps beneath the penis. Malignant tumors may evolve into the scrotal skin and the testis. If the gonad is dysplastic and associated with other GU anomalies (upper tract), this is termed scrotal tongue, with the condition representing a spectrum of penoscrotal transposition abnormalities. Surgical repair is recommended management. (See Section II: “Scrotum, Engulfment (Penscrotal Transposition),” and Image 6).

REFERENCES


SCROTUM, EPIDERMAL INCLUSION CYST

DESCRIPTION

Epidemidial inclusion cysts are benign tumors. They result from the implantation of epidermal tissue into the dermis or subcutis, from trauma or abnormal embryologic closure of the median raphe and urethral groove. These lesions appear solid on imaging and often contain a material that is a combination of keratin and cholesterol, often in a laminated configuration arising from a straddled squamous epithelial wall. They can be asymptomatic or more commonly rupture or become infected. Local excision is the treatment, since epidemidial inclusion cysts can mimic rare malignant
tumors such as liposarcoma, fibrosarcoma, and even metastatic disease.

REFERENCE

SCROTUM, FAT NECROSIS
DESCRIPTION
An uncommon lesion that is seen in prepubertal boys and can be a cause of acute scrotal pain. Typical presentation is an obese prepubertal child with recent exposure to cold, such as during swimming. Bilateral intrascrotal masses are present inferior to the testes. If the diagnosis is made with US and shows the classic presentation, conservative management can be employed.

REFERENCE

SCROTUM, GIANT NEUROLEMMOMA
DESCRIPTION
Well-encapsulated tumors of neural elements (also called neurinoma or Schwannoma) within the scrotum. Most such tumors are benign, with malignant transformation as an extremely rare occurrence. Surgical removal of the lesion is the definitive treatment.

REFERENCE

SCROTUM, HEMANGIOMA
DESCRIPTION
These lesions should be differentiated from angiokarstoma of Fournier that appear in older men (see Section II). “Angiokarstoma of Fournier (Perineal and Scrotal Angiokarstoma)” Hemangiomas represent 7% of all nonmalignant tumors and are the most common benign tumor of infancy; however, they invade the penis and scrotum only 1% of the time. Cutaneous hemangiomas also called (strawberry angiomas) are the most common benign tumor of infancy and are usually present at birth. Although such skin lesions are usually painless, they may cause functional impairment in infants. Laser therapy is necessary unless recurrent episodes of infection occur; then surgical excision may help.

REFERENCE

SEAPI INCONTINENCE CLASSIFICATION SYSTEM
DESCRIPTION
SEAPI is an acronym for stress incontinence, emptying ability, anxiety, protection, and instability. It is a useful and uniform method of following the short- and long-term outcome of stress urinary incontinence (SUI) surgery. This system is similar to the TNM tumor staging classification system in that each component is graded on a scale from 0 to 3 (normal to severe symptoms). After completion of the evaluation of the incontinent patient, a prospective subjective and objective SEAPI score is determined. These scores are then compared with postoperative SEAPI scores to assess treatment outcomes. It has been found to have a high degree of reliability and internal consistency across a wide age range in both genders.

REFERENCE

SEBORRHEIC DERMATITIS
DESCRIPTION
Commonly referred to as dandruff, this condition can be seen on the penis, anus, or pubic hair. Pruritus is the rule, with the lesions in hair-bearing areas having a red base and scaly yellow crust. While the organism Pityrosporon orbiculare is suspected, the exact agent is unknown. Standard antifungal shampoos are usually effective. Shampoo containing ketoconazole may be needed. Steroids should be used with caution, if at all, because this tends to be a lifelong problem. (See also Section II: “Pruritus, External Genitalia, Male.”)

REFERENCE

SEMIN ANALYSIS, ABNORMAL FINDINGS AND TERMINOLOGY
REFERENCE
ABNORMAL FINDINGS AND TERMINOLOGY
A significant overlap exists between fertile, subfertile, and infertile populations; therefore, absolute parameters for infertility (easest for aspermia or azoospermia) are difficult to measure precisely. In general, fertile populations demonstrate mean sperm densities of 70–80 million/mL. Assisted reproduction techniques (ART) are now able to overcome many of these abnormalities. (See also Section I: “Infertility.” Section II: “Semen Analysis, Technique, and Normal Values.” and “Semen Analysis, Abnormal Findings and Terminology.”)

Aspermia: No semen ejaculated

Azoospermia: <150 spermatozoa with forward progression of 3 or 4

Hypospermia: Poor motility and/or poor forward progression

Necrozoospermia: No live sperm in ejaculated semen

Normozoospermia(Men): Refer to a normal semen analysis

Oligoasthenospermia: Very generalized abnormalities in sperm concentration, motility, and morphology; often associated with varicocele

Oligocentrozoospermia: Significant disturbance of all 3 variables (combinations of 2 profiles may also be used)

Oligozoospermia: Low concentration of sperm (500,000–1 million/mL)

Polyospermia: Abnormally high density sperm >250 x 10^6/mL

Polyospermia: Excess number of sperm in ejaculate sample

Pycnosis/leukocytes: Excess white cells >1 white cell = 10^6/mL in semen

Teratozoospermia: Reduced percentage of morphologically normal sperm, usually <10% spermatozoa with normal morphology

REFERENCES


871
SEMEN ANALYSIS, TECHNIQUE, NORMAL VALUES

DESCRIPTION: Normozoospermia/normospermia are terms sometimes used to refer to a normal semen analysis. After 48–72 hr of abstinence, a semen specimen is collected in a wide-mouth polypropylene container with a screw top through masturbation without the use of any lubricants that could contaminate the sample. Care must be taken to capture all of the ejaculate. The sample is kept at close to body temperature as possible and delivered to the lab within 1.5 hr. Analysis includes (may vary slightly by lab) total seminal volume, sperm concentration, sperm mobility, sperm morphology, fructose content, coagulation time, liquefaction time, viscosity, and leukocyte count. Newer computer-assisted systems (CASA) can also evaluate curvilinear velocity, straight-line velocity, linearity, and amplitude of lateral head displacement. Antisperm antibodies may be considered a secondary test. Normal parameters are established by most labs. The following are general reference parameters and are typically determined on at least 2 specimens. (See also Section II: "Infertility"); and Section II: "Semen Analysis, Abnormal"; also see Section II for topics on specific semen abnormalities.

Typical Reference Lab Values for Routine Semen Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Minimum Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1.5–5.0 mL</td>
</tr>
<tr>
<td>Appearance</td>
<td>White, viscous, opaque</td>
</tr>
<tr>
<td>pH</td>
<td>7.2–7.8</td>
</tr>
<tr>
<td>Spem density</td>
<td>&gt; 20 x 10⁸/mL</td>
</tr>
<tr>
<td>Total sperm count</td>
<td>&gt; 40 x 10⁹/mL</td>
</tr>
<tr>
<td>Motility</td>
<td>&gt; 60%</td>
</tr>
<tr>
<td>Forward progression</td>
<td>&gt; 50% or &gt; 2 + 0 or a scale of 0–4; 0, no movement; 4, excellent forward progression</td>
</tr>
<tr>
<td>Morphology</td>
<td>&gt; 60% normal</td>
</tr>
<tr>
<td>Viability</td>
<td>&gt; 50% (by exclusion)</td>
</tr>
<tr>
<td>Fructose, quantitative</td>
<td>&gt; 19 mU/mL or pH 6–7</td>
</tr>
<tr>
<td>Liquefaction</td>
<td>10–20 min (measured on a scale of 0–4)</td>
</tr>
<tr>
<td>Agglutination</td>
<td>Minimal clumping (increased clumping suggests inflammatory immunologic process)</td>
</tr>
</tbody>
</table>

Normal Semen Analysis Parameters Published by the WHO

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Minimum Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>2.0 mL</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>20 million/mL</td>
</tr>
<tr>
<td>Motility</td>
<td>50%</td>
</tr>
<tr>
<td>Forward progression</td>
<td>3.0–4</td>
</tr>
<tr>
<td>Normal morphology (WHO)</td>
<td>30%</td>
</tr>
<tr>
<td>Normal morphology (WHO)</td>
<td>14%</td>
</tr>
<tr>
<td>Total sperm count</td>
<td>40 million</td>
</tr>
<tr>
<td>Total reactive sperm</td>
<td>20 million</td>
</tr>
<tr>
<td>Total functional sperm</td>
<td>6 million</td>
</tr>
</tbody>
</table>


SEMEN LEUKOCYTES

DESCRIPTION: The leukocyte is the most common nonsemen cell seen in a semen analysis, and it may be confused with immature spermatozoa on microscopy. Leukocytospermia and pyospermia are terms used to describe excess white cells in the semen specimen (> 10³/mL). Elevations usually are associated with infection, but may be linked to reactive oxygen species and may be present when there is no finding of infection or immune response. Leukocytospermia is often found in patients with unexplained infertility. Semen cultures are prone to contamination, and the use of antibiotics to treat pyospermia is controversial. (See also Section II: "Infertility"; Section II: "Semen Analysis, Abnormal Findings and Terminology"); "Semen Analysis, Technique, Normal Values"; and "Pyospermia.""


SEMEN PLASMA HYPERSENSITIVITY (SEMINAL PLASMA ALLERGY) AND HYPERSENSITIVITY TO HUMAN SEMEN (HHS)

DESCRIPTION: An allergic reaction to human semen that presents as a systemic reaction (ranging from mild to anaphylaxis) in a localized vaginal symptoms shortly after ejaculation into the vagina. Two types described in the literature the more common reaction to human seminal plasma (allergic reactions to human seminal plasma [HSP] proteins) or a response to spermatozoa (hyperreactivity to human semen [HHS]). These conditions are likely underestimated and may not be discussed or accepted in-gynecology or urology. These are seen exclusively in women (usually from 20–30 yr of age) and can be avoided through the use of condoms or less commonly through anti-allergy medications or allergen desensitization. Once established, it usually occurs with other male partners. In addition to the potential symptoms infertility is an issue.


SEMINAL VESICLE AGENESIS

DESCRIPTION: Can be unilateral or bilateral (very rare). Unilateral agenesis results from an embryologic insult before separation of the seminal bud from the mesonephric ducts. Unilateral agenesis is associated with (possibility) agenesis of the ductus deferens and with renal agenesis in 79%, (possibility) renal abnormalities in 12%, and only 8% had normal kidney bilaterally. The contralateral seminal vesicle is often hypoplastic.


SEMENAL VESICLE CALCULI AND CALCIFICATIONS

DESCRIPTION: Calcium of via deferens seems to be specific to diabetes mellitus and may be associated with calcification of the seminal vesicles. Other causes include TB, chlamydia, gonorrhea, and ureaplasma with secondary hyperparathyroidism. Intraluminal seminal vesicle calculation can be seen (Image 42).


SEMENAL VESICLE, CARCINOMA

DESCRIPTION: Primary tumors of the seminal vesicles extremely rare as there are no more than 60 historically confirmed reported cases. The seminal vesicles are often secondarily involved by cancer of surrounding structures such as prostate, bladder, or rectal carcinoma. Lymphoma of the seminal vesicles has been reported. Primary adenocarcinoma of the seminal vesicle (the most common primary type) occurs in patients ~ 50. Immunohistochemistry is helpful in diagnosis. They are PSA and PSAP negative. RF and/or cyclosporine treatment including pelvic lymph node dissection, offers curative treatment. Adjacent or neoadjuvant chemotherapy is of unproven worth, but a combination of hormonal deprivation and radiation therapy seems to be more effective than any chemotherapy.


kidney bilaterally.
SEMINAL VESICLE, CYSTS

DESCRIPTION
Cysts, of either congenital or acquired origin, located in the seminal vesicles. Many studies in the past have linked cysts to other GU issues, including renal agenesis, infertility, hematopoeisia, GU infection, and adult polycystic kidney disease. Cysts are congenital, ejaculatory duct obstruction (EDO), or a basement membrane defect, especially associated with adult polycystic kidney disease. (See also Section I: “Seminal Vesicle Masses and Cysts” and Image 2D)

TREATMENT
• No treatment is necessary if asymptomatic.
• Aquisation, manipulation, or excision, if symptomatic

REFERENCE

SEMINAL VESICULITIS

DESCRIPTION
Inflammation of the seminal vesicles that often occurs secondary to bacterial infection, causing prostatitis or epididymitis. Older literature referred to this condition as pyospermia. Symptoms are often vague and may include pain, scrotal, or perineal, painful ejaculation, hematopoeisia, lower abdominal or back pain; and LUTS. Diagnosis is often 1 of exclusion of other more common causes made with positive cultures from the ejaculate as well as imaging via transrectal US, CT, or MR. Pyospermia/leukocysteorrhea is prominent on semen analysis. Abscess formation is a complication of seminal vesiculitis and can be an initial presentation of the disease. Treatment includes culture-sensitive antibiotics, transrectal aspiration, or excision (open or laparoscopic seminal vesiculectomy) for severe cases. Tumoral seminal vesiculocystic with irrigation has been described. (See also Section II: “Pyospermia.”)

REFERENCES

SEXUAL ANHEDONIA/EJACULATORY ANHEDONIA

SEMINALOMA, CLASSIC

DESCRIPTION
The most common histologic subtype of seminomatous germ cell tumor (GCT). It accounts for ~80% of cases. Typically presents in males in the 30–50th decades of life. Syncytiotrophoblastic elements are seen in 10% of cases. These elements produce δ-hCG, which can be used as a tumor marker to help assesses prognosis or recurrence of disease after treatment. Unlike all other testicular tumors, treatment depends on tumor stage. Radical orchectomy followed by either surveillance, radiation therapy, and/or chemotherapy are performed, depending on the extent of disease. (See also Section I: “Testis, Seminoma.”)

REFERENCE

SEMINOMA, SPERMATOCYTIC

DESCRIPTION
Accounts for ~2% of all seminomatous germ cell tumor (GCT). Patients present later in life, usually in their 5th–6th decades. Unlike classic and anaplastic subtypes, spermatocytic seminoma rarely metastasizes. It is believed that this subtype arises from a different, more mature germ cell, which likely contributes to its more favorable presentation. Due to its low metastatic potential, no further treatment is often recommended after radical orchectomy. (See also Section I: “Testis, Seminoma.”)

REFERENCE

SEX REVERSAL SYNDROME (XX MALE)

DESCRIPTION
These patients demonstrate small, firm testes. Frequent gynaecomastia, a small to normal penis, and azoospermia. Testicular biopsy may demonstrate seminiferous tubuli scarring, causing elevated gonadotropins and decreased testosterone levels. Individuals are shorter than average height.

TREATMENT
• No treatment is necessary if asymptomatic.
• Further treatment is often recommended after radical orchectomy. (See also Section I: “Testis, Seminoma.”)

REFERENCE

REFERENCES

SEX-HORMONE BINDING GLOBULIN (SHBG)

DEFINITION
Testosterone (T) circulates bound to either SHBG, albumin (A), or sex-hormone binding globulin (SBG), or in an unbound form (free). SHBG-bound T is about 44% of the total T and is unavailable to cells. Albumin-bound T is about 50% of the total. Conditions that increase SHBG, include aging, hyperthyroidism, estrogen, HIV disease, anticonvulsants, heparin and heparin citrate. Conditions that decrease SHBG, include obesity, diabetes mellitus, hyperthyroidism, androgentic steroids, nephrotic syndrome, anorexia and glucocorticoids. The age-related SHBG increase means that older men may have a normal T-levels even if they are hypogonadal, as they will have low levels of free or bioavailable T. Obesity, on the other hand, decreases SHBG and T, even when the available T may be normal.

REFERENCE

SEXSOMNIA

DESCRIPTION
Sексsomnia, also known as somnambulistic sexual behavior or sleep sex is a particular form of parasomnia (disruptive sleep disorder) characterized by atypical sexual behavior during sleep. The repetition of sexual behavior during sleep can vary from explicit vocalizations with sexual content, violent masturbation, and complex sexual activities including oral sex, vaginal or anal intercourse. The exact etiology is unknown, but precipitating factors are stress, sleep deprivation/fragmentation, alcohol or drug consumption, excessive fatigue and physical overactivity in the evening.

TREATMENT
• Medications such as benzodiazepines are 1st-line therapy.
• Sleep hygiene and safety precautions should be implemented.

REFERENCE

SEXUAL ANHEDONIA/ EJACULATORY ANHEDONIA

DESCRIPTION
Lack of appropriate pleasure from sexual activity. Patients typically report a failure of genital response. Men have difficulty initiating or sustaining an erection, pre-menopausal women have difficulty with lubrication. Ejaculatory anhedonia describes lack of pleasure during ejaculation. Although a psychogenic etiology is often present, the clinician must rule-out hormonal influences. Medications such as...
SEXUAL FUNCTION SURVEY (SFS) (INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF))

DESCRIPTION: The IIEF is a 15-item, self-administered questionnaire scale for the assessment of erectile function that has been linguistically validated in 10 languages. It addresses the relevant domains of male sexual function: erectile function (EF), organic function (OF), sexual desire (SD), intercourse satisfaction (IS), and overall satisfaction. EF is represented in items 1 and 5 of the questionnaire, with a score range of 0–5, a minimum score of 0, and a maximum score of 30. IS is represented in items 9 and 10, with a score range of 0–5, a minimum score of 0, and a maximum score of 30. SD is represented in items 1 and 2, with a score range of 0–6, a minimum score of 0, and a maximum score of 30. EF, IS, and SD are each represented in 1 item of the questionnaire, with a score range of 0–15, a minimum score of 0, and a maximum score of 45. The questionnaire consists of 5 questions pertaining to the relevant domains of male sexual function: Erectile Function [IIEF] [Sexual Function Survey]."

REFERENCES


An extremely rare primary urethral malignancy that may become infected and present as a tender, fluctuant perineal nodule. Infection or inflammation of the Skene glands can cause exquisite tenderness and may be associated with dyspareunia and vulvar vestibulitis. The most common pathogens is Klebsiella pneumoniae. Treatment includes cultures of infected area along with surgical incision and drainage if abscess formation is present. Appropriate antibiotic therapy is administered. Other causes of vestibulitis or vulvodynia should be assessed and evaluated.

REFERENCES


References

Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is administered. Other causes of vestibulitis or vulvodynia should be assessed and evaluated.

REFERENCES


SKIN TAGS, EXTERNAL GENITALIA (ACROCHORDON, PEDUNCULATED PAPILLOMA, VESTIBULITIS)

DESCRIPTION: Benign, flesh-colored, soft pedunculated benign lesions that may occur anywhere on the body and generally are < 5 mm, although larger lesions can be seen. They may be pinkish, skin-colored, or hypopigmented and are more common on obese individuals. Usually asymptomatic, these lesions are often found in skin folds (neck, armpit, and labia), and rarely involve the external genitalia. They may accompany hamartomatous skin lesions in tuberous sclerosis complex or neurofibromatosis. Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is necessary, and they are usually considered clinically insignificant. If treatment is desired for cosmetic reasons, then the tags may be treated by electrocautery, simple incision or excision, suture ligation of the base, or cryotherapy.

REFERENCES


SLEEP APNEA, UROLOGIC CONSIDERATIONS

DESCRIPTION: Patients with obstructive sleep apnea may have their condition exacerbated by testosterone replacement therapy (TRT), their sleep apnea status should be monitored closely and treated if possible. Sleep apnea also may cause nocturnal hypoxia and may be a factor for erectile dysfunction (ED). Obstructive sleep apnea may also be involved with nocturnal and daytime erectile bladders in women.

REFERENCES


SHY DRAGER SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION: Shy Drager syndrome, also known as multiple system atrophy, is a progressive neurodegenerative disease in which the etiology is unknown. Bladder dysfunction causing urinary incontinence and erectile dysfunction (ED) are early features. Urinary urgency, frequency, incomplete bladder emptying as well as urinary retention or any combination are seen as urologic manifestations of the Shy Drager syndrome. In addition, weakness of the strained urethral sphincter contributes to incontinence. DO is seen on urodynamic evaluation.

REFERENCES


REFERENCES

Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is administered. Other causes of vestibulitis or vulvodynia should be assessed and evaluated.

REFERENCES


SKIN TAGS, EXTERNAL GENITALIA (ACROCHORDON, PEDUNCULATED PAPILLOMA, VESTIBULITIS)

DESCRIPTION: Benign, flesh-colored, soft pedunculated benign lesions that may occur anywhere on the body and generally are < 5 mm, although larger lesions can be seen. They may be pinkish, skin-colored, or hypopigmented and are more common on obese individuals. Usually asymptomatic, these lesions are often found in skin folds (neck, armpit, and labia), and rarely involve the external genitalia. They may accompany hamartomatous skin lesions in tuberous sclerosis complex or neurofibromatosis. Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is necessary, and they are usually considered clinically insignificant. If treatment is desired for cosmetic reasons, then the tags may be treated by electrocautery, simple incision or excision, suture ligation of the base, or cryotherapy.

REFERENCES


SLEEP APNEA, UROLOGIC CONSIDERATIONS

DESCRIPTION: Patients with obstructive sleep apnea may have their condition exacerbated by testosterone replacement therapy (TRT), their sleep apnea status should be monitored closely and treated if possible. Sleep apnea also may cause nocturnal hypoxia and may be a factor for erectile dysfunction (ED). Obstructive sleep apnea may also be involved with nocturnal and daytime erectile bladders in women.

REFERENCES


SHY DRAGER SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION: Shy Drager syndrome, also known as multiple system atrophy, is a progressive neurodegenerative disease in which the etiology is unknown. Bladder dysfunction causing urinary incontinence and erectile dysfunction (ED) are early features. Urinary urgency, frequency, incomplete bladder emptying as well as urinary retention or any combination are seen as urologic manifestations of the Shy Drager syndrome. In addition, weakness of the strained urethral sphincter contributes to incontinence. DO is seen on urodynamic evaluation.

REFERENCES


REFERENCES

Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is administered. Other causes of vestibulitis or vulvodynia should be assessed and evaluated.

REFERENCES


SKIN TAGS, EXTERNAL GENITALIA (ACROCHORDON, PEDUNCULATED PAPILLOMA, VESTIBULITIS)

DESCRIPTION: Benign, flesh-colored, soft pedunculated benign lesions that may occur anywhere on the body and generally are < 5 mm, although larger lesions can be seen. They may be pinkish, skin-colored, or hypopigmented and are more common on obese individuals. Usually asymptomatic, these lesions are often found in skin folds (neck, armpit, and labia), and rarely involve the external genitalia. They may accompany hamartomatous skin lesions in tuberous sclerosis complex or neurofibromatosis. Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is necessary, and they are usually considered clinically insignificant. If treatment is desired for cosmetic reasons, then the tags may be treated by electrocautery, simple incision or excision, suture ligation of the base, or cryotherapy.

REFERENCES


SLEEP APNEA, UROLOGIC CONSIDERATIONS

DESCRIPTION: Patients with obstructive sleep apnea may have their condition exacerbated by testosterone replacement therapy (TRT), their sleep apnea status should be monitored closely and treated if possible. Sleep apnea also may cause nocturnal hypoxia and may be a factor for erectile dysfunction (ED). Obstructive sleep apnea may also be involved with nocturnal and daytime erectile bladders in women.

REFERENCES


SHY DRAGER SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION: Shy Drager syndrome, also known as multiple system atrophy, is a progressive neurodegenerative disease in which the etiology is unknown. Bladder dysfunction causing urinary incontinence and erectile dysfunction (ED) are early features. Urinary urgency, frequency, incomplete bladder emptying as well as urinary retention or any combination are seen as urologic manifestations of the Shy Drager syndrome. In addition, weakness of the strained urethral sphincter contributes to incontinence. DO is seen on urodynamic evaluation.

REFERENCES


REFERENCES

Birt–Hogg–Dubé syndrome. Irritation and possibly HPV types 6/11 are possible causes. No treatment is administered. Other causes of vestibulitis or vulvodynia should be assessed and evaluated.

REFERENCES

REFERENCE

SMELLY GLANDS
DESCRIPTION
Smells, usually mid-urethral, are a common complaint for the treatment of intrinsic sphincteric deficiency. Smell materials are either autologous, allografts, xenografts, or synthetic. (See also Section I: “Urology, Female.”)

REFERENCE

SMITH-LEMLI–OPITZ SYNDROME
DESCRIPTION
An autosomal recessive multisystemic disease found in newborns that present with hypospadias and cryptorchidism. Anomalies in other systems include perinatal asphyxia, mental retardation, syndactyly, renal abnormalities, and microcephaly. These patients have an inborn error of cholesterol (biosynthesis defect of 3-hydroxy-3-methylglutaryl-CoA reductase), which results in deficiency of cholesterol and elevation of 7-dehydrocholesterol, a cholesterol precursor. Patients can take cholesterol with or without bile acids.

REFERENCE

SMOKING, UROLOGIC CONSIDERATIONS
DESCRIPTION
Smoking is a modifiable behavioral risk factor with an array of impact on urologic disorders. The smoking population attributable risk of bladder cancer is 50% in men and 52% in women. The relative risk of developing both renal parenchymal cancer as well as upper tract carcinoma ranged in men from 27–37% and 10–24% in women. In addition, there is a dose-response relationship as the risk of developing RCC is increased in lifelong smokers who smoke >20 cigarettes a day compared those who smoke less. Smoking may cause irreversible damage to neuromuscular and uro-endothelial mechanisms of erectile function as though only 20% of the population are smokers, 40% of men with ED are currently smokers. Smoking has also been associated with increased risk of acquiring HIV and HPV (both high and low-risk strains). The semen parameters in men who smoke have been found to be significantly decreased, especially sperm motility.

REFERENCE

SNODGRASS HYPOSPADIAS REPAIR
DESCRIPTION
Snodgrass hypospadias repair, also known as the Snodgrass method, is the most commonly performed operation to repair distal hypospadias. The key step in the procedure is a midline incision of the urethral plate. The urethral plate is then tubularized beginning at the neomeatus, which results in a slight overhang. Because sperm is highly antigenic, the inflammatory reaction creates a granuloma, which is usually asymptomatic. Some studies have shown that men who undergo vasectomy reversal have higher success rates if they have a sperm granuloma at the vasectomy site. A mass in the scrotum, often tender postvasectomy, is diagnostic.

REFERENCE

SODIUM CYANIDE NITROPRUSSIDE TEST
DESCRIPTION
A qualitative test for cystine. The assay involves the conversion by cyanide of cystine to cysteine and nitric oxide. Nitric oxide binds cysteine resulting in a purple color in 2–10 min. The test detects cystine levels above 75 mg/ml creatinine. If positive a quantitative 24-hr collection should be performed.

REFERENCE

SOLID TUMORS, RENAL
DESCRIPTION
Solitary fibrous tumors (SFTs) are mesenchymal tumors arising at any site. When involving the kidney, they arise from the capsule, renal pelvis, or hilar fatty tissue. They present similar to those with RCC. On gross appearance, the tumor is solid with a pseudocapsule. Microscopically, it shows a spindle cell proliferation. Controversy exists concerning the diagnosis of SFT and hemangiopericytoma because of overlapping immunohistochemical features. No cases of metastasis from renal SFTs has been described.

TREATMENT
Radical nephrectomy with complete excision including negative margins is needed for a favorable prognosis.

REFERENCE

SPERM GRANULOMA
DESCRIPTION
Sperm granulomas form from the injection of sperm into the scrotum and the vas deferens after vasectomy. Because sperm is highly antigenic, the inflammatory reaction creates a granuloma, which is usually asymptomatic. Some studies have shown that men who undergo vasectomy reversal have higher success rates if they have a sperm granuloma at the vasectomy site. A mass in the scrotum, often tender postvasectomy, is diagnostic.

TREATMENT
When chronic post-vasectomy pain is localized to the sperm granuloma, the lesion should be excised and occluded with electrocautery.

REFERENCES
Sperm Penetration Assay (Spa, Hamster Test)

REFERENCE

Sperm Penetration Assay (Spa, Hamster Test)

DESCRIPTION
Also called hamster ovocyte penetration assay test and in some publications (Hamster test), a test for infertility that assesses the ability of sperm to penetrate the ovum. The zona pellucida from hamster oocytes is removed, which allows capacitated human sperm to penetrate it. A test for sperm to be able to undergo capacitation, the acrosome reaction, fusion with the oocyte, and incorporation into the ooplasm. If sperm penetration is 10–30%, the sample is considered normal, but this estimation is not standardized. Some studies have shown that IVF success is correlated with a positive SPA, while others have not. These inconsistencies require that the physician become familiar with the lab performing this test. Although there are controversies surrounding SPA, it is a test that should be performed for unexplained infertility.

REFERENCE

Sperm Vitality

DESCRIPTION
Also referred to as sperm viability or sperm motility, this is 1 parameter in semen analysis during workup of male infertility. Determination of the percentage of viable and motile sperm in semen samples is helpful to determine if the sperm could be of therapeutic use for various fertilization techniques. (See also Section 1: “Infertility”, Section II: “Semen Analysis, Technique, and Normal Values.”)

REFERENCE

Spermatocord, Liposarcoma

DESCRIPTION
A low soft tissue malignancy derived from mesenchymal tissue. It is often mistaken for hydrocele, cord lipoma, or incarcerated hernia and preoperative diagnosis is rare. Most malignant paratesticular tumors are sarcomas, but 5–7% are liposarcomas. High-resolution ultrasound, CT, and MRI have become imaging of choice. Tumors in the literature have been reported to range from 0.4 cm to as large as 50 cm. The majority of tumors are low grade and well differentiated. Late recurrences and metastases may be seen, particularly with high-grade tumors. Radical orchidectomy with local excision and high ligation of the spermatocord is the treatment. Liposarcomas are radiosensitive and radiotherapy can be used to prevent local recurrence. The majority of tumors are low grade and well differentiated. The parallel tubular arrays have a spindle cell configuration. There are also rare case reports of spindle cell tumors involving the bladder and penis. The histologic features are characterized by elongated tubules and stromal changes. The stromal tumors are benign, although rare case reports of spindle cell neoplasms involving the bladder and penis. These neoplasms have been classified as leiomyosarcomas, which are benign. (See also Section 1: “Spermatocord and Torsion.”)

REFERENCE

Spina Bifida/Spina Bifida Occulta, Urologic Considerations

DESCRIPTION
Spina bifida is a brain defect that results in the incomplete closure of the embryologic neural tube, leading to incomplete development of the spinal cord and vertebral column. This usually involves the lumbar and sacral areas. As a result, many patients develop a neurogenic bladder dysfunction requiring long-term urogynecologic care. Although 90% of patients born with spina bifida have normal upper urinary tracts, over 1/3 of these patients will show signs of vesical dysfunction if no urologic intervention is performed. Spina bifida occulta is the milder form of spina bifida. The vertebrae may not fuse together, although the spinal cord and nerves are intact. Patients with spina bifida occulta may have no neurologic deficits at birth. Neurologic deficits that are present are usually mild compared to patients with spina bifida, and may develop later in life. Treatment involves appropriate urologic surveillance to preserve renal and bladder function. A neonatal renal US and voiding cystourethrography are obtained to assess for hydronephrosis and vesicoureteral reflux. Up to 20% of patients with spina bifida will have reflux. A urodynamics study (UDS) is also performed during this period to evaluate bladder compliance, detrusor pressures, capacity, leak pressures, contractions, and sphincter dysfunction. Some institutions recommend prophylactic antibiotics and CIU until the neonate’s 1st US. Patients with poorly compliant bladders with elevated filling pressures (typically above 40 cm H2O) are in danger of upper tract deterioration and are typically started on clean intermittent catheterization (CIC) and anticholinergic therapy. If the patient fails conservative medical therapy, surgical procedures such as intravesical bulking agent injection, vesicostomy, augmentation cystoplasty, or urinary diversion (continent or incontinent) may be appropriate treatment options. It should be stressed to patients and their families to have strict routine follow-up visits to evaluate bladder or upper tract deterioration. (See also Section 1: “Myelodysplasia Spinal Dysraphism, Urologic Considerations.” and Image D.)

REFERENCE

Spinal Cord Compression, Urologic Considerations

DESCRIPTION
Epidural spinal cord compression, due to a urologic etiology, is most likely bone metastasis from prostate cancer. Other types of cancer (eg, breast, lung, kidney, GI) must also be kept in mind. Venereal body metastases are present in the majority of patients dying from metastatic prostate cancer. Compression of the cord causes edema, venous congestion, and demyelination. Symptoms include back pain, progressive weakness, sensory loss, and paraparesis. Bowel and bladder dysfunction are late findings. Neurologic impairment can progress overnight, so patients must be followed carefully. Survival of patients with spinal cord compression due to metastasis is relatively poor. 40% of patients survive <6 mo, and 20–30% <2 mo. Diagnosis is based on findings of CT and MRI. (See also Section 1: “Spinal Cord Injury, Urologic Considerations.”)

REFERENCE

Spinal Shock

DESCRIPTION
After acute spinal cord injury (SCI), a period of areflexia and flaccid paralysis usually occurs below the level of injury. This period of spinal shock is variable; reflex detrusor activity usually returns after 2–12 wk, although it may take up to 1 yr. Urodynamic studies assessing bladder function are postponed until spinal shock resolve. Treatment is supportive during this period of detrusor areflexia. CIU is the recommended means of emptying the bladder, although an indwelling Foley catheter may be another alternative. (See also Section 1: “Spinal Cord Injury, Urologic Considerations.”)

REFERENCE

Spindle Cell Neoplasm, Urologic Considerations

DESCRIPTION
Mucinous tubular and spindle cell carcinoma (MUTC) is a rare neoplasm of the kidney and is distinct from the WHO as a variant of RCC. It is considered a low-grade carcinoma with a favorable prognosis. It typically presents in adult women in a 4:1 ratio. It is believed to be derived from the epithelial cells of the loop of Henle or possibly the collecting duct. There are also rare case reports of spindle cell neoplasm of the bladder and penis. The histologic features are characterized by elongated tubules and stromal arrangements, which are separated by mucinous stroma. The parallel tubular arrays have a spindle cell configuration. There are also rare case reports of spindle cell neoplasm involving the bladder and penis. These are considered low-grade carcinomas with a favorable prognosis. (See also Section 1: “Urologic Considerations.”)

REFERENCE

TREATMENT
• Diuretics
• Anticholinergics
• Intravesical botulinum toxin injection
• Vesiostomy
• Augmentation cystoplasty
• Urinary diversion

REFERENCE

Urologic Considerations

REFERENCE

Urodynamics

REFERENCE

Urodynamics

REFERENCE

Urologic Considerations

REFERENCE

Urological Considerations

REFERENCE

Urological Considerations

REFERENCE

Urological Considerations

REFERENCE

Urological Considerations

REFERENCE
STAMEY PROCEDURE (URETHROPEXY)

REFERENCE

SPINNING TOP URETHRA
DESCRIPTION Spinning top urethra (STU) is a widened posterior urethra seen mainly in girls that is seen on videourodynamic studies. The most common mechanism for dilatation of the posterior urethra is unstable bladder contractions are resisted by a voluntary increase in the tension of the external urethral sphincters. The increased pressure results in a dilatation of the posterior urethra. It is seen in patients with voiding dysfunction.

REFERENCE

SPLENIC INJURY DURING RADICAL NEPHRECTOMY
DESCRIPTION Of cases involving iatrogenic injury to the spleen, up to 12% have been reported to occur during nephrectomy. Splenic injuries usually tend to occur from excessive traction rather than direct injury or scalpel laceration; adequate exposure starting from an appropriate incision is essential. Capsular tears are the most common encountered event. The inferior portion of the spleen is typically involved, since the spleen has ligamentous associations (splenicocolic, splenorenal, splenophrenic) with the kidney and other nearby structures. The spleen has a rather loose texture and can be found crossing the upper pole of the left kidney, dividing into subcapsular branches. Optimal treatment first involves recognizing splenic injury in a timely fashion intraoperatively. Depending on the extent of injury and condition of the patient, the decision is made to proceed with either salvage of the spleen or splenectomy. Splenic salvage techniques depend on severity of injury and includes the use of topical hemostatic agents, primary suture repair, partial segmental resection, or mesh repair. Complications associated with splenic injury repair or splenectomy include subphrenic abscess, injury to the stomach, colon, or tail of the pancreas, pancreatic or pancreatico-facial fistula formation, and pleural effusion.

REFERENCE

SPLENOGONADAL FUSION
DESCRIPTION A rare congenital malformation in which an abnormal fusion exists between the spleen and the gonad or mesonephros derivatives. This fusion occurs in both sexes, but it is more common in males. Half of the cases are reported in children. The 2 types are continuous and discontinuous. In the continuous splenogonadal fusion, the main spleen is connected to the left hypogastric by a strand of tissue. This cord may be fibrous or splenic or contain beads of splenic tissue. The discontinuous type has no cord between the spleen and left gonad. 1/3 of all reported cases are associated with other congenital abnormalities, especially pernix. The majority of cases present with scrotal mass or scrotal tenderness. Some are found incidentally during herniorrhaphy or orchidectomy. Although evaluation is usually done in the operating room, a technetium99m colloid liver spleen scan can easily identify splenic tissue in the scrotum if splenogonadalfusion is suspected preoperatively. Scrotal US does not help to diagnose this entity.

TREATMENT
• Usually involves removing both the testis and adjoining mass.
• If the diagnosis of discontinuous splenogonadal fusion is made before surgery, the splenic nodule can simply be excised.
• For continuous variety, exploratory laparotomy is necessary to identify the anomaly involved and deal with the continuous cord.

REFERENCE

SPLENULES/SPLENOSIS, UROLOGIC CONSIDERATIONS
DESCRIPTION A benign condition associated with splenic rupture, typically during splenic surgery or trauma. Autotransplantation of splenic tissue occurs via seeding of spleen pulp in the abdominal or thoracic cavities. Hemangiomatous spread has also been reported. Patients are asymptomatic, and the discovery of splenules is usually incidentally on imaging studies. Splenosis in the abdominal cavity has been mistaken for primary malignancies, such as primary RCC. Similarly, thoracic splenosis can mimic metastatic uterine malignancies as well. The diagnostic modality of choice is nuclear scintigraphy. Once splenosis is confirmed and malignancy is ruled out, no treatment is necessary due to the benign nature of the condition.

REFERENCE

SPORTS HERNIA (ATHLETIC PUBALGIA, SPORTSMAN’S HERNIA)
DESCRIPTION A sports hernia is a painful, soft tissue injury that occurs in the groin area. It most often occurs during sports that require sudden changes of direction or intense twisting movements and is considered an "overuse" injury. It is a musculo-tendinous injury that involves the insertion of abdominal muscles on the pubis and the upper aponeurotic insertion of the adductor muscles. The pain develops during exercise, is generally unilateral but occasionally bilateral, and is typically located in the suprapubic and lower abdominal lateral to rectus abdominus, sometimes radiating to the testis. Although a sports hernia may lead to a traditional abdominal wall hernia, it is a different injury. A sports hernia is a strain or tear of any soft tissue (muscle, tendon, ligament) in the lower abdomen or groin area. Because different tissues may be affected and a traditional hernia may not exist, the medical community prefers the term athletic pubalgia to refer to this type of injury. The existence, significance and diagnosis of sports hernia are all controversial. The condition needs to be differentiated from a direct, indirect, or femoral groin hernia, adductor longus origin “tendinitis,” or obturator pain based on history and physical exam. The symptoms are nonspecific and can include tenderness on palpation of the medial inguinal floor, tenderness on palpation over the pubic rami, and exacerbated pain with resisted hip adduction. MRI may be useful in the differential. Rest, anti-inflammatory medications (NSAIDs) and physical therapy are beneficial. Rarely surgery may be necessary to repair the torn ligament or tendon.

REFERENCES

SQUAMOUS METAPLASIA, GENITOURINARY
DESCRIPTION The replacement of normal urothelium by metaplastic squamous epithelium. Nonkeratinizing squamous metaplasia is thought to be a normal variant in premalignant women, occurring under hormonal influence. This form is commonly seen in the ectocervix and, occasionally, it appears as a white patch. Keratinizing squamous metaplasia, also known as vesical leukoplakia, is a response to chronic irritation and infection. Some patients go on to develop squamous carcinoma. Keratinizing squamous metaplasia often occurs with long-term urinary catheterization, a bladder stone, vesical schistosomiasis; long-term observation is warranted for the development of squamous carcinoma of the bladder.

SYMPTOMS
• Pseudomembranous trigonitis
• Vesical leukoplakia

TREATMENT
Transurethral resection ablation and biopsy in cases of keratinizing squamous metaplasia.

REFERENCE


**STAMEY TEST (3-GLASS TEST, 4-GLASS TEST, MEARES–STAMEY TEST)***

**DESCRIPTION**

The 3-glass test described by Meares and Stamey is a method of collecting urine, which can provide information on the site of the urinary tract origin of RBCs or bacteria. Although this method is effective in the majority of cases of hematuria, it is more commonly used in diagnosing prostatitis. A specimen is collected from the urethra, midstream urine, and prostatic secretions. The 1st-voided 10 mL of urine is the urethral specimen (VB1). The midstream urine of 10 mL (VB2) is collected after the patient has voided about 200 mL. The patient is then instructed to stop voiding, at which time the physician massages the prostate and collects the prostatic fluid expressed prostatic secretions (EPS). Afterward, the patient voids again, and a 10-mL specimen (VB3) is collected. Cultures are sent on the 4 specimens hence the 3-glass or 4-glass test (nomenclature). When the bladder urine is sterile, vesical, and prostatic infection can be differentiated by comparing the bacterial colony counts of VB1 and prostatic fluid, EPS and VB3 counts. In urinary infections, the VB1 count is much higher than the EPS or VB3 count. The EPS and VB3 counts in prostatic infections significantly exceed the VB1 count. When interpreting bacterial colony counts, the clinician must take into account that the VB3 specimen is a 100-4 dilution of prostatic fluid. When the bladder urine is infected, the infection is localized by localization because all specimens will show heavy growth of organisms. Note that this test is often replaced by the 2-glass test, which collects a more convenient pre-postprostatic massage urine sample. The premassage and postmassage 2-glass test has strong concordance with the 4-glass test and is a reasonable alternative when EPS are not obtained. The technique and diagnostic algorithm are discussed in Section I: “Prostatitis, General” and “Prostatitis, Chronic, Bacterial (NIH VI).”

**REFERENCES**


**STEINER STRASSE**

**DESCRIPTION**

A German expression for “street of stones,” referring to multiple stone fragments in the ureter after extracorporeal shock wave lithotripsy. Characteristically, stone fragments are found in a line within the ureter, which may or may not be obstructed. The condition occasionally presents with renal colic, nausea, or vomiting. Observation is sufficient if symptoms are tolerable or absent; with severe colic or obstruction, treatment is ureteral stent placement, percutaneous nephrostomy, or ureteroscopy lithotripsy (Image 4).

**REFERENCE**


**STING PROCEDURE**

This refers to subureteral transmural injection (“STING”) of bulking agents to correct vesicoureteral reflux. The original coined term was subureteric Teflon injection (STING) using percutaneous Teflon (PTF) particles suspended in glycerol. Due to concern over migration of the Teflon to the brain and lung it was abandoned in favor of other agents. Silicone was also used as a bulking agent (Macroporl) and white effective was also abandoned due to safety concerns. Other materials such as polydilatex (cross-linked bovine collagen Contigen) and vasculocryopiapate (Cryopef) are also no longer used a bulking agents. Bulking agents such as Deflux (cross-linked dextranomer hyaluronic acid copolymer) has been accepted and is currently in widespread use. The basic technique involves the perireteral injection at the 6 o’clock position of the ureteral orifice. A modification is the hydrodistention implantation technique (HIT) where the agent is injected into the ureteral lumen filling the ureter. Overall the success rate is inferior to that of open surgery. About 70-90% have reflux resolution after 1 procedure. With repeat STING procedures, the success rate increases to 90-95%. See also Section I: “Vesicoureteral Reflux, Pediatric”; and Section II: “Bulking Agents, Intractable.”

**REFERENCES**


**STRAIGHTURIA**

**DESCRIPTION**

Slow, painful, spasmic expulsion of urine in a drip-wise fashion, usually occurring at the end of micturition due to spasm of the bladder and urethra. Associated with an irritative process in the GU system, it often refers pain to the perineum. Historically, the pathophysiology has been attributed to a significant inflammatory component. The term is not commonly used in human medicine, but is firmly entrenched in veterinary medicine.

**SYNONYMS**

• Strangury

**REFERENCES**


**STREAK GONAD**

**DESCRIPTION**

Streak gonads are hypoplastic and dysdifferentiating gonads mainly consisting of fibrous tissue. Patients with streak gonad usually present with female phenotype, primary amenorrhea, infantile breast development, sparse pubic and axillary hair, infantile external genitalia and vagina, atrophic vulvar labia, immature ovaries, high serum FSH, low urinary estrogen, and osteoporosis, as well as the streak gonad. Diagnosis is made by measuring FSH and urinary estrogen, and determining karyotype. See Section I: “General Gynecology, Mixed and Pure.”

**TREATMENT**

• Management includes laparoscopy with excision of any intra-abdominal tests or streak gonads. These masses progress to malignancies, which may develop before puberty.

• Femoral vein and reconstructive surgery are advised in cases with severely deficient visualization of the genitals.

**REFERENCES**


**STICKLER URETERAL ANASTOMOSIS**

**DESCRIPTION**

“Through an extravesical approach, a 3.5-cm tunnel encircling the ureter is made in the vagina, and a Small clamp is used to create a submucosal 3–4 cm tunnel extending out of the colon laterally. The ureter is dissected through the tunnel, the spasticity is anastomosed to the vagina, and the tapering of the ureter is closed using a transvaginal platinum wire.”

**REFERENCES**


**STROCULINERAN AMMONIUM PHOSPHATE HEXAHYDRATE**

**DESCRIPTION**

The mineral name for magnesium ammonium phosphate hexahydrate (MgNH4PO4·6H2O) stone. Struvite stones (also sometimes known as triple phosphate stones) are composed of calcium magnesium ammonium phosphate and form only in urine infected by anaerobic bacteria, such as Proteus, Providencia, and sometimes Klebsiella, Pseudomonas, and enterococcus. Because of their potential for rapid growth and substantial morbidity, early detection and eradication are essential (See also Section I: “Urolithiasis, Sheep”).

**REFERENCES**


REFERENCES

SUPERNUMERARY KIDNEY
DESCRIPTION
A supernumerary kidney is a rare condition in which a free accessory renal organ exists as a distinct entity, with its own blood supply, with presence of 2 normal kidneys. It is distinguished by its small size and abnormal abnormally-shaped kidney. It is either a component of a bilateral ureteral system or a completely duplicated system. When diagnosed, treatment for a supernumerary kidney should be based on pathologic processes affecting the kidney rather than its redundant appearance or abnormal position. Association of a normal kidney with a 2nd or 3rd (isolated) smaller kidney is an extremely rare anomaly with only a total of 81 cases reported through 2013.

REFERENCE

SUPINE STRESS TEST
DESCRIPTION
Nonurodynamic method to test for intrinsic sphincteric deficiency, it is performed by placing the patient in lithotomy position and tilting the empty bladder with 200 cc saline under gravity. The patient is then asked to cough and perform aValsalva maneuver. A test is deemed positive if fluid is seen leaking from the meatus at time of cough or Valsalva. Studies have shown that it is a relatively quick and inexpensive test that has a sensitivity of 93.5% and specificity of 90.0%.

REFERENCES

SYMPTOMATIC UROLOGY CONSIDERATIONS
DESCRIPTION
The kidney (lupus nephritis) is the organ most commonly affected by systemic lupus erythematosus (SLE), a chronic, multisystem autoimmune disease with no known cause. A variety of diseases related to SLE can affect the kidney, with renal biopsies usually necessary to identify the specific type. The renal manifestations of SLE vary from patient to patient. Proteinuria with or without an elevated creatinine is the most common manifestation of renal disease in SLE. Protein excretion typically shows a red and white blood cells per high power field and/or ≥1 cellular cast in more severe forms of disease. Immune complexes result in injury to the glomerulus, and the specific lesion is determined by renal biopsy. International Society of Nephrology classification divides the SLE glomerular disorders into different classes: Classes I and II (minimal mesangial lupus nephritis and mesangial proliferative lupus nephritis) are the mildest forms; classes III and IV (focal proliferative lupus nephritis and diffuse proliferative lupus nephritis) more severe forms; and Classes V and VI (membranous lupus nephritis and advanced sclerosing lupus nephritis) are the most severe forms. These more severe forms of lupus nephritis can cause impaired renal function, proteinuria, and the nephrotic syndrome. In addition to these glomerulopathies, SLE can also result in interstitial nephritis and renal vascular disease. Renal manifestations are dependent on the underlying cause such as infection, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid (INH), minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced lupus nephritis. Rarely, certain medications (eg, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid [INH], minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced SLE. Mild forms are not treated, but more severe forms are treated with corticosteroids (cyclophosphamide therapy) and prednisone. Renal replacement may be needed in the most severe forms.

REFERENCES

SYNONYMS
Neurosyphilis
Tetanic bladder
Tertiary syphilis
Pendulous for sphincter
Clean intermittent catheterization (CIC) for bladder atony

REFERENCE

TABES DORSALIS
DESCRIPTION
The diagnosis of Tabes Dorsalis is made by the presence of spinocerebellar ataxia and superficial sensory loss. The disease affects the most severe forms; and Classes V and VI (membranous lupus nephritis and advanced sclerosing lupus nephritis) are the most severe forms. These more severe forms of lupus nephritis can cause impaired renal function, proteinuria, and the nephrotic syndrome. In addition to these glomerulopathies, SLE can also result in interstitial nephritis and renal vascular disease. Rarely, certain medications (eg, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid [INH], minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced lupus nephritis. Rarely, certain medications (eg, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid [INH], minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced SLE. Mild forms are not treated, but more severe forms are treated with corticosteroids (cyclophosphamide therapy) and prednisone. Renal replacement may be needed in the most severe forms.

REFERENCES

SYNONYMS
Neurosyphilis
Tetanic bladder
Tertiary syphilis
Pendulous for sphincter
Clean intermittent catheterization (CIC) for bladder atony

REFERENCE

TABES DORSALIS
DESCRIPTION
DESCRIPTION
The diagnosis of Tabes Dorsalis is made by the presence of spinocerebellar ataxia and superficial sensory loss. The disease affects the most severe forms; and Classes V and VI (membranous lupus nephritis and advanced sclerosing lupus nephritis) are the most severe forms. These more severe forms of lupus nephritis can cause impaired renal function, proteinuria, and the nephrotic syndrome. In addition to these glomerulopathies, SLE can also result in interstitial nephritis and renal vascular disease. Rarely, certain medications (eg, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid [INH], minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced lupus nephritis. Rarely, certain medications (eg, antifibrin therapy [infliximab and etanercept], chlorpromazine, diltiazem, hydralazine, interferon-β, isoniazid [INH], minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced SLE. Mild forms are not treated, but more severe forms are treated with corticosteroids (cyclophosphamide therapy) and prednisone. Renal replacement may be needed in the most severe forms.

REFERENCES

SYNONYMS
Neurosyphilis
Tetanic bladder
Tertiary syphilis
Pendulous for sphincter
Clean intermittent catheterization (CIC) for bladder atony

REFERENCE
TAGHAANDAN

DESCRIPTION

The practice of forcibly snapping or cracking an erect penis to achieve rapid detumescence. This is a common cause of penile fracture in Middle Eastern countries. In Iran, 88% of penile fractures are due to this mechanism and were encountered at an average of one per week. It was described as described in Section I: “Penis, Trauma.”

REFERENCE


TAKAYASU ARTERITIS, UROLOGIC CONSIDERATIONS

DESCRIPTION

A vasculitis of unknown origin involving major arteries, which results in stenosis and aneurysmal dilatation. Involvement of renal arteries might lead to renovascular hypertension. The disease is progressive and difficult to manage and is often treated and diagnosed with angiography and surgery.

REFERENCES


TANNER STAGES/CLASSIFICATION OF SEXUAL MATURITY

DESCRIPTION

The Tanner scale defines physical measurements of the onset and development of pubertal changes based on external primary and secondary sex characteristics, such as breast and genitalia development and the growth of pubic hair. It is useful in the evaluation of delayed or precocious puberty.

- Pubic hair (boys and girls) – Stage 1: Prepubertal (none or vellus hair similar to abdomen wall)
- Stage 2: Span of growth of long, slightly pigmented hair, straight or curled, at base of penis or along labia
- Stage 3: Darker, coarser, and more curled hair, spreading sparsely over junction of pubes (male) or spreading to medial surface of thighs (female)
- Stage 4: Adult in type and quantity, with horizontal distribution (feminine type)
- External genitalia (boys) – Stage 1: Prepubertal
- Stage 2: Enlargement of scrotum and testes; scrotal skin reddens and changes in texture
- Stage 3: Enlargement of penis (length at 10°)
- Stage 4: Increased size of penis, with growth in breadth and development of glans; testes and scrotum large, skin darker
- Stage 5: Adult genitalia

- Breast development (girls) – Stage 1: Prepubertal
- Stage 2: Breast bud stage with elevation of breast and papilla; enlargement of areola
- Stage 3: Further enlargement of breast and areola; no separation of their contour
- Stage 4: Areola and papilla form a secondary mound above level of breast
- Stage 5: Mature stage. Projection of papilla only, related to recession of areola

REFERENCES


TERATOMA, SACROCOCCEAL, UROLOGIC CONSIDERATIONS

DESCRIPTION

Sacroccgeal teratomas are usually diagnosed in the neonate (1 in 40,000 births) and less often in infants or adults. Females are more affected than males. A clinical presentation is usually in the form of palpable mass, skin discoloration, or halyne hery. Related diseases include bilateral aortoarteritis, neurologic MRI, bladder or bowel dysfunction (obstruction or incontinence), high-output cardiac failure, or fetal hydrops. Sacroccgeal teratomas of the newborn are generally benign, whereas those discovered later have a 50% chance of being malignant. Wide, local excision of the tumor is primary management.

REFERENCE


TESTICULAR BIOPSY, INDICATIONS

DESCRIPTION

Testicular biopsy was once considered a cornerstone in the diagnosis of unexplained male infertility and azoospermia, but its current indications are now limited to a specific subgroup of patients. Current practice guidelines limit biopsy to those with obstructive azoospermia, those who require TESE (testicular sperm extraction), and to confirm the diagnosis of carcinoma in situ (CIS) of the testis. In men with obstructive azoospermia confirmation of the presence of normal spermigenesis is usually helpful before surgical correction of the obstruction. TESE often requires multiple testicular biopsies for sperm harvesting with part of the specimen to be used for histologic exam. In special situations where ultrasonographic abnormalities indicate the potential presence of CIS, namely testicular microcyst, intracyomugly, or a solid testicular mass, a testicular biopsy may prove to be helpful before orchiectomy.

REFERENCE


TESTIS, CARCINOID

DESCRIPTION

Carcinoid tumors of the testes are rare neoplasms that originate from neuroendocrine cells. Most carcinoid tumors are found in the Gi tract, particularly in the ileum or appendix. Because of their neuroendocrine precursors, some tumors elicit endocrine activity. 88% secrete 5-hydroxytryptamine (5-HT), a metabolite of serotonin. Carcinoind syndrome results from the vasoactive substances secreted from the tumor and can cause symptoms such as flushing, sweating, wheezing, diarrhea, abdominal pain, and fibrosis of cardiac valves. Carcinoind tumors of the testes can be divided into 3 groups: Primary metastasis to a primary site, or carcinoind tumor originating from a testicular teratoma. Most patients present with a painless scrotal mass, unlike germ cell tumors (GCT), there is no predilection unlike germ cell tumor (GCT), there is no predilection.

REFERENCES


TESTIS, CARCINOID

DESCRIPTION

Carcinoid tumors of the testes are rare neoplasms that originate from neuroendocrine cells. Most carcinoid tumors are found in the Gi tract, particularly in the ileum or appendix. Because of their neuroendocrine precursors, some tumors elicit endocrine activity. 88% secrete 5-hydroxytryptamine (5-HT), a metabolite of serotonin. Carcinoind syndrome results from the vasoactive substances secreted from the tumor and can cause symptoms such as flushing, sweating, wheezing, diarrhea, abdominal pain, and fibrosis of cardiac valves. Carcinoind tumors of the testes can be divided into 3 groups: Primary metastasis to a primary site, or carcinoind tumor originating from a testicular teratoma. Most patients present with a painless scrotal mass, unlike germ cell tumors (GCT), there is no predication for a particular age group (~16% of patients have carcinoid tumors). Tumors localized to the testes have an excellent prognosis; however long-term follow-up is needed, due to risk of late metastasizes.
As with all testicular neoplasms, treatment begins with radical orchiectomy, with high lynage of the spermatic cord. Chemotherapy or radiation therapy has been reported, but these treatment modalities have poor efficacy. Oncocytic analays have been reported to stabilize disease progression, as well as help relieve symptoms of carcinoma. Once discovered, other extratesticular sources of carcinoma should be determined. S-HAA can be measured in the urine and can be a useful adjunct. GI endoscopy, CT scan, MRI scanctigraphy, or sonomography in renatorc scintigraphy can be used to search for GI causes of carcinoma tumor.

REFERENCE


TESTIS, CARCINOMA IN SITU (CIS) / INTRATUBULAR GERM CELL NEOPLASIA (ITGCN)

DESCRIPTION

Testicular CIS is considered to be the precursor to all GCT, except for yolk sac tumors and spermatocytic seminoma. CIS may be present during infancy; however, lesions do not proliferate until adolescence, when hormonal influences come into play. Studies have shown that 50% of males with CIS developed invasive tumor growth within 5 yr. Virtually all patients with CIS will progress to testicular carcinoma. Risk factors for testicular CIS are cryptorchidism, contralateral testes cancer; extratesticular GCT, infertility, and intense patients with a Y chromosome. There is controversy concerning the screening, management, and treatment of testicular CIS. Diagnosis is made through tests biopsy. Treatment options involve surveillance, radiation, and orchiectomy. Capable baseline imaging or CIS has been associated with incomplete treatment and recurrence. High-risk patients may be offered testicular biopsy and orchiectomy, although some physicians would advocate surveillance alone. Surveillance is a viable treatment option due to the long, protracted nature of CIS, the morbidity of treatment options, and the fact that effective treatment of GCT exists. Radiation (14–20 Gy) may be performed in the patient with unilateral CIS and contralateral CIS, or in the patient with bilateral CIS. Orchiectomy is offered to the patient with unilateral CIS and a normal contralateral testis. Extensive counseling regarding the risks and benefits of surveillance vs. biopsy and subsequent treatment is needed. The option to orchiectomy sperm should be offered as well. (See also Section II “Testis, Microtubules.”) [Image 41.]

REFERENCE


TESTIS, CYSTIC LYPHANGIOMAS

DESCRIPTION

Testicular cystic lymphangiomas, benign tumors of unknown etiology, are often misdiagnosed as other conditions like hematoceles, hematoceles, watch, or possible torsion in children. Lymphangiomas are characterized by an extensive overgrowth of lymphatic vessels; 50% are present at birth, 90% are evident by the age of 2 yr. Gradual painless scrotal swelling is the common symptom. On palpation, the mass may be soft and spongy or firm and tense, usually not separable from the scrotal skin. Skin showing bluish/grayish discoloration or erythematous changes is often present. The ultrasound exam usually shows a complex multiloculated septated cystic mass without calcifications. Often, these lesions are more suggestive of hydrocele, hematocele, varicocele, or possible torsion. Ultrasound examination can be used to search for GI causes of carcinoma tumor.

REFERENCE


TESTIS, TUMORS

DESCRIPTION

Testicular hemangioma is a very rare neoplasm, usually 25 cases are in the English literature. Intratesticular tumors of vascular origin are extremely rare. Intratesticular hemangioma can mimic malignant testicular tumors on presentation and imaging. Testicular hemangioma histologically comprises 3 types: Cavernous, capillary, and epithelial. Patients usually present with testicular enlargement with or without tenderness. Although it is impossible to differentiate a hemangioma from a seminoma preoperatively, intraoperative frozen study may be helpful in the differential diagnosis. Frozen section must be performed, if the neoplasm has significant vascular proliferation identified by Doppler sonography. In these cases, testicular conservative surgical treatment by means of tumor enucleation and even radical orchiectomy over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.

In children, testicular tumors are rare and the majority are benign, especially before puberty. Radiation therapy can be used to treat testicular tumors, although radiation after puberty may be less effective. Pediatric simple testicular cysts are very rare, as most cysts occur in men 60 yr. Most can be treated with testicular-sparing surgery. The diagnostic differential of testis cysts in the pediatric population:

Hydatid cysts are rarely seen, except in the Middle East. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of postoperative pathology. Treatment has included excision and even radical orchectomy for concern over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.

In children, testicular tumors are rare and the majority are benign, especially before puberty. Radiation therapy can be used to treat testicular tumors, although radiation after puberty may be less effective. Pediatric simple testicular cysts are very rare, as most cysts occur in men 60 yr. Most can be treated with testicular-sparing surgery. The diagnostic differential of testis cysts in the pediatric population:

Hydatid cysts are rarely seen, except in the Middle East. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of postoperative pathology. Treatment has included excision and even radical orchectomy for concern over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.

In children, testicular tumors are rare and the majority are benign, especially before puberty. Radiation therapy can be used to treat testicular tumors, although radiation after puberty may be less effective. Pediatric simple testicular cysts are very rare, as most cysts occur in men 60 yr. Most can be treated with testicular-sparing surgery. The diagnostic differential of testis cysts in the pediatric population:

Hydatid cysts are rarely seen, except in the Middle East. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of postoperative pathology. Treatment has included excision and even radical orchectomy for concern over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.

In children, testicular tumors are rare and the majority are benign, especially before puberty. Radiation therapy can be used to treat testicular tumors, although radiation after puberty may be less effective. Pediatric simple testicular cysts are very rare, as most cysts occur in men 60 yr. Most can be treated with testicular-sparing surgery. The diagnostic differential of testis cysts in the pediatric population:

Hydatid cysts are rarely seen, except in the Middle East. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of postoperative pathology. Treatment has included excision and even radical orchectomy for concern over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.

In children, testicular tumors are rare and the majority are benign, especially before puberty. Radiation therapy can be used to treat testicular tumors, although radiation after puberty may be less effective. Pediatric simple testicular cysts are very rare, as most cysts occur in men 60 yr. Most can be treated with testicular-sparing surgery. The diagnostic differential of testis cysts in the pediatric population:

Hydatid cysts are rarely seen, except in the Middle East. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of postoperative pathology. Treatment has included excision and even radical orchectomy for concern over concern for malignancy. A more conservative approach with serial ultrasonographic scanning has been advocated if a clear distinction can be made between neoplastic and nonneoplastic testicular cysts. Selecting cases can potentially be managed by intraoperative frozen section to demonstrate no malignancy and enucleation of the tumor performed.
TESTIS, LYMPHOMA

DESCRIPTION
Most common testicular malignancy in men >60, and the most common secondary neoplasms of the testis. Initial presentation is usually painless testicular swelling. Diagnosis is made through orchectomy. Bilateral involvement occurs in ~50% of cases; 10% are synchronous. Treatment is multidisciplinary; orchectomy is performed, followed by systemic chemotherapy (dacarbazine, CHOP prophylaxis), and local radiation. (See also Section II: “Lymphoma, Urologic Considerations” and Image Q5.)

REFERENCES

TESTIS, METASTASIS TO

DESCRIPTION
Due to the nature of the disease, this metastasis usually presents in men >50. Spread to the testis may be hematogenous, lymphatic, or by direct extension. Most primary malignancies are prostate, lung, GI tract, melanoma, and kidney cancer (Image Q5).

REFERENCE

TESTIS, MICROLITHIASIS

DESCRIPTION
Numerous and diffuse calcifications throughout the entire testicle seen on transscrotal ultrasound. Adenocarcinoma in ultrasound technology have led to an increased detection of testicular microlithiasis. It is reported in undescended testes (0.3% incidence), prepubertal Klinefelter syndrome, and male pseudopseudophedrophimoids, and is slightly more common in postpubertal males. Infertility and malignancy have been reported to be associated with the condition, and some consider it possibly premalignant. Both seminomas and nongerm-cell-GCT have been described in association with microlithiasis. Others suggest an association with carcinoma in situ of the testis, but this is not settled. Recent studies have a prevalence of 2% in boys who undergo scrotal US, most commonly bilateral, with increased risk of malignancy. Most advocate close surveillance of patients with testicular microlithiasis, such as yearly testicular ultrasound, physical exam, and judicious tumor marker determinations (Image Qb).

REFERENCES

TESTIS, NORMAL SIZE

DESCRIPTION
Testis size measurements can be made by ultrasound (0.9) (most accurate) or Ponder orchitectometry. At birth, testicular length is ~1.5 cm with a volume of 1.1 cm³. In prepubertal boys, testicular length is usually ~2 cm and volume ~2 cm³.

Normal testicular size after puberty in an adult is about 4.5–6.5 cm with a volume ranging from 15–30 cm³.

REFERENCES

TESTIS, RETRACTILE

DESCRIPTION
A testicle that can ride high in the scrotum or near the external inguinal ring; caused by a lack of cremasteric reflex. The testicle is able to be gently manipulated into the scrotum. Usually considered a variant of normally descended testes; 3% of retractile testes may ultimately become undescended (descending or acquired undescended), and this is seen more frequently in boys <7 yo. Boys with retractile testes should be followed annually until the outcome of descent or nondescence is clear, which in many cases won’t be until puberty.

REFERENCE

TESTIS, SEX CORD STROMAL TUMORS

DESCRIPTION
These tumors arise from the supporting structures of the testes and not the germ cells. They usually present as a mass, are rarely hormonally active, and do not produce tumor markers such as hCG, usually other than the presence of tumors ranging from 15–30 cm³.

REFERENCES

TESTIS, VASOCONGESTION

DESCRIPTION
“Blue balls” is a colloquialism for acute testicular/scrotal pain in such patients. Secondary neoplasms of the testis. Initial presentation may be more common among young male adults and is usually painless testicular swelling. Diagnosis is made through testicular ultrasound, physical exam, and judicious tumor marker determinations (Image Q5).

REFERENCES

TESTIS, TERATOMA, EXTRAGONADAL

DESCRIPTION
Primary tumors of extragonadal origin are rare. In a decreasing order of frequency, the most common sites are the mediastinum, retroperitoneum, sacrococcygeal region, and pineal gland. Theses include a proliferation of primitive germ cells that takes place during early embryonic migration from the yolk sac endoderm, and pluripotent cells that persist in sequestered primitive rests during early somatic development. Histologically, all types of GCT are represented, with pure seminoma accounting for 1/2 of medullary and retroperitoneal tumors. Clinically, males are affected more than females, with the exception of sacrococcygeal tumors, where females predominates. The majority of adults present with advanced local disease and distant metastasis. Patients with mediastinal extragonadal tumors are usually diagnosed in their 20s, with or without symptoms of chest pain, cough, or dyspnea. Patients with primary retroperitoneal tumors may present with abdominal or back pain, a palpable mass, or venous obstruction. Tumors of the pineal gland usually present in children and young adults, with symptoms of increased intracranial pressure, ocular movement defects, hearing loss, hypothalamic dysfunction, or hypothalamic-pituitary disturbances. Five needle aspiration (FNA) can be used to assist in the diagnosis, but carries the risk of insufficient cellular return. When suspicion for teratoma exists, it is important to differentiate between mature and immature teratoma as immature carries the risk of malignant transformation.

TREATMENT

• Intensive chemotherapy regimens have shown some success in primary retroperitoneal seminoma.
  • The nonseminomatous version has done poorly despite surgery, radiotherapy, and chemotherapy.
  • Primary radiation therapy has been much favored for pineal tumors if CSF spread is required.

REFERENCES

TESTIS, VASOCONGESTION FROM SEXUAL AROUSAL WITHOUT EJACULATION (“BLUE BALLS”)

DESCRIPTION
“Blue balls” is a colloquialism for acute testicular/scrotal pain in such patients. Secondary neoplasms of the testis. Initial presentation may be more common among young male adults and is usually painless testicular swelling. Diagnosis is made through testicular ultrasound, physical exam, and judicious tumor marker determinations (Image Q5).

REFERENCES

TESTOSTERONE (FREE AND TOTAL) SERUM

DESCRIPTION
Measurement of serum testosterone levels is commonly used as an initial test for hypogonadism in males; it is less commonly used in the evaluation of virilization and hirsutism in females. Testosterone assays should be collected from

PH: OSO/OVY
P2: OSO/OVY
QC: OSO/OVY
T1: OSO
URW4139Y-Section-E-P2
URW1391-Gwennia
ursi short topics-xml
September 18, 2014
19:55

792
Both prostate cancer and hypogonadism become more prevalent as men age; testosterone levels can be found in complete hypogonadism, sexual dysfunction, osteoporosis, and hepatic cirrhosis.

- Generally accepted normal ranges total testosterone (may vary by lab):
  - Prepubertal children: 2–5 ng/dL.
  - Men (≥17 yr): 300–1,000 ng/dL (10.4–34.7 nmol/L).
  - Women: 20–70 ng/dL (0.7–2.6 nmol/L).
- A total testosterone level (free plus protein-bound) < 200 ng/dL (or 6.9 nmol/L) (American Association of Clinical Endocrinologists) or < 100 ng/dL (or 3.4 nmol/L) (FSH) is associated with hypogonadism and warrants further workup in an adult.
- Free testosterone (adult male range 8.8–27 pg/mL) is a useful diagnostic test as well, as elevated or decreased sex hormone-binding globulin (SHBG) changes the bioavailability of testosterone. It can be used as an adjunct to the patient with low total testosterone levels. For example, obesity is characterized by reduced total testosterone and normal free testosterone due to reduced protein binding.
- Serum SHBG concentrations increase with age. With increasing age, less of the total testosterone is free or biologically active, as SHBG binds testosterone with high affinity.
- Serum T peaks early morning and then declines over the course of the day until the nadir in the evening (10–15% lower than morning values, but may vary up to 50% in younger men).
- Testosterone replacement monitoring: For men on injections. Target T should generally be in the range of 400–700 ng/dL (13.9–27.7 nmol/L). If higher, the patient should be re-evaluated for monitoring.

Methods used to measure T: Radioimmunoassay (RIA), Enzyme-linked Immunoassay (EIA) and Liquid Chromatography-Mass Spectroscopy (LC-MS) with high affinity.

- With high affinity.
- Increasing age, less of the total testosterone is free or biologically active, as SHBG binds testosterone with high affinity.
- Serum T peaks early morning and then declines over the course of the day until the nadir in the evening (10–15% lower than morning values, but may vary up to 50% in younger men).
- Testosterone replacement monitoring: For men on injections. Target T should generally be in the range of 400–700 ng/dL (13.9–27.7 nmol/L). If higher, the patient should be re-evaluated for monitoring.

Testosterone replacement therapy following radical prostatectomy:

- Testosterone replacement therapy, prostate cancer risk

- DESCRIPTION

  Multiple published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer.

  A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES


TESTOSTERONE REPLACEMENT THERAPY, PROSTATE CANCER RISK

- DESCRIPTION

  Multiples published review articles have shown that testosterone replacement therapy (TRT) does not cause prostate cancer or placebo patients at increased risk for the development of prostate cancer. A recent audit of the UK Androgen Study showed that initiating testosterone treatment had no statistically significant effect on the incidence of prostate cancer. These findings from this study show that, with careful monitoring, men with symptoms of testosterone deficiency can be treated safely with TRT without an increased risk of developing or progressing already present prostate cancer. See also Section I: “Testosterone Replacement Therapy, General Principles.”

  REFERENCES

TREATMENT

Apply antifungal agents on overt lesions. Agents may be used for preoperative surgical planning or may be used intraoperatively as well.

REFERENCES


THORACIC KIDNEY

DESCRIPTION

A type of renal ectopia in which the kidney is found in the posterior mediastinum, partially or completely above the level of the diaphragm. The diaphragm is thin, yet envelops the protruding kidney, keeping it separate from the pleural cavity. Although in some cases they may in fact be in a position more cranially, the vast majority of patients are asymptomatic. (See also Section II: “Renal Ectopia.”)

REFERENCE


TINEA CRURIS (JOCK ITCH)

DESCRIPTION

Dermatophytic infection of the crural areas of the genitalia. Caused by dermatophytes Trichophyton soudanense, Trichophyton megacephalum, and Epidermophyton floccosum. Clinically, reddish brown lesions are seen in the crural areas of the genitalia. Penis involvement is rare. Postinflammatory hyperpigmentation may occur as a result of chronic or recurrent disease. Culture or KOH exam is necessary to confirm diagnosis. Scrupulous should be performed on the active border of the lesion and reveals branching septate hyphae. Differential diagnosis includes erythrasma, psoriasis, and seborrheic dermatitis. Renal function is not unusual, and treatment should be aimed toward active disease rather than postinflammatory hyperpigmentation. (See also Section II: “Erythrasma.”)

TREATMENT

- Prevent skin maceration by keeping skin dry.
- Apply antifungal agents or ointments. Agents include clotrimazole, miconazole, clotrimazole, and miconazole (3% or 4% cream) for 14 days (requires baseline lab monitoring CBC, LFTs).

REFERENCE


TMPRSS2-ERG GENE FUSION, PROSTATE CANCER

DESCRIPTION

Fusion of the transmembrane protease, serine 2 (TMPRSS2) and erythroblastosis virus E26 (ERG) genes is known as the TMPRSS2-ERG gene fusion. It is present in up to 80% of human prostate cancers. This gene fusion contributes to development of androgen independence in prostate cancer through disruption of androgen receptor signaling. TMPRSS2-ERG, in combination with androgen prostate cancer antigen 3 (PCA3), improved the performance of Prostate Cancer Prevention Trial risk calculator in predicting cancer on biopsy. The men were stratified into 3 groups based upon the levels of TMPRSS2:ERG and PCA3 in their urine: low, intermediate and high. Prostate cancer was diagnosed in the groups, respectively: 21%, 43%, and 69%. Grade prostate cancer (>4000 score), was diagnosed 3% in each group, respectively. TMPRSS2:ERG and PCA3 urine analysis appears to enhance the utility of serum PSA for predicting prostate cancer risk and clinically relevant cancer on biopsy. (See also Section II: “PCA3 (Prostate Cancer Gene 3) Urine Assay.”)

REFERENCE


TOILETING PROGRAMS

DESCRIPTION

Type of behavioral training to treat urinary incontinence. The patient is instructed to establish a routine voiding schedule regardless of the sensation to void. Initially, the patient is told to void at frequent intervals (e.g., every 1–2 hr), the time between voids is then increased, usually until the child establishes an acceptable period (usually 2–4 hr) of continence.

REFERENCE


TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE), UROLOGIC CONSIDERATIONS

DESCRIPTION

A useful diagnostic tool in the management of renal tumors with tumor thrombus; the TEE is used to identify the extent of tumor thrombus involvement in the inferior vena cava. This may be used for preoperative surgical planning or may be used intraoperatively as well.

REFERENCE


TRANSURETEROURETEROSTOMY REVISITED: LONG-TERM SURGICAL OUTCOMES

REFERENCE


REFERENCES

**TRICHOMONIASIS**

**DESCRIPTION**
Sexually transmitted infection caused by the protozoon *Trichomonas vaginalis*. It is a rare cause of nongonococcal urethritis in men. Common cause of vaginitis in women (from 4–10%). It is associated with a high prevalence of concomitant bacterial infection in women. STIs and associated infections include urinary discharge, dysuria, and the presence of neoplasms in uterine secretions. Some women have symptoms characterized by a diffuse, matted, yellow-green vaginal discharge with vaginal irritation. However, many women have minimal or no symptoms. Because of the high prevalence of *Trichomonas* in clinical and non-clinical settings, testing for the organism should be performed in women seeking care for vaginal discharge. Trichomoniasis has any, only minor influence on male fertility. In women, it can cause premature rupture of the membranes and premature delivery, as well as fetal infertility and cerebral palsy. Females may have an elevated vaginal pH of >4.5. A positive diagnosis is made by identification of the protozoon on wet mount (must be examined in 15–20 min). Culture on Diamond’s medium may take up to 7 days; a more rapid commercial culture method is available. (See also Section I: “Sexually Transmitted Infections.”)

**CONSIDERATIONS**
Antimicrobials (eg, metronidazole gel) are unlikely to achieve therapeutic levels in the urethra or perivaginal glands; therefore, use of this gel is not recommended. This is a common cause of coinfection and is associated with a high prevalence of coinfection of the high prevalence of *Trichomonas* in clinical and non-clinical settings, testing for the organism should be performed in women seeking care for vaginal discharge. Trichomoniasis has any, only minor influence on male fertility. In women, it can cause premature rupture of the membranes and premature delivery, as well as fetal infertility and cerebral palsy. Females may have an elevated vaginal pH of >4.5. A positive diagnosis is made by identification of the protozoon on wet mount (must be examined in 15–20 min). Culture on Diamond’s medium may take up to 7 days; a more rapid commercial culture method is available. (See also Section I: “Sexually Transmitted Infections.”)

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**DESCRIPTION**
Trichotillomania is the obsessive-compulsive habit of pulling or shaving hair from the pubic area. It is considered a willful self-harm practice. Behavioral counseling is indicated. (See also Section II: “Vaginal Discharge, Urologic Disease.”)

**REFERENCE**

**TRICHOMONAS VAGINALIS**

**DESCRIPTION**
*Trichomonas vaginalis* is a common cause of vaginitis in women. This is the most common sexually transmitted infection in the United States and is associated with a high prevalence of concomitant bacterial infection. The organism is identified and cultured on Diamond’s medium. Culture on Diamond’s medium may take up to 7 days; a more rapid commercial culture method is available. (See also Section I: “Sexually Transmitted Infections.”)

**CONSIDERATIONS**
Metronidazole gel is considerably less efficacious for treatment of trichomoniasis (<90%). Both tests are considered point-of-care diagnostic tests for trichomoniasis in women include OSOM Trichomonas Rapid Test (Genzyme Diagnostics, Cambridge, Massachusetts), an immunochromatographic rapid dipstick technology, and the AfiTray VF II (African Dickinson, San Jose, California), a rapid acid probe test that evaluates for T. vaginalis, G. vaginalis, and C. albicans. Each of these tests, which are performed on vaginal secretions, has a sensitivity of >83% and a specificity of >97%. Both tests are considered point-of-care diagnostic tests. Treatment is metronidazole 2 g PO or Tinidazole 2 g orally in a single dose for 72 h. Considered a normal finding and distinct from *Trichomonas* in women of reproductive age and in up to 75% after menopause. Considered a normal finding and distinct from *Trichomonas*, which is considered a premenopausal lesion. Cystoscopically, these are pale white-gray areas with irregular borders. This condition is not seen in men, except for some reports in men receiving estrogen for prostate cancer. Treatment is not necessary. (See also Section II: “Vaginitis, Genitourinary.”)

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**DESCRIPTION**
Trichotillomania is the obsessive-compulsive habit of cutting or shaving the hair. It is considered a willful self-harm practice. Behavioral counseling is indicated. (See also Section II: “Vaginal Discharge, Urologic Disease.”)

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**DESCRIPTION**
Trichotillomania is defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) as hair pulling by a patient’s repetitive self-pulling of hair leading to a noticeable loss of hair. Any body area, including the pubic region, can be involved. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. Most individuals start pulling their hair during childhood or adolescence and may also consume the hair. Anxiety, depression and obsessive-compulsive disorders are frequently encountered in patients with trichotillomania. Treatment is a combination of education, behavior therapy and, if necessary medication such as antipsychotics. (See also Section II: “Trichotillomania, Pubic.”)

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**

**TRICHTHOTILOMANIA, PUBIC**

**REFERENCE**
TRISOMY 20 P

DESCRIPTION
A trisomy producing microcephaly, low-set ears, deaf palate, peeled nose, and microphthalmia. Renal anomalies (e.g., renal agenesis, hypoplasia, dysplasia, and polycystic kidney) are common. Other anomalies include heart malformations, congenital diaphragmatic hernia, and limb abnormalities. Trisomy 20 P is also associated with increased risk of leukemia, Wilms tumor, and neuroblastoma.

REFERENCE

TRISOMY SYNDROME
A congenital condition characterized by the presence of 3 instead of 2 copies of any one of the autosomal chromosomes. These disorders often result in a wide range of phenotypical expressions, including GI anomalies. Examples include trisomy 18 and 13, which produce syndromes similar to Down syndrome and trisomy 21, respectively, and trisomy 21, which is associated with sporadic papillary RCC.

REFERENCE

TRUE HERMAPHRODITISM (OVO-TESTICULAR DISORDER OF SEXUAL DIFFERENTIATION (O-TESTO-SD))

DESCRIPTION
True hermaphroditism or ovo-testicular disorder of sexual differentiation (O-TESTO-SD) is 1 of the rarest varieties of all disorders of sexual differentiation. Among 5000 cases, only 100 have been reported. The gonads and histology of each patient are classified as:
- Prepubertal: Testis on 1 side and ovary on the other side
- Lateral: Testis and contralateral ovary (30%)
- Bilateral: Testicular and ovarian tissue identified on either side, usually as ovotestis (50%)
- Unilateral: Ovotestis on 1 side and testis or ovary on the other side, typically as ovotestis

REFERENCE

TUBERCULOSIS, BLADDER AND URETHRA

DESCRIPTION
The hematogenous dissemination of TB can affect the entire urinary system. Bladder TB is caused by a descending infection from renal TB. Urethral TB is rare and can present as perineal tubulitis and abscesses. Symptoms include urinary frequency, urgency, and dysuria, with mucosal ulcerations and friability, and diminished bladder capacity. (See also Section II: “Tuberculosis, Genitourinary.”)

DIAGNOSIS
- Urine culture of acid-fast bacilli: Typically 1st morning void, requires multiple sequential cultures.
- Urethral TB is typically diagnosed on biopsy.
- Imaging such as IVU and CT may be normal, but can aid in diagnosis.

TREATMENT
- Combination antituberculous treatment: Typical regimen: 6 mo of rifampicin, isoniazid, pyrazinamide, and ethambutol
- Urethral TB may require suprapubic cystostomy tube drainage and urethral dilation for stricture.

REFERENCE

TUBERCULOSIS, MALE EXTERNAL GENITALIA

DESCRIPTION
Rare manifestation of TB that may present as a papulonecrotic ulcer, tubercular granulomas, or a cold nodule, which may be clinically indistinguishable from malignant disease. Diagnosis is confirmed on biopsy, treatment is systemic antituberculous medication. (See also Section II: “Tuberculosis, Genitourinary.”)

REFERENCE

TUMOR LYsis SYNDROME (TLS)

DESCRIPTION
A syndrome associated with chemotherapy, radiation, and other treatments in which massive tumor lysis occurs, with subsequent release of large amounts of potassium, phosphate, and nucleic acids that are converted to massive amounts of uric acid. More commonly associated with chemotherapy of lymphomas and leukemias, it can be seen with any tumor type. Extensive metastatic tumor, pretreatment renal impairment, and markedly elevated LDH concentrations have been reported to be serious risk factors in developing TLS. Sub investigations would reveal hyperuricemia, hyperphosphatemia, and concurrent metabolic
acids, as well as severe hyperuricemia with eventual renal failure. If these patients are being treated with allopurinol, they are at risk of ARF and xanthine stone formation (See also Section II: “Nephropathy, Urate Acidosis, and Gouty Arthritis”).

TREATMENT
- Prevention with adequate hydration (urine output of >40–60 mL/h).
- Cautious use of xanthine; some recommend allopurinol.
- Urinary alkalization should not be done, as it may cause further precipitation of calcium phosphate in the kidney and other tissues.

REFERENCE

TUNICA VAGINALIS TUMORS
DESCRIPTION
Malignant mesothelioma of the tunica vaginalis is rare (0.3–1.5% of all malignant mesotheliomas) and often fatal. However, increased frequency has been reported since 1980. Most of the patients are 40–79 yr of age, with prior exposure to asbestos being reported in some. Microscopically, mesothelioma may be epithelial, biphasic, or a combination of both. The malignant nature of the disease is indicated by its frequent mitosis, nuclear atypia with prominent nuclei, and invasion of adjacent structures or lymphatics. Positive staining with keratin and failure to stain with CEA indicate mesothelioma. In addition, an immunoperoxidase stain has been reported to be specific for the tumor. CT and aspiration cytology may aid in preoperative diagnosis. The most important differential diagnostic considerations include mesothelial hyperplasia, adenomatoid tumor, carcinoma of the testis, and serous papillary tumors. The prognosis for this entity is poor, with a median survival of 23 mo and aggressive treatment with radical orchiectomy remains the mainstay of treatment. Adjunct chemotherapy may be tried. However, its value has not been established. (See also Section I: “Paratesticular Tumors” and “Scrotum and Testicle, Mass.”)

REFERENCE

TURNER SYNDROME (X0 SYNDROME)
DESCRIPTION
A sex chromosome abnormality with a 46, XO karyotype. It is the most common sex chromosome abnormality with an incidence of 1:10,000 newborn females. Neoplasms may have lymphomas. Clinically, patients present with short stature, primary amenorrhea, webbed neck, child-like chest, uneven pubic, and breast development. The external genitalia are female but immature, and most women with Turner syndrome are infertile. Karyotype analysis should be performed to confirm the diagnosis. Any patient with Turner syndrome who presents with virilization should also be evaluated for “Y chromosomal mosaic; as these individuals are at increased risk of gonadoblastoma or germ cell tumors.”

TREATMENT
- Endocrinopathy at diagnosis to detect cardiovascular anomalies (coronation of the aorta or a bicuspid aortic valve are most common causes of morbidity and mortality).
- Renal US to determine if GU abnormalities are present.
- Hormonal therapy in the form of growth hormone, estrogen, and medroxyprogesterone, aimed toward maximizing final height, reduction of secondary sexual characteristics, and menarche.

REFERENCE

TUNER-WARWICK INLAY URETHROPLASTY
DESCRIPTION
Through a midline scrotal incision, the urachal sinus is opened and scar tissue is removed, leaving a strip of urethra in place. The edges of the urachal incision are sutured to the urethral strip. In a 2nd stage, the mature manubialized urethra is tubularized with the surrounding scrotal skin and closed.

REFERENCE

UISS-UCLA INTERNATIONAL KIDNEY CANCER STAGING SYSTEM
DESCRIPTION
A prognostic system for renal cell carcinoma (RCC)–to-differentiate survival; the system integrates the 3 most commonly used prognostic factors: Cancer TNM stage, Furman grade, and patient performance status. Patients are categorized after nephrectomy into 3 risk groups: Low, intermediate, and high-risk for localized and metastatic disease.

REFERENCE

UNDERVIRILIZED MALE SYNDROME (MILD ANDROGEN INSENSITIVITY)
DESCRIPTION
A disorder of androgen receptor function caused by androgen receptor gene mutation. Patients with androgen receptor mutations have a 46, XY karyotype and present with a spectrum of phenotypes from complete external feminization, to ambiguous genitalia, to phenotypically intersex male, which is also known as undervirilized male syndrome. These patients present with gynecomastia at puberty, and may have scarce body hair, small penis, and complaints of impotence. Spanningnoma may or may not be impaired. Patients may have elevated lactosidase hormone, normal to slightly elevated testosterone, and high estradiol. Treatment may not be necessary, however, breast reduction surgery at puberty is sometimes necessary. Infertile men may benefit from assisted reproductive techniques (ART). (See also Section II: “Androgen Insensitivity Syndrome (AS or Androgen Resistance Syndrome). Complete and Partial Types.”)

REFERENCE

UNINHIBITED DETRUSOR CONTRACTION
DESCRIPTION
Uninhibited detrusor contraction leads to an overactive bladder. Bladder overactivity can result from damage to sensory inhibitory pathways, sensitization of peripheralafferent terminals in the bladder that unmask primitive voiding reflexes, or changes in bladder smooth muscle cells. Cystometry is essential if a definitive diagnosis is required. (See also Section II: “Overactive Bladder.”)

SYNONYMS
- Overactive bladder
- Unstable bladder

TREATMENT
- Traditionally, centers on the use of anticholinergic medications (oxybutynin, tolterodine, others).
- Estrogens may help in the postmenopausal woman.

REFERENCE

URACHAL ABNORMALITIES
DESCRIPTION
The urachus is a tubular connection between the allantoic stalk and the dome of the bladder. Fetal embryogenic resolution of this connection results in urachal abnormalities. Microscopically, urachal remnants are common, appearing in 3% of autopsy specimens, and are almost always asymptomatic. Except for the asymptomatic urachal diverticulum, the treatment of all urachal abnormalities is surgical, ie, complete excision of the abnormal structure, including a cuff of lateral. Congenital urachal abnormalities can be divided into 4 types:
- Urachal sinus: The most common urachal abnormality. The urachal sinus arises from a persistent patent urachus that drains to the umbilicus, may present with wetness, purulence, or malodorous discharge.
- Urachal cyst: Persistence of part of this channel between the bladder and umbilicus, lacking communication to either structure. The 2nd most common urachal anomaly. Most commonly presents in an older child with signs of suprapubic (Latin “calor, rubor, dolor”) in the lower abdominal wall. Occasionally, a urachal cyst will present as an asymptomatic median lower abdominal mass or tenderness.
- Urachal diverticulum of the bladder: May result from drainage of a urachal cyst to the bladder; presents with UTI.

REFERENCE
URACHAL CARCINOMA STAGING SYSTEMS

Urachal carcinoma is a malignant carcinoma that presents later in life. (See also Section I: “Urachal Carcinoma” and “Umbilical Abnormalities: Diagnostic Considerations” and Image 01.)

REFERENCE

URACHAL CARCINOMA STAGING SYSTEMS
DEFINITION
Two staging systems have been reported by Sheldon and Ashley. No formal TNM classification exists specifically for urachal carcinoma. (See also Section I: “Urachal Carcinoma.”)

Sheldon et al. (1984)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Confined to urachal mucosa and bladder (confined to urachus)</td>
</tr>
<tr>
<td>II</td>
<td>Invasion confined to urachal mucosa and bladder (extension beyond mucosal limit of urachus and bladder)</td>
</tr>
<tr>
<td>III</td>
<td>Metastatic to regional lymph nodes</td>
</tr>
<tr>
<td>IVA</td>
<td>Extension to bladder</td>
</tr>
<tr>
<td>IVB</td>
<td>Extension to peritoneum</td>
</tr>
<tr>
<td>IVC</td>
<td>Extension to other sites</td>
</tr>
</tbody>
</table>

Ashley et al. (2006)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Confined to urachal mucosa and bladder (confined to urachus)</td>
</tr>
<tr>
<td>II</td>
<td>Invasion confined to urachal mucosa and bladder (extension beyond mucosal limit of urachus and bladder)</td>
</tr>
<tr>
<td>III</td>
<td>Metastatic to regional lymph nodes</td>
</tr>
<tr>
<td>IVA</td>
<td>Extension to bladder</td>
</tr>
<tr>
<td>IVB</td>
<td>Extension to peritoneum</td>
</tr>
<tr>
<td>IVC</td>
<td>Extension to other sites</td>
</tr>
<tr>
<td>IV</td>
<td>Metastatic to nonregional lymph nodes or distant sites</td>
</tr>
</tbody>
</table>

REFERENCE

URATE, DIETARY
DESCRIPTION
Foods rich in urate should be restricted in patients with hyperuricosic calcium oxalate stone disease and in patients with acid stone disease. The intake of urate should not exceed 500 mg/day. urate-rich foods include:
- Carbohydrates, 200–500 mg urate/100 g
- Liver, 260–360 mg urate/100 g
- Kidneys, 210–255 mg urate/100 g
- Poultry skin, 300 mg urate/100 g
- Kidneys, 210–255 mg urate/100 g
- Liver, 260–360 mg urate/100 g
- Calf thymus, 900 mg urate/100 g
- Kidney, 210–255 mg urate/100 g
- Poppy seed, 300 mg urate/100 g
- Nettle, with skins: carottes, cornichons, sprats, 260–500 mg urate/100 g

REFERENCE

URAPLASMA UREALYTICUM
DESCRIPTION
Common bacterial inhabitant of the lower GI tract in adult men and women who are sexually active. As an STI it can also be transmitted vertically and from mother to offspring. It is the most common cause of nongonococcal and nonchlamydial urethritis, and can cause chorioamnionitis, pyelonephritis, and septic arthritis. It is implicated in chronic prostatitis in men, and urgency–frequency symptoms in women and in HIV-related acute epididymitis. It is also sometimes associated with decreased fertility. Diagnosis is by culture, but specific media and growth conditions are necessary. Treatment is doxycycline 100 mg/day for 2 wk or a single dose of azithromycin 1 g PO. (See also Section I: “Sexually Transmitted Diseases [STDs], General.”)

REFERENCE

URERET, AGENESIS/ATRESIA
DESCRIPTION
Isolated ureteral agenesis is incompatible with life. Unilateral ureteral agenesis indicates failure of ureteral bud development and is often accompanied by ipsilateral renal agenesis or multicystic kidney. Ureteral atresia is caused by varying degrees of failure in ureteral bud development. When either ureter or agenesis is unilateral, it is usually asymptomatic and of no clinical significance. However, it can be associated with infection (UTI) on occasion.

REFERENCE

URERET, DIVERTICULUM
DESCRIPTION
Ureteral diverticulum can be congenital or acquired, although most have been discovered in adults. Most diverticula are solitary outgrowths involving the distal ureter and upper portions of the pelvis. They are lined by urothelium, which is lined by transitional cell epithelium. Rupture of a diverticulum in the lower GU tract in adult men and women who are sexually active. As an STI it can also be transmitted vertically and from mother to offspring. It is the most common cause of nongonococcal and nonchlamydial urethritis, and can cause chorioamnionitis, pyelonephritis, and septic arthritis. It is implicated in chronic prostatitis in men, and urgency–frequency symptoms in women and in HIV-related acute epididymitis. It is also sometimes associated with decreased fertility. Diagnosis is by culture, but specific media and growth conditions are necessary. Treatment is doxycycline 100 mg/day for 2 wk or a single dose of azithromycin 1 g PO. (See also Section I: “Sexually Transmitted Diseases [STDs], General.”)

REFERENCE

URERET, DUPLICATED AND BIFID
DESCRIPTION
Duplication of ureters is a common anomaly. Duplication may be either complete or incomplete. Complete duplication is most often associated with vesicoureteral reflux, ectopic ureteral insertion, and ectopic ureteroceles, all of which are more commonly found in females than in males. Incomplete duplication is most often associated with UPJ obstruction of the lower pole of the kidney. Common clinical presentations include UTIs and urinary incontinence. Diagnosis is made usually in childhood by US, voiding urosonography, and Voiding cystourethrography. Also known as “double ureter” (partial duplication) or double ureters (if complete duplication). Treatment is urothelioysis in the presence of persistent

REFERENCE
fibroepithelial polyp. The bulk of the polyp is transitional epithelium. The incidence in ureter is 3–5% of all primary ureteral tumors. These benign tumors, hemangiomas usually cause incomplete obstruction and may eventually cause complete obstruction with dilation of the urinary tract. They predispose to UTI and may cause hematuria or abdominal flank pain. Up to 90% are associated with a duplicated collecting system in females and ~20% are nonduplicated ureters usually in males with an absent hemi-ureter. In females, the ureter typically inserts in the uterine or vaginal (dilated to the ophcyston) and cause incontinence or constant dribbling. In males the sites include the posterior urethra or seminal vesicles (no incontinence is seen) and often present later in life. Treatment is usually partial nephroureterectomy of the nonfunctioning upper pole moiety with nephrectomy often necessary for single ureter systems.

REFERENCE

URETER, FIBROEPITHELIAL POLYPS
DESCRIPTION
Fibroepithelial polyps are rare benign neoplasms. The majority of these polyps are found at the UPJ. Signs and symptoms usually associated with ureteral obstruction include flank pain and hematuria. In addition, varying degrees of hydronephrosis and ureteral intussusception have been described. Grossly, ureteral polyps are intraluminal lesions, most commonly covered with transitional epithelium. The bulk of the polyp is composed of vascularized collagenous fibrous tissue, with or without areas of chronic inflammation and edema. Ultrastructurally it is often necessary to confirm the diagnosis.

SYNONYMS
• Fibroepithyma
• Myxoma
• Fibroma
• Vascular fibrous polyps

TREATMENT
• Underscopic resection
• Open ureterotomy with polypectomy or partial ureterectomy is a reliable conservative treatment option if the diagnosis can be confirmed preoperatively.
• Many patients undergo nephroureterectomy for suspected malignancy.

REFERENCE

URETER, FISH HOOK (REVERSE J)
DESCRIPTION
A radiographic appearance of the type (fish hook) circumcaval ureter, in which the dilated proximal part of the ureter takes a characteristic fish hook or reverse J course. Universal dilatation usually ends 1–2 on lateral to the inferior vena cava, where the ureter turns upward at the border of the psoas muscle.

REFERENCE

URETER, HEMANGIOMA
DESCRIPTION
Hemangiomas are benign ureteral tumors. They may be the most common cause of chronic unilateral hematuria. Symptomatology may include hematuria, pain, hydroureter, bladder irritations, and palpable tumor. Venous lakes have also been found, but less frequently. Like other arterial tumors, hemangiomas usually cause incomplete obstruction and may eventually cause complete obstruction with dilation of the ureteral tract. They present as red, slightly elevated structures, fairly diffusely, and demarcated from their surroundings. Urethral malignancies must be excluded, especially in the elderly. Flexible ureteroscopy is considered a good diagnostic and therapeutic option in selected patients with unilateral hematuria of uncertain etiology.

REFERENCE

URETER, J HOOKING
DESCRIPTION
With progressive benign prostatic hypertrophy, elevation of the trigone occurs, resulting in a characteristic J hooking of the distal ureter. This is a reliable sign on IV of significant prostatic hypertrophy.

REFERENCE

URETER, LEIOMYOMA
DESCRIPTION
Leiomyomas of the urinary tract are rare (neoplasms of mesenchymal origin comprise <3% of all primary ureteral tumors). These benign tumors are seen predominately in the 4th–5th decade of life. The left ureter is more frequently affected. Immunohistochemical studies confirm the diagnosis. Conservative management (ureteroscopic or partial ureterectomy) is the treatment of choice.

REFERENCE

URETER, LEIOMYOSARCOMA
DESCRIPTION
Leiomyosarcoma originating from the ureter is exceedingly rare, with only 13 reported cases of primary leiomyosarcoma of the ureter. It is a disease that is very difficult to diagnose, and furthermore, it has a poor 5-year disease-specific survival. Patients present with flank pain, hematuria, and/or UTI. Radiographic workup includes IV, retrograde pyelography, and CT. Light microscopy, immunohistochemical staining and electron microscopy should be used to confirm the diagnosis of leiomyosarcoma.

TREATMENT
• Tumor resection
• Possible nephroureterectomy, depending on tumor grade and stage
• Adjunct radiation therapy may be helpful.

REFERENCE

URETER, METASTASIS TO
DESCRIPTION
Metastatic tumors of the ureter are uncommon, and 1 of the rarest causes of ureteric obstruction. Since their 1st mention in the literature in 1909 only ~400 cases are reported. Among 1/2 of the cases, the breast or gastrointestinal tract (colorectum) is the site for primary cancer. Prostate cancer and uterine cervical cancer are responsible for 35–40% of cases, with stomach and lung cancer being reported in the remaining cases. A prediction exists for the lower 1/3 of the ureter. Many are asymptomatic with the majority autopsy reports.

REFERENCE

URETER, NEPHROGENIC ADENOMA (NA)
DESCRIPTION
Nephrogenic adenoma (NA) is a rare neoplastic lesion of the ureter and assumed to be secondary to chronic irritation of the urethra. It is a benign papillary and tubular proliferation in response to trauma, infection, or limiting salivation. Although it can be seen anywhere in the urinary tract, it is most commonly observed in the bladder (55%). The incidence in ureter is ~4%. Biopsy and fulguration are appropriate, as it is treated as a low-grade urethral malignancy. Malignant transformation has not been described.

REFERENCE

URETER, NEUROFIBROMA
DESCRIPTION
Grossly, neurofibromas may be single or multiple and comprise different sized nodules. Histologically, they are composed of fascicles of elongated spindle-shaped cells with thin, wavy nuclei in a collagenized background. Neurofibromas in the ureter are very rare but have an increased incidence in von Recklinghausen disease.
A retrocaval ureter is a congenital anomaly in which the ureter passes behind the inferior vena cava (IVC). On IVP, the ureter appears straight with a narrow lumen, due to diffusely rigid changes of the wall. This results in secondary hydronephrosis.

**REFERENCE**

**URETER, PIPE-STEM**
Two types have been described. Type 1 is the more common where the ureter crosses anterior to the IVC at the level of the 3rd lumbar vertebra, and the degree of hydronephrosis is directly related to the level of the IVC. Type 2 retrocaval ureter is less common and the ureter tends to cross at a much higher level relative to the renal pelvis and the degree of hydronephrosis is usually mild. Treatment is surgery with transaction of the ureter and reanastomosis in front of the inferior vena cava. (See also Section I: “Ureter, Obstruction.”)

**REFERENCE**

**URETER, SHEPHERD’S CROOK**
Spirally twisted or “corkscrew” ureters are rare anomalies beyond the neonatal age. A spiraually twisted ureter is not considered clinically significant, unless it causes obstruction and secondary hydronephrosis. Infants frequently have a “corkscrew” appearance of the proximal segment of the ureter seen on intravenous urography, but this has been considered an imaging finding of no potential clinical significance. It may represent persistence of normal fetal developmental structures, such as congenital folds. Corkscrew configuration of the ureter may also be the result of ureteric varicosities or extrinsic ureteric obstruction when seen later in life. Obstructive uropathy is a serious clinical entity that may lead to irreversible renal damage. Corkscrew deformity of the ureter is a known cause of delayed recognition of uropathy secondary to bladder outlet obstruction (Image #).

**REFERENCE**

**URETER, SHEPHERD’S CROOK**
Spirally twisted or “corkscrew” ureters are rare anomalies beyond the neonatal age. A spirally twisted ureter is not considered clinically significant, unless it causes obstruction and secondary hydronephrosis. Infant frequently have a “corkscrew” appearance of the proximal segment of the ureter seen on intravenous urography, but this has been considered an imaging finding of no potential clinical significance. It may represent persistence of normal fetal developmental structures, such as congenital folds. Corkscrew configuration of the ureter may also be the result of ureteric varicosities or extrinsic ureteric obstruction when seen later in life. Obstructive uropathy is a serious clinical entity that may lead to irreversible renal damage. Corkscrew deformity of the ureter is a known cause of delayed recognition of uropathy secondary to bladder outlet obstruction (Image #).

**REFERENCE**

**URETER, SHEPHERD’S CROOK**
Spirally twisted or “corkscrew” ureters are rare anomalies beyond the neonatal age. A spirally twisted ureter is not considered clinically significant, unless it causes obstruction and secondary hydronephrosis. Infant frequently have a “corkscrew” appearance of the proximal segment of the ureter seen on intravenous urography, but this has been considered an imaging finding of no potential clinical significance. It may represent persistence of normal fetal developmental structures, such as congenital folds. Corkscrew configuration of the ureter may also be the result of ureteric varicosities or extrinsic ureteric obstruction when seen later in life. Obstructive uropathy is a serious clinical entity that may lead to irreversible renal damage. Corkscrew deformity of the ureter is a known cause of delayed recognition of uropathy secondary to bladder outlet obstruction (Image #).

**REFERENCE**

**URETER, STONE PASSAGE STATISTICS**
The ureter is the smallest diameter structure of the urinary tract. It is also the area most likely to be obstructed by a stone. Most stones <5 mm in diameter are likely to pass spontaneously with the likelihood of spontaneous stone passage decreasing with increased stone size. It is estimated that 2/3 of ureteral stones that pass spontaneously pass within 4 wk of the onset of symptoms.

**REFERENCE**
URETAL JETS
DESCRIPTION: Uretal jets have been studied to diagnose urethral obstruction. Uretal jets are visualized on color Doppler ultrasound as urethral urine passing into the bladder. Sensitivity of 100% and specificity of 90.9% in detecting urethral obstruction has been reported based on the absence of the urethral jet on a given side. Patients must be well hydrated and often when a prolonged imaging interval is needed to document the presence or absence of the urethral jet (Image 1).

URETAL STRICTURE FOLLOWING URINARY DIVERSION
DESCRIPTION: Urethral strictures are seen in 20–10% of patients who receive a cystotomy and urinary diversion for bladder cancer. The stricture is most commonly located at the ureterointerfacial anastomosis and more commonly involves the left ureter. Considered a late complication, strictures usually present in the 6–12 mo postoperative time period. Urethral recurrence of urethral carcinoma should be ruled out. Treatment includes percutaneous nephrostomy, indwelling ureteral stent, balloon dilation, or laser therapy.

URETERITIS
DESCRIPTION: A generic characterization given to describe inflammation of the ureter which can be further qualified into subtypes based loosely on its etiologic factors. For example, postobstructive, ureteral infections, ureteral strictures, infective or obstructive etiologies of ureteritis include ureteral amyloidosis, eosinophilic ureteritis, IgA associated ureteral inflammation, and idiopathic segmental ureteritis.

URETERITIS CYSTICA
DESCRIPTION: A benign and rare condition, ureteritis cystica is characterized by multiple cysts and space-filling defects in ureterum. Usually asymptomatic, it may present with hematuria, and if obstruction occurs, may lead to stone formation, UTI, and renal compromise. The etiology is unknown, but associated with chronic UTI. Space-filling defects seen on retrograde pyelography or excretory urography may appear as smooth, round or oval filling defects of varying sizes that protrude into the lumen. It can mimic other conditions such as bladder cancer, blood clots, air bubbles, radiolucent stones, fibroepithelial polyps, and sloughed renal papillae. It manifests as cystic areas of glandular metaplasia associated with chronic urethral inflammation; this is more commonly seen in the bladder, called cystitis cystica. Management is ureteroscopy and the mechanical disruption of cysts or infraction of chemicals such as silver nitrate to relieve obstruction.

URETERONECOSTOMYSTOSIS, TECHNIQUES AND INDICATIONS
DESCRIPTION: Ureteronecostomy, or ureteroneocystostomy, is used when there is an abnormality at the ureterovesical junction. Abnormalities include an obstructing ureteroureterostomy, ureteral reflux, distal ureteral stenosis, or urologic injuries. The surgical treatment options can be classified on the basis of the normal ureter to the bladder as intravesical, extravesical, or combined or on the relationship of the submucosal tunnel to the site of the original ureteral hiatus as suprahilar or infrahilar.

URETHRA, ADENOCARCINOMA OF ACCESSORY GLANDS
DESCRIPTION: In males, the accessory glands can develop adenocarcinoma. Adenocarcinoma of the seminal vesicles is distinct from adenocarcinoma of the epididymis. In females, the Skene glands can develop adenocarcinoma as well. Patients typically present with hematuria, dysuria, and progressive urethral obstruction. Management is similar to that for vesical adenocarcinoma. (See also Section II: “Cowper Gland Adenocarcinoma.”)

URETHRA, BLEEDING (BLOOD AT MEATUS)
SYNONYMS: Adenoma; villous polyp; hemorrhoids;
CAUSES: Posterior urethral (posterior and membranous urethra, proximal to urethral diaphragm)
PATHOPHYSIOLOGY: Prostatic-type polyps of the urethra
TREATMENT: Posterior urethral bleeding

URETHRA, BLEEDING (BLOOD AT MEATUS)
DESCRIPTION: Usually associated with GU trauma, blood at the urethral meatus is the single most important sign of urethral injury. Patients often complain of abdominal pain or inability to urinate, and report a history ofouch injury to the penis. Clinically, this finding is an absolute contraindication to immediate urethral catheter placement. Instead, urethrography should be performed (see below). This is distinct from idiopathic urethrorrhagia, which is bleeding from the urethra or blood spotting on the undergarments in preadolescents. Urethrorrhagia is a benign lesion and self-limited in most cases. (See also Section I: “Urethra, Trauma (Anterior and Posterior);” Section II: “Urethroitis, Hidradenitis.”
CAUSES:
1. Posterior urethral injury (posterior and membranous urethra, proximal to urethral diaphragm) associated with pelvic fracture and deceleration/shear injury
2. Anterior urethral injury (bulbous and pendulous urethral injury) associated with straddle injury and iatrogenic laceration
3. Traumatic urethral catheterization; more common in men
4. Neoplastic causes: idiopathic urethrorrhagia, malignancy (urethra, prostate, bladder), urethral carcinoma, urethral condyloma, urethral diverticulum, urethral stricture, benign prostatic bleeding, urethral hemangioma
TREATMENT:
1. In cases of urethral trauma, standard trauma management; shock and hemorrhage control
2. Avoid urethral catheterization
3. Retrograde urethrogram (12-Fr catheter in fossa navicularis) with 3 cc of iodine dye; retrograde injection of 20–30 cc of water-soluble dye to evaluate for extravasation beyond the urethra:
   - Positive extravasation: Immediate open bladder exploration with placement of suprapubic cystotomy tube; delayed urethral repair (3 mo after injury) with silicone urethral catheter placement concomitant with primary anastomosis
   - Negative extravasation: Careful urethral catheter placement; cystography

URETHRA, PROSTATIC TYPE POLyps
DESCRIPTION: Congenital, benign papillary-appearing lesions that occur most frequently in the prostatic urethra and contain benign prostatic epithelium. These have been reported in the anterior urethra. Cysts of the papillary projections contain prostatic stroma and glands. The lesions typically present in the 1st decade of life, but can appear at any age. Hemorrhage, erosion, and obstruction are common. Cystourethroscopy is usually diagnostic.
SYNONYMS: Urinary tract polyp; hemangioma
TREATMENT: Transurethral or suprapubic resection is curative.

URETHRA, PROSTATIC TYPE POLYPS
DESCRIPTION: Usually associated with GU trauma, blood at the urethral meatus is the single most important sign of urethral injury. Patients often complain of abdominal pain or inability to urinate, and report a history ofouch injury to the penis. Clinically, this finding is an absolute contraindication to immediate urethral catheter placement. Instead, urethrography should be performed (see below). This is distinct from idiopathic urethrorrhagia, which is bleeding from the urethra or blood spotting on the undergarments in preadolescents. Urethrorrhagia is a benign lesion and self-limited in most cases. (See also Section I: “Urethra, Trauma (Anterior and Posterior);” Section II: “Urethroitis, Hidradenitis.”
CAUSES:
1. Posterior urethral injury (posterior and membranous urethra, proximal to urethral diaphragm) associated with pelvic fracture and deceleration/shear injury
2. Anterior urethral injury (bulbous and pendulous urethral injury) associated with straddle injury and iatrogenic laceration
3. Traumatic urethral catheterization; more common in men
4. Neoplastic causes: idiopathic urethrorrhagia, malignancy (urethra, prostate, bladder), urethral carcinoma, urethral condyloma, urethral diverticulum, urethral stricture, benign prostatic bleeding, urethral hemangioma
TREATMENT:
1. In cases of urethral trauma, standard trauma management; shock and hemorrhage control
2. Avoid urethral catheterization
3. Retrograde urethrogram (12-Fr catheter in fossa navicularis) with 3 cc of iodine dye; retrograde injection of 20–30 cc of water-soluble dye to evaluate for extravasation beyond the urethra:
   - Positive extravasation: Immediate open bladder exploration with placement of suprapubic cystotomy tube; delayed urethral repair (3 mo after injury) with silicone urethral catheter placement concomitant with primary anastomosis
   - Negative extravasation: Careful urethral catheter placement; cystography

URETHRA, PROSTATIC TYPE POLYPS
DESCRIPTION: Congenital, benign papillary-appearing lesions that occur most frequently in the prostatic urethra and contain benign prostatic epithelium. These have been reported in the anterior urethra. Cysts of the papillary projections contain prostatic stroma and glands. The lesions typically present in the 1st decade of life, but can appear at any age. Hemorrhage, erosion, and obstruction are common. Cystourethroscopy is usually diagnostic.
SYNONYMS: Urinary tract polyp; hemangioma
TREATMENT: Transurethral or suprapubic resection is curative.
Carcinoma of the urethra is a rare neoplasm arising from the transitional epithelium of the urethra. It is a mixed tumor of both mesenchymal and epithelial elements. The majority of cases occur in females, with a peak age of 30–40 yr. For women, the disease is hormonally associated and many of these tumors enlarge in pregnancy. Treatment is local excision, and in most cases, there is no local recurrence. A small subset of cases may present as a mixed tumor with both adenocarcinomatous and leiomyomatous components. This type of tumor has been associated with prolonged use of azo-alpha blockers for benign prostatic hyperplasia.

**REFERENCES**

URETHRA, DIVERTICULUM

**DESCRIPTION**
Urethral diverticula are rare pathologic entities commonly found in females, with an average age at presentation of 52. Reported symptoms include urethral bleeding (most common), dysuria, genital mass, and urethral obstruction. Adenocarcinoma occurs more frequently in transitional and squamous cell cancers combined and carries a more favorable prognosis. Female urethral diverticulum can be diagnosed through MR imaging with a high index of suspicion in patients with recurrent UTIs, dysuria, urgency, and pelvic dribbling. (See Section I: “Urethra Diverticula, Female,” “Urethra, Carcinoma, General.”)

**TECHNIQUES**
- Surgical: Radical cystourethrectomy with pelvic node dissection is recommended by most authors.
- Diverticulectomy has been suggested for low-stage adenocarcinoma, if close follow-up is assured.

**REFERENCES**

URETHRA, FOREIGN BODY

**DESCRIPTION**
Cases of self-inflicted foreign body insertion in males have been reported, including objects such as fishhooks, bones, screws, safety pins, and light bulbs. Cause for inserting foreign bodies varies, including psychopathic disorder, intoxication, and erotic stimulation. Endoscopic retrieval is usually successful using modern instruments. Open surgery may also be considered. IV perioperative antibiotics followed by PO antibiotics for 1 wk has been recommended. Delayed complications include structure disease, therefore close urologic follow-up is recommended (Image 05).

**REFERENCES**

URETHRA, HEMANGIOMA

**DESCRIPTION**
Urethral hemangiomas are extremely rare tumors. The lesion is believed to be congenital, arising from the embryonic rests of unipotent angioblastic cells that fail to develop into normal blood vessels. The clinical presentation is bloody urethral discharge or frank urethral bleeding. These lesions are benign in nature. They are treated by local resection or ablation with electrocoagulation or laser. (See also Section I: “Urethra, Bleeding [Blood at Urination].”)

**REFERENCES**

URETHRA, LEIOMYOMA

**DESCRIPTION**
Rare benign neoplasm arising from smooth muscle. The majority occur in females, with a peak age of 30–40 yr. It usually presents as an asymptomatic mass, or with dysuria, UTI or obstruction, and dyspareunia. The proximal urethra is most commonly involved. No etiology is known, but it is hormonally associated and many of these tumors enlarge in pregnancy. Treatment is local excision, and prognosis is excellent as no malignant transformation or local recurrence has been reported in the literature. (See also Section I: “Urethral Mass.”)

**REFERENCES**
URETHRA, LEIOMYOSARCOMA

DESCRIPTION: Leiomyosarcoma is a smooth muscle tumor that often involves the urinary tract. Leiomyosarcomas are extremely rare tumors that are more common in females than in males. Patients present with hematuria, pain, or mass. The prognosis is poor, and the treatment is radical excision with consideration of adjuvant radiation. (See also Section I: “Urethra, Mass.”)


URETHRA, LEUKOPLAKIA

DESCRIPTION: The term leukoplakia (also called squamous metaplasia) refers to the presence of grossly discernible white patches commonly seen on the mucosal surfaces of areas of squamous metaplasia. There seems to be an increased incidence in patients with diabetes, as well as in those with chronic irritation or infection. Generally believed to be a premalignant lesion caused by chronic infection or irritation, it may progress to squamous cell carcinoma. (See also Section II: “Leukoplakia.”)


URETHRA, LYMPHOMA

DESCRIPTION: Primary malignant lymphoma (PML) of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, LYMPHOMA

DESCRIPTION: Primary malignant lymphoma of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALACOPLAKIA

DESCRIPTION: Malacoplakia is a chronic inflammatory disorder characterized by the presence of Michaelis–Gutmann bodies and von Hansemann cells. The disease shows a predilection for involving the mucosal surfaces of areas of squamous metaplasia. There seems to be an increased incidence in patients with diabetes, as well as in those with chronic irritation or infection. Generally believed to be a premalignant lesion caused by chronic infection or irritation, it may progress to squamous cell carcinoma. (See also Section II: “Leukoplakia.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Primary urinvasive malignant melanoma is rare, with <100 cases reported in the literature. 90% of patients are diagnosed in the 6th–7th decades. 80% of cases were reported to be in the fossa navicularis and the meatus. The most common presentations are dysuria, hematuria, deviated urinary stream, or urinary obstruction. Endoscopically, a pigmented nodular mucosal mass or masses, which may be ulcerated, may be seen. Local recurrence is common. Metastasis is usually to regional lymph nodes or liver, lung, and brain is also common. Staging for urothelial melanoma has not yet been standardized. Prognosis depends on the thickness of the lesion.

TREATMENT:
- Surgery: Excision of the lesion
- Chemotherapy
- Radiation therapy
- Immunotherapy
- Targeted therapy


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Primary urinvasive malignant melanoma is rare, with <100 cases reported in the literature. 90% of patients are diagnosed in the 6th–7th decades. 80% of cases were reported to be in the fossa navicularis and the meatus. The most common presentations are dysuria, hematuria, deviated urinary stream, or urinary obstruction. Endoscopically, a pigmented nodular mucosal mass or masses, which may be ulcerated, may be seen. Local recurrence is common. Metastasis is usually to regional lymph nodes or liver, lung, and brain is also common. Staging for urothelial melanoma has not yet been standardized. Prognosis depends on the thickness of the lesion.

TREATMENT:
- Surgical: Urethrectomy or penectomy with regional lymph node dissection
- Chemotherapy
- Radiation therapy
- Immunotherapy
- Targeted therapy


URETHRA, MEATUS, NORMAL CALIBER

DESCRIPTION: Normal limits of male urethral caliber are as follows:
- 6 wk–6 mo: 10 Fr
- 6 mo–6 yr: 7 Fr
- 6 yr–6 wk: 6 Fr
- 6 yr: 5 Fr
- 6 yr–6 wk: 4 Fr
- 6 wk: 3 Fr
- 6 wk: 2 Fr
- 6 wk: 1 Fr
- 6 wk: 0 Fr


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)


URETHRA, MALIGNANT MELANOMA

DESCRIPTION: Malacoplakia of the male urethra is an extremely rare neoplasm. (See also Section I: “Urethra, Mass.”)

URETHRA, POLYPS (FIBROEPITHELIAL, ADENOMATOUS, INFLAMMATORY)

DESCRIPTION

Uncertain benign polypoid of papillary lesions of the urethra, these are usually limited to male patients and occur most often in children. Polyps vary in microscopic features, which result in their classification into fibroepithelial, adenomatous, or inflammatory. Adenomatous polyps are thought to represent prostatic glandular material from a congenital developmental error. A fibroepithelial polyp consists of connective tissue inflammation, inflammatory polyps have a distinct inflammatory infiltrate. Presenting symptoms can include hematuria, hematospermia, obstruction, or UTI. Cystourethroscopy with biopsy is the test of choice. Transurethral resection with fulguration is the treatment of choice, along with removal of the source of inflammatory cells, catheter or stone removal if present. (See Section II: “Urethra, Polypoid and Polyoid.”) “Urethritis, Polypoïd.”

REFERENCES


URETHRA, PROLAPSE (FEMALE)

DESCRIPTION

Prolapse of the urethra is a rare condition, described as complete eversion of urethral mucosa through the external urethral orifice; the etiology is unknown. It is primarily associated with prepubertal girls and postmenopausal women with African-American girls more commonly affected. Vaginal bleeding is often the presenting symptom, followed by urinary complications such as dysuria. Associated factors include increased abdominal pressure, such as coughing or constipation, and trauma or infections of the vagina or urinary tract. Management ranges from conservative medical treatment to a variety of surgical corrective procedures, such as excision and urethropexy. Medical treatment includes local hygiene, sitz bath, topical antibiotics, or topical estrogen creams (adults). Surgical intervention is indicated for more severe cases, including significant bleeding, thrombosis, or gangrenous changes or if topical estrogen is contraindicated. Surgical treatment is usually accomplished with the modified Kelly–human operation. The prolapsed mucosa is excised, and the mucocutaneous junction is reaproximated with absorbable sutures.

REFERENCES


URETHRA, VILLOUS ADENOMA

DESCRIPTION

An adenomatous lesion of the urethra, usually polypoid in nature, covered by mucinous material. Masses as large as 2–4 cm in the urinary tract have been described. Etiology is possibly due to an embryonic origin similar to that of the rectosigmoid. Urinary obstruction and/or hematuria can be presenting symptoms. Best treated by complete removal, due to the premalignant changes seen in adenomas of the colon. These lesions are most commonly encountered in the male prostatic urethra. Histogenesis has been suggested to be secondary to residual cloacal epithelium in the prostatic urethra.

REFERENCES


URETHRAL HYPERMOBILITY

DESCRIPTION

Also called type II stress urinary incontinence (SUI), urethral hypermobility is caused by weak support of pelvic floor supporting structures, in which increased intra-abdominal pressure causes the descent of the bladder neck and proximal urethra. Women with hypermobility present with SUI, although some continent women have it as well. The degree of hypermobility is measured by the Q-tip test, in which a well-fabricated sterile cotton tipped applicator is placed into the bladder and then withdrawn to the point of resistance. The patient is then asked to strain and the motion of the Q-tip is observed. Hypermobility is defined as a rotating or straining angle 30% from horizontal. Treatment is per urethral collagen injection or suburethral slinging procedure.

REFERENCE


URETHRAL PRESSURE PROFILE (UPP)

DESCRIPTION

The UPP is a graphic representation of the intravesical pressure along the length of the urethra. This static study provides no assessment of physiologic urethral function during voiding. The mucosal urethral pressure profile, however, is a dynamic study that can be performed by withdrawing a catheter from the urethra during micturition. The study can define the site of urethral obstruction by demonstrating a drop in urethral pressure immediately distal to the obstructive lesion in the urethra. Controversy exists on its use in clinical practice due to the variability in the reproduction of measurements and lack of standardization.

REFERENCES


URETHRAL SLING, INDICATIONS AND ANATOMIC POSITIONS

DESCRIPTION

A urethral sling is a surgically placed to support pelvic structures or lift the urethra to enhance the bladder and pelvic floor’s ability to retain urine in patients with stress urinary incontinence (SUI). Slings can be made from autologous, alloplast, xenogenic, or synthetic tissues that provide strength. They can be placed at the proximal urethra (pubovaginal sling) or mid urethra (transvaginal tape [TVT] and transobturator [TOT] and other mid urinary slings). The urethral sling is a very effective treatment for SUI, with cure rates of 80–95% vs. other options such as the per urethral injection of bulking agents. Complications include erosion into surrounding structures such as vagina, urethra, and bladder, as well as bladder perforation, urinary tract infection, and new onset irritative voiding symptoms. (See also Section I: “Incontinence, Urinary, Adult Female”, Section II: “Sling Materials.”)

REFERENCES


URETHRAL SLING, STRUCTURE, FEMALE

DESCRIPTION

A decrease in the caliber of the urethra, as in females compared with males. Causes can include recurrent UTIs, previous endoscopic instrumentation, surgical management of urethral pathology or diverticular repair, trauma (including childbirth), neoplasia, or pelvic radiation, or it can be idiopathic. The patient usually presents with recurrent UTI or obstructive urinary symptoms (weak stream, straining to urinate, incomplete emptying). Female urethral structure has been formally defined as a fixed anatomic narrowing between the bladder neck and distal urethra of < 14 Fr preventing catheterization, with the diagnosis confirmed by cystourethroscopy, and/or videourodynamics. Interim catheterization has been used successfully, with internal urethrotomy or urethropexy also as options.

REFERENCES


URETHRAL SYNDROME

DESCRIPTION

A nonspecific term used in the past to describe symptoms such as urinary frequency, urgency, dysuria, and pelvic/perineal discomfort having no obvious cause. Because this term is so nonspecific, it is not meaningful for diagnosis or treatment planning. A more effective approach is to delineate each of the patient’s specific symptoms (e.g., frequent voiding), then pursue the differential
Chronic urethritis is a common

Centers for Disease Control and Prevention. Sexually

TREATMENT

chlamydia. Syphilis, HIV, and hepatitis B serology is

>5 WBC/HFP strongly suggests urethritis. Intraurethral

granular areas are often seen, and polyoidal masses are common. The symptoms resemble those of cystitis, although the urine is not infected. Complaints include dysuria, frequency, and nocturia. Discomfort in the urethra may be felt, particularly when walking. Urethral dilatations may help if steroids is found obsolete to 38 Ks. Empiric doxycycline or azithromycin can be tried.

REFERENCE

Urethral stricture or pelvic inflammatory disease (PID) in women, may ensue. Cause is predominantly N. gonorrhoeae and C. trachomatis infection; often together. Less common infectious agents include Ureaplasma urealyticum, Trichomonas vaginalis, herpesvirus, and Mycoplasma genitalium. Noninfectious causes include foreign bodies, soaps, douches, spermidides, and urethral instrumentation. Gram stain of discharge with >5 WBC/HFP strongly suggests urethritis. Intraurethral gram-negative diplococci are strongly indicative of gonorrhea. Cultures may be difficult to obtain, but are important for antiretroviral sensitivity testing and should be performed in all symptomatic patients. Routine urine analysis may be normal in simple urethritis. Tox and urine is often positive for leukocyte esterase and should show >5 WBC/HFP in acute urethritis. IFAF utilizing PCR assay on urine is very sensitive and specific, but costly. Wet prep of discharge may reveal Trichomonas; this is usually reserved in males who fail adequate treatment for gonorrhea and chlamydia. Syphils, HIV, and hepatitis B serology is performed as indicated to rule-out concomitant 3Ts.

TREATMENT

The United States Preventative Services Task Force recommends: screening all sexually active women >25 yo and all other women at increased risk of infection:

• All sexual partners who come in contact with the patient within 60 days should be evaluated, treated, and treated for gonorrhea and chlamydia.

• Gonorrhea Ceftriaxone 250 mg in a single IM PLUS Azithromycin 1 g orally in a single dose or doxycycline 100 mg orally twice daily for 7 days.

• Chlamydia: Azithromycin 1 g PO single dose or doxycycline 100 mg orally twice daily for 7 days.

• Trichonomiasis: Metronidazole 2 g PO single dose or 250 mg TID for 7 days or tinidazole 2 g PO in a single dose.

REFERENCE


URETHRITIS, CHRONIC, FEMALE

DESCRIPTION Chronic urethritis is a common urologic problem of females, as the distal urethra normally harbors pathogens. Infection may be increased by wearing contaminated diapers, by insertion of an introducer catheter, by spread from

can be felt, particularly when walking. Urethral dilatations may help if steroids is found obsolete to 38 Ks. Empiric doxycycline or azithromycin can be tried.

REFERENCE


URETHRITIS, POOLYPOID

DESCRIPTION A urethral counterpart of polypoid cystitis, occurs as single or multiple polypoid/ papillary lesions. A noninflammatory inflammatory lesion that is usually found in the prostatic urethra near the verumontanum. The lesions are edematous stroma with distended blood vessels and chronic inflammatory infiltrate. Usually resolves after removal of the inflammatory stimulus; if necessary, resection of the lesion usually leads to a cure. If the lesion persist, malignancy should be ruled out.

REFERENCE


URETHRITIS, SENILE

DESCRIPTION After physiologic (or surgical) menopause, hypoestrogen occurs and retroperitoneal (senile) changes take place in the vaginal (atrophy) and the urethral walls. Some evasion of the mucus at the urethral orifice, from atrophy of the vaginal wall, is usually seen and can be misdiagnosed as a cancer. Many postmenopausal women have symptoms of vesical instability (burning, frequency, urgency) and stress incontinence. Oxyuria may occur due to urine contact with the inflated atrophic tissues themselves or because of the increased incidence of UIs in these women. Best treated symptomatically or with DES vaginal suppressions 0.1 mg nightly for 3 wk. The patient may also benefit from other topical agents such as estral vaginal tablets or from conjugated estrogen cream or slow release intravaginal therapy such as the Estring.

REFERENCES


URETHROCELE

DESCRIPTION Urethroccele is a form of pelvic prolapse in which the urethra protrudes into the anterior wall of the vagina, due to loss of the normal urethral support from damage such as childbirth. Cystocele is also commonly present. In women, a urethroccele can cause voiding difficulty, some degree of incontinence, UI, and dyspareunia. The condition can also develop in children after urethralplasty, with distal obstruction causing proximal dilution of the neourethra; it is very rarely congenital. (See also Section 1, "Vulvo Vaginal [Gynecologic and Obstetric]").

REFERENCE


URETHROHETRAGIA, DIOPHATIC

DESCRIPTION Bleeding from the urethra or blood spotting on the underwear is prevalent in average age (around 10 y) is a benign condition, self-limiting in most cases. The etiology is unknown. Routine radiographic, lab, and endoscopic evaluation is unnecessary for evaluating urethrophy. Watchful waiting is indicated, as the condition resolves in 71% and 91.7% of patients at 1 and 2 y, respectively. Evaluation should be considered in patients with prolonged urethrophy because urethral fracture may be identified. (See also Section 8.1. "Urethral Bleeding [Bladder at Meatus]."

REFERENCE


URETHRAL INCONTINENCE/URETHRAL URINARY INCONTINENCE (UIU)

DESCRIPTION Urethral urinary incontinence (UI) is the involuntary leakage of urine immediately preceded by a sense of urgency. It is caused by detrusor muscle overactivity. Etiology is categorized into idiopathic; neurogenic, including stroke, diabetes, and other causes; or nonneurogenic, including infections, bladder stones, and cancer. Initial workup includes a good history and physical, evaluation for other associated urinary symptoms, check of postural residual, urine analysis. Cystoscopy should be performed in the setting of simultaneous hematuria. Urodynamie evaluation can be considered medically refractory patients. (See also Section 1. "Incontinence, Female” and “Urinary Incontinence, Male”)

TREATMENT

• Symptomatic control mainstay of treatment.

• Dietary and behavioral modifications: Limiting caffeine-containing foods, alcoholic beverages, and foods rich in vitamin A and vitamin E. Avoid wearing tight-fitting clothing.

• Biofeedback-assisted pelvic muscle training

• 1st-line medical therapy: Anticholinergics, β3 agonists

• 2nd-line therapy: Intravesical Botulinum toxin, sacral neuromodulation, and augmentation cystoplasty.

URGE INCONTINENCE/URGEO URINARY INCONTINENCE (UI)

DESCRIPTION Urge urinary incontinence (UI) is the involuntary leakage of urine immediately preceded by a sense of urgency. It is caused by detrusor muscle overactivity. Etiology is categorized into idiopathic; neurogenic, including stroke, diabetes, and other causes; or nonneurogenic, including infections, bladder stones, and cancer. Initial workup includes a good history and physical, evaluation for other associated urinary symptoms, check of postural residual, urine analysis. Cystoscopy should be performed in the setting of simultaneous hematuria. Urodynamie evaluation can be considered medically refractory patients. (See also Section 1. "Incontinence, Female” and “Urinary Incontinence, Male”)

TREATMENT

• Symptomatic control mainstay of treatment.

• Dietary and behavioral modifications: Limiting caffeine-containing foods, alcoholic beverages, and foods rich in vitamin A and vitamin E. Avoid wearing tight-fitting clothing.

• Biofeedback-assisted pelvic muscle training

• 1st-line medical therapy: Anticholinergics, β3 agonists

• 2nd-line therapy: Intravesical Botulinum toxin, sacral neuromodulation, and augmentation cystoplasty.

Persistent cloaca may allow the reflux of urine into the due to intraperitoneal bladder or upper tract atrophy and scarring. Typically this form is a subtle the renal interstitium. Deposits induce a tophus from a protracted forms of hyperuricemia. Monosodium urate crystals lead to obstruction of in the distal nephron (collecting tubules) due to its acidic environment. This can lead to Renal ultrasound with voiding cystourethrography, and paracentesis to check creatinine levels in ascitic fluid. A newer cause of urinary ascites relates to urinary extravasation following laparoscopic or robotically Correct fluid balance and electrolyte abnormalities. Direct repair at the perforation site is usually not possible. Glucose blood testing is recommended. A newer cause of urinary ascites relates to urinary extravasation following laparoscopic or robotically direct repair at the perforation site is usually not possible. Glucose blood testing is recommended. Ileal and colonic conduits can produce an abnormality that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


URINARY FLOW RATE (EUROFLOWMETRY)

DESCRIPTION

Uroflowmetry is the study of urinary flow rate (Qmax). The Qmax is defined as the product of maximum bladder capacity times the maximum flow rate. It is not a diagnostic test, but a test of bladder function. An abnormality that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


URINARY DIVERSION, RISK OF MALIGNANCY

DESCRIPTION

Symptoms of bowel used for urinary diversion have an increased risk of malignant transformation. Some studies have shown an increase in 5% to as high as 40% 10–20 yr after a urinary diversion. The etiology is unknown; adenocarcinomas, adenomatous polyps, sarcomas, TCCs, signet ring carcinomas, and ESCCs have been identified. Many investigators now recommend annual screening in patients who have intestinal segments in contact with urine beginning 10 yr after the initial surgery. Patients who have previously undergone a nephroureterectomy are at particular increased risk for development of adenocarcinoma of the sigmoid colon along the anastomotic line. It is recommended that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


URINARY FLOW RATE (EUROFLOWMETRY)

DESCRIPTION

Uroflowmetry is the study of urinary flow rate (Qmax). The Qmax is defined as the product of maximum bladder capacity times the maximum flow rate. It is not a diagnostic test, but a test of bladder function. An abnormality that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


URINARY DIVERSION, RISK OF MALIGNANCY

DESCRIPTION

Symptoms of bowel used for urinary diversion have an increased risk of malignant transformation. Some studies have shown an increase in 5% to as high as 40% 10–20 yr after a urinary diversion. The etiology is unknown; adenocarcinomas, adenomatous polyps, sarcomas, TCCs, signet ring carcinomas, and ESCCs have been identified. Many investigators now recommend annual screening in patients who have intestinal segments in contact with urine beginning 10 yr after the initial surgery. Patients who have previously undergone a nephroureterectomy are at particular increased risk for development of adenocarcinoma of the sigmoid colon along the anastomotic line. It is recommended that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


URINARY FLOW RATE (EUROFLOWMETRY)

DESCRIPTION

Uroflowmetry is the study of urinary flow rate (Qmax). The Qmax is defined as the product of maximum bladder capacity times the maximum flow rate. It is not a diagnostic test, but a test of bladder function. An abnormality that these patients undergo periodic colonoscopy to accurately define any morbidities from their previous diversion.

REFERENCES


Postoperative urinary retention


UBR61391-Section-E-P2 UBRK1391-Gonville uro short topics-u.xml September 18, 2014 19:55

URINARY TRACT INFECTION (UTI), CATHERETER-RELATED (CAUTI, CA-UTI)

DESCRIPTION: UTI is the most common hospital-acquired infection in the United States and a major focus to improve patient outcomes. Any passage of a urithal catheter can introduce bacteria into the bladder. Once the catheter is in place, bacteria enter the bladder around the catheter (extraluminal infection) and from intraluminal infection failure of closed drainage or contamination of the urine collection bag. The incidence of bacteriuria in patients with indwelling bladder catheters is directly related to the duration of catheterization. Even with optimal bladder care, 3-10% develop significant bacteriuria daily. Of these patients, 10-35% develop symptomatic UTI (catheter associated UTI or abacteriuric CAUTI), and 4% may develop bacteremia. Avoiding unnecessary catheterization, remissimg the catheter as soon as possible, and appropriate catheter management (closed catheter drainage) are the most effective methods to reduce these infections. Silver-coated urinary catheters have been shown to reduce infections. Patients who require long-term bladder drainage should be managed with intermittent catheterization, if possible. This approach is associated with a lower rate of bacteriuria and CAUTI than management with long-term indwelling catheterism. Prophylactic antibiotics are not consistently of proven benefit. Catheter-associated urinary tract infection definitions by the CDC have recently been narrowed to exclude asymptomatic bacteriuria. (See also Section E: “Urinary Tract Infection (UTI), Catheter Associated (CAUTI, CA-UTI).”)

REFERENCES


URINE, ABNORMAL COLOR

DESCRIPTION: Normal urine is clear and pale to yellowish, but urine colors can be caused by disease, medications, and dietary factors. Other factors that may affect urine color include lighting conditions and environmental factors such as humidity and air pollution. Changes in urine color can also be caused by certain medical conditions, such as kidney disease, liver disease, or cancer. (See also Section IX: “Urinalysis.”)

COLORS OF URINE

Light yellow: Normal color of urine, seen in the morning after a night of sleep, when the body is in a state of hydration.

Deep yellow: Possible signs of dehydration or kidney disease. (See also Section IX: “Urinalysis.”)

Green: May indicate a problem with the urinary tract, such as infection or stones. (See also Section IX: “Urinalysis.”)

Red: May indicate blood in the urine, such as from a kidney stone or bladder infection. (See also Section IX: “Urinalysis.”)

Black: May indicate kidney disease, liver disease, or exposure to certain medications. (See also Section IX: “Urinalysis.”)


URINE, FOAMING

DESCRIPTION: Foaming urine is a clinical finding often associated with proteinuria and kidney disease and its observation dates back to Hippocrates. Increasing degrees of proteinuria produce decreasing degrees of surface tension. In addition, the elliptical shape of protein molecules at the air-water interface produces increased surface activity. These factors exacerbate the environment in which molecules are unable to remain in a monolayer due to electrostatic repulsion; this produces foam. Occasionally, foaming is transient and caused by a focal urination into water in a toilet. (See also Section IX: “Urinalysis and Urinary Studies.”)

TREATMENT

• Treat the underlying cause of proteinuria

• Qualitative dipstick analysis; 24-hr urine collection, renal workup

REFERENCES

URINE, ODOR

DESCRIPTION

Urinary odor is related to the volume, concentration, and composition of a variety of secreted chemicals and physiological contributions from the urinary system. Normally, urine ranges from odorless to mildly aromatic, often described as fruity or “urinous.” Changes in odor are often temporary and carry little prognostic indication; however, medical conditions can occasionally present with distinct urinary odors, as described below. (See also Section IV: “Urine Studies.”)

Condition Urine Odor

Diseases
Cystine decarboxylation, cystinuria
Sulfured
Dehydration
Strong
Diabetic ketoacidosis
Sweet, fruity odor
Enterovesicular fistula
Feculent
Retained urine
Ammonia-like
Sweaty urine disease
Ammonia-like
Maple syrup urine disease
Maple syrup
Glutaric and isovaleric acidemia
Fishy
Vomiting
Gastric and lower bowel acidosis
Sweaty feet, acrid
Hawkinsuria
Swimming pool
Hypertension
Boiled cabbage
Maple syrup-urea disease
Maple syrup
Multiple carboxylase deficiency
Tomcat urine
Oatmeal urine disease
Hops-like
Phenylketonuria
Musty, mousey
Timothy phytoliminuria
Rotten fish
Tyrosinemia
Boiled cabbage, rank odor

REFERENCES


URINE, PARTICLES IN DESCRIPTION

In the gross observation of particulate matter in the urine, differential diagnoses include infection (bacteria, fungi), enterocecal fistula (meso, fores, or undigested food particles), blood clots from hematuria of any cause, papillary necrosis, ATN, thyrotoxicosis, crystalluria, bilirubinuria (cholethrombosis), urinal or other carcinoma with sloughing tissue, clumping of excessive urinary cast or protein, postextensive ileg (i.e., ureteral material), or vaginal contamination. The condition can be a normal finding with any form of urinary diversion that uses a bowel segment (usually mucous or sloughed epithelium). Note that a urine sample left standing at room temperature may cause precipitation of phosphate salts. Urine samples that will not be analyzed immediately (<2 h) should be refrigerated. Curing of the specimen after addition of a small amount of acid indicates that precipitation of salts is the probable cause. (See also Section II: “Infectious.”)

REFERENCE


URINOMA (PERINEPHRIC PSEUDOCYST)

DESCRIPTION

A collection of urine outside the urinary tract (extravesical), commonly seen from rupture of the collecting system (usually calyceal rupture) due to high pressures from obstruction (stones, posterior urethral valves, stricture, others), postoperative surgical leak (lumbar anastomosis, collecting system issues, urethral anastomosis, etc.), or traumatic disruption of the urinary tract (iatrogenic, penetrating, or blunt). Leakage of urine into the perirenal or perinephric tissues in excess of an amount that can be absorbed results in urinoma formation. The urine causes lipolysis of surrounding fat, creating a fibrous sac around the extravasated urine. Perinephric pseudocyst is the term sometimes used for an urinoma that surrounds the kidney. The urinoma fluid’s creatinine level is typically elevated, indicating urine as the source. Urinoma must be distinguished from hematoma, abscess, or collections. Classically, the urinoma is thin-walled and smooth, and the walls tend to enhance secondary to inflammatory neoangiogenesis. In contrast, the walls of abscesses and hematomas tend to be thick and more irregular with even more prominent vascularity. Typically, urinomas demonstrate homogeneous. Hounsfield units between –10 and +30 HU, and hematomas and abscesses demonstrate heterogeneous Hounsfield units. Treatment is directed at correcting the cause (relief of obstruction, stenting, or repair of leak). Small urinomas will resolve spontaneously, and drainage is not necessary. If the urinoma is large, CT or MRI-guided drainage or aspiration can be performed in perineal urinomas due to trauma to the kidney, viability of the parenchyma must be assessed by contrast-enhanced CT. If no viable tissue components extend to the collecting system (suggestive of necrosis), there is an increased risk for continued urine leak and debridement is necessary. (See also Section I: “Renal Trauma,” AATB, and Image 40.)

REFERENCE


URINOTRACHIS

DESCRIPTION

Urinotrichus is rare and refers to the presence of urine in the pleural space. It usually occurs secondary to obstructive uropathy, from the leakage of urine into a perirenal or perinephric urinoma and then its passage into the pleural space directly or via lymphatics. Cases have been reported in the setting of interventions including percutaneous nephrostomy, ESWL, and others. It is classified as a transudate. The diagnosis can be confirmed by finding a pleural fluid-to-serum creatinine ratio >1 (often >10). Relief of obstruction causing the persisting urine leak and thoracoscopy or chest tube placement is therapeutic.

REFERENCE


URODYNAMICS, INDICATIONS AND NORMAL VALUES

DESCRIPTION

A series of investigational tests to assess lower urinary tract function. Usual components include uroflowmetry, cystometry, abdominal pressure monitoring, electromyography, and voiding pressure–flow studies. Through simultaneous measurement of bladder and abdominal pressures, the detrusor pressure can be inferred and used to interpret neuromuscular events during voiding. UOS can be used to identify contributing factors to voiding dysfunction and assess their relevance, predict consequences of that dysfunction on the upper tracts, to predict the consequences and outcomes of therapeutic intervention, to confirm or understand the effects of interventional techniques, and to investigate the reasons for treatment failure. See table for Normal UOS values in Adults (Image 60).

Common urodynamics Indications Include:

• Failure of empiric treatments
• Symptomatic voiding dysfunction prior to beginning incontinence therapy
• Inability to demonstrate incontinence clinically despite subjective patient complaints
• Significantly or obviously of proposed incontinence treatment course:
• Following prior surgical therapy for incontinence, following pelvic radiation or radical pelvic surgery
• Known or suspected neurologic disorder that may influence bladder function (i.e., spinal cord injury)
• Simpler diagnostic tests have been inconclusive

Normal UOS values in Adults:

• Volume Voids (ml): 338 ± 214
• Voiding Time (sec): 28 ± 22
• Max Flow (ml/sec): M 34 ± 10, W 30 ± 10
• Average Flow (ml/sec): M 14 ± 5, W 22 ± 14
• Maximum Capacity (ml): M 552 ± 152, W 453 ± 146
• Compliance (ml/cm water): M 56 ± 37, W 71 ± 40
• Postvoid Residual (ml): ≥ 20 ± 50

M: men; W: women.

REFERENCES


UROLITHIASIS, METHOTREXATE

DESCRIPTION
Methotrexate is an anti-folate used to treat a wide variety of diseases including: Cancer, rheumatoid arthritis, lupus, ectopic pregnancy, and psoriasis. More than 90% of the drug is cleared in the urine. Drug and its metabolites are poorly soluble in acidic pH and can precipitate crystalline formation and subsequent tubular obstruction. Medication can also lead to an increase in uric acid levels in the body. Extreme care with only a few reports of renal calculi to the FDA from using this medication. [See also Section I: “Urolithiasis, Adult General” and Section II: “Urolithiasis, Drug Induced.”]

TREATMENT
• Urine alkalinization
• Hydration to induce high urine flow rates

UROLITHIASIS, MELAMINE

DESCRIPTION
An increased incidence of kidney stones and renal failure recently reported in China are believed to be associated with ingestion of infant formula contaminated with melamine. Melamine (triaminocyanurate, melamine) has industrial use as a resin or adhesive, and has been deliberately added to casein milk to boost its protein content. Although the mechanism is not clear, melamine is almost completely excreted by the kidney and appears to interact with uric acid (to be produced or associated impurity) to form crystals. Low solubility promotes precipitation in renal tubules and causes progressive blockage and significant renal degeneration.

TREATMENT
• Immediately discontinue use of melamine containing food products.
• Medically monitor renal function, fluid balance, and electrolyte status.
• Alkalize the urine.
• Treat acute kidney injury (AKI if indicated) use blood or peritoneal dialysis.
• Consider surgical pyelolithotomy in refractory cases.

REFERENCES

UROLITHIASIS, METHOTREXATE

DESCRIPTION
Methotrexate is an anti-folate used to treat a wide variety of diseases including: Cancer, rheumatoid arthritis, lupus, ectopic pregnancy, and psoriasis. More than 90% of the drug is cleared in the urine. Drug and its metabolites are poorly soluble in acidic pH and can precipitate crystalline formation and subsequent tubular obstruction. Medication can also lead to an increase in uric acid levels in the body. Extreme care with only a few reports of renal calculi to the FDA from using this medication. [See also Section I: “Urolithiasis, Adult General” and Section II: “Urolithiasis, Drug Induced.”]

TREATMENT
• Urine alkalinization
• Hydration to induce high urine flow rates

UROLITHIASIS, INFECTIOUS (STRUVITE)

DESCRIPTION
Composite of magnesium, ammonium, and phosphate mixed with carbonate. Struvite stones directly correlate with the presence of urinary-producing bacteria and active UTI. Associated with a urinary pH of >7.2, which causes struvite crystallization. They usually undergo rapid growth and may result in replacement of the entire pelvis with a stone. (See also Section II: “Urolithiasis, Drug Induced.”)

CAUSES
• Foreign body in the urinary tract
• Neurogenic bladder
• Urinary diversion
• URTs
• Indwelling catheter

REFERENCE

UROLITHIASIS, MATRIX

DESCRIPTION
Also called matrix stone, matrix nephrolithiasis, or matrix calculus in the literature, this rare renal calculus has been described as being composed of coagulated mucoids with little crystalline component. Found mostly in individuals with infection due to urease-producing organisms such as Proteus, matrix calculus can be confused with uric acid calculi because they are radiopaque. Matrix calculus, however, are usually associated with alkaline urine from a U/I, whereas uric acid calculi usually form in acidic sterile urine. Standard treatment techniques such as ureteroscopy and lithotripsy are used. (See also Section I: “Urolithiasis, Adult General”)

REFERENCE

UROLITHIASIS, MELAMINE

DESCRIPTION
An increased incidence of kidney stones and renal failure recently reported in China are believed to be associated with ingestion of infant formula contaminated with melamine. Melamine (triaminocyanurate, melamine) has industrial use as a resin or adhesive, and has been deliberately added to casein milk to boost its protein content. Although the mechanism is not clear, melamine is almost completely excreted by the kidney and appears to interact with uric acid (to be produced or associated impurity) to form crystals. Low solubility promotes precipitation in renal tubules and causes progressive blockage and significant renal degeneration.

TREATMENT
• Immediately discontinue use of melamine containing food products.
• Medically monitor renal function, fluid balance, and electrolyte status.
• Alkalize the urine.
• Treat acute kidney injury (AKI if indicated) use blood or peritoneal dialysis.
• Consider surgical pyelolithotomy in refractory cases.

REFERENCES

UROLITHIASIS, METHOTREXATE

DESCRIPTION
Methotrexate is an anti-folate used to treat a wide variety of diseases including: Cancer, rheumatoid arthritis, lupus, ectopic pregnancy, and psoriasis. More than 90% of the drug is cleared in the urine. Drug and its metabolites are poorly soluble in acidic pH and can precipitate crystalline formation and subsequent tubular obstruction. Medication can also lead to an increase in uric acid levels in the body. Extreme care with only a few reports of renal calculi to the FDA from using this medication. [See also Section I: “Urolithiasis, Adult General” and Section II: “Urolithiasis, Drug Induced.”]

TREATMENT
• Urine alkalinization
• Hydration to induce high urine flow rates

UROLITHIASIS, INFECTIOUS (STRUVITE)

DESCRIPTION
Composite of magnesium, ammonium, and phosphate mixed with carbonate. Struvite stones directly correlate with the presence of urinary-producing bacteria and active UTI. Associated with a urinary pH of >7.2, which causes struvite crystallization. They usually undergo rapid growth and may result in replacement of the entire pelvis with a stone. (See also Section II: “Urolithiasis, Drug Induced.”)

CAUSES
• Foreign body in the urinary tract
• Neurogenic bladder
• Urinary diversion
• URTs
• Indwelling catheter

REFERENCE

UROLITHIASIS, MATRIX

DESCRIPTION
Also called matrix stone, matrix nephrolithiasis, or matrix calculus in the literature, this rare renal calculus has been described as being composed of coagulated mucoids with little crystalline component. Found mostly in individuals with infection due to urease-producing organisms such as Proteus, matrix calculus can be confused with uric acid calculi because they are radiopaque. Matrix calculus, however, are usually associated with alkaline urine from a U/I, whereas uric acid calculi usually form in acidic sterile urine. Standard treatment techniques such as ureteroscopy and lithotripsy are used. (See also Section I: “Urolithiasis, Adult General”)

REFERENCE

UROLITHIASIS, MELAMINE

DESCRIPTION
An increased incidence of kidney stones and renal failure recently reported in China are believed to be associated with ingestion of infant formula contaminated with melamine. Melamine (triaminocyanurate, melamine) has industrial use as a resin or adhesive, and has been deliberately added to casein milk to boost its protein content. Although the mechanism is not clear, melamine is almost completely excreted by the kidney and appears to interact with uric acid (to be produced or associated impurity) to form crystals. Low solubility promotes precipitation in renal tubules and causes progressive blockage and significant renal degeneration.

TREATMENT
• Immediately discontinue use of melamine containing food products.
• Medically monitor renal function, fluid balance, and electrolyte status.
• Alkalize the urine.
• Treat acute kidney injury (AKI if indicated) use blood or peritoneal dialysis.
• Consider surgical pyelolithotomy in refractory cases.

REFERENCES

UROLITHIASIS, METHOTREXATE

DESCRIPTION
Methotrexate is an anti-folate used to treat a wide variety of diseases including: Cancer, rheumatoid arthritis, lupus, ectopic pregnancy, and psoriasis. More than 90% of the drug is cleared in the urine. Drug and its metabolites are poorly soluble in acidic pH and can precipitate crystalline formation and subsequent tubular obstruction. Medication can also lead to an increase in uric acid levels in the body. Extreme care with only a few reports of renal calculi to the FDA from using this medication. [See also Section I: “Urolithiasis, Adult General” and Section II: “Urolithiasis, Drug Induced.”]

TREATMENT
• Urine alkalinization
• Hydration to induce high urine flow rates
DESCRIPTION

REFERENCES

VAGINAL DISCHARGE, UROLOGIC CONSIDERATIONS
DESCRIPTION
Fluid flowing from the vaginal opening, which can be physiologic or pathologic. Timing, color, consistency, odor, and associated symptoms are all important aspects of the evaluation. (See also Section I: “Vaginitis/vulvovaginitis” and Section III: “Vaginal Discharge Algorithm.”)

CAUSES
• Noninfective: Physiologic uterine sloughing, cervical ectopy, retained foreign bodies (eg, tampon), vulval dermatitis, urethral diverticulum, sexual abuse
• Noninfectively transmitted: Bacterial vaginosis, candida infection
• Sexually transmitted infection: C. trachomatis, N. gonorrhoeae, other gonococcal vaginitis (Image 40)

REFERENCES

VAGINAL DUPLICATION
DESCRIPTION
A rare abnormality in embryologic development that results in duplication of the vagina. It is caused by failure of a primitive septum in the urovesical canal to regress or by abnormalities in the fusion of paraxial mesenchymic ducts during wk 6–9 of embryologic development of the upper vagina. The lower vagina develops from the urogenital sinus when the urovesical bulbs fuse. Abnormalities in the fusion can result in different vaginal abnormalities, including duplication. Presenting symptoms can include dysmenorrhea at menarche or a lower abdominal mass. Surgical correction of the septum is the treatment of choice for vaginal duplication.

REFERENCES
VAGINAL FUSION

DESCRIPTION
A congenital defect of the vagina may occur if the fusion of the labia minora is incomplete. This is often observed as a small opening at the external os of the cervix. Surgery is usually required to repair the defect.

REFERENCE

VAGINAL MASS, NEWBORN

DESCRIPTION
Rare intravaginal or perineal lesions are found in young girls, each with strikingly similar gross appearances; among the different etiologies listed below. Clinical exam should note exact location of lesion, urethral location, and urine flow. Workup depends on exam, although voiding cystourethrography is usually warranted.

CAUSES
- Hydroepidermis (separate hymen)
- Paracolpial cyst
- Prolapsed ectopic uretercele
- Rhombomeroepithelium of the vagina
- Urethral polyp
- Urethral prolapse

REFERENCE

VAGINAL PESSARIES, UROLOGIC CONSIDERATIONS

DESCRIPTION
A pessary intravaginal device is used to maintain the correct anatomic position of the pelvic organs and aid in urinary continence. The overall prevalence of incontinence in individuals >65 is ~30%. Pessaries provide a noninvasive management option for that subset of patients with stress urinary incontinence (SUI). Despite a wide range in published results, when combined with pelvic floor muscle rehabilitation (ie, Kegel exercise, biofeedback), pessary use may improve symptoms 50-75% of the time. This may be used as a final treatment in patients at high operative risk, or as a bridge to surgical correction of pelvic floor dysfunction.

REFERENCE

VAGINAL PROLAPSE

DESCRIPTION
Disruption of the neuromuscular, fascial, or fascial components involved in normal vaginal support, resulting in the externalization of a portion of the vaginal canal. Despite a complex anatomic framework, several key anatomic anomalies may play a role in this condition. As well, theologic anomalies are associated with inguinopelvic and femoroanterior associations in children. Posterior surgery involves the use of the posterior vaginal wall, while anterior surgery involves the anterior vaginal wall. Patients may report symptoms of stress urinary incontinence or low back pain. Diagnosis is made by examination, with further imaging as needed. The patient may be treated with a pessary, or as an acute measure, with pelvic floor muscle rehabilitation. Treatment options include: sling, mesh, and vaginal repair. The choice of treatment should be individualized, with consideration of patient age, parity, and comorbidities.

REFERENCE

VAGINOSIS

DESCRIPTION
The most common type of vaginal infection, resulting from an imbalance between the standard vaginal flora (Lactobacillus spp.) and the pessaries of the body. Many different types of pathogens have been identified, including Streptococcus, Enterococcus, and Mycoplasma. Symptoms include a foul or “fishy” odor, milky white or gray discharge, and vaginal irritation especially prominent after sex. Diagnosis can be confirmed by elevated vaginal pH (>4.5), a positive “whiff test” malodorous/fishy odor when secretions are mixed with 10% potassium hydroxide. Successful treatment is associated with restoration of normal vaginal flora and subsequent improvement in symptoms.

REFERENCE

VALSALVA MANEUVER

DESCRIPTION
A maneuver affected by a forced expiratory effort against a voluntarily closed airway, which causes increased intrathoracic and intra-abdominal pressure and impairs venous return to the right atrium. The maneuver may increase the risk of either avulsion or ureteral injury during surgical correction (11%) and postoperative association with 3% mortality. The pelvic anatomy is restored. (See also Section I: “Pelvic Prolapse” (Cystocele and Enterocele).)

- Cystocele (bladder into vagina)
- Enterocele (small intestine into vagina)
- Rectocele (rectum into vagina)
- Urethrocele (urethra into vagina)
- Uterine prolapse (uterus into vagina)
- Vaginal vault prolapse (vaginal roof through vaginal)

TREATMENT
- Abdominal sacrocolpopexy: Anterior and posterior grafts bridging vaginal wall to the sacral promontory via an abdominal incision
- Vaginal vault suspension: Apogee system (artificial suspension of the cardinal ligaments)
- Intravaginal sling. Polypropylene sling (synthetic material) or synthetic slings (cesareal supply)
- Sacropinous fixation: Elevation and fixation of vaginal apex to sacrospinous ligaments
- Robotic or vaginal hysterectomy: Vaginal incision and fixation to surrounding structures

REFERENCE

VALSALVA MANEUVER

DESCRIPTION
A maneuver affected by a forced expiratory effort against a voluntarily closed airway, which causes increased intrathoracic and intra-abdominal pressure and impairs venous return to the right atrium. The maneuver may increase the risk of either avulsion or ureteral injury during surgical correction (11%) and postoperative association with 3% mortality. The pelvic anatomy is restored. (See also Section I: “Pelvic Prolapse” (Cystocele and Enterocele).)

- Cystocele (bladder into vagina)
- Enterocele (small intestine into vagina)
- Rectocele (rectum into vagina)
- Urethrocele (urethra into vagina)
- Uterine prolapse (uterus into vagina)
- Vaginal vault prolapse (vaginal roof through vaginal)

TREATMENT
- Abdominal sacrocolpopexy: Anterior and posterior grafts bridging vaginal wall to the sacral promontory via an abdominal incision
- Vaginal vault suspension: Apogee system (artificial suspension of the cardinal ligaments)
- Intravaginal sling. Polypropylene sling (synthetic material) or synthetic slings (cesareal supply)
- Sacropinous fixation: Elevation and fixation of vaginal apex to sacrospinous ligaments
- Robotic or vaginal hysterectomy: Vaginal incision and fixation to surrounding structures

REFERENCE

VALSALVA MANEUVER

DESCRIPTION
A maneuver affected by a forced expiratory effort against a voluntarily closed airway, which causes increased intrathoracic and intra-abdominal pressure and impairs venous return to the right atrium. The maneuver may increase the risk of either avulsion or ureteral injury during surgical correction (11%) and postoperative association with 3% mortality. The pelvic anatomy is restored. (See also Section I: “Pelvic Prolapse” (Cystocele and Enterocele).)

- Cystocele (bladder into vagina)
- Enterocele (small intestine into vagina)
- Rectocele (rectum into vagina)
- Urethrocele (urethra into vagina)
- Uterine prolapse (uterus into vagina)
- Vaginal vault prolapse (vaginal roof through vaginal)

TREATMENT
- Abdominal sacrocolpopexy: Anterior and posterior grafts bridging vaginal wall to the sacral promontory via an abdominal incision
- Vaginal vault suspension: Apogee system (artificial suspension of the cardinal ligaments)
- Intravaginal sling. Polypropylene sling (synthetic material) or synthetic slings (cesareal supply)
- Sacropinous fixation: Elevation and fixation of vaginal apex to sacrospinous ligaments
- Robotic or vaginal hysterectomy: Vaginal incision and fixation to surrounding structures

REFERENCE
VASCULITIS, UROLOGIC CONSIDERATIONS

Description: Vasculitis is a common reaction to injury or caused by a multitude of different processes, including autoimmunity, infection, and hypersensitivity. Vasculitis can be divided into types depending on the vessel affected: Henoch-Schönlein purpura, PAN, hypersensitivity angiitis, Wegener granulomatosis, and lymphomatoid granulomatis.

A very strong correlation exists between the presence of anti-neutrophil cytoplasmic antibodies (ANCA) and the various types of systemic vasculitis, including autoimmunity, infection, and hypersensitivity. Depending on the type of vasculitis, patients present with different signs and symptoms. For example, some types can progress to chronic renal failure. However, upon renal biopsy, similar pathologic presentations are demonstrated. Can also result in renal hemorrhage. (See also Section II: “Henoch-Schönlein Purpura”)

Treatment:

- Abnormalities have proved to be extremely useful in the management of these patients. They are a help in diagnosis, and even more important as a guide to maintenance immunosuppressive therapy.
- Cysticercosis agents and cysticercoid are effective, depending on the type of vasculitis.


VASECTOMY REVERSAL, GENERAL CONSIDERATIONS (VASOVASOSTOMY)

Description: Usually accomplished with a 2-layer microsurgical vasovasostomy (9:10-0 nylon mucosal sutures, 9:0-0 nylon muscular sutures). Although surgical reversal of vasovasostomy can be technically performed on most patients, operative decision-making requires preoperative urologic and fertility evaluation of the female partner should be performed. Epididymal or testicular sperm aspiration combined with IVF/ICSI should be discussed. Results with microsurgical repair reach 85–90% success (appearing in semen), with postprocedural conception rates at 50–70%.

Treatment:

- Vasovasostomy (when sperm component of sperm are present, grade 1–4 vas fluid)
- Vasopexy/vasovasostomy (when no sperm are present in vas fluid)
- Postoperative scrotal support with abstention for 2 w


VASEOGRAPHY, TECHNIQUE AND INDICATIONS

Description: Vasography is the radiologic procedure used to evaluate patency of the vas deferens and ejaculatory ducts. The procedure involves injection of the contrast material into the vas deferens. Currently, seminal vesicle aspiration and vasography are originally replaced with microsurgery for the diagnosis of ESDO. Therefore, the primary indication for vasography is the assessment of vasal obstruction within the inguinal vas deferens. Infravesical obstruction of the vas deferens should be suspected in patients with azoospermia and previous surgeries, including orchietomy, hernia repair, vesicovaginal, and even appendectomy (iatrogenic injuries to the vas deferens). 4 techniques for vasovasostomy have been described: Vascupuncture, vasectomy, retrograde catheterization via cystoscopy and transvesical puncture. Isolated vasography (by vas puncture) is rarely performed because of the risk of subsequent scarring. It is usually a part of microsurgical reconstructive procedure. For this reason, it is not indicated to perform vasography at the time of testicular biopsy with the findings of normal spermatogenesis. If open vasography is planned, the bladder should be catheterized with a Foley catheter and balloon inflated with air to outline the bladder neck area. After crosstech exploration, the vas deferens is identified and isolated at the junction of the straight and convoluted portions. Under the operating microscope, the vasal sheath is isolated vertically and visual vessels preserved. A short segment of the sheath is excised and hemostasis is obtained using a 10-0 prolene suture. After a short distance of the sheath is excised and hemostasis is obtained using a 10-0 prolene suture. After a short distance of the sheath is excised and hemostasis is obtained using a 10-0 prolene suture.
DESCRIPTION
A technique in which urodynamic studies are performed at the same time as fluoroscopy of the lower urinary tract. The cystometry and pressure-flow studies are conducted in the same manner as regular urodynamics. The only difference is the addition of contrast and fluoroscopy. Radiation exposure is usually limited to <20 s. Adding simultaneous video enhances the evaluation of all patients, especially for more complex urodynamics problems. Videourodynamics is helpful when results from simple urodynamics do not agree with the clinical scenario. In complex bladder outlet obstruction, this technique can identify whether it occurs at the bladder neck, prostatic urethra, or distal sphincter. It is also helpful in the identification of bladder neck dysfunction in young men with voiding problems and in neuromuscular patients with dysmegacephaly of the distal sphincter. In incontinence evaluation, videourodynamics can help identify the presence and degree of vesical neck hypermobility, degree of proximal urethral weakness, and degree and type of cystocole present. In neuromuscular bladders, simultaneous video screening aids in diagnosing proximal and distal sphincter dysynergia and demonstrates the presence of reflux and bladder diverticula. The presence of reflux, bladder and urethral diverticula, fistula, and stones can be identified and characterized. (See also Section II: “Urodynamic.”)

VITILIGO, UROLOGIC CONSIDERATIONS

DESCRIPTION
A depigmentation of the skin in which sharply bordered patches become white. This is distinct from postinflammatory skin depigmentation in that there is no preceding inflammatory process. The etiology is probably autoimmune, and it is estimated to involve the outer germinative only in 10% of the adult male population. Treatment is optional and can include tetracycline, UV light, skin grafting, and cosmetic covering.

REFERENCES

TREATMENT
- Surgical correction
- Combination of pharmacologic injection therapy with a venous constriction system or a vacuum device

REFERENCE

VESICULOBULLOUS LESIONS, EXTERNAL GENITALIA

DESCRIPTION
Bullous lesions on the external genitalia mandate screening for STIs/STDs. They may be painful or painless, single or multiple, exophytic or ulcerated, confined to the genitália or occurring elsewhere on the body. Treatments vary widely based on etiology, and may require partner treatment in the case of STIs. (See also Section II: “Penis, Lesion, General”; “Sexually Transmitted Disease.”)

REFERENCE

VILEUS ADENOMA, BLADDER/URETHRA

DESCRIPTION
Villus adenomas of the bladder and urethra are rare and historically identical to those found in the colon. These tumors are more frequently found in the urethra at the dome of the bladder. On cystoscopy, these villous adenomas appear as exophytic papillary masses. Histologically, villous adenomas are composed of papillary structures lined by a pseudostratified epithelium containing goblet cells. Often, this tumor is associated with cystitis glandularis. Villous adenoma of the urethra has been reported in both males and females. In males, villous adenoma may be associated with urethral stricture, hematamia, and difficulty in micturition. In females, it may be less symptomatic and present with a slowly growing mass in the urethra. When villous adenomas are found, a primary intestinal tumor must be ruled out. After resection of the adenoma, the patient must be followed for recurrence or malignancy because their behavior is unpredictable. Diagnosis is made with urine cytology, cystoscopy, cystoscopy, or biopsy. Treatment is transurethral resection with selective cryotherapy.

REFERENCE

VIMENTIN, STAINING

DESCRIPTION
Monoclonal antibodies can be used to identify cell products or surface markers by directing antibodies against intermediate filaments. This facilitates the classification of otherwise poorly differentiated tumors. Vimentin is the predominant intermediate filament in mesenchymal cells, and it is found in all fibroblasts. Vimentin is less specific than the other intermediate filaments in immunocytochemistry because certain epithelial tumors (eg, RCC) may coexpress keratin and vimentin. (See also Section II: “Immunohistochemical Staining, Urologic Considerations.”)

REFERENCE

VINCENT CURTSY

DESCRIPTION
Holding maneuver used by children to postpone voiding or suppress urinary urgency. Vincent curtsy is performed by squating with a hand or heel pressed firmly into the perineum. Other common holding maneuvers including standing on tip-toe or forcible crossing of the legs (Image 6).

REFERENCE

VITILIGO, UROLOGIC CONSIDERATIONS

REFERENCE
ABRAMS P, CARDozo L, FALL M, ET AL. THE ICS IN 2002 PUBLISHED UPDATED GUIDELINES TO DEFINE AND CATEGORIZE LUTS INTO PATIENT-OVER A REPRESENTATIVE 24-HR PERIOD, TYPICALLY DOCUMENTS THE FOLLOWING:

- Time of urge to void
- Strength of urge or pain
- Time of actual void
- Voided volume
- Incontinence stress, urge, or unanne
- Amount of leakage small, medium, large

(VS. SECTION III: “VOIDING DIARY.”)

REFERENCE

VOIDING SYMPTOMS, DEFINITIONS (ICS DEFINITIONS)
DESCRIPTION
The ICS in 2002 published updated guidelines to define and categorize LUTS into 3 main groups including storage, voiding, and postmiction, as defined and subclassified here:

- Storage symptoms are experienced during storage phase of bladder:
  - Increased day-time frequency
  - Nocturia: Complaint that individual wakes up 1–2 times per night
  - Urgency: Complaint of sudden compelling desire to void
  - Training: Complaint of inability to control urine

- Voiding symptoms are experienced during voiding phase:
  - Slow stream
  - Splattering or spraying of urine stream
  - Intermittency during micturition
  - Hesitancy: Term used when individual has difficulty initiating micturition, resulting in a delay in the onset of voiding

- Postmiction symptoms are experienced immediately after miction:
  - Feeling of incomplete emptying
  - Postmiction dribble describes the involuntary loss of urine after the patient finishes passing urine.

REFERENCE

VOIDING DIARY FREQUENCY VOLUME CHART (FVC)
DESCRIPTION
A tool often used in association with pad testing to document the nature and severity of incontinence. A data sheet, maintained by the patient over a representative 24-hr period, typically documents the following:

- Voided volume
- Incontinence stress, urge, or unanne
- Amount of leakage small, medium, large

VOIDING SYMPTOMS, DEFINITIONS (ICS DEFINITIONS)
DESCRIPTION
The ICS in 2002 published updated guidelines to define and categorize LUTS into 3 main groups including storage, voiding, and postmiction, as defined and subclassified here:

- Storage symptoms are experienced during storage phase of bladder:
  - Increased day-time frequency
  - Nocturia: Complaint that individual wakes up 1–2 times per night
  - Urgency: Complaint of sudden compelling desire to void
  - Training: Complaint of inability to control urine

- Voiding symptoms are experienced during voiding phase:
  - Slow stream
  - Splattering or spraying of urine stream
  - Intermittency during micturition
  - Hesitancy: Term used when individual has difficulty initiating micturition, resulting in a delay in the onset of voiding

- Postmiction symptoms are experienced immediately after miction:
  - Feeling of incomplete emptying
  - Postmiction dribble describes the involuntary loss of urine after the patient finishes passing urine.

REFERENCE

VULVAR MALIGNANCY, UROLOGIC CONSIDERATIONS
DESCRIPTION
Vulvar carcinoma encompasses any malignancy that arises in the skin, glands, or underlying strata of the perineum, including the mons pubis, labia minora, labia majora, Bartholin glands, or clitoris. Early detection lesions (<2 cm) are critical for local control without nodal dissection. Patients presenting late in the course of disease may require radical en bloc resection of the tumor and surrounding organs. Known as pelvic exenteration. Total exenteration refers to removal of the uterus, tubes, ovaries, peritoneum, bladder, rectum or rectal segment, vagina, urethra, and a portion of the levator muscles. In an anterior exenteration, the rectum is spared, whereas in a posterior exenteration, the bladder and urethra are preserved. Urinary diversion (usually a continent catheterizable pouch) will be provided by the urologist as a portion of the pelvic reconstruction.

REFERENCE

WAGR SYNDROME (WILMS TUMOR-ANIRidia-GENital ANOMALY RETARDATION)
DESCRIPTION
WAGR syndrome is one of the Wilms tumor-associated syndromes, presenting in children <5 yr. It causes mental retardation and GU manifestations in the form of renal hypoplasia, ectopia, sacs, duplications, cystic disease, hypoplasia, cryptorchidism, and pelvic malformation. Physical exam may also reveal ear deformities, unicorneal palpebral, and anidria.

REFERENCE

WALLACE URETERAL ANASTOMOSIS
DESCRIPTION
A surgical procedure used in urinary diversion in which the ipsilateral ureter is laid adjacent and the apex of each is sutured to the other. The medial and lateral walls of the ureters are then sutured together in either an interrupted or running fashion. The Y configured ureters are then anastomosed to the end of the bowel segment used for the reservoir.

REFERENCE

WALTER REED STAGING SYSTEM, TESTIS CANCER
DESCRIPTION
Lymphangiographic criteria are used to evaluate the present and location of testicular neoplasm metastases. The following lymphangiographic patterns were found to be useful in assessing metastatic disease: filling defects, lymph node enlargement and masses, lymphatic obstruction and collateral vessel formation, and an increase or decrease in the number of lymph nodes.

REFERENCE
Nakao K, Scherer DJ. The role of lymphography in the diagnosis and treatment of malignant testicular tumors. AJR. 1972;114:482.

WATERHOUSE URETERAL STRicture REPAIR
DESCRIPTION
Through a combined abdominal and perineal approach, a wedge of pubis is resected with a Gigli saw. The membranous structure is identified and excised. The distal urethra is mobilized off the corporal bodies, and the pubicated urethral edges are reapproximated.

REFERENCE

**WATERHOUSE–FRIDERICHS LUMBAR SYNDROME**

**DESCRIPTION**
Acute adrenocortical insufficiency in infants suffering from septicaemia with *Pseudomonas* or *Meningococcus*, leading to acute hemorrhagic destruction of both adrenal glands.

**REFERENCE**

**WEDDELLITITE**

**DESCRIPTION**
Mineralogic name for renal calculi composed of calcium oxalate dihydrate. (See Section I: "Urolithiasis, Calcium Oxylate/Phosphate.")

**REFERENCE**

**WHHEWELLITE**

**DESCRIPTION**
Mineralogic name for renal calculi composed of calcium oxalate monohydrate. (See also: Section I: "Urolithiasis, Calcium Oxylate/Phosphate.")

**REFERENCE**

**WHITEHURST**

**DESCRIPTION**
An antegrade pressure–flow study to assess for renal obstruction. It is used to determine if polycystic or hydronephrotic urothelial Caix scroptography represents functional obstruction or anatomic dilation. This is a technically difficult, invasive test, requiring placement of a percutaneous antegrade catheter into the renal pelvis, with simultaneous monitoring of bladder and renal pelvic pressures during set flow rate of 10 mL/min. Evaluation of renal pelvic pressure over bladder pressure indicates some degree of renal obstruction. A Foley catheter must be in the bladder.

**SYNONYMS**

- Urologic antegrade pyelogram
- Intravenous pyelography
- Voiding cystourethrogram

**REFERENCE**

**WHITLOCKITE**

**DESCRIPTION**
Mineralogic name for renal calculi composed of tricalcium phosphate. (See Section II: "Urolithiasis, Calcium Oxylate/Phosphate.")

**REFERENCE**

**WHO 2004 HISTOLOGIC CLASSIFICATION OF TUMORS OF THE URINARY TRACT**

**UROTHELIAL NEOPLASMS**

**TUMORS OF THE URINARY TRACT**

**CLASSIFICATION OF TUMORS**

**WHO 2004 Histologic Classification of Tumors of the Urinary Tract**

**Urothelial Tumors**

- Infiltrating urothelial carcinoma
  - with squamous differentiation
  - with glandular differentiation
  - with trophoblastic differentiation

**Nodular**

- Microcystic
- Micropapillary
- Angiomyofibroblastoma

- Hemangiopericytoma

**Malignant melanomas**

- Nodular
- Lymphomatous
- Malignant melanoma

**Mesenchymal tumors**

- Rhabdomyosarcoma
- Leiomyosarcoma
- Angiosarcoma
- Leiomyoma

**Miscellaneous tumors**

- Carcinoma of Skene, Cowper and Little glands
- Metastatic tumors from other organs

**OTHER UROTHELIAL NEOPLASMS**

- Adenocarcinoma
- Sarcoma

**REFERENCES**


**DESCRIPTION**
At a consensus conference of the World Health Organization (WHO) and the International Society of Urologic Pathologists (ISUP) in 1998, the WHO/ISUP classification of urothelial neoplasms of the bladder was developed. The innovations of this consensus included the elimination of grades of dysplasia, with high-grade dysplasia equated with carcinoma in situ, as well as a condensation of cytologic grading of urothelial carcinoma (ie, grades 1–3) to low- and high-grade carcinoma. In addition, a new entity was recommended for low-grade papillary lesions, entitled papillary urothelial neoplasms of low-malignant

**REFERENCE**

**WHO 2004 Histologic Classification of Tumors of the Urinary Tract**

**Urothelial Tumors**

- Infiltrating urothelial carcinoma
- with squamous differentiation
- with glandular differentiation
- with trophoblastic differentiation

**Nodular**

- Microcystic
- Micropapillary
- Angiomyofibroblastoma

- Hemangiopericytoma

**Malignant melanomas**

- Nodular
- Lymphomatous
- Malignant melanoma

**Mesenchymal tumors**

- Rhabdomyosarcoma
- Leiomyosarcoma
- Angiosarcoma
- Leiomyoma

**Miscellaneous tumors**

- Carcinoma of Skene, Cowper and Little glands
- Metastatic tumors from other organs

**OTHER UROTHELIAL NEOPLASMS**

- Adenocarcinoma
- Sarcoma

**REFERENCES**


**DESCRIPTION**
At a consensus conference of the World Health Organization (WHO) and the International Society of Urologic Pathologists (ISUP) in 1998, the WHO/ISUP classification of urothelial neoplasms of the bladder was developed. The innovations of this consensus included the elimination of grades of dysplasia, with high-grade dysplasia equated with carcinoma in situ, as well as a condensation of cytologic grading of urothelial carcinoma (ie, grades 1–3) to low- and high-grade carcinoma. In addition, a new entity was recommended for low-grade papillary lesions, entitled papillary urothelial neoplasms of low-malignant
WILMS TUMOR STAGING SYSTEM, INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY (SIOP)

WINTER CORPORAL SHUNT

DESCRIPTION: A shunt between the corpora and glans penis created to treat priapism. A Tru-Cut biopsy needle is inserted through the tip of the glans and into the corpora, and a core of tissue is removed. Through the same glans puncture site, the Tru-Cut can be reinserted in order to create 2 fistulas at the end of both corpora. It is also referred to as a percutaneous glanducavernous shunt.


WOLFFIAN DUCT REMNANTS

DESCRIPTION: Normally, an embryo develops 2 sets of paired (mullerian and wolfian) mesonephric ducts. In females, obliteration of the mullerian system fails to occur, and wolfian vestiges may persist as the epididymis, ductus deferens, ejaculatory duct, and seminal vesicles. The normal end of the wolfian duct occasionally persists as a vesical remnant, the appendix epididymis. Remnants of the mesonephric tubules may persist as a spinal structure, the paradidymis. See also Section I: “Torsions, Testicular Appendages.”


REFERENCES

A unified system developed to aid the conduct of clinical trials now widely used for clinical staging treatment decisions (see table). The National Wilms Tumor Study (NWTS) system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the United States and Canada (see table below). (See also Section I: “Wilms tumor”; Section II: “Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP).”

REFERENCES

Bilateral renal tumors at initial diagnosis


REFERENCES

Diffuse peritoneal contamination by the tumor

REFERENCE: A shunt between the corpora and glans penis created to treat priapism. A Tru-Cut biopsy needle is inserted through the tip of the glans and into the corpora, and a core of tissue is removed. Through the same glans puncture site, the Tru-Cut can be reinserted in order to create 2 fistulas at the end of both corpora. It is also referred to as a percutaneous glanducavernous shunt.


REFERENCES

A unified system developed to aid the conduct of clinical trials now widely used for clinical staging treatment decisions (see table). The National Wilms Tumor Study (NWTS) system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the United States and Canada. The SIOP system is based upon postchemotherapy surgical evaluation and is used extensively in Europe. (See also Section I: “Wilms tumor”; Section II: “Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP).”

REFERENCES

A shunt between the corpora and glans penis created to treat priapism. A Tru-Cut biopsy needle is inserted through the tip of the glans and into the corpora, and a core of tissue is removed. Through the same glans puncture site, the Tru-Cut can be reinserted in order to create 2 fistulas at the end of both corpora. It is also referred to as a percutaneous glanducavernous shunt.


REFERENCES

A unified system developed to aid the conduct of clinical trials now widely used for clinical staging treatment decisions (see table). The National Wilms Tumor Study (NWTS) system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the United States and Canada. The SIOP system is based upon postchemotherapy surgical evaluation and is used extensively in Europe. (See also Section I: “Wilms tumor”; Section II: “Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP).”

REFERENCES

A unified system developed to aid the conduct of clinical trials now widely used for clinical staging treatment decisions (see table). The National Wilms Tumor Study (NWTS) system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the United States and Canada (see table below). (See also Section I: “Wilms tumor”; Section II: “Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP).”

REFERENCES

A unified system developed to aid the conduct of clinical trials now widely used for clinical staging treatment decisions (see table). The National Wilms Tumor Study (NWTS) system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the United States and Canada. The SIOP system is based upon postchemotherapy surgical evaluation and is used extensively in Europe. (See also Section I: “Wilms tumor”; Section II: “Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP).”

REFERENCES
SYNONYMS
- Parke-Davis
- Aspergilliosis

REFERENCE

WOUND DEHISCENCE, UROLOGIC CONSIDERATIONS
DESCRIPTION
Development of a postoperative gap or deficit in the peritoneal suture line, with or without extravasation. Prevalence is in 1–3% of patients and carries a risk of mortality as high as 44%. Risk factors include anemia, hypobulinemia, advanced age, male gender, chronic lung disease, malnutrition, wound infection, and emergent procedure. Surgical variables include suture type, use of prosthetic material, incision location, hypothermia, perfusion, and oxygenation. Primary repair of initial dehiscence carries a 96% success rate with sutures and/or re-tensions, whereas the use of an interposition mesh confers an initial 100% success rate.

REFERENCE

WOUND INFECTION, POSTOPERATIVE, UROLOGIC CONSIDERATIONS
DESCRIPTION
Surgical site infections and postoperative UTIs are common causes of patient morbidity, complicating 5% and 20% of clean cases, respectively. Patient-related risk factors include advanced age, anatomic urinary anomalies, poor nutrition, tobacco use, corticosteroid use, immunodeficiency, diabetes, insulin-dependent pregnancy, diabetes, candidiasis, vaginal infection, prolonged hospitalization. The need for perioperative antimicrobial prophylaxis has been well documented. Antibiotics should be given within 60 min of procedure start time, and selected based on patient history, as well as an anticipated procedure. (See Section II: “Propylptic Antibiotics, AUA Guidelines.”) Treatment for wound infection is summarized below.

REFERENCE

KANTHOGRAMMATOSIS (ERDHEIM-CHESTER DISEASE)
DESCRIPTION
Erdheim-Chester disease is a rare non-Langerhans form of histiocytosis with a poor prognosis. This disease occurs most commonly in patients older than 50 presenting with xanthoma-like skin nodules and bilateral lower limb bone pain. Most disseminated forms of the disease can have renal failure caused by retromental and perirenal infiltrative or constrictive changes. These patients can also have cardiopulmonary insufficiency and CNS involvement and may have a progressive and fatal disease. The pathophysiology is limited with established treatments.

REFERENCE

KANTHOMA, BLADDER
DESCRIPTION
Collection of foamy histocytes found in the lamina propria in patients with disorders of lipid metabolism.

REFERENCE

X-LINKED SPINAL AND BULBAR ATROPHY SYNDROME (KENNEDY SYNDROME)
DESCRIPTION
Kennedy syndrome is a late-onset, bulbopspinal type of muscular atrophy. There is an X-linked recessive inheritance genetic marker CAAG repeat sequences in the androgen receptor gene (Xq28). The majority of evidence of androgen sensitivity is inherited to exaggerated or persistent adolescent gynecomastia, and the mildly high LH, testosterone, and estradiol levels characteristic of other forms of androgen insensitivity. The condition becomes prominent in the 4th–5th decades, with proximal muscle weakness and wasting; bulbar signs; fasciculations in skeletal muscles; subtle signs of endocrine dysfunction, such as diabetes, gynecomastia, or testicular atrophy, and oligospermia. The progression is very slow, and these patients can expect a normal lifespan; it is essential to distinguish this syndrome from other, often more severe neurologic diseases.

REFERENCE

XXY SYNDROME
SYNONYMS
- Klinefelter’s

REFERENCE
Albi G, del Campo L, Tagarro D. Wunderlich syndrome: Kennedy syndrome is a late-onset, bulbopspinal type of muscular atrophy. There is an X-linked recessive inheritance genetic marker CAAG repeat sequences in the androgen receptor gene (Xq28). The majority of evidence of androgen sensitivity is inherited to exaggerated or persistent adolescent gynecomastia, and the mildly high LH, testosterone, and estradiol levels characteristic of other forms of androgen insensitivity. The condition becomes prominent in the 4th–5th decades, with proximal muscle weakness and wasting; bulbar signs; fasciculations in skeletal muscles; subtle signs of endocrine dysfunction, such as diabetes, gynecomastia, or testicular atrophy, and oligospermia. The progression is very slow, and these patients can expect a normal lifespan; it is essential to distinguish this syndrome from other, often more severe neurologic diseases.

REFERENCE

XX YONOMYS
REFERENCE

XX MALE REVERSAL SYNDROME (XX MALE)
DESCRIPTION
A rare disorder of phenotypic males who have a 46, XX karyotype. Physical exam may reveal short stature; small, firm testes, a small to normal-sized penis; hypogonadism, and gynecomastia. Azospermia is typical. Seminiferous tubule sclerosis can be shown on testicular biopsy. Lab investigation reveals high gonadotropin levels and decreased testosterone levels. In most cases, other fragments from the short arm of the Y chromosome can be detected in the distal and the short arm of the X chromosome.

REFERENCE

XX SYNDROME (TRIPLE X SYNDROME, TRIPLO-X)
DESCRIPTION
Triplet X chromosome abnormalities occur in 1–2:10,000 newborn females. There are no specific diagnostic features. Mental irregularities and mental retardation have been reported. Fertility is usually preserved, and many XXX females have normal offspring.

REFERENCE

XX SYNDROME
DESCRIPTION
Rare variant of Klenefer syndrome (47, XXXY) with an additional X chromosome (48, XXXY). Phenotype is similar to 47, 48, XXXY
XXY SYNDROME (KLINEFELTER SYNDROME)

XXY with more pronounced features; these patients frequently exhibit microphalia, hypogonadotropic hypogonadism, and gynecomastia. They are infertile (azoospermia), usually are mentally retarded, and have characteristic facies.

**TREATMENT**

Supplemental testosterone may be beneficial for growth retardation and have characteristic facies.

**REFERENCE**


**XXY SYNDROME (KLINEFELTER SYNDROME)***

**DESCRIPTION**

A syndrome characterized by the presence of an extra X chromosome (usually 47, XXY), resulting in a hypogonadal male. It is the most common chromosomal aberration among men, with an estimated frequency of 1:1,500 among newborns. Caused by a nondisjunction of the sex chromosomes of the gametes from either parent, affected individuals are tall, with a eunuchoid habitus, small firm testes, and gynecomastia. Mental retardation and psychiatric disturbances have also been identified. Elevated gonadotropins and azoospermia are typically present. Seminiferous tubule sclerosis is a common finding on testicular biopsy. The diagnosis may be made by a chromatin-positive buccal smear, indicating the presence of an extra X chromosome. Karyotypes usually demonstrate 47, XXY or the milder mosaic pattern, 46, XY, 47, XXY.

**TREATMENT**

- No therapy improves spermatogenesis in Klinefelter syndrome.
- In mosaic Klinefelter syndrome with severe oligospermia, intracytoplasmic injection with IVF is technically possible.

**REFERENCES**


**FOLK SAC TUMOR, BLADDER**

**DESCRIPTION**

Follicle cell tumor of the bladder is very rare and appears to have a predilection for the urachal remnant. It has the same pathological characteristics as its counterparts in any other part of the body, and it is managed in the same way. (See Section II: “Malignant Tumor, Prostate.”)

**REFERENCE**


**FOLK SAC TUMOR, PROSTATE**

**DESCRIPTION**

Endodermal sinus tumor located in the prostate, similar to yolk sac tumor also called endodermal sinus tumor) found in the testis. A primary site of presentation in the prostate is extremely rare, with only a few reported cases. An increased incidence of extragonadal GCT is reported with Klinefelter syndrome, with postmenarche levels are commonly elevated, and are used as a tumor marker. Human chorionic gondadropin is not elevated. Schiller–Duval bodies are evident on histology. Treatment is multimodal, using cisplatin-based combination chemotherapy and radical surgery.

**REFERENCE**


**YOUNG CLASSIFICATION OF POSTERIOR URETHRAL VALVES**

**DESCRIPTION**

Young described 3 general types of posterior urethral valves:
- Type I: The valves are continuous with the ureterovesical junction and take an anterior course, dividing into 2 forks-like processes in the region of the bulbovesical junction. Usually, anterior fusion of the valves is not complete; however, some cases exhibit complete anterior fusion and drift between the 2 vestibule posteriorly. A subdivision of type I consists of a simple, instead of double, valve. Type I valves are the most common.
- Type II: Same as type I, but the valve, rather than taking an anterior course, tends to pass from the upper aspect of the verumontanum toward the external sphincter, where it divides into 2 fork-like processes. (Note: Type II valves are now thought to be nonexistent.)
- Type III: The valves have no relation to the verumontanum; instead, they are attached to the internal sphincter and the bladder neck.

**REFERENCE**


**YOUNG-DEAS-LEADBETTER BLADDER RECONSTRUCTION**

**DESCRIPTION**

This procedure was used to achieve a functional bladder neck closure for a persistent vesicoureteral reflux. It is no longer widely used. Although EDO accounts for <1% of infertility, it is a treatable entity, using transurethral resection of ejaculatory duct.

**REFERENCE**


**ZIPPER ENTRAPMENT**

**DESCRIPTION**

Usually an emergency department presentation, this penile problem usually results from the entrapment of the foreskin between the frenulum of the glans and the corona of the glans. The condition is caused by implanted sepsis, causing epispidiastomy, and treated by azospermidastomy. Birth rates remain poor.

**REFERENCE**


**ZINNER SYNDROME**

**DESCRIPTION**

Ejaculatory duct obstruction (EDO) resulting from a unilateral seminal vesicle cystic with associated obstructive kidney agenesis, the condition is caused by a congenital multicystic/lymphatic cystic abnormality. Although EDO accounts for <1% of infertility, it is a treatable entity, using transurethral resection of ejaculatory duct.
ORTHOPEDIC BONE PLIERS (see below). An alternate method of release involves cutting the closed portion of the actuator (upper teeth) with trauma shears to release the closed portion of the zipper from around the tissue.

- To remove a zipper, local anesthetic is injected into the area. Mineral oil is used to lubricate the zipper, and then 1 attempt is made to unzip the zipper. If this attempt is unsuccessful, a sturdy wire cutter (diagonal cutter) is used to cut the median bar on the top of the zipper slider, which connects its front and back plates. Then the slider falls off in 2 pieces, and the zipper teeth come apart readily (Image 1).

REFERENCES


ZONA PELLUCIDA BINDING ASSAY

DESCRIPTION
An assay used to counsel patients about their chances of success with IVF. Being species-specific, the human sperm-zona pellucida binding requires human oocytes. Different sources of oocytes can be used, such as postmortem, IVF surplus, or surgical specimens. Oocytes are bisected, and 1/2 of the zona acts as the control. Different preservation methods are available, such as salt storage, dimethyl sulfoxide freezing, or ultra-low-temperature freezing. The assay is essentially composed of 2 steps: Initial attachment, followed by irreversible binding. After repeated rinsing, the number of tightly bound spermatozoa to ZP is counted using phase contrast microscopy. This can be expressed as the hemizona index, which is the number of the patient's bound spermatozoa divided by the bound spermatozoa from the fertile control donor, multiplied by 1,003. Using a cut off of 35%, the hemizona index has been used by some to predict IVF success rate. (See also Section II: “Sperm Penetration Assay [Hamster Test].”)

REFERENCE
SECTION III

Algorithms

Section Editor: Stanley Zaslaw, MD, MBA, FACS
Abdominal Pain, Lower

**ABDOMINAL PAIN, LOWER**

- Common causes: Appendicitis, ovarian cyst, diverticulitis, UTI, cholecystitis, IBS, IBD, constipation, pregnancy, PID, ruptured AAA, pancreatitis
- Check labs/imaging: CBC, amylase, lipase, UA, abdominal XR (pelvic US, colonoscopy, abdominal CT)

- **Right lower**
  - Gradual onset
  - Mesenteric adenitis
  - Appendicitis
  - Pyelonephritis
  - Crohn disease

- **Hypogastric**
  - Sudden onset
  - Ovarian torsion
  - Ruptured cyst
  - Cecal diverticulitis
  - Meckel diverticulitis

- **Left lower**
  - Sigmoid diverticulitis
  - IBD
  - Constipation
  - Pyelonephritis
  - Crohn disease

- **Genitourinary**
  - Ruptured AAA
  - Abdominal wall hematoma
  - Psoas or abdominal abscess
  - Incarcerated or strangulated hernia

- **Gastrointestinal**
  - Cystitis
  - Pyelonephritis
  - Nephrolithiasis
  - PID
  - Endometriosis
  - Mittelschmerz
  - Ovarian torsion
  - Ectopic pregnancy

- **Constipation**
  - IBD
  - Ischemic colitis

---


822
Acid Phosphatase Elevation

**ACID PHOSPHATASE ELEVATION**

Acid phosphatase is produced by the prostate, RBCs, seminal fluid, and bony turnover.

- Common causes: Prostate cancer (most common), neoplasm, multiple myeloma, Paget’s, Gaucher’s, ITP, liver disease, renal failure, hyperparathyroidism, trauma.

Rectal exam

- PSA

Abnormal rectal exam or PSA

- Irregular prostate: Skeletal survey and urology referral

Normal rectal exam and PSA

Search for other causes:
- CBC, electrolytes, alkaline phosphatase, SPEP, UPEP, ESR, LFTs, B12, and TSH, TSH.

Anemia

- Determine type of anemia (ie, hemolytic). Begin treatment.
  - High ALK: Paget’s, advanced Gaucher’s
  - Low ALK: Hypothyroidism, B12 deficiency, Celiac disease, Malnutrition

No anemia

- Liver disease, early Gaucher’s, multiple myeloma

---

Acute Scrotum

**ACUTE SCROTUM**

- Acute scrotal swelling
  - With perineal edema?
    - Yes
    - External genitalia trauma?
      - Yes
      - Testicular torsion, Epididymitis, Orchitis, Abscess, Torsion of appendix testis or appendix epididymis (late)
    - No
    - Cellulitis, Fourrier gangrene
      - Yes
      - Testis enlarged?
        - Yes
        - Hydrocele, Hernia with hydrocele, Spermatocele
        - No
        - Transilluminates?
          - Yes
          - Idiopathic edema, Henoch–Schonlein Purpura (scrotal wall vasculitis), Kawasaki disease, Fat necrosis scrotal wall
          - No
          - Varicocele, Hernia
        - No
        - Testicular tumor, Paratesticular tumor, Leukemia, Antenatal torsion (newborn)
      - No
      - Reduced swelling?
        - Yes
        - Scrotal wall swelling?
          - Yes
          - Hernia
          - No
          - Transilluminates?
            - Yes
            - Idiopathic edema, Henoch–Schonlein Purpura (scrotal wall vasculitis), Kawasaki disease, Fat necrosis scrotal wall
            - No
            - Varicocele, Hernia
        - No
        - Testicular tumor, Paratesticular tumor, Leukemia, Antenatal torsion (newborn)
    - No
    - Generalized edema?
      - Yes
      - Renal diseases (Nephrotic Syndrome, Fluid overload, Cardiac Failure, Liver disease)
      - No
      - Gastrointestinal disease
        - Yes
        - Hematocele, Hernia
        - No
        - Fat necrosis scrotal wall
      - No
      - Testicular rupture, Spermatocele/hydrocele rupture, Epididymitis, Torsion
        - Yes
        - Torsion of appendix testis or appendix epididymis (late)
        - No
        - Hydrocele, Hernia with hydrocele, Spermatocele
    - No
  - No
  - Peritoneal mass
    - Yes
    - Allergic dermatitis, Erythema nodosum
    - No
  - Pain?
    - Yes
    - Testicular tumor, Paratesticular tumor, Leukemia, Antenatal torsion (newborn)
    - No
    - Reduced swelling?
      - Yes
      - Scrotal wall swelling?
        - Yes
        - Hernia
        - No
        - Transilluminates?
          - Yes
          - Idiopathic edema, Henoch–Schonlein Purpura (scrotal wall vasculitis), Kawasaki disease, Fat necrosis scrotal wall
          - No
          - Varicocele, Hernia
        - No
        - Testicular tumor, Paratesticular tumor, Leukemia, Antenatal torsion (newborn)
      - No
      - Testicular tumor, Paratesticular tumor, Leukemia, Antenatal torsion (newborn)

Adapted from AUA University: Acute Scrotum (http://www.auanet.org/education/acute-scrotum.cfm) and The Royal Children’s Hospital Melbourne Clinical Practice Guidelines (http://www.rch.org.au/clinicalguide/guideline_index/Acute_Scrotal_Pain_or_Swelling/)
Addison Disease (Adrenocortical Insufficiency)

ADDISON DISEASE (ADRENOCORTICAL INSUFFICIENCY)

Common causes: Corticosteroid withdrawal, TB, HIV, malignancy, pituitary disorders

Recent corticosteroid use

Yes

Corticosteroid withdrawal

No

Check: HIV test, PPD, RPR, ACTH, CT of adrenals, brain MRI

Infections

TB, HIV, Syphilis, Fungal infection

Metastatic disease

Lung, Breast, Colon, Lymphoma

Adrenal abnormality

Meningococcemia, Sepsis, Thrombotic disorder

Pituitary ACTH deficiency

Turner Aneurysm Infarction Sheehan syndrome
Adrenal Mass, Solid

**ADRENAL MASS, SOLID**

- History and physical evaluation: dexamethasone suppression test or late-night salivary cortisol test, 24 hr urinary fractionated metanephrines

**功能性的肾上腺肿瘤**

- Functional adrenal mass
  - Surgical removal in most cases
  - CT
    - Delayed washout
    - Low attenuation and rapid washout
    - Surgical removal
  - MRI
    - Low signal T2
    - Follow with serial imaging and remove if enlarging or becomes functional

**非功能性的肾上腺肿瘤**

- Nonfunctional adrenal mass
  - Size ≤ 4 cm
  - MRI
    - Low signal T2
    - Surgical removal
  - Size ≥ 4 cm
    - MRI
      - High signal T2
      - Surgical removal
Anuria or Oliguria

**ANURIA OR OLIGURIA**

- **Common causes:**
  - Obstruction, acute renal failure, shock

- Check labs: UA, BUN, creatinine

- Catheterize bladder

- Urine in bladder
  - Bladder neck obstruction
    - BPH
    - Tumor

- No urine or very little
  - Low BP
    - CHF
    - Hypovolemia

  - Normal or elevated BP
    - Renal disease
    - Medications
      - Aminoglycosides
      - Gold
      - Amphotericin B
      - Chemotherapy


828
BLADDER TRAUMA

Intraperitoneal bladder rupture

Operative management

Yes

- Inadequate catheter drainage
- Vaginal or rectal injury
- Bladder neck injury
- Candidate for ORIF
- Bony fragments in bladder
- Laparotomy for other reasons

No

Cystogram

Normal

Extraperitoneal bladder rupture

Foley catheter

Pelvic ring fracture with gross or microscopic (5+ or >30 RBC/HFPF) hematuria
Gross hematuria in presence of otherwise unexplained free intraperitoneal fluid
Penetrating injury to low abdomen or pelvis with any degree of hematuria
Posterior urethral injury

Relative indications:
- Pelvis fluid collection
- Inability to void
- Elevated serum creatinine
- Abdominal distention
- Suprapubic tenderness
- Intoxicated or unresponsive
- Poorly functioning Foley catheter
- Pelvic fracture pattern
- Large pubic symphysis diastasis
- Displaced obturator ring fracture

Intraperitoneal bladder rupture

Normal

Extraperitoneal bladder rupture
**Bladder Tumor**

**BLADDER TUMOR**

- Transurethral resection of bladder tumor (TURBT)

**Staging**: Exam under anesthesia, imaging of abdomen and pelvis with upper tract imaging, check x-ray, Comprehensive Metabolic Profile (CMP)

**Primary treatment**
- Chemotherapy
- Radical cystectomy, urinary diversion (continent or conduit), and pelvic lymph node dissection is standard
- Partial cystectomy with pelvic lymphadenectomy considered in patients with no CIS, negative random bladder biopsies, no prostate involvement, and tumor located in favorable anatomical position such as a diverticulum or dome of bladder
- Multimodality treatment with chemotherapy, radiation, aggressive TURBT is being investigated
- Neoadjuvant chemotherapy provides a survival benefit. Surgery performed soon after recovery from chemotherapy

**Nonmuscle invasive**

- **Ta**
  - Low grade
  - High grade
- **T1**
  - Low grade
  - High grade
- 6-wk course of intravesical chemotherapy or BCG for the following:
  - Multifocal tumors
  - Large tumor (>2 cm)
- Repeat TURBT within 4 wk.
- 6-wk induction course of BCG followed by maintenance therapy
- Consider initial radical cystectomy in bulky high-grade disease, presence of CIS with T1 disease, presence of lymphovascular invasion
- Follow-up with cystoscopy, cytology, and interval upper tract imaging
- If CIS not present after induction BCG, start maintenance BCG
- If CIS present after induction BCG, consider cystectomy or 2nd induction course of BCG

**Muscle invasive**

- **T4b, stage IV, M1**
- Primary treatment chemotherapy
- Radical cystectomy, urinary diversion (continent or conduit), and pelvic lymph node dissection is standard
- Partial cystectomy with pelvic lymphadenectomy considered in patients with no CIS, negative random bladder biopsies, no prostate involvement, and tumor located in favorable anatomical position such as a diverticulum or dome of bladder
- Multimodality treatment with chemotherapy, radiation, aggressive TURBT is being investigated
- Neoadjuvant chemotherapy provides a survival benefit. Surgery performed soon after recovery from chemotherapy

**Follow-up with cystoscopy, cytology, and interval upper tract imaging**

- If recurrence, give 2nd 6-wk induction of BCG or consider radical cystectomy
- If CIS present after induction BCG, consider cystectomy or 2nd induction course of BCG

**Introduction BCG**

- BCG
- If CIS not present after induction BCG, start maintenance BCG
- If CIS present after induction BCG, consider cystectomy or 2nd induction course of BCG

**Repeat TURBT within 4 wk.**
Candida urinary infection (Candiduria)

**Candiduria**

- **Candiduria in asymptomatic patient**
  - Repeat clean catch urine culture
    - **Negative:** Stop
    - **Positive:** Assess for predisposing factors
      - Diabetes
      - Renal impairment
      - Broad spectrum antibiotics
      - Indwelling catheter
      - Stone disease
      - **Risk factors present**
        - Image the GU tract, r/o obstruction
        - Stop antibiotics if possible
        - Change or remove catheter
        - Glucose control in Diabetic
    - **Risk factors present**
      - Image the GU tract, r/o obstruction
      - Stop antibiotics if possible
      - Change or remove catheter
      - Glucose control in Diabetic
      - **Follow-up culture:** usually resolves in weeks to months
Cushing Syndrome

**CUSHING SYNDROME**

Common causes: Pituitary adenoma, adrenal tumor, paraneoplastic syndrome, exogenous corticosteroids

- Long-term steroid medication
  - Oral corticosteroids
  - Inhaled corticosteroids

- No long-term steroid use
  - Overnight dexamethasone suppression test or late-night salivary cortisol X2 or 24-hr urinary free cortisol X2
    - Suppressed cortisol levels
      - Pituitary adenoma
    - Normal or high levels
      - Adrenal tumor
      - Adrenal hyperplasia
      - Oat cell lung cancer


832
Cystocele and/or Enterocele

**CYSTOCELE AND/OR ENTEROCELE**

- **Cystocele and/or enterocele management**
  - (anterior compartment/pelvic organ prolapse)
  - Based on history/physical exam

**Surgical management:**
- **Vaginal approach**
  - Pelvic floor muscle therapy
  - Pessary
  - Sacrospinous ligament fixation
  - Uterovaginal ligament fixation
  - Mesh repair
  - Kelly-Kennedy plication
  - Paravaginal repair
  - Open approach
  - Laparoscopic/robotic sacrospinous ligament fixation

**Nonsurgical management:**
- Pelvic floor muscle therapy
- Pessary

**If successful, continue management:**
- Consider surgical management via vaginal or abdominal approach

**Failure to respond:**
- If there is occult stress urinary incontinence?
  - Yes
    - Consider sling
  - No
    - Conservative management

**Abdominal approach**
- Surgical management: Abdominal approach
Delayed Puberty

**DELAYED PUBERTY**

History/Physical exam: Growth pattern (stalled vs. delayed), sexual development, nutrition and exercise habits, family history (height and pubertal history), medication, and medical history

Labs:
* Basic CBC, ESR, creatinine, BUN, liver function enzymes, TSH/free T4
* Hormones: FSH, LH, prolactin, DHEA, estradiol (girls), total testosterone (boys)

Images: Bone age of left hand and wrist

Primary hypogonadism: Elevated FSH, LH

Secondary hypogonadism: Normal or low FSH, LH

Decreased estradiol

Primary gonadal failure

Decreased testosterone

Functional hypogonadotropic hypogonadism

Constitutional delay of growth and puberty

Permanent hypogonadotropic hypogonadism

**Primary hypogonadism**

Diabetes mellitus, sickle cell anemia, CIN3 disease, chronic renal failure, celiac, other chronic disease

**Idiopathic gonadal failure**

Decreased estradiol

Chronic disease

History of chemotherapy or radiation

Albino or diminishing testicular volume

**Decreased testosterone**

Primary hypogonadism

Idiopathic gonadal failure

Decreased testosterone

Decreased estradiol

Decreased testosterone

Decreased estradiol

Decreased testosterone

Decrease estradiol

Primary gonadal failure

Decreased testosterone

Functional hypogonadotropic hypogonadism
Disorders of Sexual Development (DSD)

**DISORDERS OF SEXUAL DEVELOPMENT (DSD)**

- **Ambiguous genitalia**
  - Disorder of sexual development
  - Gonads palpable:
    - Ultrasound
    - Karyotype
  - Müllerian structures absent
  - Poly X-Y
  - Variant of seminiferous tubule
    - T/DHT normal
    - Androgen insensitivity
      - Dysgenic testis
      - Leydig cell defect
  - XY or XXY
  - T/DHT elevated
  - 17-OH progesterone not elevated:
    - Consider another form of CAH if ACTH elevated
  - 17-OH progesterone elevated
  - Mixed or partial gonadal dysgenesis
  - True hermaphrodite
  - Undervirilized male

- **Müllerian structures present**
  - Müllerian structures present
    - Müllerian structure present
    - Müllerian structures absent
    - XX Müllerian structure present
    - 21-hydroxylase deficiency
    - Undervirilized male
    - True hermaphrodite
    - Gonadal dysgenesis
    - XY
    - Masculinized female
    - XX, XY, or XXXY
    - True hermaphrodite
    - Gonadal dysgenesis
    - Undervirilized male
Dyspareunia

**DYSPAREUNIA**

Common causes: Dermatitis, skin infections, UTI, vulvodynia, vaginal atrophy, vulvovaginitis, vaginal dryness, endometriosis, adenomyosis, pelvic inflammatory disease (PID), irritable bowel syndrome, inflammatory bowel disease (IBD), vaginismus, ovarian cysts, carcinoma (vulvar, cervical, lichen sclerosus, endometrial, ovarian)

Location of symptoms

- Superficial
  - Inadequate lubrication
  - Vulvodynia
  - Vulvar atrophy
  - Vaginitis
  - Vaginosus
  - Urethritis
  - Vulvar dermatitis
  - Lichen sclerosus

- Deep
  - Vaginal dryness
  - Vaginal atrophy
  - Retracted uterus
  - Endometriosis
  - PID
  - Endometrial carcinoma
  - Carcinoma
  - Cervical carcinoma

- Midline
  - Cystitis
  - IBD

- Lateral Pain
  - Ovarian cyst
  - Ovarian carcinoma
  - IBD
  - Diverticulitis

- Diffuse
  - Functional


836
DYSURIA

Causes

Common causes: Cystitis, STIs, vaginitis, prostatitis

Infectious

Noninfectious

Others

Infection of one of the following:

• Local trauma
• Labial adhesions
• Chemical urethritis

• Urinary stones
• Urethral strictures
• Reactive arthritis
• Behçet disease
• Lichen sclerosus

Genitourinary

• Pyelonephritis
• UTI
• Urethritis
• Prostatitis

Perineum

• Vaginitis (fungal, bacterial)
• Balanitis
• Pelvic inflammatory

Systemic

Less common

• Pelvic inflammatory disease
• Acropedic vaginitis
• Vulvar disease
• Vaginal warts

Urine clean catch on every patient.

Urine analysis

Urine pregnancy test

(+) Nitrates
(+ ) Pyuria

(−) Nitrates
(− ) Pyuria

Acute bacterial cystitis

Vaginal discharge

Urethral discharge

Cervical discharge

Ejaculation, Premature

**EJACULATION, PREMATURE**

**History and physical**
**Detailed sexual history**
**History of concurrent erectile dysfunction**

**Oral medication**
- Treat ED 1st if present

**Consider PDE5 inhibitors**
- SSRIs (off-label)
  - Fluoxetine
  - Paroxetine
  - Sertraline
  - Dapoxetine (EU approved)

**Topical anesthetics**
- Apply 20–30 min prior to intercourse
- Stop-start technique, squeeze technique, “quiet vagina”

**Behavioral therapy**
- Stop-start technique
- Squeeze technique
- “Quiet vagina”

**Treat ED 1st if present**

**Daily dosage or episodic dosage 3–4 hr prior to intercourse can be used**

**Dosage can be titrated up weekly until benefit**

**Enuresis**

**Wetting while asleep in a child 5 yr and older**

**ENURESIS**

- **UA/UC Positive?**
  - Yes
    - **Monosymptomatic (MSE) (Enuresis + normal UA)**
    - **Focused H&P, fluid intake, stool, and voiding diary**
    - **Daytime bladder sx**
    - **Constipation (consider functional enuresis)**
    - **No abnormality on H&P, or diary.**
    - **Persistent enuresis**
      - **Parent/child education. Behavioral therapy**
      - Resolves
      - **Enuresis alarm**
    - **Return to MSE path**
    - **Continue therapy × 6 mo**
    - **Resolves**
    - **Subspecialist referral**
    - **Evaluate for obstructive sleep apnea (OSA)**
    - **Subspecialist referral**
    - **Psychological sx (anxiety, major depressive disorder (MDD), child abuse, Attention Deficit Hyperactivity Disorder (ADHD), conduct disorder)**
    - **Immediate subspecialist referral**
    - **Subspecialist referral**
    - **Stop alarm after 14 consecutive dry nights**
    - **Family to decide if daily vs. occasional tx**
    - **Enuresis due to infection**
    - **Nonmonosymptomatic (NMSE) (enuresis + other lower urinary tract symptoms)**
    - **Focused H&P, fluid intake, stool, and voiding diary**
    - **Urinalysis & culture (UA/UC)**
    - **No abnormality on H&P, or diary.**
    - **Persistent enuresis**
      - **Parent/child education. Behavioral therapy**
      - Resolves
      - **Enuresis alarm**
    - **No**
      - **Subspecialist referral**
      - **Evaluate for obstructive sleep apnea (OSA)**
      - **Subspecialist referral**
      - **Continued medical management**
      - **Subspecialist referral**
      - **Treat underlying condition (diabetes mellitus, diabetes insipidus, chronic renal failure, seizure disorder, sickle cell, constipation, pinworm)**
      - **Immediate subspecialist referral**
      - **Subspecialist referral**
      - **Enuresis alarm**
      - **No**

**References**

Erectile Dysfunction

**ERECTILE DYSFUNCTION**

- History and focused physical exam
  - Identify common conditions that may predispose to ED
    - Hypertension
    - Diabetes
    - Cardiovascular disease
    - Hyperlipidemia
    - Depression
    - Alcoholism
    - Smoking
  - Labs: Fasting glucose, lipids, hormone panel

- If possible psychogenic cause, may consider nocturnal penile tumescence monitoring
- History of perineal trauma
- Consider vascular evaluation:
  - Combine intracavernous injection and stimulation
  - Arteriography
- Treat hormonal
- Oral phosphodiesterase type 5 (PDE5) inhibitors
- If failure and/or patient intolerance, penile prosthesis may be considered

Success:
- Periodic follow-up for efficacy, side effects, and any change in health status

Failure:
- Ensure adequate medication was performed
  - Titrate dosage
  - Switch PDE5 inhibitor
- Alprostadil intraurethral suppositories
- Intracavernous drug injection
- Vacuum constriction devices

Fecal incontinence management

Multicomponent treatment:
- Increase dietary fluid and fiber
- Improve bowel habits
- Pelvic floor muscle exercises
- Urge reduction strategies
- Barrier cream

Diarhea/loose stool consistency

- Fiber
- Loperamide
- Cholestyramine

Constipation/normal stool consistency

- Fiber
- Secondary treatment of constipation:
  - Glycerin suppositories
  - Remove causes of overflow fecal incontinence
  - Daily enemas

Biofeedback sessions

- Neuromodulation
- Artificial Sphincter
- Colostomy
Foley Catheter Problem (Difficult Placement, Male)

**FOLEY CATHETER PROBLEM (DIFFICULT PLACEMENT, MALE)**

- **History and physical:** Assess need for cathetered with admitting service. Digital rectal exam. Assess history of LUTS/BPH/urologic surgery. Give dose of antibiotic if possible infection.
- **Intraurethral lidocaine jelly:** Attempt placement of 20–22 Fr Foley or Coude catheter. Try different catheters if unsuccessful.
- **Flexible cystoscopy:** History of urologic surgery or structure disease. History of urologic trauma.
- **History of urologic surgery or structure disease:** Consider attempting 10–12 Fr catheter or initial flexible cystoscopy.
- **Retrograde urethrogram:** Suprapubic tube may be needed.
- **Flexible cystoscopy:** Able to place wire under cystoscopy. Unable to pass wire under cystoscopy.
- **Serial dilation over wire with placement of council catheter over guide wire:** Serial for possible urethrotomy or urethroplasty.
- **No stricture:** Place council catheter over guide wire.
- **Structure:** Able to place wire under cystoscopy. Unable to pass wire under cystoscopy. Serial dilation over wire with placement of council catheter over guide wire. Serial for possible urethrotomy or urethroplasty.
Genital Ulcers

Common causes: Herpes simplex, syphilis, chancroid, granuloma, inguinale

Check labs: RPR, HIV, GC, and chlamydia culture or DNA probe

Lesions painful?

Yes

No

Vesicles on erythematous base

Evolves from pinpoint ulcer to a large sore, yellowish base; associated with recurrent oral ulcers

Gram stain shows gram-negative rods, “school of fish” appearance; culture difficult

Unroof new vesicle to culture fluid

RPR +, may confirm with FTA-ABS

Punch biopsy at ulcer edge

Herpes simplex

Chancroid

Behçet disease

Syphilis

Granuloma inguinale

Genital Ulcers


843
Groin and Hip Pain

GROIN AND HIP PAIN

Common causes: OA, osteonecrosis, sciatica, stress fracture

Yes

Traumatic

No

Fracture dislocation labral tear/loose body

Yes

History of childhood pathology (such as developmental dysplasia, slipped capital femoral epiphysis, Legg–Calvé–Perthes)

No

Groin pain can be elicited by ranging hip in flexion, internal rotation or flexion, external rotation, or a resisted straight leg raise

Yes

Intra-articular

No

Extra-articular

Numbness, paresthesias or shooting pain

Location

Other

Inability to reproduce pain at site with physical exam, but exam at another site reproduces pain

Yes

Anterior iliospina tendinitis

No

Abdominal pathology must be ruled out (such as PID, nephrolithiasis, appendicitis, ovarian cysts, aneurysms, etc.)

Exercise induced?

Yes

Stress fracture

Anti-occlusive disease


844
GYNECOMASTIA

Common causes: Testicular dysfunction, drug use, congenital disorders, hypopituitarism, liver, renal, thyroid disease, obesity, carcinoma.

- Review medications
- Drug effect
- ACE inhibitor
- Marijuana
- Spironolactone
- Cimetidine
- Antiandrogens
- Alcohol
- Others
- No obvious drug
- Adolescent
- Obesity

If no other complaints and normal exam, normal findings may last 1–2 yr

- Check labs: TSH, LFTs, testosterone, serous hCG, beta hCG
- Normal findings
- Low TSH
- Hyperthyroidism
- Abnormal LFTs
- Chronic liver disease
- Testicular exam
- Abnormal
- Normal

Evidence of feminization
- Evidence of feminization
- Liver disease
- Adrenal tumor
- beta hCG-producing tumor
- Hyperprolactinemia
- Klinefelter syndrome

- Beta hCG
- Elevated
- Scrotal US
- Normal
- Testosterone

- Normal
- Scrotal US
- Mass
- Testicular germ cell tumor
- CT abdomen
- Increased LH
- Increased hCG
- Decreased LH

- Decreased LH
- Normal
- Testosterone
- Increased
- Normal
- Inhibin and/or estradiol
- Decreased LH

HEMATURIA, ADULT

Microscopic hematuria (MH): ≥3 RBCs per HPF in 2 specimens

- History and physical to assess possible causes of MH (UTI, trauma, recent urologic procedure, menstruation, etc.)
- Repeat UA/micro after treatment of other cause(s)
- Release from care

If CT urogram contraindicated, less optimal imaging:
- MR urogram
- Retrograde pyelograms in combination with non-contrast CT, MRI, or US

Renal function testing (BUN, creatinine, eGFR)
Upper tract imaging – CT urogram
Concurrent nephrology workup if indicated (proteinuria, dysmorphic RBCs, impaired renal function, etc.)

High-risk patient:
- Age >35 yr
- Smoking history
- Irritative voiding symptoms
- Chemical exposure
- Gross hematuria
- History of urologic disease

Low-risk patient

- Urinary cytology and diagnostic cystoscopy

Treat condition accordingly
Follow-up with UA/micro yearly × 2 yr
Release from care
Follow persistent MH with annual UA. Consider nephrology evaluation. Repeat anatomic evaluation every 3–5 yr or sooner if symptoms/risk factors change

Follow-up as indicated by diagnosis:
Re-evaluate for MH after resolution of condition
Release from care

HEMATORURIA, MACROSCOPIC (GROSS) PEDIATRIC

- Symptoms of glomerulonephritis, i.e., edema, HTN, proteinuria, RBC casts
  - Yes
  - No

- History of trauma
  - Yes
  - No

- Urine culture & renal US
  - Yes
  - No

- Renal ultrasound & 24-hr urine collection for metabolic stone profile
  - Yes
  - No

- Signs/symptoms of UTI
  - Yes
  - No

- Family history of kidney stone
  - Yes
  - No

- Renal US, urine culture, test parents for hematuria, hemoglobin electrophoresis, urine calcium/creatinine ratio
  - Yes
  - No

- Tumor or structural abnormality
  - Yes
  - No

- Cystoscopy with/without retrograde ureteropyelograms
  - Yes
  - No

- Treat accordingly

- Check basic metabolic panel, complete blood count, complement C3, albumin, antistreptolysin titer & streptozyme
  - Yes
  - No

- Tests consistent with post-infectious glomerulonephritis
  - Yes
  - No

- Supportive therapy
  - Yes
  - No

- Hypertension, hyperkalemia, and/or azotemia present
  - Yes
  - No

- Refer to pediatric nephrologist

- Yes
  - No
HEMURIA, PEDIATRIC MICROSCOPIC ISOLATED ASYMPTOMATIC

Repeat urinalysis weekly × 2 (without exercise)

Persistent hematuria

Test parents and siblings for hematuria

Follow-up urinalysis with physical exam

No

Positive

Family history of kidney stone

Benign familial hematuria

Consider hearing test, renal ultrasound, and hemoglobin electrophoresis depending on level of concern

Check urine calcium/creatinine ratio

Normal

If no other concerning signs/symptoms then follow with yearly urinalysis
HEMATURIA, TRAUMATIC

Hemodynamically stable
- Blunt trauma
- Microscopic hematuria
  - No hypotension
  - Adult or <50 RBCs/HPF in child
    - Repeat UA in 2–3 wk.
  - Hypotension
    - >50 RBCs/HPF in child
      - CT scan with IV and PO contrast with delayed images and CT cystogram

Hemodynamically unstable
- To OR for exploratory laparotomy with on-table IVP (2.2 mL/kg bolus IV contrast)
- IVP abnormal
  - Expanding and/or pulsatile retroperitoneal hematoma
  - Extraperitoneal bladder injury
- Repair injuries

Treat injuries or repeat UA in 2–3 wk if no injuries

Hyperaldosteronism, Primary (Aldosteronism, Conn Syndrome)

**HYPERALDOSTERONISM, PRIMARY (ALDOSTERONISM, CONN SYNDROME)**

- **Common causes:** Adrenal adenoma, adrenal hyperplasia, Cushing syndrome, renal artery stenosis, cirrhosis, nephrotic syndrome

  - **Check labs:** Plasma renin, morning plasma aldosterone, urinalysis

  - **Check medications:** Diuretics, hydralazine, laxatives

  - **Low plasma renin activity (PRA), high plasma aldosterone/PRA ratio**

  - **Confirmatory tests:** Fludrocortisone suppression, oral sodium loading test, IV saline infusion test, captopril suppression test. If negative, primary hyperaldosteronism unlikely

  - **Primary hyperaldosteronism**

  - **Adrenal adenoma, Bilateral adrenal hyperplasia**

  - **Excision or embolization**

  - **Secondary hyperaldosteronism**

  - **Renal artery stenosis**

  - **Renal disease**

  - **CHF**

  - **Cirrhosis**

  - **Dehydration**

  - **Polycystic kidneys**

  - **Glomerulonephritis**

  - **Bartter syndrome**

Hypercalcemia

Common causes:
- Hyperparathyroidism
- Malignancy
- Hyperthyroidism
- Vitamin D toxicity
- Milk-alkali syndrome
- Medications

Medications

Thiazides
Antacids
Calcium supplements
Vitamin D supplements
Lithium

Milk-alkali syndrome

PTH elevated
Phosphorus low/normal

Hyperparathyroidism
Parathyroid adenoma
Ectopic PTH secretion
Lithium

Suppressed
TSH

Barrett's disease

Paraneoplastic syndrome

Metastatic

Lung cancer
Breast cancer
Multiple myeloma
Lymphoma
Leukemia

Ovarian
Renal
Head and neck

PTH suppressed

Malignancy
- Metastatic or paraneoplastic syndrome
- Paget disease

Paget disease

Suppressed
TSH

Sarcoidosis

Check labs: PTH, phosphorus, CBC, serum protein electrophoresis (SPEP), TSH

Hyperkalemia

K+ >5.5 mEq/L

Common causes: Specimen delay and hemolysis, renal insufficiency, acidosis, rhabdomyolysis, insulin deficiency, adrenal insufficiency, medications, massive blood transfusions, tumor lysis, ischemic bowel

Clinical manifestations
- Weakness, nausea, paresthesias, palpitations, ileus, flaccid paralysis
- EKG changes: Peaked T waves, ↑ PR interval, ↑ QRS width, sine wave pattern, PEA

Repeat test

Normal
- Pseudohyperkalemia: (VF with K+ hemolyzed sample
- Check medications
- No suspicious medications
- ABGs, GFR, Cr, BUN, glucose, electrolytes, digoxin levels, CPK, urine K+

Abnormal
- Angiotensin-converting-enzyme inhibitor (ACEI), Angiotensin II receptor blockers (ARBs), β-blockers, NSAIDS, penicillin VK, TMP-SMX, digitals, K+-sparing diuretics, heparin, cyclosporine, tacrolimus, pentamidine, succinylcholine
- Discontinue medication or adjust dose

Urine K+ >30 mEq/L
- Transcellular shift

Urine K+ <30 mEq/L
- Impaired renal excretion

Acidosis
- Rhabdomyolysis
- Hyperglycemia
- Burns

Renal insufficiency
- Adrenal insufficiency
- Hyporeninemic Hypoaldosteronism

Urine K+ <30 mEq/L: Impaired renal excretion

No suspicious medications

Abnormal

Common causes: Specimen delay and hemolysis, renal insufficiency, acidosis, rhabdomyolysis, insulin deficiency, adrenal insufficiency, medications, massive blood transfusions, tumor lysis, ischemic bowel

Clinical manifestations
- Weakness, nausea, paresthesias, palpitations, ileus, flaccid paralysis
- EKG changes: Peaked T waves, ↑ PR interval, ↑ QRS width, sine wave pattern, PEA

Repeat test

Normal
- Pseudohyperkalemia: (VF with K+ hemolyzed sample
- Check medications
- No suspicious medications
- ABGs, GFR, Cr, BUN, glucose, electrolytes, digoxin levels, CPK, urine K+

Abnormal
- Angiotensin-converting-enzyme inhibitor (ACEI), Angiotensin II receptor blockers (ARBs), β-blockers, NSAIDS, penicillin VK, TMP-SMX, digitals, K+-sparing diuretics, heparin, cyclosporine, tacrolimus, pentamidine, succinylcholine
- Discontinue medication or adjust dose

Urine K+ >30 mEq/L
- Transcellular shift

Urine K+ <30 mEq/L
- Impaired renal excretion

Acidosis
- Rhabdomyolysis
- Hyperglycemia
- Burns

Renal insufficiency
- Adrenal insufficiency
- Hyporeninemic Hypoaldosteronism

Urine K+ <30 mEq/L: Impaired renal excretion

No suspicious medications

Abnormal

Common causes: Specimen delay and hemolysis, renal insufficiency, acidosis, rhabdomyolysis, insulin deficiency, adrenal insufficiency, medications, massive blood transfusions, tumor lysis, ischemic bowel

Clinical manifestations
- Weakness, nausea, paresthesias, palpitations, ileus, flaccid paralysis
- EKG changes: Peaked T waves, ↑ PR interval, ↑ QRS width, sine wave pattern, PEA

Repeat test

Normal
- Pseudohyperkalemia: (VF with K+ hemolyzed sample
- Check medications
- No suspicious medications
- ABGs, GFR, Cr, BUN, glucose, electrolytes, digoxin levels, CPK, urine K+

Abnormal
- Angiotensin-converting-enzyme inhibitor (ACEI), Angiotensin II receptor blockers (ARBs), β-blockers, NSAIDS, penicillin VK, TMP-SMX, digitals, K+-sparing diuretics, heparin, cyclosporine, tacrolimus, pentamidine, succinylcholine
- Discontinue medication or adjust dose

Urine K+ >30 mEq/L
- Transcellular shift

Urine K+ <30 mEq/L
- Impaired renal excretion

Hypernatremia

**HYPERNATREMIA**

**History and volume status**

**Hypovolemic:**
- Dermal losses
- GI losses
- Diuretics
- Postobstruction
- Acute and chronic renal disease
- Hyperosmolar nonketotic coma

**Euvolemic:**
- Diabetes insipidus (central, nephrogenic)
- Hypodipsia
- Fever
- Hyperventilation
- Mechanical ventilation

**Hypervolemic:**
- Hypervolemic
- Hypovolemic
- Diabetes insipidus (hypertonic saline, tube feedings, antibiotic containing sodium)
- Hyperaldosteronism
- Cushing disease

Obtain urine and plasma osmolality and urinary sodium

**Urine osmolality/plasma osmolality < 0.7 mOsm/kg**

- Diabetes insipidus
- Hypodipsia
- CNS lesion

**Urine osmolality/plasma osmolality > 0.7 mOsm/kg**

- Urine sodium < 20 mEq/L

- Renal:
  - Diuretics (osmotic, loop)
  - Interstitial renal disease
  - High-protein diet

- Endocrine:
  - Cushing disease
  - Primary hyperaldosteronism
  - Diabetes mellitus

- GI losses:
  - Lactulose malabsorption
  - Infectious diarrhea

- Respiratory losses:
  - Hyperventilation

- Skin losses:
  - Excessive sweating


853
Hypertension and Elevated Blood Pressure, Treatment

HYPERTENSION AND ELEVATED BLOOD PRESSURE, TREATMENT

BP: SBP <120 and DBP <80

Measured on 2 separate office visits

Yes

No

At goal?

Yes

No

DM or CKD

Goal BP: <140/90

Lifestyle modifications:
DASH diet, weight reduction, moderate consumption of alcohol, limit NSAIDs, physical activity, smoking cessation

First-line: Thiazide type diuretics
Second-line: Consider ACE-I, BB, CCB, or combination

Compelling Comorbidities
Include: CAD, CVA, CHF (ACEi or BB for CHF)
Add other antihypertensive drugs to meet goal: Diuretics, ACE-I, BB, CCB as needed

Lifestyle modifications:
DASH diet, weight reduction, moderate consumption of alcohol, limit NSAIDs, physical activity, smoking cessation

First-line: Thiazide type diuretics AND Second-line: Consider ACE-I, BB, CCB, or combination until goal is met

Heart failure
Initial therapy options: Thiazide, BB, ACE-I, ARB, Aldosterone antagonist

Postmyocardial infarction Initial therapy options: BB, ACE-I, ARB, Aldosterone antagonist

High CAD risk
Initial therapy options: Thiazide, BB, ACE-I, CCB

Diabetes
Initial therapy options: Thiazide, ACE-I, ARB, CCB

Chronic kidney disease
Initial therapy options: ACE-I, ARB

Recurrent stroke prevention
Initial therapy options: Thiazide, ACE-I


854
Hypocalcemia

**HYPOCALCEMIA**

Common causes: Lab error, chronic renal failure, postsurgical hypoparathyroidism, hypoalbuminemia, hypomagnesemia, hyperphosphatemia, medication, PTH deficiency or resistance, vitamin D deficiency or resistance.

Check labs: Repeat serum calcium, ionized calcium, electrolytes, BUN, creatinine, magnesium, phosphorus, albumin, LFTs, PT, PTT, PTH.

**Serum calcium >8.5 mg/dL**
- Bound to albumin
- If ionized calcium not available, correct calcium for albumin; calcium concentration falls by 0.8 mg/dL for every 1 g/dL fall in albumin.

**Calcium <8.5 mg/dL, ionized or corrected calcium low, albumin normal or slightly low**
- Magnesium low
- Phosphorus low
- PTH high
- PTH low
- Hypomagnesemia
- Hypoparathyroidism
- Rickets
- Abnormalities of vitamin D metabolism
- Pseudohypoparathyroidism

**Calcium <8.5 mg/dL, ionized or corrected calcium normal, albumin low**
- Hypoalbuminemia
- Cirrhosis
- Nephrotic syndrome
- Malnutrition
- Burns
- Chronic illness
- Sepsis

Hypokalemia

**HYPOKALEMIA**

**HISTORY TAKING**

- No transcellular shift, adequate K intake, obtain serum electrolytes, BUN, Cr, Urine Na, K, and osmolality

**INADEQUATE INTAKE**
- Potassium deficient diet:
  - Tea and toast diet
- Eating disorders:
  - Anorexia, bulimia, starvation, pica
  - inability to eat potassium-poor TPN

- **AML:** Acute myelogenous leukemia,
- **OD:** Overdose
- **GI:** Gastrointestinal,
- **UK:** Urine potassium;
- **TTKG:** transtubular potassium gradient
- **UCl:** urine chloride

**SPURIOUS**
- Leukocytosis (WBC >100K)
- AML: Severe lipemia

**TRANSCELLULAR SHIFT**
- Gill-adrenergic agonists:
  - Epinephrine
- Decongestants:
  - Pseudoephedrine, phenylpropanolamine
- Bronchodilators: Abuterol, terbutaline, isoproterenol, ephedrine, malatoperoentol
- Tocolytic: ritodrine, nylidin
- Theophylline
- Chloroquine
- Caffeine
- Verapamil
- Insulin
- Alkalosis
- Increased anabolic state
- Increased in RBC production: Pericusic anemia (Wt Hb)
- Neutropenia (Gl-CSF)
- Thyrototic periodic paralysis
- Barium intoxication
- Pheochromocytoma
- Hypokalemia periodic paralysis
- Refeeding syndrome
- Hypothermia
- Delirium Tremens

**RENAL LOSS**
- Profuse sweating
- UK >30 mEq/d
- TTKG** >7
- UK <25 mEq/d
- TTKG** <3

**GI LOSS**
- Vomiting
- Diarrhea
- GI suction
- Draining GI fistula
- laxatives
- Secretory tumors:
  - Villous adenoma,
  - VIPoma,
  - Zolinger–Ellison syndrome
- Inability to eat potassium-poor TPN

**INSENSIBLE LOSS**
- Hypnormotensive
- Base status

**ACIDEMIC**
- DKA
- RTA type II
- Some distal RTA type I

**VARIABLE**
- Mg deficiency:
  - Amphotericin B
  - Cisplatinum
  - Aminoglycosides:
  - Foscarnet
  - Poor Mg intake

- <20 Vomiting
- NGT

**ALKALEMIC**
- UCI
- >20 Diuretics
- Bartter’s/Gilberman’s

**Hypertensive**
- Primary hypaldosteronism: Conn syndrome
- Secondary hyperaldosteronism:
  - renovascular disease, renin-secreting tumor
- Nonaldosterone mineralocorticoid:
  - Cushing’s, Liddle’s, exogenous mineralocorticoid, licorice

**INADEQUATE INTAKE**
- Potassium deficient diet:
  - Tea and toast diet
- Eating disorders:
  - Anorexia, bulimia, starvation, pica
  - inability to eat potassium-poor TPN

**MEDICATIONS**
- Diuretics
- Bicarbonate
- Methylenanthrene OD
- Amphotericin B
- Cisplatin
- Chloroquine intoxication
- Verapamil OD
- Beta agonist intoxication
- Ephedrine

**TTKG** = Urine K⁺ x serum osmolality/Serum K⁺ x urine osmolality
- <3 kidney is not wasting excessive potassium >7 significant renal loss


856
Hypomagnesemia

**HYPOMAGNESEMIA**

- **Common causes:**
  - GI loss
  - Malnutrition
  - Malabsorption
  - Diuretics
  - Alcoholism

- **24-hour urinary magnesium**

- **FE_{Mg} = \frac{U_{Mg} \times P_{Cr}}{(0.7 \times P_{Mg}) \times U_{Cr}} \times 100**

- **FEMg < 2% or**
  - 24 hr U_{Mg} > 30 mg

- **FEMg > 2% or**
  - 24 hr U_{Mg} < 10 mg

- **Renal**
  - Impaired renal function: GFR < 60
  - Normal renal function: GFR > 80

- **Acquired:**
  - Chronic renal failure
  - Acute tubular necrosis
  - Renal tubular acidosis
  - Postobstructive diuresis
  - 1° Aldosteronism
  - Hyperparathyroidism
  - Hyperthyroid
  - SIADH
  - Hyperaldosteronism

- **Redistribution:**
  - Hungry bone syndrome
  - Pancreatitis
  - Insulin treatment
  - Transfusion
  - Refeeding syndrome

- **Endocrine:**
  - Hyperparathyroidism
  - Hyperthyroid
  - SIADH
  - Hyperaldosteronism

- **Malabsorption:**
  - Celiac sprue
  - Crohn disease
  - Small bowel resection

- **Poor intake:**
  - Malnutrition
  - Starvation
  - Mg-free IVF
  - TPN

- **GI loss:**
  - Vomiting
  - Diarrhea
  - NG suction
  - Intestinal fistula

- **Miscellaneous:**
  - Chronic alcoholism
  - Diabetes mellitus

- **Medications:**
  - Diuretics: loop/thiazide
  - PPI
  - Aminoglycoside
  - Amphotericin B
  - Cisplatin
  - Cyclosporin
  - Cetuximab
  - Tacrolimus
  - Foscarnet
  - Pentamidine

- **Congenital:**
  - Bartter syndrome
  - Gitelman syndrome

**FEMg =** Fractional excretion of magnesium
**UMg =** urinary magnesium
**UCr =** Urinary creatinine
**PCr =** Plasma creatinine


857
Hyponatremia

**HYPONATREMIA**

Serum osmolality

- <280 mEq/L
  - Pseudohyponatremia:
    - Hyperlipidemia
    - Hyperproteinemia
    - Hyperglycemia
    - Mannitol

- ≥280 mEq/L
  - Hypovolemic:
    - Poor skin turgor, dry mucous membranes
  - Hypervolemic:
    - Edema, ascites
    - 3rd heart sound

What is the volume status?

- Hypovolemic: U Na <20 mEq/L
  - GI losses
  - Sweating
  - Burns
  - Cystic fibrosis
  - Exercise
  - Bleeding

- Hypervolemic: U Na >20 mEq/L
  - CHF
  - Nephritic syndrome
  - Liver failure
  - Pregnancy

- Euvolemic
  - U Na <20 mEq/L
  - CHF
  - Addison disease
  - SIADH
  - Cerebral salt wasting

- U Na >20 mEq/L
  - Diuretic use

U Na = Urinary sodium

Hypospadias

**HYPOSPADIAS**

- With chordee
  - Release chordee without preservation of urethral plate
  - Two-stage graft urethroplasty using buccal mucosal graft or prepuce
  - Release chordee with preservation of urethral plate
- Without chordee
  - Release chordee without preservation of urethral plate
  - Preputial island tube urethroplasty
  - Tubularized incised plate onlay island flap (with bad urethral plate)
  - Tubularized incised plate
  - Tubularized incised plate Glans approximation procedure
  - Glans approximation procedure Meatal advancement and glanduloplasty (MAGPI)
  - Proximal/midshaft
  - Distal
  - Coronal
  - Glandular
Incontinence, Female

INCONTINENCE, FEMALE

- History and physical exam
- Urine analysis and culture
- Uroflowmetry and postvoid residual
- Symptom and quality-of-life questionnaire
- Micturition diary
- Urodynamics if indicated:
  - Simpler tests inconclusive
  - Empirical treatment fails
  - Proposed surgery
  - History of pelvic surgery/radiation
  - Neurologic conditions
- Voiding cystourethrogram in select patients
- Cystourethroscopy in select patients

Incontinence associated with poor bladder emptying or retention

VCUG
Urodynamics
Identify correct pathology:
- Iatrogenic from prior surgery
- Pelvic organ prolapse
- CIC if underactive detrusor muscle

Evaluate and treat possible fistula or ectopic ureter

Continuous incontinence
Urgo incontinence
Mixed incontinence: Treat main problems first
Stress incontinence

Initial treatment options:
- Pelvic floor muscle training/behavior modification
- Biofeedback
- Oral anticholinergic agents (eg, oxybutinin, tolterodine, mirabegron, etc.)
- Intravesical agents (Botulinum toxin, etc.)
- Percutaneous tibial nerve stimulation

Surgery considered when less-invasive treatments fail or are not tolerated:
- Sacral neuromodulation
- Augmentation cystoplasty
- Urinary diversion

Initial treatment options:
- Pelvic floor muscle training/behavior modification
- α-adrenergic agents (limited utility)
- Imipramine
- Duloxetine (not FDA approved)
- Pessary

Minimally invasive options:
- Urethral bulking agents

Surgical options:
- Slings
- Suspensions
- Prosthesis repair
- Artificial urinary sphincter

Initial treatment options:
- Pelvic floor muscle training/behavior modification
- Biofeedback
- Oral anticholinergic agents (eg, oxybutinin, tolterodine, mirabegron, etc.)
- Intravesical agents (Botulinum toxin, etc.)
- Percutaneous tibial nerve stimulation

Surgery considered when less-invasive treatments fail or are not tolerated:
- Sacral neuromodulation
- Augmentation cystoplasty
- Urinary diversion

Initial treatment options:
- Pelvic floor muscle training/behavior modification
- Biofeedback
- Oral anticholinergic agents (eg, oxybutinin, tolterodine, mirabegron, etc.)
- Intravesical agents (Botulinum toxin, etc.)
- Percutaneous tibial nerve stimulation

Surgery considered when less-invasive treatments fail or are not tolerated:
- Sacral neuromodulation
- Augmentation cystoplasty
- Urinary diversion
Incontinence, Male

**INCONTINENCE, MALE**

- Urinary incontinence, male

  - Post-micturition dribble
  - Post-prostatectomy incontinence
  - Incontinence with urgency/frequency

**STRESS INCONTINENCE**

- Urethral milking
- Pelvic floor muscle training

**MIXED INCONTINENCE**

- General assessment
- Urinary diary and symptom score
- Assess quality of life and desire for treatment
- Physical examination: abdominal, rectal, sacral neurologic
- Urinalysis ± urine culture ➞ If infected, treat and reassess
- Assess PVR: physical exam./catherization/ultrasound

**URGE INCONTINENCE**

- Lifestyle interventions
  - Pelvic floor muscle training
  - Bladder retraining
- Antimuscarinics

**Specialized management**

- Failed initial therapy
  - Urethrocystoscopy
  - Urodynamics

**Post-prostatectomy**

- Incontinence on physical activity
- Incontinence with urgency/frequency

**OVERFLOW INCONTINENCE**

- Sphincteric incompetence
  - If initial therapy fails:
    - Artificial urinary sphincter
    - Sling procedures
    - Bulking agents

- Overactive detrusor
  - If initial therapy fails:
    - Neurostimulation
    - Sacral blockade
    - Botulinumtoxin detrusor injections
    - Bladder augmentation/substitution

- Underactive detrusor
  - Intermittent catheterization (IC)
  - Alpha-blockers
  - 5-α-reductase inhibitors
  - Neurostimulation
  - Correct anatomic defects

- Bladder outlet obstruction
- Consider:
  - Urethrocystoscopy
  - PVR/flow rates
  - VCUG/urethrogram
  - Ultrasound/IVP

- Lower urinary tract anomaly/pathology
  - Correct anomaly
  - Treat pathology


861
Incontinence, Pediatric

INCONTINENCE, PEDIATRIC

Pattern of wetting

Normal with nocturnal enuresis

Maturational delay

- Lumbar-sacral spine x-ray
- Renal US

<8 y/o

Normal
- VCUG
- MRI of spine
- Urodynamics

Abnormal
- Education
- Bed wetting alarm

>8 y/o

Normal with diurnal enuresis

Continuous

VCUG, Renal US

Intermittent

Dysfunctional voiding

VCUG, Renal US

- Timed voiding
- Bowel regimen
- Pharmacotherapy

Neurogenic abnormality

No UTI

UTI

Eccopic ureter

Exstrophy

Urodynamics

Medical or surgical treatment

- Timed voiding
- Bowel regimen
- Pharmacotherapy
- Need for clean intermittent catheterization (CIC)

>8 y/o

<8 y/o

Neurogenic abnormality

Ectopic ureter

Exstrophy

Surgery

Medical or surgical treatment
Infertility

Infertility

Common causes: Endocrine disorders (Polycystic ovary syndrome [PCOS], thyroid disease, hyperprolactinemia), pelvic structural abnormalities, azoospermia/oligospermia, unexplained infertility, poor coital timing/frequency

Evaluate coital timing and frequency

Female factor

Male factor

Patient history, physical, pelvic exam

Semen analysis

Uterine/tubal evaluation hysterosalpingogram

Assess ovulation using basal body temperature chart, urine LH ovulation predictor kit, and midultral serum progesterone

Positive for gonorrhea/chlamydia

Evaluate and treat for PID

Normal semen

Abnormal semen

Uterine abnormality

Tubal abnormality

Consider genetic evaluation

Consider testicular biopsy

History and physical exam

Endocrine evaluation

Normal

Abnormal

Ovulatory

Oligoovulation

If >35 y/o evaluate ovarian resistance with menses day-3 serum FSH or clomiphene citrate challenge test

Measure serum FSH, LH, TSH, and prolactin (PRL) levels

If low/normal FSH/LH or high PRL perform CT scan or MRI to evaluate for hypothalamic/pituitary disorder

Progestin challenge test

If hirsutism present determine serum 17-hydroxyprogesterone and testosterone levels to evaluate for PCOS and congenital adrenal hyperplasia (CAH)

If low/normal FSH/LH or high PRL perform CT scan or MRI to evaluate for hypothalamic/pituitary disorder

Semen analysis

Normal semen

Abnormal semen

Measure serum FSH, LH, testosterone, PRL

History and physical exam

Endocrine evaluation

If hirsutism present determine serum 17-hydroxyprogesterone and testosterone levels to evaluate for PCOS and congenital adrenal hyperplasia (CAH)

INFERTILITY, MALE ABNORMAL SEMEN

- Infertility, male – abnormal sperm parameters
  - Semen analysis × 2
    - Morning testosterone, LH, FSH, prolactin (PRL)
      - Abnormal
        - Low testosterone, Low FSH/LH
          - Secondary testicular failure
            - Karyotype
              - Y-chromosome microdeletion
                - Normal prolactin
                  - Rule out pituitary tumor
                    - Normal
                      - Other causes
                        - Medical or surgical treatment
        - High FSH, LH, Low testosterone
          - Primary testicular failure
            - Sertoli only
              - High prolactin
                - Head MRI
                  - Normal
                    - Abnormal
      - Normal
        - High LH, High testosterone
        - Androgen resistance
        - High FSH only
          - Sertoli only
            - No varicocele
              - Palpable varicocele
                - Repair
        - Check for varicocele
          - Low testosterone, Low FSH/LH
        - Secondary testicular failure
INFERTILITY, MALE, LOW SEMEN VOLUME

Semen analysis > 2 with >48 hr of abstinence

Semen volume <2 mL

Cystoscopy/Retrograde Urethrogram if:
1. Obstructive symptoms
2. History of strictures
3. Risk for stricture

Post-ejaculate urinalysis

Sperm present

Retrograde ejaculation

Sperm absent

TRUS with seminal vesicle aspiration

Dilated seminal vesicle or ejaculatory

Transurethral resection of ejaculatory duct
Lower Urinary Tract Symptoms (LUTS), Male

LOWER URINARY TRACT SYMPTOMS (LUTS), MALE

History and physical
Digital rectal exam
Urinalysis
PSA in select patients
Urine cytology in at-risk patients

Presence of the following clearly related to benign prostatic hypertrophy (BPH):
- Bladder stones
- Renal insufficiency
- Persistent gross hematuria
- Recurrent UTI

Mild symptoms (AUA/IPSS ≤ 7) or symptoms not bothersome
Watchful waiting

Moderate (AUA/IPSS 8–19) or severe (AUA/IPSS 20–35) symptoms
Watchful waiting

AUA/IPSS symptom index
Assessment of patient bother

Surgery

Mild symptoms (AUA/IPSS ≤ 7) or symptoms not bothersome
Watchful waiting

Optional tests:
- Uroflow
- PVR

Discussion of treatment options

Patient chooses noninvasive therapy
Watchful waiting

Patient chooses invasive therapy

Optional tests:
- Urodynamics
- Cystoscopy
- Prostate US

Surgery or minimally invasive therapy

Lymphadenopathy

**LYMPHADENOPATHY**

- **Localized** (1 site)
  - Low risk of malignancy: Tender, rubbery movable LNs
    - Yes
      - Apparent infectious or inflammatory disease?
        - Yes
          - Guided FNA/excisional biopsy
        - No
          - Observe for 3–4 wk
    - No
      - LN ultrasoundography: Round, absent hilus, Doppler with disorganized peripheral vascular pattern
        - Yes
          - Diagnostic?
            - Yes
              - Follow-up
              - Reactive pattern
              - Positive for malignancy
              - Inconclusive
              - CT scan directed to drainage area for diagnostic/staging purposes
              - Tissue diagnosis of primary tumor
            - No
              - Reassurance
          - No
            - Reassurance
    - Persistent?
      - Yes
        - Guided FNA/excisional biopsy
      - No
        - Reassurance

- **Generalized** (2 or more sites)
  - Risk of malignancy: Nontender, hard, fixed or matted, progressively enlarging LNs, supravacular location
    - Yes
      - Review history:
        - Search clues for infectious, inflammatory, autoimmune or neoplastic diseases. Review medications.
        - Chest x-ray, CBC, mononucleosis, and CMV serology, PPD, RPR, ANA, HBsAg, HIV, protein electrophoresis, LDH
      - CT scan directed to drainage area for diagnostic/staging purposes
        - Yes
          - Tissue diagnosis of primary tumor
        - No
          - Repeat biopsy
    - No
      - Infectious:
        - HIV
        - Syphilis
        - CMV
        - EBV
        - Hepatitis
        - Tuberculosis
      - Inflammatory:
        - Sarcoidosis
        - Autoimmune:
          - Rheumatoid Arthritis
          - Lupus
        - Neoplastic:
          - Hodgkin disease
          - Non-Hodgkin Lymphomas
          - Leukemia
          - Drugs:
            - Allopurinol
            - Atenolol
            - Captopril
            - Carbamazepine
            - Cephalosporins
            - Gold
            - Hydralazine
            - Penicillin

Follow-up

Metabolic Acidosis

**METABOLIC ACIDOSIS**

- **Anion gap (AG)**

  \[ \text{AG} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) \]

- Normal: \(<12 \text{ mEq/L} \)

- **Calculate** \( \Delta/\Delta \) (delta/delta ratio)

  \[ \frac{\text{AG} - 12}{\text{HCO}_3^- - 24} \]

- **AG**

  - \( \geq 12 \) AG
  - \(< 12 \) AG

**1–2 Metabolic acidosis**

- Check urine or serum ketones (or \( \beta \)-hydroxy butyrate if pH < 7.1 & ketone negative)

**≤1 AG metabolic acidosis & nonanion gap metabolic acidosis**

**>2 Metabolic acidosis & metabolic alkalosis or respiratory acidosis**

**Normal glucose**

**Elevated glucose**

- Elevated BUN/creatinine

  Yes: DKA

  No: Consider malnutrition, alcoholic ketoacidosis

- No: Serum lactate

  Yes: Renal failure–induced metabolic acidosis

- Decreased or normal: Check osmolar gap = measured osmolality – calculated (2[Na+] + glucose + BUN/2.8 + ethanol/4.6)

- Elevated: Lactic acidosis (hypoperfusion), shock, sepsis, liver or renal failure

- <10 mOsm: Obtain salicylate level

- ≥10 mOsm: Obtain ethylene glycol and methanol levels


868
**METABOLIC SYNDROME, TREATMENT**

1. **Identify risk factors**
   - Abdominal obesity, insulin resistance, physical inactivity, high BMI, high-carb diet, cigarette smoking, Western diet, 1–2 sugar-sweetened beverages/day, patients with known cardiovascular disease.

2. **Assess**
   - Is waist circumference >40” (102 cm) - men or >35” (88 cm) - women?
   - Serum triglycerides ≥1.7 mmol/L (150 mg/dL) or on lipid lowering therapy.
   - Serum HDL <1.03 mmol/L (40 mg/dL) in men or <1.3 mmol/L (50 mg/dL) in woman.
   - SBP ≥130 mm Hg or DBP ≥85 mm Hg or treatment of previously diagnosed HTN.
   - Fasting plasma glucose ≥5.6 mmol/L (100 mg/dL) or previously diagnosed DM2.

3. **Does patient meet 2 of 4 criteria above?**
   - Yes
   - No

4. **Treat physical inactivity**
   - Regular moderate-intensity physical activity; 30–60 min of continuous or intermittent exercise 5 d/wk. (Level 3)

5. **Treat abdominal obesity**
   - 7–10% body weight reduction in 1st year of therapy. Weight maintenance/reduction through balanced physical activity, reduced caloric intake, and lifestyle changes. (Level 3)

6. **Treat elevated BP**
   - Physical activity (see above)
   - Weight reduction
   - Pharmacotherapy if indicated for BP >140/90. (Level 3)

7. **Treat elevated glucose**
   - Physical activity (see above)
   - Weight reduction
   - Pharmacotherapy if necessary to delay progression to DM. (Level 3)

8. **Consider and treat alternative**
   - Hypertension, hyperlipidemia, diabetes, obesity

Nephrotic Syndrome

Suggesting symptoms and signs:
Edema, foamy urine, weight gain, hypoalbuminemia

Urine dipstick analysis

≥3–4 + protein

Yes

SPOT URINE COLLECTION
Random urine protein/creatinine

Yes/conformation

≥3–3.5 g/24 h

Yes

24-HOUR URINE COLLECTION
Gold standard

Obtain:
- CBC w/diff., ESR, BUN/creatinine, electrolytes, glucose, serum albumin, lipid panel, HIV, hepatitis panel, RPR, ANA, anti-dsDNA, complement (C3 and C4) levels.
- Symptoms or History of: DM, SLE, Hep B or C, NSAID use/abuse, pregnancy, multiple myeloma?

Renal biopsy

Normal-appearing glomeruli on renal biopsy microscopy; effacement of foot processes on electron microscopy

Thickening of the glomerular basement membrane on electron microscopy; IgG and C3 deposits with immunofluorescent staining

Sclerosis and hyalinosis of segments of <50% of all glomeruli on electron microscopy deposits with immunofluorescent staining

Minimal change disease

Membranous nephropathy

Focal segmental glomerulosclerosis

SECONDARY NEPHROTIC SYNDROME

Diabetic nephropathy

Systemic lupus

Hepatitis B & C

Preeclampsia

Multiple myeloma

HIV

Amyloidosis

Nocturia

**NOCTURIA**

- **Voiding diary**
  - NPI (nocturnal polyuria index) >35%
  - Diminished nocturnal bladder capacity (NBC)
  - 24-hr urine volume >40 mL/kg

**Nocturnal polyuria**
- CHF
- Diabetes mellitus
- Peripheral edema
- Excessive nighttime fluid intake
- Sleep apnea
- Medications
- Venous stasis

**Mixed (nocturnal polyuria + low nocturnal bladder capacity)**

**Low nocturnal bladder capacity**
- Detrusor overactivity (neurogenic/non neurogenic)
- Voiding dysfunction
- Inflammatory (UTI, radiation cystitis, stones)
- Neoplasia (BPH, urothelial carcinoma of the bladder or CIS)

**24-hr (global) Polyuria**
- Diabetes mellitus
- Diabetes insipidus
- Primary polydipsia

**NPI**: Night-time urine output greater than 35% of the daily total in older adults.
Parathyroid Hormone, Elevated Serum

**PARATHYROID HORMONE, ELEVATED SERUM**

Common causes:
- Parathyroid adenoma, parathyroid hyperplasia, ectopic PTH, renal failure, lithium, small bowel disease, chronic pancreatitis, low calcium intake, vitamin D deficiency, familial hypocalciuric hypercalcemia (FHH), MEN 1

Check labs:
- Total serum calcium, PO4, 25-hydroxy vitamin D, urinary Ca:Cr

Serum Ca on 2 occasions; ± clinical signs of hypercalcemia

Primary hyperparathyroidism

- Parathyroid adenoma
- Parathyroid hyperplasia
- Ectopic PTH
- Lithium
- MEN 1

Or if urinary Ca:Cr

Tertiary hyperparathyroidism: follows long-standing secondary hyperparathyroidism

Secondary hyperparathyroidism

- Renal failure
- Chronic pancreatitis
- Low calcium intake
- Vitamin D deficiency

Familial hypocalciuric hypercalcemia (FHH)

PELVIC PAIN, FEMALE

Common causes: Menstrual cramps, PID, ectopic pregnancy, fibroid uterus, endometriosis, ovarian cyst

Pregnancy test

+ Pregnancy test
  - Ectopic pregnancy
  - Normal gestation

- Pregnancy test
  - Cyclic pain
  - Acute pain
  - Gradual onset

Menstrual cramps
Endometriosis
Adenomyosis

PID
Ovarian torsion
UTI
Appendicitis
Diverticulitis

Uterine fibroids
Ovarian tumor
Functional disorder

Penis, Squamous Cell Carcinoma

**PENIS, SQUAMOUS CELL CARCINOMA**

- History and physical
- Incisional–excisional biopsy of lesion
- Exam inguinal lymph nodes (IGN) with CT scan if palpable nodes
- Penile US assess proximal extent

- Tumor on prepuce
- Circumcision with intraoperative frozen section analysis

- Distal tumor
- Partial penectomy with intraoperative frozen section analysis >2 cm

- Proximal tumor
- Total penectomy

- Tis, Ta, T1G1–2, no vascular invasion
- If IGN are palpable give 4 wk of antibiotics and reassess

- T2–T4, vascular invasion, grade 3
- Palpable IGN
- Ipsilateral superficial and deep inguinal and pelvic node dissection. Contralateral superficial inguinal dissection.

- Nonpalpable IGN
- Observe

- Consider FNA and excisional biopsy for Tis and Ta tumors prior to node dissection

- Consider adjuvant chemotherapy if T4 disease, >2 nodes positive, bilateral metastasis, extranodal extension, or positive

- Perform deep inguinal and pelvic lymph node dissection if superficial dissection positive on that side

- Bilateral superficial inguinal node dissection
PENIS, TRAUMA

History and physical
Urine analysis
Retrograde urethrogram (RUG) in most cases

Traumatic amputation
Penetrating injury
Penile fracture

Immediate exploration
Close corporal defects with 2-0 or 3-0 absorbable suture
Inspect spongiosum and urethra

Partial urethral injury
Over-sew with fine absorbable sutures over catheter

Complete urethral injury
Debride, mobilize, and primary anastomosis over urethral catheter

Microvascular reimplantation if severed part available, close corpora and spatulate urethral neomeatus if severed part not available. Consider suprapubic tube.

<16-hr cold ischemia
OR
<4-hr warm ischemia
Polyuria

**Common causes:** Diabetes mellitus, diabetes insipidus, medication, hyperparathyroidism, renal disease

**Check labs:** Urinalysis, glucose, BUN, creatinine, calcium

- **Elevated glucose**
  - Diabetes mellitus
  - Medication effect

- **Normal glucose**
  - No medication effect

- **Presence of WBC, leukocyte esterase, nitrates**

- **Diuretics**
  - Lithium
  - Demeclocycline

- **Elevated calcium**
  - Hyperparathyroidism
  - Elevated BUN, creatinine, or abnormal urine sediment

- **Normal calcium**
  - Normal renal tests
  - Suppressed TSH

- **Low urine specific gravity, low urine osmolality, normal serum osmolality, hypernatremia**

- **Diabetes insipidus**

---


876
Precocious Puberty

**Precocious Puberty**

- Signs of secondary sexual development in boys >9 and girls >8

**Common causes:**
- Medication, pituitary tumor, congenital, adrenal hyperplasia, adrenal tumor, ovarian tumor, pseudoprecocious puberty

**X-ray to determine bone age**

- **Bone age > chronologic age**
  - Basal LH levels
  - <5 mIU/mL: GnRH stimulation test, LH, FSH
  - >5 mIU/mL: Gonadotropin-independent (peripheral) precocious puberty
  - Elevated LH, FSH, estradiol, testosterone, TSH, MRI of brain
  - LH, FSH increased
  - Absent LH response

- **Bone age = chronologic age**
  - Incomplete precocious puberty (premature adrenarche or thelarche)

**Gonadotropin-dependent (central) precocious puberty**

- Elevated hCG in β
- Germ cell tumor
- Elevated 17-hydroxyprogesterone
- McCune–Albright syndrome
- Elevates DHEA, DHEAS, findings on imaging

- Congenital adrenal hyperplasia
- Elevated DHEA, DHEAS, findings on imaging
- Adrenal tumor on cancer

**Gonadotropin-independent (peripheral) precocious puberty**

- Very high level of testosterone in β
- Leydig cell tumor
- Elevated testosterone in β and estradiol in β, with bone and skin findings

- Elevated testosterone in β and estradiol in β
- Exogenous sex steroids

**Incomplete precocious puberty**

- Testosterone, estradiol, LH, FSH, cortisol, DHEA, DHEAS, 17-hydroxyprogesterone, hCG (males), abdominal and pelvic US

**Common causes:**
- Medication, pituitary tumor, congenital, adrenal hyperplasia, adrenal tumor, ovarian tumor, pseudoprecocious puberty

**Priapism**

PRIAPISM

- History and physical
  - Duration of erection (treat when >4 hr)
  - Degree of pain
  - Previous history of priapism
  - Use of drugs that may have caused priapism
  - History of pelvic, genital, or perineal trauma
  - History of sickle cell disease
  - History of other hematologic abnormality
  - Labs: CBC, urine analysis, urine toxicology

- Treat any underlying disease, such as sickle cell, simultaneously

- Penile blood gas
- Color duplex US of perineum and penis

- Ischemic:
  - $pO_2 < 30$, $pCO_2 > 60$, $pH < 7.25$ on penile blood gas

- Nonischemic:
  - $pO_2 > 90$, $pCO_2 < 40$, $pH = 7.40$ on penile blood gas

- Place patient on cardiac monitor
- Give dose of Ancef or similar spectrum antibiotic
- Possible dorsal penile back

- Aspiration with or without irrigation
- Phenylephrine 100–500 mcg/mL normal saline

- Distal shunts
- Arteriography and embolization
- Surgical ligation

- Repeal distal shunt or proximal shunt
- Implementation of penile prosthesis controversial

Prostate cancer, rising PSA following androgen ablation (Castration resistant prostate cancer [CRPC]) Rising PSA with testosterone <50 ng/mL

Radiographic evidence of metastasis?

No

Yes

Confirn and maintain castrate testosterone level (<50 ng/mL)

Consider clinical trial

PSADT ≤ 10 mo: Antiandrogen withdrawal
Ketoconazole
Corticosteroids
DES or other estrogen

Periodic radiographic imaging

With radiographic evidence of metastasis treat as mCRPC

PSADT >10 mo: Continue observation

Sipuleucel-T

Antiandrogen withdrawal
Abiraterone
Enzalutamide
Ketoconazole
Corticosteroids
DES or other estrogen
Docetaxel
Clinical trial

If post-docetaxel: Abriraterone, cabazitaxel, radium-223 (symptomatic bone mets)
Salvage chemotherapy
Docetaxel rechallenge
Mitoxantrone
Other secondary hormonal therapy: Antiandrogen, antiandrogen withdrawal, ketoconazole, corticosteroids, DES or other estrogen
Sipuleucel-T
Clinical trial
Best supportive care

Progression

Symptomatic?

No

Yes

Docetaxel
Radium-223 (bone mets only)
Mitoxantrone
Abiraterone
Enzalutamide
Palliative RT or radionuclide for symptomatic bone mets
Clinical trial
Best supportive care

Metastatic castrate resistant prostate cancer (mCRPC)

Confirm and maintain castrate testosterone level (<50 ng/mL)

Denosumab or zoledronic acid with bone metastasis

Clinical trial

Prostatitis

**PROSTATITIS**

- **Prostatitis, general**
  - History and physical
    - Check UA and urine culture
      - Meares–Stamey 4-glass test
      - Suspect acute bacterial prostatitis (NIH I)
        - CBC, admit for IV antibiotics if febrile; treat 4–6 wk oral antibiotics
        - VB1: Initial 5–10 mL
        - VB2: 16 mL midstream voided urine
        - EPS: Expressed prostatic secretions
        - VB3: Post-EPS voided urine
          - All cultures positive
            - Bacterial cystitis. Treat cystitis and repeat test
          - EPS, VB3 culture positive, WBC in EPS
            - Chronic bacterial prostatitis (NIH II)
          - WBC in EPS, culture negative
            - Chronic pelvic pain syndrome inflammatory (NIH IIIa)
          - VB1 cultures positive
            - Urethritis or urethral colonization
          - All cultures negative
            - Chronic pelvic pain syndrome noninflammatory (NIH IIIb)
        - EPS: expressed prostatic secretions
          - NIH: National Institutes of Health classification of prostatitis
          - VB: voided bladder urine
Proteinuria

Common causes: Nephrotic syndrome, diabetes mellitus, multiple myeloma, CHF, medications

Check labs: BUN, creatinine, glucose, serum protein, repeat urine protein

Proteinuria resolved

Fever
Vigorous exercise
Cold exposure
Dehydration

Yes

No

Age <30

Rule out orthostatic proteinuria

Elevated BUN
creatinine

Check: Renal US 24-hr urine for protein and creatinine clearance

Normal renal function

Elevated serum protein

Check labs: serum protein electrophoresis (SPEP)

Glomerular disease
Poly cystic kidney disease
Diabetic nephropathy
Acute tubular necrosis

Nephrotic medications
Renal artery stenosis

Salicylates
Carbamazepine
Aminoglycosides

CHF

Multiple myeloma
Waldenström macroglobulinemia

The use of PSA for prostate cancer screening and the definition of "abnormal" PSA is controversial. No absolute PSA can determine the presence or absence of prostate cancer. Age specific median population values in men:

- 40’s: 0.5–0.7 ng/mL
- 50’s: 0.9 ng/mL
- 60’s: 1.3 ng/mL
- 70’s: 1.7 ng/mL

PSA < 4 ng/mL: 15% prostate cancer risk
PSA 4–10 ng/mL: 30–35% prostate cancer risk
PSA > 10 ng/mL: >67% prostate cancer risk

Screening PSA based on informed consent in an asymptomatic man with >10 yr life expectancy and normal DRE.

Normal or abnormal PSA based on the suspicion of the presence of prostate cancer in a man with or without symptoms (e.g., suspicious rectal exam [nodularity/firmness], proctalgia, pelvic/osteoblastic bone metastasis).

PSA > 1 ng/mL: Repeat every 1–2 yr
PSA < 1 ng/mL: Repeat at age 50
PSA < 3 ng/mL: no other indications for biopsy repeat every 1–2 yr
Any PSA > 3 ng/mL:

Standard transrectal ultrasound (TRUS) directed prostate biopsy for tissue diagnosis (12 core sets and lesion directed).

PSA Adjuncts:
- PSA velocity/PSA density
- % free PSA (<10% suspicious for cancer)
- PCA3 urine score (>35 suspicious for cancer)
- Prostate Health Index (PHI) (>35 suspicious for cancer)

Follow-up based on risk factors:

- Atypia, ASAP, suspicious for cancer
- High-grade PIN in biopsies (≥2 sites)
- Repeat biopsy within 6 mo

Prostate cancer staging and discussion management options (locally advanced vs. metastatic).

After two negative TRUS biopsies, cancer is not commonly found. For repeat biopsy consider anterior and transition zone. Multiparametric MRI and TRUS/MRI fusion biopsy may be useful. High-risk patients may benefit from calculation including transperineal template approaches.
PULMONARY EMBOLISM, DIAGNOSIS

- Clinical signs/symptoms of DVT > Clinical signs/symptoms of DVT
  - Alternate Dx less likely than PE
  - Heart rate >100
  - Immobility/surgery in last 4 wk
  - Previous DVT/PE
  - Hemoptysis
  - Malignancy

Pulmonary Embolism, Diagnosis

D-Dimer

- Normal: PE ruled out
- Elevated (0.5 g/mL): 
  - <2: Low probability
  - ≥2: High probability
  - Consider initiated Tx prior to confirmation

- Clinical signs/symptoms of DVT > Clinical signs/symptoms of DVT
  - Alternate Dx less likely than PE
  - Heart rate >100
  - Immobility/surgery in last 4 wk
  - Previous DVT/PE
  - Hemoptysis
  - Malignancy

- Critically ill: Multidetector CT available
- Not critically ill: Transthoracic/ transesophageal echocardiogram to evaluate for right ventricular strain or dysfunction

- Right ventricular dysfunction seen
- Multidetector CT unavailable
- No dysfunction, no injury
- Dysfunction, no injury
- Dysfunction, and injury

- Admit to inpatient service or consider treatment at home
- Admit to inpatient service anticoagulation
- Consider to admit to ICU. Consider thrombolysis anticoagulation

- Thrombosis, surgery, catheter anticoagulation

- After PE is diagnosed, follow-up and monitor for 2 yr in office, as there is a high rate of recurrence.

Pulmonary Embolism, Treatment

**PULMONARY EMBOLISM, TREATMENT**

Probability of pulmonary embolism above treatment threshold

- IV C filter
  - Yes
  - No
    - Massive pulmonary embolism? (SBP < 90 for > 15 min)
      - Yes
        - Thrombolysis contraindicated?
          - Yes
            - Thrombolysis
          - No
            - No
            - Embolotomy, per local expertise
      - No
        - Evidence of increased severity that suggests potential benefit of thrombolysis:
          - 1. Hemodynamic instability.
          - 2. Worse respiratory insufficiency.
          - 3. Severe RV strain, and/or
          - 4. Major myocardial necrosis?
            - Yes
              - History of heparin-induced thrombocytopenia (HIT)?
                - Yes
                  - Consider fondaparinux or argatroban.
                - No
                  - Absolute contraindications to thrombolysis:
                    - Prior intracranial bleed
                    - Ischemic stroke < 3 mo
                    - Suspected aortic dissection
                    - Active bleeding diathesis
                    - Recent brain or spinal surgery
                    - Closed head or facial trauma
            - No
              - Consider fondaparinux or argatroban.


884
Pyuria

Common causes: Cystitis, pyelonephritis, urethritis, nephritis, appendicitis, vaginal contamination

Check labs: Urine culture

Positive

Fever and/or flank pain
Pyelonephritis

No fever, flank pain
Cystitis

Negative

Acute abdominal pain

Renal disease

Appendicitis
Pelvic inflammatory disease (PID)
Pancreatitis

Glomerulonephritis
Interstitial nephritis

Other infections

Urethritis
Prostatitis
Renal TB

Vaginal contamination
Interstitial cystitis

Rectal Injury

RECTAL INJURY

Rectal injury during radical prostatectomy or radical cystectomy

Identified intraoperatively

Prior pelvic radiation or septic/unstable

No

Immediate layered closure with omental or peritoneal flap

Diverting colostomy, delayed colorectal anastomosis

Cystourethrogram prior to Foley catheter removal; if persistent rectourethral fistula, continue Foley vs. delayed repair (transrectal advancement flap)

Suspected postoperatively

Confirm with distended tender abdomen, fever, elevated WBC, abdomino-pelvic axial imaging with free air and perirectal fluid

Yes

Consider proximal bowel diversion with an end colostomy
Rectocele and Enterocele

**RECTOCELE AND ENTEROCELE**

Rectocele and/or enterocele management (posterior compartment prolapse) based on history, physical exam findings

- **Conservative management**
  - Pelvic floor muscle therapy
  - Pessary
  - If successful, continue management

- **Failure to respond?**
  - Consider surgical approach

- **Surgical approach**
  - Midline fascial plication
  - Site-specific repair
  - Transrectal rectocele repair
  - Graft augmentation
  - Sacral colpopexy with mesh extension

- **Is there occult stress urinary incontinence?**
  - Yes: Consider sling
  - No: Conservative management
Renal Colic Management

RENAL COLIC MANAGEMENT

Helical CT abdomen/pelvis (non-contrast)

CT confirms renal/ureteral stone

Urgent intervention required

Obstructed infected upper tract
impending renal deterioration
intractable pain nausea vomiting
patient preference

Nonurgent pathway

CT shows no renal/ureteral stone

Nonurgent pathway

Consider nonurologic causes

Assess likelihood
of spontaneous
stone passage

Observation

Consider metabolic
stone risk

Intervention required

Assess stone composition,
location, size, upper tract
anatomy, patient preference

Uric acid stone

Dissolution therapy

Consider metabolic
stone risk

Nonuric acid stone

Urologic intervention

Consider metabolic
stone risk


888
Acute kidney injury (AKI, previously called acute renal failure) is an acute loss of kidney function over days to weeks resulting in an inability to excrete nitrogenous wastes and creatinine. Patients are often asymptomatic, and are recognized by an increase in serum creatinine level (>0.5 mg/dL from baseline). Prerenal disease (PD) is one category of AKI where the injury occurs outside the nephron; it is marked by diminished renal blood flow leading to a decrease in glomerular filtration rate (GFR).

Common causes: True volume depletion, hypotension, edematous states, selective renal ischemia, and drugs affecting autoregulation.

Workup: History and physical, serum chemistries, CBC with differential, LFTs including serum albumin urinalysis with microscopy, urine sodium, and creatinine and if diagnosis remains obscure, imaging (x-ray, US, CT).

Volume depletion

Hypotension

Edematous states (decreased effective blood volume)

Selective renal ischemia

Drugs affecting autoregulation

Dehydration/Poor PO intake: Dry mucous membranes, pallor, orthostatic hypotension, weight loss, perspiration, decreased skin turgor.

GI losses: Eructation, diarrhea

Renal losses: Overdiuresis with diuretics, osmotic diuresis with hyperglycemia.

Infectious: Fever, chills, leukocytosis (with left shift).

Hemorrhage

Insensible losses: Perspiration, burns.

Large vessel diseases: Arterial thrombus (hypercoagulable syndromes), emboli (atherosclerotic disease), aortic dissection (connective tissue disease, trauma).

Shock

Septic: Evidence of infection, hypotension, acidosis, constitutional symptoms, leukopenia or leukocytosis, tachycardia, tachypnea.

CHF: JVD, pulmonary rales, pitting edema, hepatomegaly, dyspnea

Cirrhosis: Ascites, varices, pruritus, jaundice, anemia, bruising, edema, elevated LFTs, hypalbuminemia

Nephrotic syndrome: Hypoalbuminemia, proteinuria, foamy urine, hypertension, facial and peripheral edema.

Hepatorenal syndrome: Portal hypertension, oliguria, hyperammonemia, constitutional symptoms

Bilateral renal artery stenosis: Possible history of hypertension, atherosclerosis, fibromuscular dysplasia/worsened by ACE inhibitors or ARBs.

ACE inhibitors: Vasodilation of arterial arterioles

NSAIDs: Vasostenogen of arterial arterioles

Calcineurin inhibitors: Vasostenogen of arterial arterioles

FENa <1% is seen in contrast nephropathy and pigment nephropathy (rhabdomyolysis), both of which cause intrinsic renal failure. FENa can be >1% with diuretics if overdiuresis is severe, and also if prerenal failure develops in patients with chronic kidney disease.

Prerenal disease

Serum BUN: Creatinine ≤20:1

Urine osmolality >400 mOsm

Urine sediment: Bland, few hyaline casts

FENa <1%* (with exceptions)

Intrinsic

Serum BUN: Creatinine >20:1

Urine osmolality 200–300 mOsm

Urine sediment: Variable depending on etiology (eg., acute tubular necrosis [ATN], acute interstitial nephritis [AIN], glomerulonephritis [GN])

FENa >2%*

Postrenal/Obstructive

Urine sediment: Blurred, few hyaline casts, possible RBCs

Anuria if complete bilateral urinary tract obstruction is present.

ACE inhibitors:

Vasodilation of arterial arterioles

NSAIDs:

Vasostenogen of arterial arterioles

Calcineurin inhibitors:

Vasostenogen of arterial arterioles

Renal Mass

**RENAL MASS**

- **Cystic**
  - Bosniak I or II
  - No need to follow if asymptomatic
  - Surveillance with periodic US, CT, or MRI

- **Solid**
  - Bosniak IF
  - Surgical removal
  - Likely RCC, follow with serial imaging and remove as indicated
  - Bosniak III–IV
  - Enhancing >15
  - Concern for metastasis to kidney or lymphoma
  - Fat present
  - MRI if concern for renal vein involvement
  - Staging with imaging of abdomen, chest x-ray, complete metabolic panel

Bosniak Classification:
- I: simple cyst
- II: benign cysts with few thin septae fine calcification in wall
- IF: cysts with increased septae, minimal enhancement or thickened wall. Calcifications present but no soft tissue mass.
- III: thickened, irregular walls or septae with enhancement
- IV: clearly malignant cystic masses (characteristics of Class III with enhancing soft tissue masses)

- **Nephroureterectomy with endoscopic treatment on select cases**
- **TCC**
- **MRI** if concern for renal vein involvement
- **Staging with imaging of abdomen, chest x-ray, complete metabolic panel**

Size <3 cm, advanced age, comorbidities, patient preference

- **Tumor ablation (eg., cryotherapy or radio frequency ablation [RFA])**
- **Active surveillance**
- **Partial nephrectomy**
- **Radical nephrectomy**

Amenable to nephron sparing surgery (eg., Stage T1a [<4 cm] and select T1b [4–7 cm])

- Large tumor, locally invasive, venous involvement, lymphadenopathy, patient preference

Likely AML, follow with serial imaging and remove as indicated

Likely RCC

Diagnostic ureteroscopy or retrograde pyelogram if concern for urothelial carcinoma

Staging with imaging of abdomen, chest x-ray, complete metabolic panel

TCC

Nephroureterectomy with endoscopic treatment on select cases

TCC
RENAL MASS, INTRAOPERATIVE CONSULT

Preop imaging available & enhancing solid mass:
1. Evaluate contralateral kidney with available labs/imaging ± IRBx & FS
2. Attempt to perform PN after family discussion (if present)

Preop imaging unavailable, patient stable:
• Obtain Doppler US

Solid elements, normal contralateral kidney, and amenable to PN
• Perform PN

Radical required for technical reasons

RN required for technical reasons: perform if evidence of normal contralateral kidney function and:
1. Absolute indication for RN (≥cT3, vascular compromise, adjacent organ involvement)
2. After IRBx and FS show evidence of malignancy

Evidence of benign disease, severe CKD, and/or abnormal contralateral kidney function
• Defer treatment until discussion of risk of dialysis

Abbreviations:
- RN = radical nephrectomy
- PN = partial nephrectomy
- IRBx = intraop renal biopsy
- FS = frozen section analysis
- CKD = chronic kidney disease
Renal Trauma, Hemodynamically Stable

**RENAL TRAUMA, HEMODYNAMICALLY STABLE**

- CT abdomen/pelvis with delayed images

- **Grade I–III**
  - Nonoperative management:
    - Observation
    - Bed rest until gross hematuria resolves
    - Serial hematocrit
  - Repeat CT at 36–72 hr for grade IV nonvascular
  - Place ureteral stent for significant enlarging urinoma
  - Continued observation and reimaging with possible surgical repair if persistent

- **Grade IV nonvascular**
  - Nonoperative management:
    - Observation
    - Bed rest until gross hematuria resolves
    - Serial hematocrit
  - Englarging hematoma CT or >4–6 units pRBCs required for declining hematocrit
  - Selective angioembolization and continued observation

- **Grade IV vascular and any grade V**
  - Operative management generally required for pedicle avulsion injuries
  - Long-term BP monitoring
  - Repeat angioembolization or surgical repair if continued bleeding

- **Grade IV nonvascular**
  - Observation
  - Bed rest until gross hematuria resolves
  - Serial hematocrit
  - Repeat CT at 36–72 hr for grade IV nonvascular
  - Place ureteral stent for significant enlarging urinoma
  - Continued observation and reimaging with possible surgical repair if persistent

- **Repeat CT at 36–72 hr for grade IV nonvascular**
  - Englarging hematoma CT or >4–6 units pRBCs required for declining hematocrit
  - Selective angioembolization and continued observation

- **Long-term BP monitoring**
  - Repeat angioembolization or surgical repair if continued bleeding

**CT abdomen/pelvis with delayed images**
**SCROTUM AND TESTICLE, MASS**

- **History and physical**
  - If trauma, suspect testis fracture or hematoma
  - Painful and suspect torsion
    - Bilateral orchiopexy
  - Not painful and/or torsion not suspected
    - Scrotal US with Doppler
  - Inguinal hernia
    - Surgical repair
  - Abscess
    - Surgical
  - Epididymo-orchitis
    - Anti-inflammatories
    - Antibiotics
    - Rare surgical excisions
  - Torsion of testicular
    - Hydrocele
    - Surgical repair or observation
  - Epididymal mass
    - Cystic
    - Spermatocele, epididymal head
    - Labs: LDH, AFP, β-hCG, LFTs, CBC, Cr
    - Chest x-ray
    - Consider CT abdomen with IV/PO contrast preoperatively, but can also be done postoperatively
  - Solid testicular mass
    - Cystic
    - Solid
  - Spermatic cord mass
    - Cystic
    - Varicocele
    - Radical inguinal orchiectomy with high litigation of spermatic cord
SCROTUM AND TESTICLE, TRAUMA

History and physical
Type of injury
Other injuries
Urine analysis

Blunt

Physical exam suggestive of testicular injury

Penetrating

Immediate surgical repair with goal of testis salvage

If presence of hematuria, consider associated urethral injury

Scrotal US with Doppler

Presence of:
- Testicular fracture
- Inhomogeneity of testicular parenchyma
- Occlusion of tunica albuginea
- Testicular torsion
- Intratesticular hematoma
- Large or expanding hematocoele
Testis Cancer, Nonseminoma

TESTIS CANCER, NONSEMINOMA

Testis Cancer, nonseminomatous Germ cell tumor

Stage 1

RPLND vs. surveillance vs. chemotherapy

Presence of: 
- >T2 
- >40% embryonal 
- Lymphatic or vascular invasion

Primary chemotherapy

Template vs. bilateral RPLND

Stage IIA-III

Primary RPLND

Stage IIC-III or stage IV

Primary chemotherapy based on risk category: Good, intermediate, and poor

Complete response on imaging

Partial response on imaging and markers normal

Poor response on imaging and/or markers elevated

Observation

Bilateral RPLND

Salvage chemotherapy

Tumor in specimen

Teratoma

Fibrosis

Salvage chemotherapy based on tumor left behind

Observation

NO

N1

≥N2

Observation

Adjuvant chemotherapy

Bilateral RPLND

Salvage chemotherapy
Testis Cancer, Seminoma

**TESTIS CANCER, SEMINOMA**

CT abd/pelvis
AFP (5 wk postorchietomy)
hCG (1 wk postorchietomy)
Chest x-ray
Chest CT if x-ray abnormal

Pure seminoma

Stage I
- Spermatocytic seminoma
  - Observation
  - Tumor <4 cm
    - No vascular or lymphatic invasion
      - Observation
      - Relapse
      - Radiation therapy
      - Chemotherapy
    - Tumor >4 cm
      - Vascular or lymphatic invasion
      - Low-dose radiation therapy or investigational chemotherapy
      - Relapse
      - Chemotherapy
      - Relapse

Stage IIA and IIB
- Classic and anaplastic seminoma
  - Observation
  - Elevated hCG
  - Chemotherapy

Stage IIC and III
- Radiation therapy
  - Residual mass
  - Consistent with desmoplastic response
    - Observe

Platinum-based chemotherapy

Tumor >4 cm
- Vascular or lymphatic invasion
  - Low-dose radiation therapy or investigational chemotherapy
  - Relapse
  - Chemotherapy

Tumor <4 cm
- No vascular or lymphatic invasion
  - Observation
  - Relapse
  - Radiation therapy

Consistent with desmoplastic response
- Observe

Discrete mass >3 cm:
- Surgical resection

Necrosis/fibrosis
- Germ cell
  - Salvage chemotherapy or XRT

Necrosis/fibrosis
- Germ cell
  - Salvage chemotherapy or XRT

Pure seminoma

AFP (5 wk postorchietomy)
Chest x-ray
Chest CT if x-ray abnormal

Chest CT if x-ray abnormal
**Testosterone Deficiency (Hypogonadism)**

**TESTOSTERONE DEFICIENCY (HYPOGONADISM)**

- Clinical suspicion of testosterone deficiency
  - Metabolic syndrome
  - Erectile dysfunction
  - Clinical symptoms or physical signs

Measure morning total testosterone (7–11 AM)

- <300 ng/dL
  - Repeat morning total testosterone (consider free or bioavailable T if suspect altered SHBG)
  - Low testosterone
  - Exclude reversible causes: illness, medications, nutritional deficiency
  - Measure: FSH, LH, SHBG
  - Low testosterone
  - Normal testosterone
  - Elevated LH and FSH

Low testosterone

- Primary hypogonadism: Congenital anorchidism, cryptorchidism, mumps orchitis; genetic and developmental conditions (Klinefelter syndrome, Sertoli cell only syndrome, etc.); radiation treatment, chemotherapy, testicular trauma

Secondary hypogonadism: Genetic conditions (Kallmann syndrome, Prader-Willi syndrome), Pituitary (tumors, granulomas, abscesses), Hyperprolactinemia, cranial trauma or radiation, medications

Mixed (primary and secondary) hypogonadism

Undescended Testicle (Cryptorchidism)

**UNDESCENDED TESTICLE (CRYPTORCHIDISM)**

- Tests exam by experienced observer

**Nonpalpable**
- Consider US
  - Overweight
  - Uncooperative

**Palpable**
- Retractile
- Distal to external ring

**Large contralateral testis >2 SD**
- No palpable appendage
- Scrotal nubbin
  - Consider scrotal orchidopexy

**Normal contralateral testis**
- No intrascrotal structures
- Yearly exams and parental observation
- Inguinal orchidopexy with or w/o hernia repair

**Inguinal orchiectomy**
- Hyptrophic, short vas, dysgenetic, or postpubertal
  - 1- or 2-stage Fowler–Stephens orchidopexy
  - Laparoscopic orchidopexy

**Consider contralateral testicular fixation**
- No further intervention
- Inguinal exploration
  - Viable testis
  - Consider microvascular orchidopexy
  - Laparoscopic orchidopexy
  - 1- or 2-stage Fowler–Stephens orchidopexy
  - Hypotrophic, short vas, dysgenetic, or postpubertal

**Inguinal repair**
- Laparoscopy
  - Long-term F/U Counseling the family and self-exam

**Patent PV**
- Distal to external ring
- Consider scrotal orchidopexy

**Consider staged approach**
- Yearly exams and parental observation
- Inguinal orchidopexy with or w/o hernia repair
- Patent PV

Urethral Discharge

URETHRAL DISCHARGE

Common causes:
Gonorrhea, chlamydia, trichomonas, urethral strictures, reactive arthritis (formerly Reiter's syndrome)

Check labs: Culture or urine DNA probe for GC and chlamydia, wet mount

+ STI/STD test

Gonorrhea
Chlamydial infection
Trichomoniasis

- STI/STD test

Joint pains
Urethral stricture

+ PPD

Reactive arthritis
(Formerly Reiter syndrome)
Undifferentiated spondyloarthropathy

Tuberculosis

Urinary Retention, Male

**Suspect acute bacterial prostatitis:**
- Suprapubic catheter preferred if septic

**History and physical exam:**
- LUTS history
- Urologic surgery
- Diabetes, neurologic conditions
- History of strictures, STDs
- Neurologic exam
- GU exam including DRE
- Medication history
- Bladder sonogram/scan

**Neurologic findings concerning for cord compression (ie, due to prostate cancer or other CNS lesion):**
- Foley catheter placement
- MRI or CT scan of spine
- Neurosurgery consultation

**Drain bladder:**
- Larger or coude type catheters may be needed
- Cystoscopy with placement of catheter over wire

**Bladder drained:**
- Record initial output
- Send urine analysis and culture
- Send electrolytes, CBC

**Stop possible precipitating medications**
Start α-blocker therapy
Consider starting 5α-reductase inhibitor
Course of antibiotics if suspect infection

**Voiding trial in 1–2 wk**

**Pass:**
- Continue medical management for presumed BPH
- Surgery if indicated for BPH
- Check PSA in 4–6 wk and consider prostate cancer as cause

**Fail:**
- Further evaluation options: Cystoscopy, urodynamics, imaging, PSA
- Consider prostate cancer
- Treat as indicated: Clean intermittent catheterization, surgery, sacral

**Suspect urethral stricture:**
- Attempt smaller catheter
- Obtain RUG or perform cystoscopy to confirm
- Suprapubic tube preferred over repeated dilation

**Suspect prostate cancer:**
- Obtain PSA
- Bone scan and CT scan if indicated

**Bladder drained:**
- Record initial output
- Send urine analysis and culture
- Send electrolytes, CBC

**Stop possible precipitating medications**
Start α-blocker therapy
Consider starting 5α-reductase inhibitor
Course of antibiotics if suspect infection

**Voiding trial in 1–2 wk**

**Pass:**
- Continue medical management for presumed BPH
- Surgery if indicated for BPH
- Check PSA in 4–6 wk and consider prostate cancer as cause

**Fail:**
- Further evaluation options: Cystoscopy, urodynamics, imaging, PSA
- Consider prostate cancer
- Treat as indicated: Clean intermittent catheterization, surgery, sacral

**If acute renal failure, electrolyte abnormalities, or no urinary output for >24 hr consider admission for monitoring of electrolytes and postobstructive diuresis**
Urine Leak From Vagina

**URINE LEAK FROM VAGINA**

Urine leakage from vagina (vesicovaginal and ureterovaginal fistula)

- Cystoscopy, retrograde pyelogram or CT–IV urogram

Ureter unobstructed

- Cystoscopy, bladder distention, dye test
- Confirm vesicovaginal fistula
- Surgical repair

Ureter obstructed

- Retrograde ureterogram/pyelogram
- Confirm ureteral obstruction and/or leakage
- Attempt to pass ureteral catheter

Successful

- Observe

- Fistula repairs naturally

Unsuccessful

- Fistula remains patent

- Ureteroneocystostomy
Urolithiasis

Common causes: Idiopathic, gout, medication effect, hyperparathyroidism, renal disease, colitis

Stone analysis if possible to determine diagnosis

No stone available

Medication effect

Diuretics
Calcium antacids, Indinavir

No medication effect

Check labs: Electrolytes, BUN, creatinine, calcium, uric acid, urine for calcium, oxalate, acid, uric acid

Serum calcium elevated

Parathyroid hormone (PTH) elevated

Hyperparathyroidism

Urine uric acid and/or serum uric acid

Elevated

Normal

Gout
Acidic urine

Urine calcium level

Elevated

Normal

Idiopathic stone formation

Colitis
Chronic diarrhea

Renal disease

Polygenic kidney disease
Renal tubular acidosis

Urolithiasis, Ureteral Calculi

**UROLITHIASIS, URETERAL CALCULI**

- **History and physical**
- **Urine analysis**
- **CBC**
- **Basic metabolic panel**
- **CT scan without contrast**

**Signs of sepsis**

**Proximal ureter**
- Stone <10 mm
  - Symptomatic controlled
  - Normal contralateral kidney function
  - Patient preference

**Distal ureter**
- Stone removal indicated:
  - Persistent obstruction
  - Failure of stone progression
  - Uncontrolled pain

- **Trial of medical expulsive therapy:**
  - α-blocker preferred
  - Periodic imaging

- **Mid ureter**
  - >10 mm
  - <10 mm

- **ESWL may be preferred over ureteroscopy**
- **ESWL or urerteroscopy acceptable**

- **Ureteroscopy may be preferred over ESWL. If uncomplicated, may omit ureteral stent placement**

- **Urgent percutaneous drainage or ureteral stenting with delayed definitive treatment**

UTI, Adult Female

**UTI, ADULT FEMALE**

Complicating factors for UTI & pyelonephritis treatment
- Women >55 yrs
- Symptoms lasting >7 days
- Diabetes mellitus
- Structural abnormality of urinary tract (eg, renal calculi, tumor, abscess)
- Spinal cord injury
- Multiple sclerosis
- Pregnancy
- Chronic catheterization
- Recurrent UTI

Signs and symptoms of suspected UTI
- Dysuria in combination with frequency, urgency, suprapubic pain, and/or hematuria
- Usually in the absence of vaginal symptoms
- Pyuria on routine urinalysis
- Nitrite positive (for gram negatives)

Presence of additional signs & symptoms?
- Fever (Temperature ≥38.5°C)
- Flank pain
- Abdominal or pelvic pain
- Nausea/vomiting
- Costovertebral tenderness

UTI unlikely
- Pelvic exam to detect vaginal or cervical infection; consider urine culture

History and physical most consistent with UTI
- Dipstick UA shows leukocyte esterase or nitrites
- Microscopic UA
  - >15 WBC/HPF
  - >5 RBC/HPF (or not available)

Empiric antibiotics: 3 day regimen
- trimethoprim/sulfamethoxazole
- ciprofloxacin
- nitrofurantoin

Consider urine culture, cervical culture or KON or wet mount to detect other diagnoses (vaginal infection, chlamydia, etc.). Need follow-up for clearing of hematuria

UTI, Pediatric

**UTI, PEDIATRIC**

- History and physical
- Urine analysis and culture
- Antibiotics
- Voiding cystourethrogram (VCUG) and renal/bladder ultrasound (RUS) after

**Renal VCUG and RUS**

**Vesicoureteral reflux**

**Hydronephrosis**

- Observe and if recurrent UTIs:
  - Nuclear VCUG may be more sensitive in detecting VUR
  - Manage constipation and dysfunctional voiding
  - Consider prophylactic antibiotics if UTIs continue and no abnormalities
  - Consider PICC if recurrent febrile UTIs

- Prophylactic antibiotics
  - Treat dysfunctional voiding and constipation.
  - Consider DMSA scan, serum creatinine if febrile UTIs and/or hypertension.

- Rule out secondary causes of VUR:
  - Dysfunctional voiding
  - Posterior urethral valves
  - Neurogenic bladder

**UPJ obstruction**

- Ureterocoele
- Ectopic ureter
- Megareuter
- Prune belly syndrome
- Posterior urethral valves

**Recurrent UTIs**

- Evidence of further renal scarring
- Parent preference for surgery
- Reflux nephropathy
- Elevated creatinine
- Noncompliance

**Principles of Management:**
- VUR often resolves spontaneously for grades I–III VUR
- The higher the grade of VUR, the less likely it will spontaneously resolve
- Prophylactic antibiotics are generally benign and are 1st-line therapy

**Absent**

- Recurrent UTIs
- Evidence of further renal scarring
- Parent preference for surgery
- Reflux nephropathy
- Elevated creatinine
- Noncompliance

- Continue antibiotics and follow with interval VCUG (nuclear or fluoroscopic) until reflux resolves and no more UTIs

**Present**

- Surgical correction of VUR
  - Open

- Document resolution of VUR with VCUG (nuclear or fluoroscopic)
VAGINAL BLEEDING, ABNORMAL

Common causes: PCOS, uterine polyp, uterine tumor, infection, cervical pathology, luteal phase defect

Prepubescent

Child abuse, tumor, anovulatory bleeding of adolescence

Reproductive age

Obtain US, FSH, TSH, prolactin, coagulation studies

Obtain HCG, genital cultures

Workup normal

Pelvic exam, Pap, genital C/S, US and/or endometrial biopsy: TSH, prolactin

Postmenopausal

Common causes: PCOS, uterine polyp, uterine tumor, infection, cervical pathology, luteal phase defect

Ovulatory

Obtain US, FSH, TSH, prolactin, coagulation studies

Hypothyroidism

Normal

Weight loss, excessive exercise

Hyperprolactinemia

Abnormal

Anorexia nervosa

Pituitary adenoma

Yes

Check: LH, DHEA-S, endometrial biopsy

No

Bulimia

Anorexia nervosa

Polycystic ovary syndrome

Uterine tumor

Regular bleeding at cycles >35 days

Regular bleeding at cycles <21 days

Cervical pathology

Menorrhagia

Regular bleeding between 21 and 35 days

Luteal phase defect

Oligomenorrhea

Uterine tumor

Bleeding disorder

Yes

No

Anovulatory

Age >35 yr

Check: Endometrial biopsy, CBC, PT/PTT


907
Vaginal Discharge

VAGINAL DISCHARGE

Common causes: Bacterial vaginosis, candida vulvovaginitis, trichomoniasis

Less common causes: Atrophic vaginitis, cervicitis, foreign body, irritants, and allergens

History and pelvic exam

Vulvar or vaginal lesions/abnormalities (consider carcinoma)

Foreign body

Check pH*

pH < 4.5

Wet prep with KOH

Clue cells

Consider atrophic vaginitis, erosive lichen planus, lichen sclerosus, pemphigoid, or desquamative inflammatory vaginitis

pH > 4.5

Wet prep

PMNs

Motile flagella

Trichomoniasis

Culture for N. gonorrhoeae and chlamydia

Metronidazole 2 g × once OR 500 mg PO b.i.d. × 7 days

Candida vulvovaginitis

Fluconazole 150 mg PO × once

Hyphae or budding yeast

Yes

Consider physiologic leukorrhea, contact irritant, seborrheic dermatitis, psoriasis

No

Cervicitis

Clue cells +/- KOH "whiff" test

Bacterial vaginosis

Metronidazole 500 mg PO BID × 7 days OR Clindamycin 2% cream 5 g QHS × 7 days

* pH for diagnosis is less useful for women at the extreme ages

**VAS DEFERENS, CONGENITAL ABSENCE**

- Nonpalpable vas deferens
- Vas deferens absent unilaterally
  - Cystic fibrosis evaluation of patient CFTR (cystic fibrosis transmembrane conductance regulator) gene analysis
    - Negative for cystic fibrosis trait
      - Evaluate cystic fibrosis status of partner
        - Partner negative for cystic fibrosis
          - In vitro fertilization via surgical sperm extraction/aspiration
        - Partner positive for cystic fibrosis
          - Counsel patient and partner about cystic fibrosis
    - Positive for cystic fibrosis trait
      - Renal US CFTR testing

Vitamin D Deficiency

**VITAMIN D DEFICIENCY**

Risk factors/common causes:
- Age >65
- Insufficient sunlight exposure (homebound, veiled)
- Renal disease
- Liver disease
- Depression
- Chronic use of anticonvulsants
- Dark skin
- Insufficient dietary intake
- GI malabsorption
- Obesity (BMI >30)
- Immigrants to colder climates
- Chronic use of glucocorticoids
- Periosteal bone pain (eg., sternum, ilia)
- GI malabsorption:
  - Celiac, cystic fibrosis,
  - Inflammatory bowel disease
- Pregnancy
- Medications: Anticonvulsants, antiretroviral
  and glucocorticoids
- Gastrectomy or extensive bowel surgery

**Infants and children:**
- <1 y/o: 400 IU (D) per day
- >1 y/o: 400–1,000 IU (D) per day + adequate sun exposure (5–30 minutes twice weekly depending on time of day, between 10 AM and 3 PM and skin pigmentation)
- Infants >1 y/o with ‘Obesity or Malabsorption Syndrome’, consider pediatric endocrine evaluation; if unavailable, 5,000 units/day for 2 mo; if labs are normal/normal physical exam and normal x-ray. Maintenance dose: 600 units/day

**Significant risk factors?**
- Level <20 ng/mL (vitamin D deficiency)
- Treatment: Start 50,000 IU (D2 or D) once per week for 8 wk, then 1,000–4,000 IU per day thereafter
- Then 1,000 IU (D) per day thereafter
- After 6 mo, consider repeating serum 25 OH vitamin D level

- Level <20 ng/mL (vitamin D deficiency)
- Consult endocrinology if no malabsorptive disease

**Lab: Serum 25-hydroxyvitamin D concentration**
- Level >30 ng/mL normal
- Level <30 ng/mL (vitamin D insufficiency)
- Treatment: 800–1,000 IU (D) per day
- Maintenance: 800–1,000 IU (D) per day

- Level <20 ng/mL (vitamin D deficiency)
- Treatment: Start 50,000 IU (D2 or D) once per week for 8 wk, then 1,000–4,000 IU per day thereafter
- Then 1,000 IU (D) per day thereafter
- After 6 mo, consider repeating serum 25 OH vitamin D level

- Level <20 ng/mL (vitamin D deficiency)
- Consult endocrinology if no malabsorptive disease

SECTION IV
Urinalysis and Urine Studies

Section Editor: Leonard Gomella, MD, FACS
I. URINE ANALYSIS

URINE ANALYSIS PROCEDURE

For a routine urine analysis, a fresh (<1 hr old), clean-catch urine sample is acceptable. If the analysis cannot be performed immediately, refrigerate the sample. (When urine stands at room temperature for a long period, casts and red blood cells undergo lysis, and the urine becomes alkalized with precipitation of salts.)

1. Pour 5–10 mL of well-mixed urine into a centrifuge tube.
2. Check for appearance (color, turbidity, odor). If a urine sample looks grossly cloudy, it is sometimes advisable to examine an unspun sample. If an unspun sample is used, make note that you have done so. In general, for routine urine analysis, an unspun sample is more desirable.
3. Spin a capped sample at 3,000 rpm for 3–5 min.
4. While the sample is in the centrifuge, use the dipstick (Chemstrip, etc.) to perform the dipstick evaluation on the remaining sample. Read the results according to the color chart on the bottle. Allow the correct amount of time before reading the test (usually 1–2 min) to avoid false results. Chemstrip 10 provides 10 tests (specific gravity, pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, and blood). Other strips may provide more agents. Agents that color the urine red, phenoxyethylparaben (p-hydroxyacetanilide) may interfere with the reading. Dipstick specific gravity is also available on some assay strips.
5. Decant and discard the supernatant. Mix the remaining sediment by flicking it with your finger and pouring or pipetting 1 or 2 drops onto a microscopic slide. Cover with a coverslip. Compare with a normal urine.
6. Examine 10 low-power fields (×150, i.e., 10× objective for epithelial cells, casts, crystals, and mucus. Casts are usually reported as number of low-power fields and tend to collect around the periphery of the coverslip.
7. Examine several high-power fields (×400, i.e., 40× objective) for epithelial cells, crystals, RBCs, WBCs, bacteria, amorphous substances (all usually unimportant). RBCs, WBCs, and bacteria are usually reported as number per high-power field.

Normal Urine Analysis Values

- Appearance: Yellow, clear, straw-colored
- Specific gravity: Normal: 1.012
- pH: Normal: 6.0–7.5
- Glucose: 0–4/HPF
- Protein: 0–4/HPF
- Leukocyte esterase: Negative
- Blood: Negative
- Nitrite: Negative
- WBC: 0–4/HPF
- RBC: 0–4/HPF
- Epithelial cells: Occasional
- Mucus: Occasional
- Bacteria: None

Differential Diagnosis for Routine Urine Analysis

- Appearance (see Section II Urine, Abnormal Color; Section IV, Urine, Odor, and Urine, Particles in)
  - Acidic: High-protein (meat) diet, ammonium citrate, methicillin, and other medications (due to ketoacidosis [starvation, diabetes], chronic obstructive pulmonary disease [COPD]),
  - Basic: Urate uric acid infections (UTI), renal tubular acidosis, diet (high-vegetable, milk, immediately after meal), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diabetic therapy
- Specific gravity:
  - Usually strongly to slightly, except with osmotic diuresis. A value <1.012 indicates normal renal concentrating ability:
    - Increased: Volume depletion, congestive heart failure (CHF), adrenal insufficiency, diabetes mellitus, inappropriate antidiuretic hormone (ADH), increased proteins (nephrosis); if markedly increased (1.040–1.050), suspect artifact or excretion of radiographic contrast media
    - Decreased: Diabetes insipidus, pheochromocytoma, glomerulonephritis, water load with normal renal function
- Bilirubin:
  - Positive: Obstructive jaundice (myeloproliferative and metastatic), hepatitis (Note: False positive with stool contamination)
- Blood:
  - Positive: See Section I Hematuria, gross and microscopic, adult and Hematuria, microscopic, pediatric
  - Note: If the dipstick is positive for blood, but no RBCs are seen, free hemoglobin may be present from trauma, from a transfusion reaction, or from lysis of RBCs (RBCs will lysis if the pH is <5.0 or >8.0); or there may be myoglobin present because of a crush injury, burn, or tissue ischemia.
- Ketones:
  - Detects primarily acetone and acetoacetic acid and not by hydroxybutyric acid
  - Positive: Starvation, high-fat-low-carbohydrate diet, diabetic ketoacidosis, vomiting, diarrhea, hyperthyroidism, pregnancy, fatty livers (especially in children)
- Glucose:
  - Positive: Fructose, lactose, sucrose, alcohol, urine
  - Negative: Fructose, lactose, alcohol, urine
- Nitrates:
  - Detects primarily potassium nitrate and potassium nitrate
  - Positive: Infection (A negative test does not rule out infection, because some organisms, such as Shigella flexneri and other gram-positive cocci), will not produce nitrates, and the urine must also be retained in the bladder for several hours to allow the bacteria to take place)

- Protein:
  - Indicated by dipstick of persistent proteinuria
- Leukocyte esterase
  - Positive: Pyelonephritis, glomerulonephritis, Kimura disease, nephrotic syndrome, myeloma, polycystic disease, colic stone ingestion, and malignancies of the lower tract, functional causes (fever, stress, heavy exercise), malignant hypertension, congestive heart failure
- Urobilinogen
  - See Section I Pyuria:
  - This test detects ≤1 WBC/HFP if voided WBCs. When combined with the nitrite test, it has a predictive value for UTI of 74% if both tests are positive, and >97% if both tests are negative
  - Positive: Infection (false-positive with vaginal contamination)
- Urobilin
  - Positive: Cholestasis, CHF with hepatic congestion, nephritis, hyperthyroidism, suppression of gut flora with antibiotics (Note: With obstructive jaundice, urobilinogen is usually normal, but bilirubin is elevated)
- Leukocytes
  - Positive: Glaucoma, fracture, gout, sarcoidosis
- Leukocyte esterase
  - Positive: Pyelonephritis, urinary tract infections (UTI), renal tubular acidosis, diet (high-vegetable, milk, immediately after meal), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diabetic therapy
- Blood
  - Positive: Pyelonephritis, urinary tract infections (UTI), renal tubular acidosis, diet (high-vegetable, milk, immediately after meal), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diabetic therapy
- Nitrite
  - Positive: Infection (A negative test does not rule out infection, because some organisms, such as Shigella flexneri and other gram-positive cocci), will not produce nitrates, and the urine must also be retained in the bladder for several hours to allow the bacteria to take place)
- Protein
  - Indicated by dipstick of persistent proteinuria
- Leukocyte esterase
  - Positive: Pyelonephritis, glomerulonephritis, Kimura disease, nephrotic syndrome, myeloma, polycystic disease, colic stone ingestion, and malignancies of the lower tract, functional causes (fever, stress, heavy exercise), malignant hypertension, congestive heart failure
- Urobilinogen
  - See Section I Pyuria:
  - This test detects ≤1 WBC/HFP if voided WBCs. When combined with the nitrite test, it has a predictive value for UTI of 74% if both tests are positive, and >97% if both tests are negative
  - Positive: Infection (false-positive with vaginal contamination)
- Urobilin
  - Positive: Cholestasis, CHF with hepatic congestion, nephritis, hyperthyroidism, suppression of gut flora with antibiotics (Note: With obstructive jaundice, urobilinogen is usually normal, but bilirubin is elevated)
- Leukocytes
  - Positive: Glaucoma, fracture, gout, sarcoidosis
- Leukocyte esterase
  - Positive: Pyelonephritis, urinary tract infections (UTI), renal tubular acidosis, diet (high-vegetable, milk, immediately after meal), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diabetic therapy
- Blood
  - Positive: Pyelonephritis, urinary tract infections (UTI), renal tubular acidosis, diet (high-vegetable, milk, immediately after meal), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diabetic therapy
- Nitrite
  - Positive: Infection (A negative test does not rule out infection, because some organisms, such as Shigella flexneri and other gram-positive cocci), will not produce nitrates, and the urine must also be retained in the bladder for several hours to allow the bacteria to take place)
II. SPOT OR RANDOM URINE STUDIES

The so-called spot urine is often ordered to aid in diagnosing various conditions. It relies on only a small sample (10–20 mL) of urine:

- **Spot urine for Jβ/microglobulin (<0.3 mg/L):** A marker for renal tubular injury.
- **Increased:** Diseases of the proximal tubule (ATN, interstitial nephritis, pyelonephritis), drug-induced nephropathy (aminoglycosides), diabetes, trauma, sepsis.

- **Spot urine for electrolytes:** The serum levels of this assay is limited because of large variations in daily fluid and salt intake, and the results are usually underestimated if a diuretic has been given. (See section III. eGFR and other factors such as age, sex, and race and has generally replaced 24-hr urinary creatinine determinations. Online calculators for adults and children can be found at: http://clinical.niddk.nih.gov/lab-evaluation/calculators.html. (Accessed April 19, 2014)

- **Spot urine for creatinine:** A marker of renal tubular injury.
- **Increased:** Dehydration, CHF, hypercalcemia, hypothyroidism, interstitial nephritis, pyelonephritis, diabetes mellitus, nephrotoxin, virus.
- **Granular casts:** Breakdown of cellular casts leads to waxy casts; dirty brown granular casts typical in the early morning.

- **Spot urine for osmolality:** (Present with Hansell/Wright staining and white light microscopy):
  - **Increased:** Diabetes insipidus, acute renal failure, medications (azathioprine, indinavir, itraconazole).
  - **Decreased:** Nephrogenic diabetes insipidus, acute tubular necrosis, DI within the context of diabetes insipidus, SIADH, acute tubular necrosis, nephrogenic diabetes insipidus.

- **Spot urine for myoglobin:** (qualitative negative): Positively; skeletal muscle conditions (crush injury, etc.). If the values in the previous example were for a 12-hr-old boy who weighed 70 lb (1.1 m2), the clearance would be: 70 mL/min (1.1 m2) × 7.1 mL/min = 75 mL/min.

III. CREATININE CLEARANCE AND GLOMERULAR FILTRATION RATE

**CREATININE CLEARANCE**

- **Renal male:** Total creatinine 1–2 g/24 h (8.8–17.7 mmol/L), clearance 85–125 mL/min/1.73 m2.
- **Renal female:** Total creatinine 0.8–1.8 g/24 h (7.1–15.9 mmol/L); clearance 75–115 mL/min/1.73 m2.
- **Child:** Total creatinine (3 yr) 12–10 mg/kg/24 h (1.08–1.44 mL/min/1.73 m2).
- **Decreased:** A decreased creatinine clearance results in an increase in serum creatinine, usually secondary to renal insufficiency. See Section II. Filtration Rate.

**DETERMINATION OF CREATININE CLEARANCE**

- **Creatinine clearance (CrCl):** A measure of the glomerular filtration rate (GFR) in the absence of renal disease.

- **Increased:** Early diabetes mellitus, pregnancy

**Estimated glomerular filtration rate (eGFR):**

**Estimated glomerular filtration rate (eGFR):**

**Estimated glomerular filtration rate (eGFR):**

- **Creatinine clearance:** A marker of renal tubular injury.
- **Increased:** Dehydration, CHF, hypercalcemia, hypothyroidism, interstitial nephritis, pyelonephritis, diabetes mellitus, nephrotoxin, virus.
- **Granular casts:** Breakdown of cellular casts leads to waxy casts; dirty brown granular casts typical in the early morning.

- **Spot urine for protein:** (Present with Hansell/Wright staining and white light microscopy):
  - **Increased:** Diseases of the proximal tubule (ATN, interstitial nephritis, pyelonephritis), drug-induced nephropathy (aminoglycosides), diabetes, trauma, sepsis.

- **Spot urine for electrolytes:** The serum levels of this assay is limited because of large variations in daily fluid and salt intake, and the results are usually underestimated if a diuretic has been given. (See section III. eGFR and other factors such as age, sex, and race and has generally replaced 24-hr urinary creatinine determinations. Online calculators for adults and children can be found at: http://clinical.niddk.nih.gov/lab-evaluation/calculators.html. (Accessed April 19, 2014)

- **Spot urine for creatinine:** A marker of renal tubular injury.
- **Increased:** Dehydration, CHF, hypercalcemia, hypothyroidism, interstitial nephritis, pyelonephritis, diabetes mellitus, nephrotoxin, virus.
- **Granular casts:** Breakdown of cellular casts leads to waxy casts; dirty brown granular casts typical in the early morning.

- **Spot urine for osmolality:** (Present with Hansell/Wright staining and white light microscopy):
  - **Increased:** Diabetes insipidus, acute renal failure, medications (azathioprine, indinavir, itraconazole).
  - **Decreased:** Nephrogenic diabetes insipidus, acute tubular necrosis, DI within the context of diabetes insipidus, SIADH, acute tubular necrosis, nephrogenic diabetes insipidus.

- **Spot urine for myoglobin:** (qualitative negative): Positively; skeletal muscle conditions (crush injury, etc.). If the values in the previous example were for a 12-hr-old boy who weighed 70 lb (1.1 m2), the clearance would be: 70 mL/min (1.1 m2) × 7.1 mL/min = 75 mL/min.

**Estimated glomerular filtration rate (eGFR):**

**Estimated glomerular filtration rate (eGFR):**

- **Creatinine clearance:** A measure of the glomerular filtration rate (GFR) in the absence of renal disease.

- **Increased:** Early diabetes mellitus, pregnancy

**DETERMINATION OF CREATININE CLEARANCE**

- **Creatinine clearance (CrCl):** A sensitive indicator of early renal insufficiency and is a measure of the glomerular filtration rate (GFR); however, the GFR does not provide information on the vogue of the renal disease. CrCl decreases with age, with a CrCl of 10–20 mL/min indicating severe renal failure, and usually the need for dialysis. The National Kidney Disease Education Program (NKDEP) recommends using an estimation of GFR (eGFR) from serum creatinine in adults (>18 yr) with chronic kidney disease (CKD) and those at risk for CKD (diabetes, hypertension, and family history of kidney failure).

**METHODS**

1. Formal 24-hr Urinary Collection for Creatinine Clearance

Order a concurrent serum creatinine (SCr) and a 24-hr urine creatinine. A shorter time interval can be used (e.g., 12 hr), but the formula must be corrected for this change; a 24-hr sample is less prone to collection errors.

- **Creatinine x total urine volume**

**Example:** The following are calculations of (a) CrCl from a 24-hr urine sample with a volume of 1,000 mL, (b) a urine creatinine of 108 mg/100 mL, and (c) a Scr of 1 mg/100 mL (1 mg/dL), where time = 1.440 min for 24-hr collection is used.

- **Clearance (CrCl):**
  - **CrCl = 125 mL/min** (1 mL/dL) = 75 mL/min

To determine if there is a valid, full 24-hr collection, the sample should contain 18–25 mg/kg/h of creatinine for adult males or 12–20 mg/kg/h for adult females. If the patient is an adult (110 lb = body surface area of 1.73 m2), adjustment of the clearance for body size is not routinely done. Adjustment for the pediatric patients is a necessity. If the values in the previous example were for a 12-hr-old boy who weighed 70 lb (1.1 m2), the clearance would be:

- **CrCl = 75 mL/min (1.1 m2) = 71 mL/min

2. **Estimated Creatinine Clearance (eGFR)**

- **Estimated glomerular filtration rate (eGFR):** Based on Scr combined with other factors such as age, sex, and race and has generally replaced 24-hr urinary creatinine determinations. Online calculators for adults and children can be found at: http://clinical.niddk.nih.gov/lab-evaluation/calculators.html. (Accessed April 19, 2014)

**Reference Table for Population Mean eGFRs from National Health and Nutrition Examination Survey (NHANES) III**

<table>
<thead>
<tr>
<th>Age (Yr)</th>
<th>Mean eGFR (mL/min/1.73 m2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1yr</td>
<td>118</td>
</tr>
<tr>
<td>1–3yr</td>
<td>91</td>
</tr>
<tr>
<td>4–5yr</td>
<td>61</td>
</tr>
<tr>
<td>6–8yr</td>
<td>42</td>
</tr>
<tr>
<td>9–10yr</td>
<td>35</td>
</tr>
<tr>
<td>11–13yr</td>
<td>30</td>
</tr>
<tr>
<td>14–15yr</td>
<td>27</td>
</tr>
<tr>
<td>16–17yr</td>
<td>23</td>
</tr>
<tr>
<td>&gt;17yr</td>
<td>20</td>
</tr>
</tbody>
</table>

**Reference Table for Population Mean eGFRs from National Health and Nutrition Examination Survey (NHANES) III**
IV. 24-HR URINE STUDIES

**Cysteamine urine.** See also Section II Hypercalciuria (Absorbptive, Nrenal and Receptive) and Metabolic Stone Evaluation (24-hr urine studies) — Normally ordered as part of a urinalysis metabolic evaluation:
- Normal: Calculi-free diet: 150 mg 24-hr (3.7 mmol/L), average calcium diet: (600–800 mg)/24-hr (2.5–6.2 mmol/L).
- Increased: Hyperparathyroidism, hyperparathyroid, hyperparathyroid tumor, and achondroplasia. Normal: 10–55 mg/24-hr (600–800 mg/24-hr).

**Creatinine, fractionated.** (Nonprotein, secondary, and-disposable):
- Used to evaluate creatinine and paraproteinemia. Avoids drugs that can interfere with the test, leading to false high creatinine values. Totropic steroids, diuretics, calcium, acetaminophen, aspirin, warfarin, alcohol, and aspirin. All these drugs should be discontinued 2 wk prior to testing.
- Normal: Values are variable and dependent on the assay method used. Nonprotein 15–80 mg/24-hr (86–478 mmol/24-hr), protein 0–25 mg/24-hr (0–5.0 mmol/24-hr), uric acid 65–400 mg/24-hr (3.5–20 mmol/24-hr).
- Increased: Phenylketonuria levels are = twice the upper normal value, paraproteinemia, epinephrine administration. Presence of drug (see above).

**Cortisol, free.** — Used to evaluate adrenal cortical function; screening test of choice for Cushing syndrome:
- Normal: 10–55 μg/d (27–150 nmol/L).
- Increased: Cushing syndrome (adrenal hyperplasia from a primary tumor secreting ACTH or ectopic secretion of ACTH by other tumors such as bronchial carcinoma or adrenal tumor secreting cortisol), stress during collection, pregnancy.

- **Cyclophosphamide:**
  - Used to treat proteinuria, microscopic: Normal: 30–45 mg/24-hr (0.6–0.9 mmol/L).
  - Increased: Cyclophosphamide (60 mg/24-hr (1.7 mmol/L)); cyclophosphamide and vincristine syndrome. Up to 250 mg/24-hr (1 mmol/L).

- **Electrophoresis, protein (24-hr urine protein, 24-hr urine globulins):** — Used to evaluate overall serum function; screen for myeloma, monoclonal gammopathy, lymphoma, amyloidosis; can differentiate types of proteinuria (see table below).

**Pattern Description (Type of Proteinuria)**

<table>
<thead>
<tr>
<th>Protein</th>
<th>Normal</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>Sp</th>
<th>α</th>
<th>β</th>
<th>γ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>150</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Albumin</td>
<td>150</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Overflow, acute-phase response</td>
<td>150</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Overflow, monoclonal spike</td>
<td>150</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Electrophoretic Zones**

- **5-Hydroxyindoleacetic acid (5-HIAA).**
  - Used in diagnosing carcinoid syndrome.
  - Normal: 10–60 μg (10.4–61.6 mmol)/24-hr urine collection.
  - Increased: Carcinoid tumors (except rectal), may or may not be present; other tumors: kidney, breast, bladder, ovary, stomach, testes, pancreas.

**Heavy metals:

- **Lead:** Measures urinary lead concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
- **Mercury:** Measures urinary mercury concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
- **Cadmium:** Measures urinary cadmium concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
- **Copper:** Measures urinary copper concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.

**Urinary nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**

- Measures urinary nitrogen concentration.
  - Normal: 15–20 mg/24-hr (28–69 mmol/L); increased: 20–50 mg/24-hr; note: Low values in prepubertal children.
  - Increased: Adrenal cortex abnormalities (renal adenoma, adrenal carcinoma, Cushing syndrome).

**Urea nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**

- Measures urea nitrogen concentration.
  - Normal: 12,000–20,000 mg/24-hr (31–52 mmol/L); note: Low values in prepubertal children.
  - Increased: Adrenal cortex abnormalities (renal adenoma, adrenal carcinoma, Cushing syndrome).

**Urea nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**

- Measures urinary nitrite concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
  - Decreased: Decreased pyridoxal phosphate, Addison disease.

**Vitamin D deficiency:**

- Measures vitamin D deficiency. Normal: 20 mg/24-hr (7.1 mmol/L) in adults, 10 mg/24-hr (3.4 mmol/L) in children.

**Vitamine D deficiency:**

- Measures vitamin D deficiency. Normal: 20 mg/24-hr (7.1 mmol/L) in adults, 10 mg/24-hr (3.4 mmol/L) in children.

**Electrophoretic Zones**

- **5-Hydroxy-indole-acetic acid (5-HIAA):**
  - Used in diagnosing carcinoid syndrome.
  - Normal: 10–60 μg (10.4–61.6 mmol)/24-hr urine collection.
  - Increased: Carcinoid tumors (except rectal), may or may not be present; other tumors: kidney, breast, bladder, ovary, stomach, testes, pancreas.

- **Heavy metals:**
  - **Lead:** Measures urinary lead concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
  - **Mercury:** Measures urinary mercury concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
  - **Cadmium:** Measures urinary cadmium concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
  - **Copper:** Measures urinary copper concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.

- **Urinary nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**
  - Measures urinary nitrogen concentration.
    - Normal: 15–20 mg/24-hr (28–69 mmol/L); increased: 20–50 mg/24-hr; note: Low values in prepubertal children.
    - Increased: Adrenal cortex abnormalities (renal adenoma, adrenal carcinoma, Cushing syndrome).

- **Urea nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**
  - Measures urea nitrogen concentration.
    - Normal: 12,000–20,000 mg/24-hr (31–52 mmol/L); note: Low values in prepubertal children.
    - Increased: Adrenal cortex abnormalities (renal adenoma, adrenal carcinoma, Cushing syndrome).

- **Urea nitrogen, urine (urine nitrogen, nitrogen balance, blood-urea nitrogen, BUN):**
  - Measures urinary nitrite concentration. Normal: 100–100 mg/24-hr (1.6–4.0 mmol/L); increased: Exposure.
    - Decreased: Decreased pyridoxal phosphate, Addison disease.

- **Vitamine D deficiency:**
  - Measures vitamin D deficiency. Normal: 20 mg/24-hr (7.1 mmol/L) in adults, 10 mg/24-hr (3.4 mmol/L) in children.

**REFERENCES**


SECTION V

Alternative and Complementary Urologic Therapies

Section Editors: Franklin Lowe, MD, MPH
Sven Wenske, MD
Introduction

National Center for Complementary and Alternative Medicine (NCCAM), a division of the National Institutes of Health (NIH), conducts and supports research and provides information about complementary health. In a recent national survey, 38% of adults used some form of complementary and alternative medicine (1). “Complementary medicine” refers to use of Complementary and Alternative Medicine (CAM) together with conventional medicine, such as using acupuncture in addition to usual care to help lessen pain. Most use of CAM by Americans is complementary. “Alternative medicine” refers to use of CAM in place of conventional medicine. “Integrative medicine” combines treatments from conventional medicine and CAM for which there is some high-quality evidence of safety and effectiveness. It is also called integrated medicine.

CAM practices are often grouped into broad categories, such as natural products, mind and body medicine, and manipulative and body-based practices. Although these categories are not formally defined, they are useful for discussing CAM practices and some CAM practices may fit into more than 1 category. This chapter provides an overview of some of the CAM practices that are used or are related to the practice of urology.

Mind and Body Medicine

Mind and body practices focus on the interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote health. Many CAM practices embody this concept in different ways. Meditation techniques, yoga, and acupuncture are some of these techniques.

Acupuncture, the application of solid needles inserted into defined spots in the skin, has been described thousands of years ago as part of ancient Chinese medicine. Although its main application has been to treat a variety of chronic conditions, such as back pain, obesity, addictions, and many others, more recently acupuncture has found its way into modern medicine and is now also part of daily clinical routine in many urologic practices. Especially urologic diseases that are difficult to treat, such as premature ejaculation, lower urinary tract symptoms (LUTS) and overactive bladder (OAB), chronic prostatitis/chronic pelvic pain syndrome (CPPS), or side effects (eg, hot flashes) of androgen-deprivation therapy (ADT) for advanced/metastatic prostate cancer, are the primary targets of acupuncture in urology (2).

Results from a clinical study in patients with LUTS or CPPS, 1 of the most difficult to treat urologic conditions, or patients with increased urinary frequency and urgency after radical prostatectomy, showed good results of acupuncture in decreasing symptoms and improving quality of life (3). Good success has also been reported in studies on patients that receive acupuncture for hot flashes, 1 of the most common side effects of ADT. A randomized placebo-controlled study showed recently the effects of acupuncture in the treatment of premature ejaculation in comparison to placebo and the standard treatment using paroxetine (4). Whereas paroxetine reduced the validated Premature Ejaculation Diagnostic Tool (PEDT) score from 17 to 10.5, acupuncture achieved a reduction from 16 to 11, which was significantly better than placebo. Usually, treatments are being applied twice per week for the 1st 6 wk. If patients respond to the treatment and if symptoms improve, the treatment frequency is reduced to once per week, and continues for a total of 12 wk. After that, a maintenance treatment schedule may be needed to prevent recurrent or increasing symptoms.

While the mechanisms of acupuncture are still not entirely understood, the main hypothesis is that certain neurotransmitters (eg, serotonin, endorphins) are being released under needle stimulation, and that there exists an alternative connective tissue communication system unrelated to the peripheral and central nervous systems.

In addition to acupuncture, also pelvic floor muscle training (PFMT), relaxation, and yoga have all been shown to decrease muscle contractions and stress of the pelvic floor. One analysis from Stanford University studied the treatment of intra- and extrapelvic myofascial trigger point release therapy, and training in paradoxical relaxation including cognitive behavioral methods in patients with CPPS, with good results (5).

Overall, especially after exhausting standard treatments for common benign urologic disorders, acupuncture and other complementary therapy offer good alternative treatment approaches with limited potential for adverse events.

Manipulative and Body-Based Practices

Manipulative and body-based practices focus primarily on the structures and systems of the body, including the bones and joints, soft tissues, and circulatory and lymphatic systems. 2 commonly used therapies fall within this category: Spinal manipulation and massage therapy. Limited data is available but the literature suggests that 2 methods of manual therapy (myofascial physical therapy and global therapeutic massage) may benefit patients with urologic CPPS (6).
ACTIVE HEXOSE CORRELATED COMPOUND (AHCC)
AHCC is derived from the mycelia (branches) of the mushroom Lentinula edodes, and contains beta-glucans, a component that is known for its antiviral properties. It is used in the treatment of chronic immune conditions.

CAROTENOID POWDER SUPPLEMENT (Vaccinium macrocarpon)
Carotene powder is derived from cranberry extract and is used in the treatment of prostatitis.

CAUSAL SPECIES (Capsicum annuum)
Capsicum annuum is a species of the Capsicum genus and is used in the treatment of pain and inflammation.

COMMON NATURAL PRODUCTS USED IN UROLOGY
Several natural products are used in the treatment of urological conditions, including cranberry juice, saw palmetto, and pygeum.

CUTEBITUM (Luteolin subalpino)
Cutebitum is a natural supplement derived from the plant Luteolin subalpino and is used in the treatment of urological conditions.

GINKGO BILoba
Ginkgo biloba is derived from the seed of the Ginkgo biloba tree and is used in the treatment of a variety of conditions, including cognitive impairment and cardiovascular disease.

HOLISTIC PRODUCTS AND HERBS
A variety of holistic products and herbs are used in the treatment of urological conditions, including cranberry, saw palmetto, and pygeum.

L-BENEFIC (Polyphenol extract)
L-Benific is a product derived from the leaves of the plant L. officinalis and is used in the treatment of urological conditions.

LUTETIA (Luteolin officinate)
Lutetia is a natural supplement derived from the plant L. officinate and is used in the treatment of urological conditions.

MASTODON (Radix urticae)
Mastodon is a natural supplement derived from the root of the plant Urtica dioica and is used in the treatment of urological conditions.

MELATONIN (Melatonin)
Melatonin is a hormone derived from the pineal gland and is used in the treatment of urological conditions.

POLYVINYL (Polyvinyl alcohol)
Polyvinyl is a synthetic polymer used in the treatment of urological conditions.

PROSTATE SUPPORT (Pygeum africanum)
Pygeum africanum is a natural supplement derived from the bark of the African plum tree and is used in the treatment of prostate conditions.

QUINOSIL (Quinone silicate)
Quinonisol is a natural supplement derived from the plant Quinone silicate and is used in the treatment of urological conditions.

SMALLRICE (Spermatozoon)
Smallrice is a natural supplement derived from the sperm of the plant Spermatozoon and is used in the treatment of urological conditions.

SPIDER CRANBERRY (Vaccinium macrocarpon)
Spider cranberry is derived from the berry of the plant V. macrocarpon and is used in the treatment of urological conditions.

SUPPLEMENTS (Vaccinium macrocarpon)
Supplements derived from the cranberry are used in the treatment of urological conditions.

TURMERIC (Curcumin)
Turmeric is a natural supplement derived from the plant Curcuma longa and is used in the treatment of urological conditions.

VITAMIN D (Calciferol)
Vitamin D is a nutrient derived from the food we eat and is used in the treatment of urological conditions.

WATERFORD (Aquatic plant)
Waterford is a natural supplement derived from the aquatic plant Waterford and is used in the treatment of urological conditions.
Overall, the protective effect of lycopene is unclear, as studies have found it to have potential anticancer effects against damage from free radicals. In several pigment acts basically as an antioxidant, protecting cells against damage from free radicals. Lycopene is a major carotenoid component of tomato, which has been reported to cause tachyarrhythmias. Phytoestrogens of the prenyl-flavone family. It has estrogenic due to the presence of novel potent (27,28). However, extracts of epimedium are strongly antihypertensive and antiandrogenic, and antiestrogenic effects (38). It has almost no effect upon prostate size and no effect upon PSA levels (39). There are no known significant health risks or adverse effects.

POMEGRANATE (Punica granatum)

Pomegranate juice is known for its high vitamin C content, as well as vitamin B6 (pyridoxine), potassium, and natural phenols, such as ellagitannins and flavonoids with extremely effective free radical-scavenging properties. Increasing evidence shows that pomegranate juice has potential to inhibit growth and induce the invasion of prostate cancer cells both in vitro and in vivo. A phase II clinical trial, in which patients with rising PSA after primary treatment with curative intent of prostate cancer were given 8 oz of pomegranate juice per day, showed that the mean PSA doubling time increased significantly in men under treatment with pomegranate juice from 15 to 54 mo (p < 0.001) (40). One of the hypothesized mechanisms in which pomegranate juice affects many of the cellular processes involved in cell death and also affects signaling pathways that could inhibit cell migration and invasion (41).

PUMPKIN SEED (Cucurbita pepo)

Fresh and dried seeds are taken whole or ground for the treatment of BPH or OAB. Active compounds are thought to be phytosterols (42,43). There are no recent clinical trials and therefore no evidence establishing its efficacy. There are no known side effects.

RESVERATROL

Resveratrol is a potent antioxidant found in wine, especially in high concentration in Pino Noir, but also in grapes and berries. Research has demonstrated that it inhibits cancer growth through reduction of cell proliferation and metastasis, and reduction of cell apoptosis. On a molecular level, it has been shown that mechanisms involved are Inhibition of Akt and suppression of KRAS 1 oncogene expression (44). These antitumor effects of resveratrol were observed in in vitro and in vivo preclinical studies with the common prostate cancer cell lines PC3, DU145, and LNCaP.
A pollen extract obtained by microbial digestion and extraction by water and organic solvents. Cernilton is the branded product. Active ingredients are thought to be β-sitosterols (45). It is used for the treatment of BPH and prostatitis and CPPS (46). In vitro inhibition of synthesis of prostaglandin and estradiol metabolites has been demonstrated (47). No long-term conclusive clinical studies exist. Side effects are reportedly minimal.

**SAW PALMETTO BERRY** *(Serenoa repens, Sabal verruculata)*

There are many different extraction processes and therefore many different brands of saw palmetto. The composition of these brands is variable. A recent NIH-sponsored double-blind, placebo-controlled study using the Indra brand showed no statistical difference between placebo and saw palmetto berry treatment for BPH/LUTS. Proenase brand is the most widely studied product (see “Premenopausal” above). Minimal side effects are associated with saw palmetto. Saw palmetto berry extract (SBPE) compounds are also sold as “prostate health.” SBPE includes ingredients such as β-sitosterol and stigmasterol with no reliable clinical data to support their use. A recent large meta-analysis documented no significant clinical benefit of Saw palmetto on LUTS or prostate volume (10). Saw palmetto extract does not affect serum prostate-specific antigen more than placebo, even at relatively high-dose (48). In addition it appears safe with the saw palmetto extract used in the CAMUS trial showed no evidence of toxicity at doses up to 3 times the usual clinical dose during an 18-mo period.

**SELENIUM**

A trace mineral that may prevent the development of prostate cancer. Epidemiologic studies suggest a chemopreventive effect (49). A study of patients with high-grade PIN suggested that selenium reduced the incidence of prostate cancer on subsequent biopsy. The National Cancer Institute-sponsored SELECT trial was a 10 yr prospective trial that began in 2001 of over 35,000 men studying the prostate cancer chemopreventive effects of selenium and vitamin E alone and in combination (49). The data monitoring safety board (DMSB) halted the trial in the fall of 2006. Their concerns were that the supplements did not appear to offer any benefit. Although there was a statistically nonsignificant trend to increasing prostate cancer with vitamin E alone and increased diabetes risk in men on selenium alone.

**SOUTH AFRICAN STAR GRASS** *(Hypoxis rooperi)*

This extract is taken for BPH/LUTS. The active compound is thought to be β-sitosterols, which are thought to induce apoptosis by transforming growth factor (TGF) signaling (46). Initial studies showed dramatic improvements in symptom scores and flow rates; however, confirmatory studies are still needed (51). Adverse effects are believed to be minimal.

**STINGING NETTLE** *(Urtica dioica, Urtica radix)*

Razors is a branded form of this extract; (see Razors section above). The clinical evidence of the effectiveness of nettle root is based primarily on open studies, and the significance of this must be confirmed (14, 52). Minimal toxicity is associated with stinging nettle use.

**VITAMIN D3 (Cholecalciferol)**

As a fat-soluble vitamin, vitamin D3 plays a key role in overall health, as it mainly maintains calcium and phosphate homeostasis. However, it has also been shown to exhibit antineoplastic effects on various types of cancer such as colon, breast, and prostate cancer (53). The Institute of Medicine (IOM) has reviewed and updated the dietary reference intakes (DRIs) for vitamin D. It found that there is strong evidence to support the use of vitamin D with calcium for bone health, but it was lacking for other health conditions. Dosages for patient with various health issues differ. The recommended daily allowance (RDA), as set in 2011, is based on age, as follows: For those 1–70 yr of age, 600 IU daily, for those 71 yr and older, 800 to daily, and for pregnant and lactating women, 1,200 to daily. The IOM further recommended that serum 25(OH)D levels of 20 ng/mL (50 nmol/L) is adequate, and levels ≥ 50 ng/mL (125 nmol/L) could have potential adverse effects. However, dosages for unselected patients may differ based on underlying health disorders and concomitant medications (underlying osteopenia, ADT, therapy with bisphosphonates in patients with metastatic prostate cancer, etc.)

**VITAMIN E (α-Tocopherol)**

Vitamin E, another fat-soluble essential vitamin, was initially thought to prevent prostate cancer (80). However, the National Cancer Institute–sponsored SELECT trial, studying prostate cancer chemopreventive effects of selenium and vitamin E alone and in combination (50). The follow-up publication in 2011 even reported a significantly increased prostate cancer risk in healthy men with dietary supplementation with vitamin E (51). In addition, vitamin E supplementation above dosages of 400 IU per day was found to significantly increase risks of cardiovascular events.

**YOHBININE (Paussinystalla yohimbe) YOCON, YOHIMEX**

An extract of the bark of the yohimbe tree has been used for erectile dysfunction and decreased libido. The mechanism of action is an α2-adrenergic agonist. Conflicting studies show both positive and no effect when compared to placebo (52). It appears to have greatest utility for men with psychogenic impotence. Despite the advent of phosphodiesterase 5 (PDE5) inhibitors, there is widespread utilization of this over-the-counter product. Side effects include anxiety, tremors, diziness, hypertension, and tachycardia. Do not use with antidepressants (eg, MAOIs or similar agents).

**ZYFLAMEND**

A formula containing 10 different herbs, is a dietary supplement marketed for the support of cardiovascular and joint function and healthy inflammation response. It is thought to have anti-inflammatory, antiproliferative, and antiangiogenic properties. Several in vitro studies have shown that Zyflamend decreases COX-1 and COX-2 enzymatic activity, induces apoptosis, and reduces angiogenesis receptor expression in NCI/CA1 cells (57). Moreover, it was found to inhibit angiogenic acid pathways in human prostate cancer PZC cells. Moreover, it also inhibits the proliferation of oral squamous carcinoma, pancreatic cancer, and melanoma cells in vitro. In an animal model, it inhibited the growth of both hormone-naïve and castrate-resistant prostate cancer, and reduced the expression of PSA. However, the latter could not be shown in a phase I clinical trial in men with PIN at Columbia University Medical Center, where Zyflamend was well tolerated, but did not lead to any significant changes in serum PSA levels (58).

**REFERENCES**


920

REFERENCES


SECTION VI

Urologic Drug Reference

Section Editors: T. Ernesto Figueroa, MD, FAAP, FACS
Leonard G. Gomella, MD, FACS
Kevin R. Loughlin, MD, MBA, FACS
Jack H. Mydlo, MD
This section is designed to be a quick reference of medications commonly used in urology or of those that have significant impact on the GU system. Although some general information about the drug may be presented, this is not intended to be a complete authoritative listing for each medication; the focus here is on the practice of urology. You should be familiar with all the indications, contraindications, adverse effects, and drug interactions of any medication that you prescribe. Such detailed information is beyond the scope of this book but can be found in the manufacturer’s package insert, product websites, in the Physicians’ Desk Reference (PDR), or from the American Hospital Formulary Service.

Medications are listed by generic name, with some of the more common trade names noted. Common uses and urology-specific uses are listed in addition to the official labeled indications (FDA approved), because many available medications are used to treat various conditions based on the medical literature, and these uses are not listed in the package insert. Asterisks are placed before and after the official US FDA approved indications. This additional use information is based on the editorial review of the literature and is representative of urology practice patterns primarily in the US. Where no pediatric dosage is provided, the implication is that the use of the agent is not well established in this age group. Controlled substances are indicated by the symbol [C]. Increasingly, drug interaction and medication side effects can be related to a drug’s metabolism and the enzymes of the cytochrome P450 system are essential for the metabolism of many medications. There are more than 50 CYP450 enzymes, but the CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 enzymes metabolize 90% of drugs and are predominantly expressed in the liver. The table at the end of the chapter (page 975) summarizes some of the common medications and their CYP450 interactions that are noted for many of the medications listed here.

### MEDICATION KEY

Medications are in alphabetical order by their generic name. Some of the more commonly recognized trade names in the US are listed for each (in parentheses after the generic name). If a drug is available without prescription, it is noted as OTC (over-the-counter).

**GENERIC DRUG NAME (SELECTED COMMON BRAND NAMES) [CONTROLLED SUBSTANCE DESIGNATION] [OTC]**

**WARNING:** Summarized versions of the Black Box precautions deemed necessary by the FDA. These are significant precautions and contraindications concerning the individual medication. **Usual:** This includes both FDA-labeled indications bracketed by **~** and other “off-label” uses of the medication. Because many medications are used to treat various conditions based on the medical literature, and these uses are not listed in their package insert, we list common uses of the medication in addition to official labeled indications (FDA approved) based on input from our editorial board. **Action:** How the drug works. This information is helpful in comparing classes of drugs and understanding side effects and contraindications. **Spectrum:** Specifies activity against selected microbes for antimicrobials. **Dose:** Adults & Peds: When no specific pediatric dose is given, the implication is that this drug is not commonly used or indicated for that age group. At the end of the dosing line, important dosing modifications may be noted (ie, take with food, avoid antacids, etc.). **IP:** (Warning/Precaution): (Pregnancy/fetal risk categories, breast-feeding [as noted below]) Cautions concerning the use of the drug in specific settings. **C:** Contraindications. **Disp:** Common dosing forms. **SE (Side Effects):** Common or significant side effects. **Notes:** Other key useful information about the drug, including additions made by our editorial board.

### CONTROLLED SUBSTANCE CLASSIFICATION

Medications under the control of the US Drug Enforcement Agency (DEA) (Schedules I–V controlled substances) are indicated by the symbol (C). Most medications are uncontrolled and do not require a DEA prescriber number or a special prescription pad. The following is a general description for the schedules of DEA-controlled substances.

**Schedule (C-I):** All nonresearch use forbidden (eg, heroin, etc.).

**Schedule (C-II):** High addictive potential; medical use accepted. No telephone call-in prescriptions; no refills.

**Schedule (C-III):** Low to moderate risk of physical dependence, high risk of psychologic dependence; prescription usually must be rewritten after 6 mo or 5 refills (eg, codeine, oxycodone).

**Schedule (C-IV):** Limited potential for dependence; prescription rules same as for Schedule III (eg, buprenorphine, propoxyphene).

**Schedule (C-V):** Very limited abuse potential; prescribing regulations often same as for uncontrolled medications; some states have additional restrictions.

### FDA FETAL RISK CATEGORIES

**Category A:** Adequate studies in pregnant women have not demonstrated a risk to the fetus in the 1st trimester of pregnancy; there is no evidence of risk in the last 2 trimesters.

**Category B:** Animal studies have not demonstrated a risk to the fetus, but no adequate studies have been done in pregnant women.

**Category C:** Animal studies have shown an adverse effect on the fetus, but no adequate studies have been done in humans. The benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

**Category D:** Animal studies have shown an adverse effect on the fetus; but adequate studies in pregnant women have not demonstrated a risk to the fetus during the 1st trimester of pregnancy, and there is no evidence of risk in the last 2 trimesters.

**Category X:** Animal studies have shown an adverse effect on the fetus, but no adequate studies have been done in humans. The benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

### BREAST-FEEDING CLASSIFICATION

<table>
<thead>
<tr>
<th>Classification</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. A</td>
<td>Compatible with breast feeding. You should be familiar with all the indications, contraindications, adverse effects, and drug interactions of any medication that you prescribe. Such detailed information is beyond the scope of this book but can be found in the manufacturer’s package insert, product websites, in the Physicians’ Desk Reference (PDR), or from the American Hospital Formulary Service. Medications are listed by generic name, with some of the more common trade names noted. Common uses and urology-specific uses are listed in addition to the official labeled indications (FDA approved), because many available medications are used to treat various conditions based on the medical literature, and these uses are not listed in the package insert. Asterisks are placed before and after the official US FDA approved indications. This additional use information is based on the editorial review of the literature and is representative of urology practice patterns primarily in the US. Where no pediatric dosage is provided, the implication is that the use of the agent is not well established in this age group. Controlled substances are indicated by the symbol [C]. Increasingly, drug interaction and medication side effects can be related to a drug’s metabolism and the enzymes of the cytochrome P450 system are essential for the metabolism of many medications. There are more than 50 CYP450 enzymes, but the CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 enzymes metabolize 90% of drugs and are predominantly expressed in the liver. The table at the end of the chapter (page 975) summarizes some of the common medications and their CYP450 interactions that are noted for many of the medications listed here.</td>
</tr>
<tr>
<td>Classifications</td>
<td>Notes</td>
</tr>
<tr>
<td>Schedule (C-I)</td>
<td>All nonresearch use forbidden</td>
</tr>
<tr>
<td>Schedule (C-II)</td>
<td>High addictive potential; medical use accepted. No telephone call-in prescriptions; no refills</td>
</tr>
<tr>
<td>Schedule (C-III)</td>
<td>Low to moderate risk of physical dependence, high risk of psychologic dependence; prescription usually must be rewritten after 6 mo or 5 refills (eg, codeine, oxycodone)</td>
</tr>
<tr>
<td>Schedule (C-IV)</td>
<td>Limited potential for dependence; prescription rules same as for Schedule III (eg, buprenorphine, propoxyphene)</td>
</tr>
<tr>
<td>Schedule (C-V)</td>
<td>Very limited abuse potential; prescribing regulations often same as for uncontrolled medications; some states have additional restrictions.</td>
</tr>
<tr>
<td>Category A</td>
<td>Adequate studies in pregnant women have not demonstrated a risk to the fetus in the 1st trimester of pregnancy; there is no evidence of risk in the last 2 trimesters.</td>
</tr>
<tr>
<td>Category B</td>
<td>Animal studies have not demonstrated a risk to the fetus, but no adequate studies have been done in pregnant women.</td>
</tr>
<tr>
<td>Category C</td>
<td>Animal studies have shown an adverse effect on the fetus, but no adequate studies have been done in humans. The benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.</td>
</tr>
<tr>
<td>Category D</td>
<td>Animal studies have shown an adverse effect on the fetus; but adequate studies in pregnant women have not demonstrated a risk to the fetus during the 1st trimester of pregnancy, and there is no evidence of risk in the last 2 trimesters.</td>
</tr>
<tr>
<td>Category X</td>
<td>Animal studies have shown an adverse effect on the fetus, but no adequate studies have been done in humans. The benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.</td>
</tr>
<tr>
<td>Gender-specific uses</td>
<td>Common uses and urology-specific uses are listed in addition to the official labeled indications (FDA approved), because many available medications are used to treat various conditions based on the medical literature, and these uses are not listed in the package insert. Asterisks are placed before and after the official US FDA approved indications. This additional use information is based on the editorial review of the literature and is representative of urology practice patterns primarily in the US. Where no pediatric dosage is provided, the implication is that the use of the agent is not well established in this age group. Controlled substances are indicated by the symbol [C]. Increasingly, drug interaction and medication side effects can be related to a drug’s metabolism and the enzymes of the cytochrome P450 system are essential for the metabolism of many medications. There are more than 50 CYP450 enzymes, but the CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 enzymes metabolize 90% of drugs and are predominantly expressed in the liver. The table at the end of the chapter (page 975) summarizes some of the common medications and their CYP450 interactions that are noted for many of the medications listed here.</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>If a drug is available without prescription, it is noted as OTC (over-the-counter).</td>
</tr>
<tr>
<td>Medications are listed by generic name. Some of the more commonly recognized trade names in the US are listed for each (in parentheses after the generic name). If a drug is available without prescription, it is noted as OTC (over-the-counter).</td>
<td></td>
</tr>
<tr>
<td>Medications are listed by generic name, with some of the more common trade names noted. Common uses and urology-specific uses are listed in addition to the official labeled indications (FDA approved), because many available medications are used to treat various conditions based on the medical literature, and these uses are not listed in the package insert. Asterisks are placed before and after the official US FDA approved indications. This additional use information is based on the editorial review of the literature and is representative of urology practice patterns primarily in the US. Where no pediatric dosage is provided, the implication is that the use of the agent is not well established in this age group. Controlled substances are indicated by the symbol [C]. Increasingly, drug interaction and medication side effects can be related to a drug’s metabolism and the enzymes of the cytochrome P450 system are essential for the metabolism of many medications. There are more than 50 CYP450 enzymes, but the CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 enzymes metabolize 90% of drugs and are predominantly expressed in the liver. The table at the end of the chapter (page 975) summarizes some of the common medications and their CYP450 interactions that are noted for many of the medications listed here.</td>
<td></td>
</tr>
</tbody>
</table>
**ACETAMINOPHEN (CODEINE) (TYLENOL NO. 2, 3, AND 4) [C-II, C-V]**

**USES:**
- Mild-mild pain (No. 2–3); moderate pain (No. 4).
- Combined APAP and narcotic analgesic.

**DOSE:**
- Adults: 1–2 tabs q4-h to 30–60 mg/codeine q4–6h based on codeine content (max. dose APAP = 4 g/day). 
- Pediatric: 325–650 mg PO or PR q4–6h or 1,000 mg q6h; max. 4 g/d.

**NOTES:**
- Associated w/ doses 4 g/d; limit SEs (hypokalemia and hypertension); if taken with warfarin; serious skin rxns (SJS, TEN), photosensitivity, hyperglycemia.
- Absorption may be reduced w/ CYP3A4 substrates/CYP3A4 inhibitors or inducers; do not use w/ severe liver insufficiency.

**DISP:**
- Tablets 500 mg.

**ACETYLCYSTEINE (ACETADOTE, MUCOMYST)**

**USES:**
- Mucolytic, antioxidant to acetaminophen hepatotoxicity, adjacent treat chronic bronchopulmonary disease & cystic fibrosis; prevent contrast-induced renal dysfunction.

**ACTIONS:**
- Splits mucoprotein disulfide linkages; reduces glutathione in acetaminophen OD to protect liver.

**DOSE:**
- Adult: PO or IV: 140 mg q4-h, then 70 mg q8-h × 7 days (dose may be limited ≤1.5 mg/kg q6-h for patients ≤65 kg or ≤25 mg/kg q6-h for patients >65 kg).
- Adult: PO or IV: 35 mg/kg q8-h × 7 days (dose may be limited ≤1.5 mg/kg q6-h for patients ≤65 kg or ≤25 mg/kg q6-h for patients >65 kg).

**NOTES:**
- Activated charcoal adsorbs PO
- Sodium bicarbonate may increase availability; use only if severe toxicity.

**ACIDOPHILUS, OMIFRIM IV (Rx), TYLENOL, OTHER GENERIC**

**NOTC**

**W/ Rx:**
- May cause acute liver failure; associated w/ doses > 4,000 mg/d & taking APAP in > 1 product.

**DOBIEF:**
- Mild–mod pain, HA, fever

**ACTIONS:**
- Nonspecific analgesic; CVS synth of prostaglandin & hypotensive & hypothermic effect.

**DOSE:**
- Adults: 125–450 mg PO or PR q4-h to 1,000 mg PO q4–8-h; max. 4 g/d, max. 4 g/d.
- Pediatric: 0.5–8 mg/kg q4–6h; max. 4 g/d.
- Pediatric: < 12 kg: 10–15 mg/kg q4–6h; max. 5 g/d.
- Pediatric: 12–25 kg: 15 mg/kg q4–6h; max. 10 g/d.
- Pediatric: 25–50 kg: 12.5 mg/kg q4–6h max. 7.5 mg/kg q4–6h.

**W/P:**
- [C] + w/ high-dose aspirin and acetazolamide, as readministration. With serious reactions occur, d/c use.

**NOTES:**
- Additive toxicities to sulfonamides (e.g., Stevenson–Johnson syndrome [SJS], toxic epidermal necrolysis [TEN], hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias). Sensitizations w/ a sulfonamide is possible, cross-sensitivity may be possible.

**ACETYLCYSTEINE**

**USES:**
- Prevent renal injury risk.

**ACTIONS:**
- Adjunct for chronic urea-splitting UTI infection.

**DOSE:**
- Adult: 325 mg of APAP/325 mg codeineudent until available. FDA advisory has rec’d in max. dose to 3,000 mg/d.

**ACETAMINOPHEN (APAP, N-ACETYL-O-AMINOHEXANOL) (ACEPHEN, OMIFRIM IV [Rx]), TYLENOL, OTHER GENERIC [(OTC)]

**WARNING:**
- May cause acute liver failure; associated w/ doses > 4,000 mg/d & taking APAP in > 1 product.

**DOSE:**
- Adults: 125–450 mg PO or PR q4-h to 1,000 mg PO q4–8-h; max. 4 g/d, max. 4 g/d.
- Pediatric: 0.5–8 mg/kg q4–6h; max. 4 g/d.
- Pediatric: < 12 kg: 10–15 mg/kg q4–6h; max. 5 g/d.
- Pediatric: 12–25 kg: 15 mg/kg q4–6h; max. 10 g/d.
- Pediatric: 25–50 kg: 12.5 mg/kg q4–6h max. 7.5 mg/kg q4–6h.

**W/P:**
- [C] + w/ high-dose aspirin and acetazolamide, as readministration. With serious reactions occur, d/c use.

**NOTES:**
- Additive toxicities to sulfonamides (e.g., Stevenson–Johnson syndrome [SJS], toxic epidermal necrolysis [TEN], hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias). Sensitizations w/ a sulfonamide is possible, cross-sensitivity may be possible.

**ACETAMINOPHEN (APAP, N-ACETYL-O-AMINOHEXANOL) (ACEPHEN, OMIFRIM IV [Rx]), TYLENOL, OTHER GENERIC [(OTC)]

**WARNING:**
- May cause acute liver failure; associated w/ doses > 4,000 mg/d & taking APAP in > 1 product.

**DOSE:**
- Adults: 125–450 mg PO or PR q4-h to 1,000 mg PO q4–8-h; max. 4 g/d, max. 4 g/d.
- Pediatric: 0.5–8 mg/kg q4–6h; max. 4 g/d.
- Pediatric: < 12 kg: 10–15 mg/kg q4–6h; max. 5 g/d.
- Pediatric: 12–25 kg: 15 mg/kg q4–6h; max. 10 g/d.
- Pediatric: 25–50 kg: 12.5 mg/kg q4–6h max. 7.5 mg/kg q4–6h.

**W/P:**
- [C] + w/ high-dose aspirin and acetazolamide, as readministration. With serious reactions occur, d/c use.

**NOTES:**
- Additive toxicities to sulfonamides (e.g., Stevenson–Johnson syndrome [SJS], toxic epidermal necrolysis [TEN], hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias). Sensitizations w/ a sulfonamide is possible, cross-sensitivity may be possible.
ALDESKLEUKIN (IL-2) (PROLEUKIN)

WARNING: Restrict to pts w/ IL-2 cardiac/pulmonary functions as defined by formal testing. Caution w/ IL-2 cardiac dysfunction. Administer in hospital setting w/ physician experienced w/ antinecotic agents. Aux: w/ capillary leak syndrome (CLS) characterized by ↓ BP and organ perfusion w/ potential for cardiac/respiratory tox, GI bleeding/infection, renal insufficiency, edema, and mental status changes; ↓ risk of sepsis and bacterial endocarditis. Thrush bacterial infection before use. Pts w/ central lines are at ↑ risk for infection. Propofol w/ oxacillin, nafcillin, ciprofloxacin, or vancomycin may reduce staphylococcal infection. Hold w/ moderate-severe lethargy or somnolence; continue use may result in coma.

USES: Met RCC & melanoma.

ACTIONS: Acts via T-2 receptor; many immunomodulatory effects.

DOSE: 6,000 IU/kg q8h = max. 1.4-doses daily 1-5 day and days 15-19 of 28-day cycle (DAYSA schedule for RCC); other schedules (eg, “high dose” schedule for RCC); other schedules (eg, “high dose” schedule for RCC); other schedules (eg, “high dose” schedule for RCC);

ALFUSOZIN (UROXATRAL, GENERIC)

USES: "Symptomatic BH*.

ACTIONS: α-Blockers

DOSE: 10 mg PO daily immediately after the same meal, do not crush/hold.

W/P: [B, C, T] w/ any Hx

BP: ↓, ↓ BP: ≤ 80/60 mmHg, urine output ≤ 0.5 mL/kg body weight/h; ↓ BP: ≤ 80/60 mmHg, urine output ≤ 0.5 mL/kg body weight/h

SE: Headache, syncope, dizziness; rare priapism.

NOTES: Do not cut or crush.

ALLOPURINOL (ALLOPRIM, ZYLOPRIM, GENERIC)

USES: "Gout, hyperuricemia of malignancy, uric acid urolithiasis, recurrent calcium oxalate calcium uric acid urolithiasis, recurrent calcium oxalate calculi (w/ urinary uric acid > 800 mg/dL in males and 700 mg/dL in females).* "

ACTIONS: Xanthine oxidase inhibitor; ↓ uric acid production.

DOSE: Adults: 100–400 mg PO bid; up to 800 mg/d in renal impairment.

W/P: [B, C, T] ≤ 30 mL/min. w/ NSAID

SE: Headache, nausea, vomiting, diarrhea, abdominal pain, drug fever, rash, pruritus, urticaria, urticarial rash, pruritic rashes, urticaria, GI bleed/infarction, renal & mild hematologic tox (w/ transfusion), WBC, eosinophilia, worsening renal function; 80% have desquamative skin rash, fever, hepatic dysfunction, hematologic tox including leukopenia, anemia, thrombocytopenia; 13% have flu-like syndrome (malaise, fever, chills), 3% with fever, chills, rigors, headache, fatigue, weakness, myalgia, arthralgia; 30% have fever, chills, malaise, myalgia, arthralgia, flu-like syndrome.

ALPROSTADIL, INTRACAVERNOUS (CAVERJECT, CAVERJECT IMPULSE, EDEX)

USES: "Erectile dysfunction.* ACTIONS: A form of prostaglandin E1; relaxes smooth muscles, dilates cavernous arteries, 1 LAKURAR a 80% have desquamative skin rash, fever, hepatic dysfunction, hematologic maladoption, penis deformity/erection, men in whom sexual activity inadvisable.

Counsel about priapism, penile fibrosis, & hematoma risks.

ALPROSTADIL, URETHRAL SUPPOSITORY (MUSE)

USES: "Erectile dysfunction.* ACTIONS: A form of prostaglandin E1; urethral absorption, vasodilator, relaxes smooth muscle of corpus cavernosum.

Dose: 125–200 μg PRN to achieve erection (max. 2 systems/24 h) duration 30–60 min.

W/P: [B, C, T] ≤ 30 mL/min. w/ NSAID

SE: Headache, nausea, vomiting, diarrhea, abdominal pain, drug fever, rash, pruritus, urticaria, urticarial rash, pruritic rashes, urticaria, GI bleed/infarction, renal & mild hematologic tox (w/ transfusion), WBC, eosinophilia, worsening renal function; 80% have desquamative skin rash, fever, hepatic dysfunction, hematologic tox including leukopenia, anemia, thrombocytopenia; 13% have flu-like syndrome (malaise, fever, chills), 3% with fever, chills, rigors, headache, fatigue, weakness, myalgia, arthralgia; 30% have fever, chills, malaise, myalgia, arthralgia, flu-like syndrome.

ALVIMOPAN (ENTEREG)

WARNING: for short-term hospital use only (max. 14 days).

USES: "Accelerate the time to upper and lower gastrointestinal recovery following partial or small bowel resection surgery with primary anastomosis.* ACTIONS: (opioid μ) receptor antagonist; selectively binds GI receptors, antagonizes effects of opioids on GI motility/acidity.

Dose: 12 mg 30 min-3 h preop PO, then 12 mg 8h up to 7 days, max. 15 doses.

W/P: [B, C, T] ≤ 30 mL/min. w/ NSAID

SE: Headache, nausea, vomiting, diarrhea, abdominal pain, drug fever, rash, pruritus, urticaria, urticarial rash, pruritic rashes, urticaria, GI bleed/infarction, renal & mild hematologic tox (w/ transfusion), WBC, eosinophilia, worsening renal function; 80% have desquamative skin rash, fever, hepatic dysfunction, hematologic maladoption, penis deformity/erection, men in whom sexual activity inadvisable.

Counsel about priapism, penile fibrosis, & hematoma risks.

NOTES: Do not cut or crush.

NOTES: Do not cut or crush.

NOTES: Do not cut or crush.

NOTES: Do not cut or crush.

NOTES: Do not cut or crush.

NOTES: Do not cut or crush.
AMLODIPINE/VALSARTAN (HA EXFORGE)

**AMLODIPINE (MIDAMOR, GENERIC)**

**USES:** Calcium channel blocker w/ angiotensin II receptor blocker.

**DOSE:**
- Adults: Initial 5 mg PO q day, max 10 mg PO q day.
- BP: 0–125 mg/mL, w/ hepatic impairment.
- W/P: [D, ?]

**ACTIONS:**
- Calcium channel blocker; relaxes smooth muscle, reduces vascular resistance, decreases total peripheral resistance, and decreases myocardial oxygen demand.

**DISP:** Tabs 2.5, 5, 10 mg.

**NOTES:** Take w/o regard to meals.

**ADVERSE EFFECTS:**
- Edema, headache, palpitations, flushing, dizziness.
- Take w/o regard to meals.

**AMLODIPINE/OLMESARTAN (AZOR)**

**USES:**
- Calcium channel blocker w/ angiotensin II receptor blocker.
- **DOSE:**
  - Initial 4.5 mg PO q day, max 10 mg PO q day.
  - **BP:** With [D, ?] w/o regard to meals.
  - **NOTES:** Take w/o regard to meals.

**ACTIONS:**
- Calcium channel blocker; relaxes coronary vascular smooth muscle.

**DOSE:**
- Adults: 2–3 g PO, q 12 h, w/ hepatic impairment.
- W/P: [C, ?]

**DISP:** Tabs 2.5, 5, 10 mg.

**NOTES:** Take w/o regard to meals.

**AMLODIPINE/OLMESARTAN (HA EXFORGE)**

**USES:** Calcium channel blocker w/ angiotensin II receptor blocker.

**DOSE:**
- Adults: Initial 5 mg PO q day, max 10 mg PO q day.
- BP: [D, ?] w/o regard to meals.
- **NOTES:** Take w/o regard to meals.

**ACTIONS:**
- Calcium channel blocker; relaxes coronary vascular smooth muscle.

**DISP:**
- Adults: Initial 4.5 mg PO q day, max 10 mg PO q day.
- **BP:** With [D, ?] w/o regard to meals.
- **NOTES:** Take w/o regard to meals.

**AMLODIPINE (RANOLIN, EXFORGE)**

**USES:**
- Calcium channel blocker.

**DOSE:**
- Adults: Initial 5 mg PO q day, max 10 mg PO q day.
- BP: [D, ?] w/o regard to meals.
- **NOTES:** Take w/o regard to meals.

**ACTIONS:**
- Calcium channel blocker; relaxes coronary vascular smooth muscle.

**DISP:**
- Adults: Initial 4.5 mg PO q day, max 10 mg PO q day.
- **BP:** With [D, ?] w/o regard to meals.
- **NOTES:** Take w/o regard to meals.
AMLODIPINE/VALSARTAN/HCTZ (EXFORGE HCT)

AMLODIPINE/VALSARTAN/HCTZ (EXFORGE HCT)

WARNING: Use of renin-angiotensin agents in PREGNANCY can cause fetal injury and death, so C5 immediately when PREGNANCY detected.

USES: + Hypertension (not initial therapy).

ACTIONS: Calcium channel blocker, angiotensin II receptor blocker, β-blocker diuretic.


SE: Edema, dizziness, headache, fatigue, t. & k laboratory changes, renal impairment, hypotension, syncope, rash.

ACTIONS: β-blocker, angiotensin receptor blocker, diuretic.

DOSE: Adults: 250–500 mg PO q8h or 875 mg q12h, XR 2,000 mg PO q12h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMPHOTERICIN B LIPID COMPLEX (ABELCET)

USES: "Refactory invasive fungal infection in pts resistant to conventional amphotericin B.

DOSE: Adults & Peds: 3–6 mg/m² IV q10–14d.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMPHOTERICIN B LIPOSOMAL (AMBISOME)

USES: "Refactory invasive fungal infection w/ intolerance to conventional amphotericin B/cryptococcal meningitis in HIV, empiric for fungal meningitis, visceral leishmaniasis.

DOSE: Adults & Peds: 3–6 mg/m² IV q10–14d.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMPICILLIN (GENERIC)

USES: "Neutropenia, G.幽门螺杆菌, E. coli, B, & inhibitor (SIB prophylaxis).

DOSE: Adults & Peds: 250–500 mg PO q6–8h or up to 250 mg PO q4h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMPICILLIN (AMOXIL)

USES: "Ear, lower resp, skin, urinary tract infections from susceptible gram(-) bacteria; +/−Lactam antibiotic; a cell wall synth. Spectrum: (gran-) B, & enterococcus (G), S, & enterococcus (G).

DOSE: Adults: 3–4 mg/kg/d; 1 mg/kg/h IV, q6–8h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMLLODIPINE/VALSARTAN/HCTZ (EXFORGE HCT)

USES: "H. pylori endocarditis prophylaxis, + Lactam antibiotic; a cell wall synth. Spectrum: (gran-) B, & enterococcus (G).

DOSE: Adults: 250–500 mg PO q8h or 875 mg q12h, XR 2,000 mg PO q12h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMOXICILLIN/CLOVANILIC ACID (AUGMENTIN, AUGMENTIN ES-600, AUGMENTIN XR)

USES: "Ear, lower resp, skin, urinary tract infections caused by β-lactamase-producing H, influenzae, S, pneumoniae, & E. coli.


DOSE: Adults: 250–500 mg PO q8h or 875 mg q12h, XR 2,000 mg PO q12h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

AMMONIUM ALUMINIUM SULFATE (ALUM) [OTC]

USES: "Hemorrhagic cystitis when saline bladder irrigation fails.

ACTIONS: Alginates, forms precipitates over bladder surface.

DOSE: Adults/Peds: 1–4 mg col w/ constant NS bladder irrigation 200–250 mL/h.

W/P: [B, ?].

SE: Constipation, nausea, vomiting.

AMPHOTERICIN B (FUNGIZONE)

USES: "Severe, systemic fungal infections; oral & cutaneous candidiasis.

ACTIONS: Binds ergosterol in fungal membrane, alters permeability.

DOSE: Adults: 3–6 mg/kg/d q12h; max. dose 10/320/25 mg.

W/P: [B, enters breast milk].

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not substitute 250 mg tabs for one 500-mg tab (possible OD of clavulanic acid).

BENZYL BENZilate (AMPHOTEC)

USES: "Abscesses; systemic candidiasis.

ACTIONS: Binds ergosterol in fungal membrane, alters permeability.

DOSE: Children: 3–4 mg/kg/d; 1 mg/kg/h IV, q6–8h.

SE: Anaphylaxis, fever, chills, headache, J, P, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

BREZOZ (AMPHOREX)

USES: "Parenteral nutrition, drug eluting devices, hyperkalemia.

ACTIONS: Improves hemodynamics, reduces peripheral vascular resistance.

DOSE: Adults: 1,000–2,000 mg or 8–12 or 250–500 mg PO q8h.

SE: Hypotension, nausea, vomiting, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.

BREZOZ (GENERIC)

USES: "Parenteral nutrition, drug eluting devices, hyperkalemia.

ACTIONS: Improves hemodynamics, reduces peripheral vascular resistance.

DOSE: Adults: 1,000–2,000 mg or 8–12 or 250–500 mg PO q8h.

SE: Hypotension, nausea, vomiting, N/V, P, K, <Mg, BP, anemia.

NOTES: Do not use in-line filter; check LFTs/lytes.
AMPICILLIN-SULBACTAM (UNASYN, GENERIC)

**USES:** Gynecologic, intra-abdominal, skin infections, w/ lactamase-producing S. aureus, Enterococci, H. influenzae, P. mirabilis & Bacteroides sp.

**ACTIONS:** β-Lactam antibiotic & β-lactamase inhibitor; Spectrum: gram + & – as amp alone; also in combination, Aminopenicillin, Bacteriostatic.

**DOSE:**

- **Adults:** 1.5–3 g IV or IV gtt.
- **Ped:** 100–400 mg ampicillin/kg (150–300 mg UnasyN gtt)/q6h; ↓ w/ renal insufficiency.

**W/P:** (R, M).

**Disp:** Powder for injection 1 g (ampicillin 577 mg & sulbactam 423 mg).

**Notes:** A 2:1 ratio ampicillin:sulbactam.

**ANIDULAFUNGIN (ERAXIS)

**USES:** Candidiasis, esophageal candidiasis, other Candida infections (peritonitis, intra-abdominal abscesses).

**ACTIONS:** Echinocandin; ↓ cell wall synthesis. Spectrum: C. albicans, C. glabrata, C. parapsilosis, C. krusei.

**DOSE:**

- **Adults:** 200 mg IV × 1, then 150 mg IV daily [T, 4 days after last (±) culture]. 1.1 mg/m² max, Inf rate.
- **Ped:** 3–4 mg/m² 

**W/P:** (R, M)

- **Cl:** Aminocandin hypersens.

**Disp:** Powder 50, 100 mg

**Notes:** ↓ Inf rate to < 1.1 mg/m² in IV injections.

**APIXABAN (ELIQUIS)

**Warning:** Risk of spinal epidural hematoma w/ paralysis & 3° thoracic events w/ DC in all pts, monitor closely.

**Uses:** Prevents CV death in nonvalvular AF.

**ACTIONS:** Factor Xa inhibitor.

**Dose:** 5 mg BD, 2.5 mg w/ the following:

- **Adults:** Warfarin 60 mg q4 (may be 1.5, 2.5 mg w/ strong dual inhibitor of CYP3A4 and P-glycoprotein; if on 2.5 mg do not use w/ strong dual inhibitor of CYP3A4 and P-glycoprotein.

**W/P:** (R, M)

- **Cl:** Do not use w/ prophylactic values.

**Disp:** Tablets 2.5, 5 mg

**Notes:** ↓ Inf apixaban.

**ATENOLOL (TENORMIN, GENERIC)

**Warning:** Avoid abrupt withdrawal (esp. CAO emb, syndromal T2DM, acute HR, TNF inhibitors).

**Uses:** HTN, angina, post-MI.

**ACTIONS:** Selective β-adrenergic receptor blocker.

**Dose:** 50 mg PO up to 50 mg PO/d; ↓ renal impairment.

**W/P:** (M), D, bronchospasm, abrupt DC can exacerbate angina & ↑ HR risk.

- **Cl:** HR, congestive shock, cardiac failure, 2nd/3rd-degree AV block, sino-atrial dysfunction, pulm edema.

**Disp:** Tablets 25, 50, 100 mg

- **S.E:** HR, β, BF, 2nd/3rd-degree AV block, dizziness, fatigue.

**ATENOLOL & CHLORHLIDONE (TENORETIC)

**Uses:** Malignant HTN.

**ACTIONS:** β-Adrenergic blockade w/ diuretic.

**Dose:** 50–100 mg PO based on atenolol, ↓ dose w/ CVD 25–35 ml/min.

**W/P:** (D), β, ↓, DM, bronchospasm.

- **Cl:** See atenolol; anuria, softening, cyanosis.

**Disp:** Atenolol 50 mg/chlorthalidone 25 mg, aminophylline 100 mg/chlorthalidone 25 mg.

- **SE:** HR, BF, 2nd/3rd-degree AV block, dizziness, fatigue, ↓ K⁺, photosensitivity.

**AVANAFIL (STENDRA)

**Uses:** Erectile dysfunction.

**ACTIONS:** Phosphodiesterase type 5 (PDE5) responsible for GMP breakdown; ↑ cGMP activity to relax smooth muscle in 5° flow to corpus cavernosum, onset 30–60 min (delayed 1–1.25 hr with high fat meals).

**Dose:** 25 mg PO as early as 15 min before sex activity, no more than 1–2x/week; ↓ dose 50–200 mg based on effect; do not use w/ strong CYP3A4 inhibitor, use 50 mg w/ mod CYP3A4 inhibitor; w/ or w/o food.

**W/P:** (M)

- **Cl:** Priapism risk. Hypersensitivity w/ BP meds or substantial alcohol; seek immediate attention w/ hearing loss or acute vision loss (may be NAION; w/ substantial alcohol; seek immediate attention w/ hearing loss or acute vision loss (may be NAION).

**Disp:** Tablets 50, 100, 200 mg.

**Notes:** Mean capitol onset w/ sildenafil (15–30 min).

**ATROPINE, BENZODIAZEPIN, HYDROXYCINNAMIC ACID, METHENAMINE, METHYLENE BLUE, PHENYL SALICYLATE (URISED)

**Uses:** Lower urinary tract dysfunction.

**ACTIONS:** Methylamine in acidic urine neutralizes fornicate/methanet (cardiotonic), methylene blue (cardiovascular-acidic) (imidazolacetic), phenyl salicylate (imidazolacetic), hyoscine and atropine (parasympatholytic; ↓ muscle spasm).

**Dose:**

- **Adults:** 2 tablets PO QID.

- **Ped:** 6 yr: Individually.

**W/P:** (R, M)

- **Cl:** Nausea, vomiting; w/ sulfonamides.

**Disp:** Tablets: atropane 0.5 mg, hyoscyamine 0.05 mg, methylamine blue 4.5 mg, phenyl salicylate 18.1 mg.

**S.E:** Rash, dry mouth, flushing, ↑ pulse, diastolic, blurred vision, unreflex diastasis, voiding difficulties.

**Notes:** Take w/ plenty of fluid; can cause crystalluria; see also hyoscine and methenamine listings.

**AVANAFIL (STENDRA)

**Uses:** Erectile dysfunction.

**ACTIONS:** Phosphodiesterase type 5 (PDE5) responsible for GMP breakdown; ↑ cGMP activity to relax smooth muscle in 5° flow to corpus cavernosum, onset 30–60 min (delayed 1–1.25 hr with high fat meals).

**Dose:** (M) only 100 mg PO as early as 15 min before sex activity, no more than 1–2x/week; ↓ dose 50–200 mg based on effect; do not use w/ strong CYP3A4 inhibitor, use 50 mg w/ mod CYP3A4 inhibitor; w/ or w/o food.

**W/P:** (M)

- **Cl:** Priapism risk. Hypersensitivity w/ BP meds or substantial alcohol; seek immediate attention w/ hearing loss or acute vision loss; may be NAION; w/ CYP3A4 inhibitor (eg. ketoconazole; rifampin, erythromycin) ↑ effect; do not use w/ severe retinal/vascular impairment.

- **Cl:** Severe of use if not advised.

**Disp:** Tablets 50, 100, 200 mg.

**Notes:** Mean capitol onset w/ sildenafil (15–30 min).
AZITHROMYCIN (ZITHROMAX)

USES: Community-acquired pneumonia, pharyngitis, otitis media, skin infections; nongonococcal (chlamydial) urethritis, chancroid & pharyngitis, otitis media, skin infections, PID; Treat & prevention of MAC in HIV.

DOSE: Adults: 5 mg PO q2-3d; then 5 mg PO qd; 25 mg/d q1–2wk, target dose 2–3 mg/kg/d.

adiran of use or dose by ½ if usual or strong CYPLA4A inhibitor.

DISP: Tabs 250, 500, 600 mg; 2 Pack (5-dg, 250 mg); Tri Pack (500 mg tabs x 3); susp 2 g; single-dose unit-dose (Zmax) FR susp (2 x 2) susp 100, 200 mg/mL; inj powder 500 mg, 2.5 mL.

SE: GI upset, metallic taste.

AZTREONAM (AZACTAM)

USES: Acute gonorrhea – UTIs, lower resp, intra-abdominal, skin, genitourinary infections & septicemia.

ACTIONS: Monobactam; 1 Cell-wall synth.

DISP: Intramuscular, IM; optimal number of induction instillations and resection; do not administer intravesical forms SQ or IM;

SE: GI upset, metallic taste.

BACITRACIN, NEOMYCIN, & POLYMYXIN B, TOPICAL (BACIGUENT); BACITRACIN & POLYMYXIN B, TOPICAL (NEOSPORIN); BACITRACIN, NEOMYCIN, & POLYMYXIN B, TOPICAL (CORTISPORIN)

USES: Prevent/Treat of minor skin infections.

ACTIONS: Topical antibiotics w/ added components (anti-inflammatory & analgesics).

DOSE: Apply sparingly BID-QD.

SE: Not for deep wounds, punctures, or animal bites.

BASILIXIMAB (SIMULECT)

WARNING: Use only under the supervision of a physician experienced in immunosuppressive therapy in an appropriate facility.

USES: Prevent acute transplant rejection.

AEs: Myelosuppression; malignancies; risk of infections.

DISP: Powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.


DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

BASILIXIMAB (SIMULECT)

WARNING: May not be effective in immunosuppressed patients.

USES: Myelosuppression; malignancies; risk of infections.

DISP: Powder 10, 20 mg.

SE: GI upset, metallic taste.

BASILIXIMAB (SIMULECT)

WARNING: Myelosuppression; malignancies; risk of infections.

DOSE: Adult: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.

DOSE: Adult & Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV 4 days post-transplant.

Peds: >35 kg: 10 mg 2 hr prior to transplant; same dose 4 days post-transplant.

SE: Hypersensitivity to murine proteins.

DISP: mg powder 10, 20 mg.

SE: Edema, J, HTN, Headache, dizziness, fever, pain, infection. GI effects, electrolyte disturbances.

NOTES: A neutrophilic M.
BROMOCRIPTINE (PARLODEL)

**USES:** Parkinson’s disease, hyperprolactinemia, acromegaly, pharyngitis.

**DOSE:** Oral: 0.015–0.1 mg/kg PO q6–24h (max. 10 mg/d).

**ACTIONS:** Agonist to striatal dopamine receptors; reduces prolactin secretion. USES: hyperprolactinemia, acromegaly, pituitary tumors.

**SE:** Edema from CHF, hepatic cirrhosis, & renal disease. May induce withdrawal in opioid dependency. NOTE: May induce withdrawal in opioid dependency.

**BUPIVACAINE (MARCAINE, SENSORCANE, GENERIC)

**WARNING:** Avoid 0.75% for OB anesthesia due to reports of cardiac arrest and death.

**USES:** Local or regional anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures.

**DOSE:** Local anesthetic: 1–3 mg/mL; duration 5–7 hr; max. 300 mg.

**ACTIONS:** Local anesthetic: 1–3 mg/mL; duration 5–7 hr; max. 300 mg.

**SE:** Drowsiness, dizziness, nasal congestion.

**DISP:** Note for withdrawal if opioid dependent.

**BUTABARBITAL, HYDROXYCaine, PHENAZOPyrIDine**

**USES:** Atropine-like, pain & migraine headache.

**ACTIONS:** Opiate agonist-antagonist w/ central analgesic actions.

**DOSE:** Use: Acute pain: 5–40 mg IM or IV or 50–100 units SQ; in renal impairment.

**SE:** Urinary tract pain w/ UTI, procedures, trauma.

**DOSE:** 1 PO OD, pc & fc; w/ antiacid for UTI.

**BUTABARBITAL, HYDROXYCaine, PHENAZOPyrIDine**

**USES:** Atropine-like, pain & migraine headache.

**ACTIONS:** Opiate agonist-antagonist w/ central analgesic actions.

**DOSE:** Use: Acute pain: 5–40 mg IM or IV or 50–100 units SQ; in renal impairment.

**SE:** Urinary tract pain w/ UTI, procedures, trauma.

**DOSE:** 1 PO OD, pc & fc; w/ antiacid for UTI. 2 days max.

**CALCITONIN (FORTICAL, MICALCIN)

**USES:** Hypercalcemic deaths reported; check CBCs, Cl w/ AKI > 1500 calcium; severe hypercalcemia (exsymptomatic, ↓ BP; bronchospasm) may occur, D/C if no response w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**ACTIONS:** Microtuble inhibitor.

**DOSE:** 25 mg/m² at 1 hr; duration 5–7 hr; may titrate w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**SE:** N/V/diarrhea, renal function deterioration.

**CALCITONIN (FORTICAL, MICALCIN)

**USES:** Hypercalcemic deaths reported; check CBCs, Cl w/ AKI > 1500 calcium; severe hypercalcemia (exsymptomatic, ↓ BP; bronchospasm) may occur, D/C if no response w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**ACTIONS:** Microtuble inhibitor.

**DOSE:** 25 mg/m² at 1 hr; duration 5–7 hr; may titrate w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**SE:** N/V/diarrhea, renal function deterioration.

**CALCITONIN (FORTICAL, MICALCIN)

**USES:** Hypercalcemic deaths reported; check CBCs, Cl w/ AKI > 1500 calcium; severe hypercalcemia (exsymptomatic, ↓ BP; bronchospasm) may occur, D/C if no response w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**ACTIONS:** Microtuble inhibitor.

**DOSE:** 25 mg/m² at 1 hr; duration 5–7 hr; may titrate w/ bisphosphonates, sepsis, N/V/diarrhea, shock & sepsis.

**SE:** N/V/diarrhea, renal function deterioration.
CALCITROL (ROCALCITROL, CALCICUE)

USES: Probable decrease of FPTH levels to treat bone disease. Ca2+ on dialysis.

ACTIONS: 1,25-Dihydroxycholecalciferol (vit D analog); Ca2+ and phosphorus absorption; Ca bone mineralization.

DOSE: Adults: Initial, 0.25 μg PO, 0.25 μg q=4 wk PRN; 0.5–4 g diet to control serum phosphate discomfort. Nonaluminum phosphate binders and low phosphate tox.

DISP: Chew tabs 350, 420, 500, 550, 750, 850 mg; CI: [C, ?].

W/P: [C, ?].

SE: Can vary; ± GI distress.

CI: [B, M].

W/P: [C, ?].

OTHERS) (CALCICUE, CALCIJEX)

USES: Calcium carbonate (Tums, Alka-Mints) [OTC]

USES: NEPHRO-ASSOCIATED HYPERPARATHYROIDISM (HPT) * ACTIONS: Ca2+ spike in serum to PTH absorption.

DOSE: 2–4 tabs PO w/ meals; usual 2,001–2,668 mg PO w/ meals.

W/P: [C, ?].

SE: ↑ GI, possible w/ antacids.

CI: ↑ Ca2+; ↓ GI toxic.

DISP: Hx: ↑ GI, renal calculi.

SE: ↑ Ca2+; ↓ GI toxic.

W/P: [C, ?].

CALCIUM CARBONATE TUMS, ALKA-MINTS [OTC]

USES: Hypochlorhydric-associated gastrointestinal disorders, infant formula, etc. – calcium supplementation.

ACTIONS: Neutrophil granulocytes.

DOSE: 500 mg–2 PO PRN; [G, 70 mg, ]; w/ renal impairment.

W/P: [C, ?].

CI: Hx: ↑ Ca2+; renal calculi, suspected digoxin tox.

DISP: Chew tabs 330, 420, 500, 550, 750, 850 mg; susp.

SE: ↑ Ca2+; ↓ PO 60%, constipation.

W/P: [C, ?].

CULCIONATE (CALCIONATE) [OTC]

USES: Treat & prevent calcium deficiency. 

ACTIONS: Calcium supplement.

DOSE: Adults: 1,000–2,000 mg/d – doses.

Peds: 200–1,300 mg/d.

W/P: [C, ?].

DISP: PO susp 1.8–9.5 g elemental Ca 110–220 mL.

SE: ↑ Ca2+, ↓ PO 60%, constipation.

SE: ↑ PO, ↓ Ca2+.

W/P: [C, ?].

CALCIMET (CALCIUM SALTS) [PHOSPHATE, GLUCONATE, GLUCOPATE]

USES: Calcium replacement, VF, calcium blocker tox (calcium channel block,); severe ↑ hypomagnesemia tetany, hyperparathyroidism in ESRD.

ACTIONS: Calcium supplement replacement.

DOSE: Adults: Replacement: 1–2 g PO. Tetany: 1 g CaO over 10–30 min; repeat in 6 hr PRN.

Hypercalcemia/hyperphosphatemia/calcium channel blocker overdose: 500–1,000 mg (5–10 min of 10% calcium IV); repeat PRN; comparable dose of 10% calcium gluconate 15–30 ml.

Peds: Tetany: 10 mg/kg CaO (5–10 min); repeat in 6–8 hr or use Inf (200 mg/kg max). Hypercalcemia/hyperphosphatemia/calcium channel blocker overdose: Calcium chloride or gluconate 20 mg/kg (11.2 mg/kg slow IV); repeat PRN; renal venous stasis preferred.

Adults & Peds: ↓ calcium oral chelated blood tox in; 0.45 mlg Ca100 mL chelated blood tox (in renal impairment).

W/P: [C, ?].

CI: ↑ Ca2+, suspected digoxin tox.

DISP: SPC: CaH10 10% = 100 mg/ml Ca 27.2 mgmL; CaH10 10% = 100 mg/ml Ca, 28.5 mg/cc; 735 mg Ca; 975 mg Ca; 1 g = 95 mg Ca; Ca glucopate 200 ml = 1 mg/ml; 10% CaO IV; repeat PRN; calcium gluconate 13–30 mL.

Peds: Tetany: 10 mg/kg CaO (5–10 min); repeat in 6–8 hr or use Inf (200 mg/kg max).

Hypercalcemia/hyperphosphatemia/calcium channel blocker overdose: Calcium chloride or gluconate 20 mg/kg (11.2 mg/kg slow IV); repeat PRN; renal venous stasis preferred.

Adults & Peds: ↓ calcium oral chelated blood tox in; 0.45 mlg Ca100 mL chelated blood tox (in renal impairment).

W/P: [C, ?].

CI: ↑ Ca2+, suspected digoxin tox.

DISP: SPC: CaH10 10% = 100 mg/ml Ca 27.2 mgmL; CaH10 10% = 100 mg/ml Ca, 28.5 mg/cc; 735 mg Ca; 975 mg Ca; 1 g = 95 mg Ca; Ca glucopate 200 ml = 1 mg/ml; 10% CaO IV; repeat PRN; calcium gluconate 13–30 mL.

Peds: Tetany: 10 mg/kg CaO (5–10 min); repeat in 6–8 hr or use Inf (200 mg/kg max).

Hypercalcemia/hyperphosphatemia/calcium channel blocker overdose: Calcium chloride or gluconate 20 mg/kg (11.2 mg/kg slow IV); repeat PRN; renal venous stasis preferred.

Adults & Peds: ↓ calcium oral chelated blood tox in; 0.45 mlg Ca100 mL chelated blood tox (in renal impairment).

W/P: [C, ?].

SE: ↑ PO, ↓ Ca2+.

CI: [C, ?].

W/P: [C, ?].

CALCIFEROL (VITAMIN D3, ROCALTROL) [GENERIC]

USES: Treat & prevent vitamin D deficiency.

ACTIONS: Calciferol.

DOSE: Adults: 0.5–4 g diet to control serum phosphate discomfort. Nonaluminum phosphate binders and low phosphate tox.

DISP: Chew tabs 350, 420, 500, 550, 750, 850 mg; susp.

SE: ↑ GI, renal calculi, suspected digoxin tox.

DISP: Chew tabs 330, 420, 500, 550, 750, 850 mg; susp.

SE: ↑ PO, ↓ Ca2+.

W/P: [C, ?].
CEFDROXIL (GENERIC)

USES: *Infections of the nose, skin, bone, & urinary tract.*

ACTIONS: 1st-gen cephalosporin; j cell wall synth. Spectrum: Good gram (+) bacilli & cocci (Streptococcus, Staphylococcus) except Enterococcus); some gram (E. coli, Proteus, Klebsiella).

DOSE: Adults: 1–2 g PO, ↓ doses. Peds: 25–100 mg/kg IV → 6–8 h; ↓ in renal impairment.

W/P: [B, M].

SE: Cephalosporin/PCN allergy.

Disp: Caps 300 mg; susp 250, 375 mg/5 mL.

CI: Cefadroxil/PCN allergy.

W/P: [B, M].

3rd-gen cephalosporin; j cell wall synth. Spectrum: Good gram (+), + (Bacteroides); anaerobic: ↑ (not B. fragilis). Spectrum: S. pneumoniae, S. pyogenes, M. catarrhalis, H. influenzae, some anaerobes (not B. fragilis).

DOSE: Adults: 400 mg PO → daily-BID. Peds: 8 mg/kg PO → daily-BID; ↓ in renal impairment.

W/P: [B, M].

SE: N/V/diarrhea, rash, pruritus, cellulitis, eosinophilia, ↑ LFTs.

Disp: Susp 100, 200, 400 mg/5 mL.

CI: Cefadroxil/PCN allergy.

W/P: [B, M].

4th-gen cephalosporin; j cell wall synth. Spectrum: Most gram (+) - (except Enterococcus); some gram (E. coli, Proteus, Klebsiella). Use with severe infections.

DOSE: Adults: 1–2 g IV q4–8h. Peds: 20 mg/kg q8h for febrile neutropenia; ↓ doses.

W/P: [B, M].

SE: N/V/diarrhea, rash, pruritus, cellulitis, eosinophilia, ↑ LFTs.

Disp: Caps 500 mg; tabs 1 g; susp. 250, 500 mg/mL.

CI: Cefadroxil/PCN allergy.

W/P: [B, M].

50 mg/kg q8h for febrile neutropenia; ↓ doses.

W/P: [B, M].

NOTES: May interfere w/ warfarin.

CEFOTAXIME (CLAFORAN, GENERIC)

USES: *Infections of lower resp tract, skin, bone & joint, urinary tract, meningitis, sepsis, PCP, GC.*

ACTIONS: 3rd-gen cephalosporins; j cell wall synth. Spectrum: Most gram (+) - (except Pseudomonas, some gram (-) cocci S. pneumoniae, S. aureus (penicillinase-resistant pneumococci produced), enterococci [including ampicillin resistant], not Enterobacter; many PCN-resistant pneumococci.

DOSE: Adults: Unconjugated infection: 1 g IVIM q12h; Abdomen sepsis: 1–2 g IVIM q6–8h. Enterococcus: 2 g IVIM q8–12h; G. vini; enterococci, catalase in hemol: 0.5 mg/d PO; ↑; Viocin: G. vini: 1 g/d PO; ↑;

Peds: 50–200 mg/kg/d IV q4–8h; ↓ in renal/hepatic impairment.

W/P: [B, M].

SE: Arthralgia w/ rapid inj; ↑ LFTs.

Disp: Powder for inj 500 mg, 1, 2, 10 g; premixed sol 25 mg/mL, 40 mg/mL.

SE: diarrhea, rash, pruritus, cellulitis, eosinophilia, ↑ transaminases.

CEFOTETAN (GENERIC)

USES: *Infections of the upper & lower resp tract, skin, bone, urinary tract, abdominal & gynecologic system.*

ACTIONS: 2nd-gen cephalosporins; j cell wall synth. Spectrum: Some active against gram (+) anaerobes including B. fragilis, gram (+), including E. coli, Klebsiella, & Proteus.

DOSE: Adults: 1–3 g PO/L/IV. Peds: 20–40 mg/kg/dose IV → q12h (6–12 kg max); ↓ in renal impairment.

W/P: ↓ 1; ↑ 1/2 h; ↑ in renal impairment.

SE: Diarrhea, rash, pruritus, cellulitis, ↑ transaminases, hypoprothrombinemia, & bleeding (1–3 MIT side chain).

NOTES: May interfere w/ warfarin.

CEFOTAXIM (GENERIC)

USES: *Infections of the upper & lower resp tract, skin, bone, urinary tract, Abdominal & gynecologic system.*

ACTIONS: 2nd-gen cephalosporins; j cell wall synth. Spectrum: Good gram (+) - against enteric bacilli (E. coli, Klebsiella, & Proteus), anaerobic & fragilis.

DOSE: Adults: 2–6 g IV q8h. Peds: 80–160 mg/kg/d IV q4–8h (12 kg max); ↓ in renal impairment.

W/P: [B, M].

CI: Cefadroxil/PCN allergy.

Disp: Powder for inj 1, 2, 10 g.

SE: Diarrhea, rash, eosinophilia, ↑ transaminases.
CEFPODOXIME (GENERIC)

USES: "Throat, ear, skin, & urinary tract infections." 

ACTIONS: 3rd-gen cephalosporin; j, cell wall synth. 
Spectrum: β-lactamase–producing H. influenzae, acute uncomplicated N. gonorrhoeae, zone unconfmed gram−. (cf. clavulanate, Proxna) 

DOSE: 
- Adults: 100–400 mg PO q12h. 
- Peds: 10 mg/kg PO – RID; ↓ in renal impairment, w/ food. 

W/P: [R, X]. 

Cl: Cephalosporin/PCN allergy. 

DISP: Caps 250, 500 mg; susp, 125, 250 mg; susp premixed 20, 40 mg/mL. 

CI: Sulfonamide allergy, perioperative CABG. 

W/P: [C/D (3rd tri), ?] w/ renal impairment. 

NOTES: Watch for Sxs of GI bleed; no effect on plt/bleeding time; can affect drugs metabolized by COX-2 pathway. 

CEFIBUTEN (CEDAX)

USES: "Throat, ear, skin, & urinary tract infections, & otitis media."

ACTIONS: 3rd-gen cephalosporin; j, cell wall synth. 
Spectrum: N. influenzae & M. catarrhalis; weak against S. pneumonia. 

DOSE: 
- Adults: 400 mg/d PO. 
- Peds: 9 mg/kg PO, ↓ in renal impairment; take on empty stomach (susp). 

W/P: [R, X]. 

Cl: Cephalosporin/PCN allergy. 

DISP: Caps 400 mg; susp 90 mg/mL. 

CI: Sulfonamide allergy, perioperative CABG. 

NOTES: See "Warning," GI upset, HTN, edema, renal failure, headache. 

CEFTRIAXONE (ROCEPHIN, GENERIC)

WARNING: Avoid in hypothyroidism or confusion w/ calcium-containing products. 

USES: "Throat, ear, skin, bone, abdominal & urinary tract infections, meningitis, septicaemia, GC, PID, perioperative." 

ACTIONS: 3rd-gen cephalosporin; j, cell wall synth. 
Spectrum: fried gram−, excellent β-lactamase producers. 

DOSE: 
- Adults: 1–2 g IM/IV q12–24h. 
- Peds: 50–100 mg/kg IM/IV − q12–24h; decrease dose with renal insuficiency. 

W/P: [R, X]. 

Cl: Proximal acute renal failure (PARF) in children may require dialysis. 

Cl: Cephalosporin allergy, hypothyroidism/neonates. 

DISP: Powder for inj 160 mg, 250 mg IV q8h. 

W/P: [R, X]. 

Cl: Cephalosporin allergy. 

DISP: Caps 50, 100, 200, 400 mg. 

CI: Sulfonamide allergy, perioperative CABG. 

NOTES: See "Warning," GI upset, HTN, edema, renal failure, headache. 

CEFTRIAXONE (CETIN PO, ZINACEF (PARENTERAL), GENERIC)

USES: "Upper & lower resp tract, skin, bone, urinary tract infections, meningitis, & septicaemia." 

ACTIONS: 2nd-gen cephalosporins; j, cell wall synth. 
Spectrum: β-lactamase–producing H. influenzae, acute uncomplicated N. gonorrhoeae, zone unconfmed gram−. (cf. clavulanate, Proxna) 

DOSE: 
- Adults: 250–500 mg PO q6h. 
- Peds: 15–25 mg/kg PO q6h; ↓ in renal impairment; take PO w/ food. 

W/P: [R, X]. 

Cl: Cephalosporin allergy. 

DISP: Caps 250, 500 mg; susp, 125, 250 mg; susp premixed 20, 40 mg/mL. 

CI: Sulfonamide allergy, perioperative CABG. 

NOTES: Cefuroxime film coated tabs & susp not bioequivalent; do not substitute on a mg/mg basis; IV crosses blood–brain barrier. 

CELECOXIB (CELEBREX)

WARNING: ↑ Risk of serious CV thrombotic events, MI, & stroke; can be fatal; ↑ Risk of serious GI adverse events including bleeding, ulceration, & perforation of the stomach or intestine; can be fatal. 

USES: "Osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute pain, primary dysmenorrhea." 

ACTIONS: NSAID; decreases urine pH. 

DISP: Caps 200 mg, 400 mg PO q12–24h; decrease dose w/ hepatic impairment. 

CI: Hypersensitivity; anaphylaxis; HTN, edema, renal failure, jaundice. 

NOTES: Watch for Sxs of GI bleed; no effect on pitibinding time; can affect drugs metabolized by P450 pathway. 

CEPHEALXIN (KLEXF, GENERIC)

USES: "Nasal, bone, upper/lower resp tract (streptococcal pharyngitis), otitis media, uncompy synths infections." 

ACTIONS: 1st-gen cephalosporin; j, cell wall synth. 
Spectrum: Streptococcus (including β-hemolytic), Staphylococcus, E. coli, Proteus, & Klebsiella. 

DOSE: 
- Adults & Peds: > 15 yr: 250–1,000 mg PO q8h; < 15 yr: 7–14 days (4 g/d max.). 
- Peds: 30–125 mg/kg PO q8h. 

W/P: [R, X]. 

Cl: Cephalosporin allergy. 

DISP: Caps 250, 500 mg; susp, 125, 250 mg; susp premixed 20, 40 mg/mL. 

CI: Sulfonamide allergy, perioperative CABG. 

NOTES: Cefuroxime film coated tabs & susp not bioequivalent; do not substitute on a mg/mg basis; IV crosses blood–brain barrier. 

CHLOROTHIAZIDE (DIURIL)

USES: "HTN, edema." 

ACTIONS: Thiazide diuretics; decreases urine calcium. 

ACTIONS: 2nd-gen cephalosporins; j, cell wall synth. 
Spectrum: β-lactamase–producing H. influenzae, acute uncomplicated N. gonorrhoeae, zone unconfmed gram−. (cf. clavulanate, Proxna) 

DOSE: 
- Adults: 250–1,5 g IV q8h or 250–500 mg PO bid. 
- Peds: 15–100 mg/kg IV − q8h or 20–30 mg/kg PO − BID; ↓ in renal impairment; take PO w/ food. 

W/P: [R, X]. 

Cl: Cephalosporin allergy. 

DISP: Caps 250, 500 mg; susp, 125, 250 mg; susp premixed 20, 40 mg/mL. 

CI: Sulfonamide allergy, perioperative CABG. 

NOTES: Cefuroxime film coated tabs & susp not bioequivalent; do not substitute on a mg/mg basis; IV crosses blood–brain barrier. 

933
CHLORTHALIDONE (GENERIC)

DOSE:
- Adults: 500–1 mg PO daily; 50–1,200 mg IV (for edema only).
- Peds: ≤ 6 mo: 10–20 mg/kg/d PO ⇒ BID; 4 mg/kg ⇒ daily IV; OK w/ food.
- W/P: (+, +, +).
- Cl: Sensitivity to thiazide/sulfonylureas, anemia.
- DISP: Tabs 250, 500 mg; susp 250 mg/mL IV ⇒ 500 mg/mL
- SE: ↑ K+, Na+, dizziness, hypertension, hyperuricemia, sexual dysfunction; 25–50 mg/d for idiopathic hypercalcemia.
- NOTES: Do not use (M/O) take early in the day to avoid nocturia; use sunblock; monitor lym.

CHLORTHALIDONE (GENERIC)

USES: ↑ HTN, edema.

ACTIONS: Thiazide diuretic.

DOSE:
- Adults: 25–100 mg PO daily.
- Peds: (Not FDA approved) 0.3–2 mg/kg/dose PO ⇒ 1–2 mg/kg/dose IV ⇒ in renal impairment; OK w/ food, NR.
- W/P: (+, +, +).
- Cl: Cross-sensitivity w/ thiazides or sulfonamides; anemia.
- DISP: Tabs 25, 100, 150 mg.
- SE: ↑ K+, dizziness, photosensitivity, ↑ glucose, hyperuricemia, sexual dysfunction; 25–50 mg/d for idiopathic hypercalcemia.

CHOLECALCIFEROL (VITAMIN D3) (DELTA D)

USES: Dietary sup to Tract vitamin D deficiency.

ACTIONS: ↑ Intestinal Ca2+ absorption.

DOSE: 400–1,000 IU PO.

W/P: (D dose above the RDA), + (+).

Cl: ↑ Ca2+, hypercalciuria, allergy.

DISP: Tabs 400, 1,000 IU.

SE: ↑ Ca2+ renal failure, HTN, psychosis.

NOTES: 1 mg cholecalciferol = 40,000 IU ⊥ D activity.

CIPROFLOXACIN (CIPRO, CIPRO XR)

WARNING: ↑ Risk Achilles tendon rupture and tendinopathy. ↑ in risk ⇒ 40–60 y on thiazide or w/ organ transplant; axial w/ myopathy–myalgia, may ↑ muscle weakness.

USES: Treat lower resp tract, urinary, skin & skin structure, bone/joints, complex intra-abdominal infection (peritonitis, typhoid, infectious diarrhea), urticaria GC, inhaled asthma, futures including poscid; Peds only for multi resistant UTI not as first agent.


DOSE: Adults: 250–750 mg PO q2–4h; XR 500–1,000 mg PO q2–4h; 200–400 mg IV q12h; J ⇒ renal impairment.

CITRIC ACID, GLUCONOLACTONE, AND MAGNESIUM CARBONATE (RENACIN)

USES: Chemolysis of calculi: dissolution; insoluble Ca2+ of the urinary tract composed of apatite (calcium phosphate) or struvite (magnesium ammonium phosphate) in nonsurgical candidates; adjunctive therapy to dissolve residual urothelial/tract fragments postop; partial dissolution of calculi to facilitate surgical removal.

ACTIONS: dissolution of calcium by exchange of Mg2+ from irrigating solution for insoluble Ca2+ in calculus. Mg2+ salts are soluble in the citrate irrigating solution, dissolving calculus.

DISP: (Invertment & blind) irrigation: 30–50 mL via Foley, stumped for 30 mins, repelled TID for 3–5 or bladder stones; irrigation via dual nephrostomy tube (without cuffing) or into ureteral catheter with nephrostomy drainage; essential to keep pressure >80 cm H2O by manipulation.

W/P: (+, +) Caution ⇒ irrigating the renal pelvis of patients w/ impaired renal function. Observe for early signs/symptoms of hypermagnesemia (nausea, lethargy, confusion and hypotension). Severe hypermagnesemia may result in hyporeflexia, dyspnea, apneic episodes, cardiac arrest, and subsequent death. Monitor magnesium levels and deep tendon reflexes should be evaluated.

CI: Obstructed urinary tract, extravasation, UPI.

DISP: Solution: Se: Hypermagnesemia, limitation, sialosis, other infections.

NOTES: fluid solution G was modified by addition of magnesium salts to create Renacidin.

CLARITHROMYCIN (BIAxin, Biaxin LR)

USES: ↑ Upperson flap tract, skin & skin structure infections, H. pylori infections, & infections caused by nontuberculous (atypical) Mycobacterium; prevention of MAC infections in HIV infection.


DOSE:
- Adults: 250–500 mg PO BID or 1,000 mg (2 × 500 mg X tab)/t/d (Macrolide carbonic 500 mg PO PO)
- Peds: ≤ 6 mo: 7.5 mg/kg PO PO; BD; ↓ renal impairment.

W/P: (+, +) Antibiotic-associated colitis; rare ↑ QT & ventricular arrhythmias; not rec w/ PDE5 inhibitors.

Cl: Macrolide allergy; w/ H pylori w/ Biaxir; w/ aspirin, piroxicam, atorvastatin, leflunomide, ergotamines, PDE5 inhibitors (sildenafil, others); w/ corticosteroids; w/ cimetidine & renal impairment; w/ statins, ↑ QT or ventricular arrhythmias.

DISP: Tabs 250, 500 mg susp 125, 250 mg/mL; 500 mL NX tab.

SE: ↑ QT interval; causes metabolic taste, Vomiting, abdominal pain, rash.

NOTES: Multiple drug interactions; ↑ theophylline & carbamazepine levels, do not refrigerate susp.

CLINDAMYCIN (Cleocin, Cleocin-T, Others)

WARNING: Pseudomembranous colitis may range from mild to life threatening.

USES: ↑ aerobic & anaerobic infections; topical for severe acne & Vag infections.

ACTIONS: Bactericidal interferes w/ protein synthesis. Spectrum: Streptococci (eg, pneumococci, staphylococci), & (find ↔ anaerobes, no activity against gram) – aerobes.

DOSE:
- Adults: PO: 150–450 mg PO q6–8 h. IV: 300–400 mg q4–8 h ⇒ 900 mg IV q4 h. Vag cream: 1 applicator ⇒ 7 days. Vag supp: Insert 1 qhs ⇒ 3 days. Topical: Apply 1% gel, lotion, or ointm BD.

Ped: (Avoid use; contains benzyl alcohol) 10–15 mg/kg/day IV ⇒ q8–12 h. Children > 3 y: 30–50 mg/kg/d4 h ⇒ 48–49 h. ↑ to a max of 1.8 g/d PO or 4.8 g IV. Topical: Apply 1%, gel, lotion, or ointm BD, ↓ in severe hepatic impairment.
**COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)**

**WARNING:** Corporal rupture, severe hematoma, mild allergic reactions (pruritus).

**NOTES:** For details of procedure see package insert; administer only by experienced provider. If the deformity < 15 degrees after any treatment cycle subsequent cycles should not be administered.  

**Ped:** Analgesic: 0.5–1 mg/kg/dose PO q4–6h PRN. Antitussive: 1–1.5 mg/kg/24h PO q4–6h max. 30 mg/24h; 1 mg renal/hepatic impairment.

**W/P:** JC: (D prolonged use or high dose at term), ox (CNS depression), Hr drug abuse, severe hepatic impairment.

**CI:** Component sensitivity.

**DISP:** Tabs: 15, 30, 60 mg; soln: 30 mg/5 mL; inj: 15, 30 mg/5 mL.

**SE:** Drowsiness, constipation, J BP.

**NOTES:** Usually combined w/ vasoepinephrine for pain or as agents (eg, terbutyl hydrazide) as an antispasmodic, 120 mg Hying 10 mg IM morphine.

---

**CODEINE [C-II]**

**USES:** Mild–mod pain; symptomatic relief of acute coronary syndrome.

**ACTIONS:** Narcotic analgesic, J cough reflex.

**DOSE:** Adults: Analgesic: 15–60 mg PO or IM q4h PRN; 360 mg max/24h. Antitussive: 10–20 mg PO q4h PRN; max. 120 mg.

**SE:** Ovarian enlargement, vasomotor flushes.

**DISP:** tabs: 0.1, 0.2, 0.3 mg.

**CI:** Component sensitivity.

**DISP:** Tabs: 0.1, 0.2, 0.3 mg.

**SE:** Drowsiness, orthostatic, J BP, serotonina, constipation, J MR, dizziness.

**NOTES:** More effective for HTN if combined w/ diuretics; withhold slowly, naranbolic HTN w/ abrupt D/C of doses >0.2 mg BID. (Duloxad oral is used for chronic, cancer pain.

---

**COLONICPHEN (CLomid, Serophene, Generic)**

**USES:** 1x ovulatory dysfunction in women desiring pregnancy.

**ACTIONS:** Nonsteroidal ovulatory stimulant; estrogen antagonists, increase FSH and LH through blocking feedback inhibition on the pituitary.

**DOSE:** 50 mg × 5 days; If no ovulation × 10 mg × 5 days @ 30 day; ovulation usually 5–10 days postcourse, time cycling w/ expected ovulation time.

**DISP:** Tabs 0.1, 0.2, 0.3 mg.

**SE:** Ovarian enlargement, vasomotor flushes.

**NOTES:** Off-label use in males to increase testosterone or for low sperm counts; >10% of men w/ azospermia and hypospermidion have return of sperm to ejaculate after 1 treatment using clomifene.

---

**CLOMIDONE, ORAL (CATEAPRS)**

**USES:** Clomiphene citrate, Clomid, Serophene, Generic.

**ACTIONS:** Clomiphene citrate, Clomid, Serophene, Generic.

**DOSE:** Adults: 50 mg/d; full effects take several days.

**ACTIONS:** D/C drug w/ diazepam, evaluate for C. diff.

---

**CODEINE [C-II]**

**USES:** Mild–mod pain; symptomatic relief of acute coronary syndrome.

**ACTIONS:** Narcotic analgesic, J cough reflex.

**DOSE:** Adults: Analgesic: 15–60 mg PO or IM q4h PRN; 360 mg max/24h. Antitussive: 10–20 mg PO q4h PRN; max. 120 mg.

**SE:** Drowsiness, constipation, J BP.

**NOTES:** More effective for HTN if combined w/ diuretics; withhold slowly, naranbolic HTN w/ abrupt D/C of doses >0.2 mg BID. (Duloxad oral is used for chronic, cancer pain.

---

**COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)**

**W**arning: Corporal rupture, severe hematoma, mild allergic reactions (pruritus).

**NOTES:** For details of procedure see package insert; administer only by experienced provider. If the deformity < 15 degrees after any treatment cycle subsequent cycles should not be administered.  

**Ped:** Analgesic: 0.5–1 mg/kg/dose PO q4–6h PRN. Antitussive: 1–1.5 mg/kg/24h PO q4–6h max. 30 mg/24h; 1 mg renal/hepatic impairment.

**W/P:** JC: (D prolonged use or high dose at term), ox (CNS depression), Hr drug abuse, severe hepatic impairment.

**CI:** Component sensitivity.

**DISP:** Tabs: 15, 30, 60 mg; soln: 30 mg/5 mL; inj: 15, 30 mg/5 mL.

**SE:** Drowsiness, constipation, J BP.

**NOTES:** Usually combined w/ vasoepinephrine for pain or as agents (eg, terbutyl hydrazide) as an antispasmodic, 120 mg Hying 10 mg IM morphine.

---

**COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)**

**WARNING:** Corporal rupture, severe hematoma, mild allergic reactions (pruritus).

**NOTES:** For details of procedure see package insert; administer only by experienced provider. If the deformity < 15 degrees after any treatment cycle subsequent cycles should not be administered.  

**Ped:** Analgesic: 0.5–1 mg/kg/dose PO q4–6h PRN. Antitussive: 1–1.5 mg/kg/24h PO q4–6h max. 30 mg/24h; 1 mg renal/hepatic impairment.

**W/P:** JC: (D prolonged use or high dose at term), ox (CNS depression), Hr drug abuse, severe hepatic impairment.

**CI:** Component sensitivity.

**DISP:** Tabs: 15, 30, 60 mg; soln: 30 mg/5 mL; inj: 15, 30 mg/5 mL.

**SE:** Drowsiness, constipation, J BP.

**NOTES:** Usually combined w/ vasoepinephrine for pain or as agents (eg, terbutyl hydrazide) as an antispasmodic, 120 mg Hying 10 mg IM morphine.

---

**CODEINE [C-II]**

**USES:** Mild–mod pain; symptomatic relief of acute coronary syndrome.

**ACTIONS:** Narcotic analgesic, J cough reflex.

**DOSE:** Adults: Analgesic: 15–60 mg PO or IM q4h PRN; 360 mg max/24h. Antitussive: 10–20 mg PO q4h PRN; max. 120 mg.

**SE:** Ovarian enlargement, vasomotor flushes.

**DISP:** tabs: 0.1, 0.2, 0.3 mg.

**CI:** Component sensitivity.

**DISP:** Tabs: 0.1, 0.2, 0.3 mg.

**SE:** Drowsiness, orthostatic, J BP, serotonina, constipation, J MR, dizziness.

**NOTES:** More effective for HTN if combined w/ diuretics; withhold slowly, naranbolic HTN w/ abrupt D/C of doses >0.2 mg BID. (Duloxad oral is used for chronic, cancer pain.

---

**COLIODIGEL (PLAXIV, GENERIC)**

**USES:** ‘Reduce attherosclerotic events, acute coronary syndrome.’

**ACTIONS:** J PR aggregation.

**DOSE:** 75 mg; ACL: 350–400 mg PO loading dose, then 75 mg PO, full effects take several days.
CONIVAPTAN HCL (VAPRISOL)

- Hold pressure for 30 s and release, after 30 s repeat, repeat 3 times.
- Patient should perform self-modeling with spontaneous erection and stretch flaccid penis

CONIVAPTAN HCL (VAPRISOL)

USES: Edematous & hyponatremic hypovolemia.

ACTIONS: Dual arginine vasopressin 2 receptor antagonist.

DOSE: 20 mg IV 1–2 max. dose, then 20 mg cont for 24 h; 20 mg IV load for 1–3 more days; may ↑ 1 mg/hr if Na+ not responding; 4-day max; use, use large vial, change site q24h.

W/P: [C, ↓] Rapid↑ Na+ (12 mEq/L) may cause cardiac decompensation, impaired renal function, high aldosterone levels, CYP3A4 inhibitor.

CL: Hyponatremic hypovolemia, w/ CYP344 inhibitor, anuria.

DISP: IV 20 mg/100 mL.

SE: Ile ile reactions, headache, IVN/Dxanthea, constipation, J, K, orthostatic, J, RP, thirst, pain, dry mouth, paresthesia, pitting, infection.

NOTES: Monitor Na+, vol and neurologic status; Na+ w/ vol replacement.

CORTISONE

See Textbook Systemic and Topical Pages 968, 969

CYCLOSPORINE (GENGRAF, NEORAL, SANDIMMUNE)

WARNING: Risk nephrotoxic, risk of malignancies, risk H/TN and nephrotoxic.

USES: Organ rejection in kidney, liver, heart, rheumatoid arthritis, psoriasis.

ACTIONS: Immunosuppressant reversible inhibition of immunocompetent lymphocytes, a calcineurin.

DOSE: Adults & Peds: PO: 15 mg/kg/12 h transplantant; after 2 wk, taper by 5 mg/kg/d to 6–10 mg/kg/d or PO: 75 mg PO BID; do not chew/crush; NPO, give 1/3 PO dose IV; DID 15–30 mL/min

W/P: [C, ↓] CYP3A4 inhibitor.

CL: Decreased renal, hepatic dysfunction, cirrhosis.

DISP: Caps 25, 75 mg.

SE: Trough:
- Headache, dizziness, anxiety, nephrotox, pulm edema, pain, anaphylaxis/hypersens.
- Administer w/in 4 hr of prep.
- Follow WBC cystine or plasma cysteamine levels.
- Risk neoplasm, irreversible testicular atrophy possible; cardiotox rare; anorexia; N/V; hepatotox; rare interstitial pneumonitis; allergic reactions; anaphylaxis; rash; myalgia; headache; diarrhea; flushing; fever; hypotension; increase BUN & Cr and mimic transplant rejection; peds up to 12 yr: Maint 1.3 g/m2/d; patients with normal renal function 0.75 g/m2/d.

NOTES: Monitor renal function.

CYTOSPORIN

See Textbook Systemic and Topical Pages 988, 997

CYTOXAN, NEOSAR

WARNING: Risk aplasia, myelosuppression, risk WBC, risk of malignancies, risk H/TN, risk of malignancies.

USES: Hodgkin disease & NHLs; multiple myeloma; chronic lymphocytic leukemia, ovarian, cervical, melanoma, tumors; neuroblastoma; retinoblastoma; acute leukemias; allogeneic & ABMT in high doses; severe rheumatologic disorders (SLE, JRA, Weger granulomatosis); “internal change” nephrotic syndrome in children.

ACTIONS: Alkalizing agent.

DOSE: Adults: (per protocol) 500-1,500 mg/m2 qm o .

W/P: [C, ↓] Risk of TTP and/or thrombocytopenia.

CL: GI absorption.

DISP: Caps 25, 75 mg.

SE: Myelosuppression, N/V, anorexia, vomiting, abdominal pain, renal ischemia.

NOTES: Monitor BUN & Cr and mimic transplant rejection.

CYSTAMINE (CYSTAGON, PROCYBSI)

DOSE: Risk of thrombosis; risk of malignancies.

ACTIONS: Benemid corticosteroid.

DOSE: Benemid: 500 mg–1g/m2 qm o .

W/P: [C, ↓] Risk of TTP and/or thrombocytopenia.

CL: GI absorption.

DISP: Caps 25, 75 mg.

SE: Nausea, vomiting, anorexia and abdominal pain, lethargy.

NOTES: Follow WBC cystine or plasma cysteamine levels.

DABIGATRAN (PRADAXA)

WARNING: Pradaxa D/C if inadequate anticoagulation may 1 stroke risk, epidural or spinal hematomas may occur.

USES: ↑ Risk stroke/systemic embolism w/ nonvalvular AF; treat DVT and PE in patients who have been treated with a parenteral anticoagulant for 5–10 days.

ACTIONS: Thrombin inhibitor.

DOSE: C/O: [C, ?] QD 30 mg/m2/150 mg PO BID.

W/P: [C, ↓] Dose at 2-wk intervals; 1.8 g/m2–160 mg/kg (or 15 mg/kg/12 h pretransplant; 10.7% at 12 yr.

CL: Prevention of acute organ rejection.

DISP: Caps 75, 150 mg.

SE: Bleeding, gastritis, dyspepsia.

NOTES: See label to convert between anticoagulants; caps sensitive to humidity (30-day life span).

DACLIZUMAB (ZENAPAX)

WARNING: Administer in glass container; N/O to Sandimmune and Neoral (Sandimmun); avoid refeeding HCQ patients after D/C.

ACTIONS: Δ Proliferative activity, immunosuppression.

DOSE: Adult: 10 mg/kg IV/IM/Inj 3 times weekly; 5–10 days.

W/P: [C, ↓] Δ Risk of wound infection.

CL: GI absorption.

DISP: Caps 50, 150 mg.

SE: Trough:
- Headache, dizziness, anxiety, nephrotox, pulm edema, pain, anaphylaxis/hypersens.
- Administer in w/ IV 4 hr of prep.

DACLIZUMAB (ZENAPAX)
**DACTINOMYCIN (COSMEGEN)**

**WARNING:** Administer under skilled supervision in properly equipped facility; powder and citric acid, dextrose, mannitol, potassium hydroxide, and thiomersal; avoid exposure and use precautions.

**USES:** Choriocarcinoma, Wilms' tumor, Kaposi and Ewing sarcomas, rhabdomyosarcoma, uterine and testicular cancer.

**DOSE:**
- Adults: 15 µg/mL for 5 for 5 qh 6–8 wk or 400–600 µg/m² q4–6 wk.
- Pediatric: S/C.

**ACTIONS:** DNA-intercalating agent.

**SIDE Effects:** Hypersensitivity, pyrexia, fever, chills, abdominal pain, vomiting, diarrhea, nausea, stomatitis, anorexia, vomiting, retching, hypotension, fever, chills, rash, erythema, arthralgia, myalgia, edema, urticaria and angioedema.

**NOTES:** Classified as antibiotic but not used as antibacterial.

---

**DALBANVANCIN (DALVANCE)**

**USES:** Acute bacterial skin & skin structure infections (ABSSSI), complicated skin & skin structure infections (cABSSSI).

**DOSE:**
- Adults: 2,500–5,000 U SQ 1–2 hr.
- Pediatric: Adjust to appropriately for age and weight.

**ACTIONS:** Glycopeptide antibacterial (blocks cell wall synthesis).

**SIDE Effects:** Nausea, vomiting, anaphylaxis reported; avoid rapid inf; severe infusion reactions include hemodynamic instability, hypotension, anaphylaxis and anaphylactoid reactions.

---

**DARIFENACIN (ENABLEX)**

**USES:** Overactive bladder with symptoms of urge incontinence, urgency and frequency.

**DOSE:**
- Adults: 15 mg p.o. in 1 or 2 doses.

**ACTIONS:** Muscarinic receptor antagonist.

**SIDE Effects:** Diarrhea, constipation, dyspepsia, flatulence.

---

**DARITONTE (DANTIUM, REVONTO)**

**WARNING:** Hepatic reported; DC after 45 days. May not be beneficial.

**USES:** Treat spasticity due to upper motor neuron disorders (eg, spinal cord injury, stroke, CP, MS), malignant hyperthermia.

**DOSE:**
- Adults: 25, 40, 60, 100, 200, 300 µg/kg single IV or SQ qwk; titrate, do not exceed target Hgb of 12 g/dL; use lowest doses possible; see PI to convert from Hemoprep.

**ACTIONS:** Erythropoiesis, recombinant human EPO (rHuEPO).

**SIDE Effects:** Headache, hypertension, vertigo, chest pain, abdominal pain, back pain, myalgia, edema, edema, rash, urticaria and angioedema.

---

**DEGARELIX (FIRMAGON)**

**USES:** Advanced prostate cancer.

**DOSE:**
- Adults with mHSPC: 3.6 mg SC at baseline and 6 months.

**ACTIONS:** Reversible LHRH antagonists; LH and testosterone (obv) saw use in prostate (obv) and testicular (obv).

**SIDE Effects:** Hot flashes, sexual dysfunction, fatigue, mood swings, abdominal pain.

---

**DENOSUMAB (PROLIA, XGEVA)**

**USES:** Multiple myeloma postmenopausal women; 1 BMD in men on ADT (Prolia); prevent skeletal events in bone metastases (Xgeva).

**DOSE:**
- Prolia: 60 mg SQ giv, in upper arm, thigh, abdominal.
- Xgeva: 120 mg SQ q6mo; in upper arm, thigh, abdominal.

**ACTIONS:** RANK ligand (RANKL) inhibitor (human Fc fusion protein).

**SIDE Effects:** Tenderness, pain at injection site, subcutaneous fat atrophy, arthralgia, myalgia.

---

**DESMPRESSIN (ddAVP, DDAVP NASAL SPRAY, STIMATE)**

**USES:** Amniotic fluid levels in women with severe polyhydramnios.

**DOSE:**
- Adults: 10–40 µg/mL in 1–3 doses.
- Pediatric: 3–12 yrs:
  - 0.50–0.63 µg/mL in 1 or 2 doses.

**ACTIONS:** Nonselective LHRH receptor agonist.

**SIDE Effects:** Nausea, vomiting, diarrhea, abdominal pain, retentive, abnormal vision, dizziness, asthenia.

---

**DENTROHEMOCRINE (DANTRIUM, REVONTO)**

**WARNING:** Hepatic reported; DC after 45 days. May not be beneficial.

**USES:** Treat spasticity due to upper motor neuron disorders (eg, spinal cord injury, stroke, CP, MS), malignant hyperthermia.

**DOSE:**
- Adults: 25, 40, 60, 100, 200, 300 µg/kg single IV or SQ qwk; titrate, do not exceed target Hgb of 12 g/dL; use lowest doses possible; see PI to convert from Hemoprep.

**ACTIONS:** Erythropoiesis, recombinant human EPO (rHuEPO).

**SIDE Effects:** Headache, hypertension, vertigo, chest pain, abdominal pain, back pain, myalgia, edema, edema, rash, urticaria and angioedema.

---

**DERIVATIONS (DANTRIUM, REVONTO)**

**SIDE Effects:** Diarrhea, constipation, dyspepsia, flatulence.

---

**DEGARELIX (FIRMAGON)**

**USES:** Advanced prostate cancer.

**DOSE:**
- Adults with mHSPC: 3.6 mg SC at baseline and 6 months.

**ACTIONS:** Reversible LHRH antagonists; LH and testosterone (obv) saw use in prostate (obv) and testicular (obv).

**SIDE Effects:** Hot flashes, sexual dysfunction, fatigue, mood swings, abdominal pain.

---

**DENOSUMAB (PROLIA, XGEVA)**

**USES:** Multiple myeloma postmenopausal women; 1 BMD in men on ADT (Prolia); prevent skeletal events in bone metastases (Xgeva).

**DOSE:**
- Prolia: 60 mg SQ giv, in upper arm, thigh, abdominal.
- Xgeva: 120 mg SQ q6mo; in upper arm, thigh, abdominal.

**ACTIONS:** RANK ligand (RANKL) inhibitor (human Fc fusion protein).

**SIDE Effects:** Tenderness, pain at injection site, subcutaneous fat atrophy, arthralgia, myalgia.

---

**DESMPRESSIN (ddAVP, DDAVP NASAL SPRAY, STIMATE)**

**USES:** Amniotic fluid levels in women with severe polyhydramnios.

**DOSE:**
- Adults: 10–40 µg/mL in 1–3 doses.
- Pediatric: 3–12 yrs:
  - 0.50–0.63 µg/mL in 1 or 2 doses.

**ACTIONS:** Nonselective LHRH receptor agonist.

**SIDE Effects:** Nausea, vomiting, diarrhea, abdominal pain, retentive, abnormal vision, dizziness, asthenia.
**DEXAMETHASONE (DECADRON)**

See steroids, Spernic and steroids, Topical: Pages 968, 969.

**DEXAMETHASONE (DECADRON)**

**USES:**

- Minimize paralytic ileus, Treat postoperative ileus.

**ACTIONS:**

- Cholinergic agent.

**DOSE:**

- Relief of pain: 2–3 tabs PO TID. Present postoperative ileus: 250–500 mg IM stat, repeat in 2 hr; then q8h PNI, IM: 500 mg IM stat, repeat in 2 hr; then q8h IM.

**W/P:**

- Cef: Hemophilic, mechanical bowel obstr.

**DISP:**

- 150 mg IM; cream 2% (Parabrodin chew [OTC]).

**SIDE EFFECTS:**

- GI cramps, heartburn, rash, GI ulceration, urinary retention.

**NOTES:**

- Do not crush tabs, watch for GI bleed; check CBC, U/S.

---

**DILTIAZEM (CARDIZEM, CARDIZEM CD, CARDIZEM LA, CARDIZEM SR, CARTIA XT, DILACOR XR, DILTIA XT, TAZTIA XT, TIZAC)**

**USES:**

- Angina, prevention of reinfarction, HTN, AF or A flutter.

**ACTIONS:**

- Calcium channel blocker.

**DOSE:**

- HTN: 2R 120–360 mg PO BID, 1 to 360 mg PO max. 2R or XR: 120–380 mg PO max. 540 mg PO or LA 180–360 mg PO.

**W/P:**

- CEF: + Effect w/ amiodarone, diltiazem, ranolazine, tiotidine, digoxin, H blockers, thiazides.

**CI:**

- All blocks, AM, R patient.

**DISP:**

- Cardizem CD: Caps 120, 180, 240, 300, 360 mg; Cardizem LA: Tabs 120, 180, 240, 360, 420 mg; Cardizem SR: Caps 60, 90, 120 mg; Cardizem: Tabs 10, 60, 90, 120 mg; Cartia XT: Caps 120, 180, 240, 300 mg; Dilacor-XR: Caps 120, 180, 240 mg; Ziac: Tabs 120, 180, 240, 300, 360, 420 mg, 540 mg; Taztia XT: 120, 180, 240, 300, 360 mg.

**SE:**

- Sinus hypoplasia, AV block, ECG abnormalities, peripheral edema, dizziness, headache.

**NOTES:**

- Cardizem CD, Dilacor XR, Tiazac not interchangeable.

---

**DIMETHYL SULFOXIDE (DMSO) (RIMSO-50)**

**USES:**

- Intravenous cystoscopy.

**ACTIONS:**

- Sterilizes.

**DOSE:**

- Intratwuos, 50 ml retain for 15 min; repeat q2hr until relief.

**W/P:**

- CEF: + See cystitis, w/ urinary retention.

**CI:**

- Component sensitivity.

---

**DIPHENHYDRAMINE (BENADRYL, GENERIC) [OTC]**

**USES:**

- Treat & prevent allergic reactions, motion sickness, postoperative nausea, sedation, cough suppression, Thrust of extrapontal reactions.

**ACTIONS:**

- Anticholinergic, antihistamine.

**DOSE:**

- Adults: 25–50 mg PO, IM or IM-TID-QID.

**Ped:**

- 2 yr: 0.5–1 mg/Kg/24 hr PO or IA – QID (max. 300 mg/d, ↓ during infancy w/ minimal-severe renal insufficiency).

**W/P:**

- CEF: Elderly, narrow-angle glaucoma, BPH, or MAOIs.

**CI:**

- Acute asthma.

**DISP:**

- Tabs & caps 25, 50, 100; chew tabs 12.5 mg, oral 6.25 mg PO, 25 mg PO or IM; 12.5 mg PO or IM; 12.5 mg/mL; IM; 50 mg/mL cream, gel, inj 2%.
DIPHENOXYLATE/ATROPINE (LOMOTIL, LONOX, GENERIC) [C-V]

USES: Sensitivity to meds w/ polysorbate 80, component sensitivity.

CI:

W/P: Elderly, w/ renal impairment.

DOSE:

ACTIONS:

USES:

∗

NOTES:

DORIPENEM (DORIBAX)

USES: Complicated intra-abdominal infection and G1 including pelvic.

ACTIONS:

USES:

NOTES:

SE:

DISP:

DOSE:

ACTIONS:

USES:

†

NOTES:

DOXAZOSIN (CARDURA, CARDURA XL, GENERIC)

USES: Hypertension.

ACTIONS: α-1-Adrenergic blocker; relaxes bladder neck smooth muscle.

USES:

∗

NOTES:

DOXORUBICIN (ADRIMYACIN, GENERIC)

USES: Acute leukemias; Hodgkin disease & NHLs; soft tissue, osteo & body carcinomas; Wilms' tumor; neuroblastoma; bladder, breast, ovarian, gastric, thyroid, & lung cancers*; intravesical for bladder cancer.

ACTIONS: Interleukin DNA; DNA topoisomerase I & II.

DOSE:

†

NOTES:

DOXYCYCLINE (ADOXA, ORACEL, VIBRAMYCIN, VIBRA-TABS)

USES: Broad-spectrum antibiotic*; acne vulgaris, uncomplicated UTI, chlamydia, PID, lymphocytic inflammation, anthrax, malaria prophylaxis.

ACTIONS: Tetracycline; bacteriostatic; spectrum: Limited gram (+) and (−), Rickettsia sp, Chlamydia sp, Mycoplasma, B. anthracis.

DOSE:

NOTES:

d-PENICILLAMINE (CUPRIMINE, DEPEN)

WARNING: Physicians planning to use penicillamine should thoroughly familiarize themselves with its toxicity, special dosage considerations, and therapeutic benefits. Penicillamine should never be used casually. Each patient should remain under the close supervision of the physician. Patients should be warned to report promptly any symptoms suggesting toxicity.

ACTIONS: Chelating agent.

DOSE:

NOTES:

d-PENICILLAMINE (CUPRIMINE, DEPEN)

WARNING: Physicians planning to use penicillamine should thoroughly familiarize themselves with its toxicity, special dosage considerations, and therapeutic benefits. Penicillamine should never be used casually. Each patient should remain under the close supervision of the physician. Patients should be warned to report promptly any symptoms suggesting toxicity.

ACTIONS: Chelating agent.

DOSE:

NOTES:

d-PENICILLAMINE (CUPRIMINE, DEPEN)

WARNING: Physicians planning to use penicillamine should thoroughly familiarize themselves with its toxicity, special dosage considerations, and therapeutic benefits. Penicillamine should never be used casually. Each patient should remain under the close supervision of the physician. Patients should be warned to report promptly any symptoms suggesting toxicity.

ACTIONS: Chelating agent.

DOSE:

NOTES:

939
DUOXETINE (CYMBALTA)

SE: Allergic reactions in up to 39%; azoselerosis, aplastic anemia, dizziness, diarrhea, abdominal pain, dermatologic manifestations, nephrotic syndrome.

NOTES: Do not discontinue therapy in; interruptions of a few days can cause hypersecretion with re-emergence of therapy; monitor CBC, CRP (proteins, hematologic, urinary, systemic levels), use PTH/8 if intact or use parathyroid.

DULOXETINE (CYMBALTA)

WARNING: antidepressants may ↑ risk of suicidality; consider risk/benefit of use. Easily monitor for clinical worsening, suicidality, or behavior change, not for peels.

USES: Depression, diabetic peripheral neuropathic pain, generalized anxiety disorder (GAD), fibromyalgia, chronic osteoarthritic & back pain.

ACTIONS: Selective serotonin & norepinephrine reuptake inhibitor (SSNRI).

DOSE: Depression: 60–40 mg PO; 80–60 mg PO; 120 mg/d; Fibromyalgia, Osteoarthritis/back pain: 60 mg/d PO; neuropathy: changes; not for peds.

USES: Treatment of moderate to severe chronic pain.

ACTIONS: Sympathomimetic; stimulates α & β receptors; bronchodilator.

DOSE: Adults: 0.25–1 mg/kg IV; 1.25–10 mg IV/q4h; Peds: 0.05–0.1 mg/kg IV PO q2–4h; ↑ in renal impairment.

ECONAZOLE (ECOZA, SPECTAZOLE, GENERIC)

USES: Tinea, candidiasis, & tinea versicolor infections.

ACTIONS: Antifungal.

DOSE: Topical formulations 0.5–1% BID q4–24h.

EMLA (LIDOCAINE 2.5%, PRilocaine 2.5%, GENERIC)

USES: nummular eczema, dysesthesias.

ACTIONS: Topical anesthetic.

DOSE: Apply to areas BID q12h.

ENZALUTAMIDE (XTANDI)

USES: Metastatic castration-resistant prostate cancer w/ or w/o previous docetaxel.

ACTIONS: Androgen receptor inhibitor.

DOSE: Oral (only) 160 mg daily, do not chew/nail caps.

EPIPHEN (EPHEDRINE, GENERIC)

USES: Acute bronchospasm, bronchial asthma, nasal congestion, ↑ BP, nasal spray, ephedrine, & isoprenaline gels.

ACTIONS: Symptomomimetic; stimulates β1 receptors; bronchodilators.

DOSE: Adults: 12.5–25 mg PO q4h PRN expectorant; 1–2 mg/kg IV q1–2h; 30–60 mg IM q2–4h; 0.5–1 mg/kg SQ q6–12h; 100–200 mg SC q4–6h.

ENOXAPARIN (LOVENOX)

USES: Recent or anticipated epidural/spinal anesthesia, ↑ risk of spinal epidural hematoma w/ subsequent paralysis.

ACTIONS: LMW heparins; inhibit thrombin by complexes w/ antithrombin III.

DOSE: Adults: Prevention & Treat of DVT; Treat PE: unstable angina & non-Q SBMI.

WARNING: Recent or anticipated epidural/spinal anesthesia, ↑ risk of spinal epidural hematoma w/ subsequent paralysis.

USES: Prevention & Treat of DVT; Treat PE: unstable angina & non-Q SBMI.

ACTIONS: LMW heparins; inhibit thrombin by complexes w/ antithrombin III.

DOSE: Adults: Prevention: 30 mg SQ 12 or 40 mg SQ BID; DVT/PE Treat: 1 mg/kg SQ 2H or 1.5 mg/kg SQ 4H; SCI: 30 mL/m² 1 to 1.5 mg/kg SQ 4H.

Ped: Prevention: 0.5 mg/kg SQ 2H; DVT/PE Treat: 1 mg/kg SQ 2H; 2 dose w/ SCI: 30 mL/m².

W/P: [C, ?] not for prophylaxis in prosthetic heart valves.

CI: Active bleeding, heparin induced thrombocytopenia-Ah, heparin, clot, skin, mass.

DISP: IV 10 mg/1 mL; SQ 0.5 mg/kg SQ 12H; 120, 150 mg SQ; 300 mg/mL multi-dose vial.

SE: Bleeding, hemarthrosis, bruising, thrombocytopenia, local, pain/hematoma at site, ↑ A/G.

NOTES: ↑ risk on bleeding time, function, PT, or aPTT; monitor SIH for heparin-induced thrombocytopenia, clinical bleeding, may monitor antifactor Xa kit for PT.
EPOETIN ALFA (Erythropoietin, Epo) (EPOGEN, PROCRIT)

**WARNING:** Inj. Morbidity, serious CV thromboembolic events, and tumor progression. Renal failure pts experienced greater risks (death/CV events) on erythropoiesis-stimulating agents (ESA) to target Hgb 11 g/dL, Maintain Hgb 10–12 g/dL. In cancer pts, ESA survival advantage progression in some cancer when dosed Hgb > 2 g/dL. Use lowest dose needed. Use only for myelosuppressive some cancer when dosed Hgb


ESAs dose needed. Use only for myelosuppressive some cancer when dosed Hgb


In cancer pt, ESAs target Hgb levels 11 g/dL. Maintain Hgb 10–12 g/dL.


thrombocytosis, ↑ Can give IM


SE:


CI:


W/P:


Peds:


Adults:


DOSE:


α


NOTES:


Refrigerate; monitor baseline & posttreatment Hct/Hgb, BP, ferritin.


DISP:


Inj 2,000, 3,000, 4,000, 10,000, 20,000, 40,000 U/mL.


ILOTYCIN, GENERIC (ERTAPENEM (INVANZ)


ESTRADIOL, ORAL (DELESTROGEN, ESTRACE, FEMTRACE, GENERIC)


DOSE:


Adults: Base 250–500 mg PO q12–16 hr or erythropoietin 400–800 mg q12–14 hr, 100 mg–1 g IV q6h. Prophylactic: 250 mg PO TID 20 min ac.


PO: 30–50 mg/kg PO = q4–6h or 20–40 mg/kg IV q6h, max = 2 g/kg.


W/P: [X, ↓, ↓] May ↑ thyroid binding globulin (TBG) or thyroxine disease. ↓


CI:


W/P: [X, ↓]↑


SE:


DVT. Consider DVT prophylaxis.


CI:


↑ Mortality, serious CV thromboembolic events, and tumor progression. Renal failure pts experienced greater risks (death/CV events) on erythropoiesis-stimulating agents (ESAs) to target Hgb 11 g/dL, Maintain Hgb 10–12 g/dL. In cancer pts, ESA survival advantage progression in some cancer when dosed Hgb > 2 g/dL. Use lowest dose needed. Use only for myelosuppressive some cancer when dosed Hgb


In cancer pt, ESAs target Hgb levels 11 g/dL. Maintain Hgb 10–12 g/dL.


thrombocytosis, ↑ Can give IM


SE:


CI:


W/P:


Peds:


Adults:


DOSE:


α


NOTES:


Refrigerate; monitor baseline & posttreatment Hct/Hgb, BP, ferritin.


DISP:


Inj 2,000, 3,000, 4,000, 10,000, 20,000, 40,000 U/mL.


ILOTYCIN, GENERIC (ERTAPENEM (INVANZ)


ESTRADIOL, ORAL (DELESTROGEN, ESTRACE, FEMTRACE, GENERIC)


DOSE:


Adults: Base 250–500 mg PO q12–16 hr or erythropoietin 400–800 mg q12–14 hr, 100 mg–1 g IV q6h. Prophylactic: 250 mg PO TID 20 min ac.


PO: 30–50 mg/kg PO = q4–6h or 20–40 mg/kg IV q6h, max = 2 g/kg.


W/P: [X, ↓, ↓] May ↑ thyroid binding globulin (TBG) or thyroxine disease. ↓


CI:


W/P: [X, ↓]↑


SE:


DVT. Consider DVT prophylaxis.


CI:


↑ Mortality, serious CV thromboembolic events, and tumor progression. Renal failure pts experienced greater risks (death/CV events) on erythropoiesis-stimulating agents (ESAs) to target Hgb 11 g/dL, Maintain Hgb 10–12 g/dL. In cancer pts, ESA survival advantage progression in some cancer when dosed Hgb > 2 g/dL. Use lowest dose needed. Use only for myelosuppressive some cancer when dosed Hgb


In cancer pt, ESAs target Hgb levels 11 g/dL. Maintain Hgb 10–12 g/dL.


thrombocytosis, ↑ Can give IM


SE:


CI:


W/P:


Peds:


Adults:


DOSE:


α


NOTES:


Refrigerate; monitor baseline & posttreatment Hct/Hgb, BP, ferritin.


DISP:


Inj 2,000, 3,000, 4,000, 10,000, 20,000, 40,000 U/mL.


ILOTYCIN, GENERIC (ERTAPENEM (INVANZ)


ESTRADIOL, ORAL (DELESTROGEN, ESTRACE, FEMTRACE, GENERIC)


DOSE:


Adults: Base 250–500 mg PO q12–16 hr or erythropoietin 400–800 mg q12–14 hr, 100 mg–1 g IV q6h. Prophylactic: 250 mg PO TID 20 min ac.


PO: 30–50 mg/kg PO = q4–6h or 20–40 mg/kg IV q6h, max = 2 g/kg.


W/P: [X, ↓, ↓] May ↑ thyroid binding globulin (TBG) or thyroxine disease. ↓


CI:


W/P: [X, ↓]↑


SE:


DVT. Consider DVT prophylaxis.


CI:


↑ Mortality, serious CV thromboembolic events, and tumor progression. Renal failure pts experienced greater risks (death/CV events) on erythropoiesis-stimulating agents (ESAs) to target Hgb 11 g/dL, Maintain Hgb 10–12 g/dL. In cancer pts, ESA survival advantage progression in some cancer when dosed Hgb > 2 g/dL. Use lowest dose needed. Use only for myelosuppressive some cancer when dosed Hgb


In cancer pt, ESAs target Hgb levels 11 g/dL. Maintain Hgb 10–12 g/dL.


thrombocytosis, ↑ Can give IM


SE:


CI:


W/P:


Peds:


Adults:


DOSE:


α


NOTES:


Refrigerate; monitor baseline & posttreatment Hct/Hgb, BP, ferritin.


DISP:


Inj 2,000, 3,000, 4,000, 10,000, 20,000, 40,000 U/mL.


ILOTYCIN, GENERIC (ERTAPENEM (INVANZ)


ESTRADIOL, ORAL (DELESTROGEN, ESTRACE, FEMTRACE, GENERIC)


DOSE:


Adults: Base 250–500 mg PO q12–16 hr or erythropoietin 400–800 mg q12–14 hr, 100 mg–1 g IV q6h. Prophylactic: 250 mg PO TID 20 min ac.


PO: 30–50 mg/kg PO = q4–6h or 20–40 mg/kg IV q6h, max = 2 g/kg.


W/P: [X, ↓, ↓] May ↑ thyroid binding globulin (TBG) or thyroxine disease. ↓


CI:


W/P: [X, ↓]↑


SE:


DVT. Consider DVT prophylaxis.


CI:


↑ Mortality, serious CV thromboembolic events, and tumor progression. Renal failure pts experienced greater risks (death/CV events) on erythropoiesis-stimulating agents (ESAs) to target Hgb 11 g/dL, Maintain Hgb 10–12 g/dL. In cancer pts, ESA survival advantage progression in some cancer when dosed Hgb > 2 g/dL. Use lowest dose needed. Use only for myelosuppressive some cancer when dosed Hgb


In cancer pt, ESAs target Hgb levels 11 g/dL. Maintain Hgb 10–12 g/dL.


thrombocytosis, ↑ Can give IM
ESTRADIOL, SPRAY (EVAMIST)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Vasomotor sx in menopause.

ACTIONS: Estrogen supl.

DOSE: Spray on inner surface of forearm. 
W/P: [X, ↓–↓] May ↑ PT/PTT aggregation w/ thyroid disease.

CI: Unspecified genitai bleeding, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis, recent MI, pregnancy, severe hepatic disease.

DISP: 1.9 mg spray [16–spray container].

NOTES: Contains alcohol; caution around flames until dry; not for Vag use.

ESTRADIOL, TRANSDERMAL (ALORA, CLIMARA, ESTRADERM, VIVELLE DOT)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Severe menopausal vasomotor sx; female hypogonadism.

ACTIONS: Estrogen supl.

DOSE: Start 0.0375 mg/24 h patch ↑ to 0.05–0.075 mg/24 h w/ intact uterus cycle 3 wk ↑ 0.1 mg/24 h/wk. 
W/P: [X, ↓–↓] May ↑ PT/PTT aggregation w/ thyroid disease; toxic shock reported.

CI: Unspecified genitai bleeding, breast cancer; estrogen-dependent tumors; thromboembolic disorders; thrombophlebitis, recent MI, pregnancy, severe hepatic disease.

DISP: 1 patch 1–2 wk.

NOTES: Contains alcohol; caution around flames until dry; not for Vag use.

ESTRADIOL, VAGINAL (ESTRING, FEMRING, VAGIFEM)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Postmenopausal Vag atrophy (EstrinG™), vulvar and vaginal atrophy associated w/ menopause (Ferring™), atrophic vaginitis (Vagifem™).

ACTIONS: Estrogen supl.

DOSE: Estring: Insert ring into upper 3rd of Vag vault; remove and replace after 90 d; reassess 3–6 mo. 
W/P: [X, ↓–↓] May ↑ PT/PTT aggregation w/ thyroid disease; toxic shock reported.

CI: Unspecified genitai bleeding, breast cancer; estrogen-dependent tumors; thromboembolic disorders; thrombophlebitis, recent MI, pregnancy, severe hepatic disease.

DISP: Estring ring: 0.0075 mg/24 h, Ferring ring: 0.05 and 0.1 mg/24 h [Ferring 10 μg].

SE: Headache, leukorhea, back pain, candidiasis, vaginitis, Vag discomfort/hemorrhage, arthralgia, insomnia, abdominal pain; see estradiol, oral notes.

ESTRADIOL/LEVONORGESTREL, TRANSDERMAL (CLIMARA PRO)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Menopausal vasomotor sx; prevent postmenopausal osteoporosis.

ACTIONS: Estrogen & progestrone.

DOSE: 1 patch ↑ to 4 wk.
W/P: [X, ↓–↓] thyroid.

CI: AUB, estrogen-sensitive tumors, he thromboembolism, liver impairment, pregnancy, hypertension.

DISP: Estraderm 0.045 mg/levonorgestrel 0.015 mg/day patch.

SE: Site reaction, Vag bleeding, spotting, breast changes, abnormal bleeding/spotting, headache, retention fluid, edema, ↑ BT.

NOTES: Apply to lower abdomen; for osteoporosis give CA2+↑ BT↓ sup; follow breast exams.

ESTRADIOL/NORETHINDRONE (ACTIVELLA, FEMHRT, GENERIC)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Menopausal vasomotor sx; prevent postmenopausal osteoporosis.

ACTIONS: Estrogen/progestrone; plant derived.

DOSE: 1 tab start w/ lowest dose combo.
W/P: [X, ↓–↓] ↑ BT↑ PTH↑. 
CI: Pregnancy; he breast cancer; estrogen-dependent tumor; abnormal genitai bleeding; he DVT, he OR related disorder; recent (≤ 15 yr) arterial thromboembolic disease (CVs, MI).

DISP: Femhrt: Tab. 2.5/0.1, 2.5/0.3 mg ↓ BT↓ PTH↑. 
ACTIVELLA: Tabs: 10/0.5, 0.5 mg/0.1 mg.

SE: Thrombosis, dizziness, headache, blood changes, insomnia, emotional instability, breast pain.

NOTES: Use in women w/ intact uterus; caution in heavy smokers; combo also used as oral contraceptive.

ESTRAMUSTINE PHOSPHATE (EMCYT)

USES: Palliative treatment of metastatic and/or advanced carcinoma of the prostate.

ACTIONS: Estradiol w/ nitrogen mustard; exact mechanism unknown.

DOSE: 0.4 mg/kg/d in 3–4 doses; on empty stomach, no dairy products.
W/P: [X, ↓–↓] not used in females.
CI: Active thromboembolism or thromboembolic disorders.

DISP: Caps 140 mg.
SE: ↑ N/V; exacerbation of pre-existing CHF, edema, hepatic disturbances, thrombophlebitis, MI, PE, gynecomastia in 20–100%.

NOTES: Low-dose breast irradiation before may ↓ gynecomastia.

ESTROGEN, CONJUGATED (PREMARIN)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Mid–severe menopausal vasomotor sx; atrophic vaginitis; hypogonadism; palliation of advanced breast and prostate cancer; prevention osteoporosis.

ACTIONS: Estrogen replacement.

DOSE: 0.3–1.25 mg PO; Intramuscular cream 0.5–2 g x 21 days, then off x 7 days or 0.5 mg twice weekly.
W/P: [X, ↓–↓] thyroid.

CI: Severe hepatic impairment, genitai bleeding of unknown cause, breast cancer; estrogen-dependent tumors, thromboembolic disorders, thrombosis, thrombophlebitis, recent MI.

DISP: Caps 0.3, 0.45, 0.625, 0.9, 1.25 mg; Vag cream 0.625 mg/d.
SE: ↑ Risk of endometrial cancer, galbladder disease, thromboembolism, headache, & possibly breast cancer.

NOTES: Generic products not equivalent.

ESTROGEN, CONJUGATED/ MEDROXYPGROGESTERONE (PREMPRO, PREMPHASE)

WARNING: Risk endometrial cancer. Do not use to prevent CV disease or dementia. ↑ risk MI, stroke, breast cancer (PL), and DVT in postmenopausal (50–79 yr). ↑ Dementia risk in postmenopausal (≥ 65 yr).

USES: Mid–severe menopausal vasomotor sx; atrophic vaginitis; prevent postmenopausal osteoporosis.

ACTIONS: Hormonal replacement.
FENTANYL, INJECTION (SUBLIMAZE, GENERIC) [C-II]

DOSE: Prempro 1 tab PO daily, Premphase 1 tab PO daily.
W/P: [K, L].
CI: Severe hepatic impairment, genital bleeding of unknown cause; breast cancer, estrogen-dependent tumors; thromboembolic disorders, thrombosis, thrombophlebitis.

DOSE: [As estrogen/progestogen replacement] Prempro: Tabs 0.315, 0.451/3, 0.625/2.5, 0.625/5 mg; Premphase: Tabs 0.625/10 (days 1–14) & 0.625/5 mg (days 15–28).
SE: Gallbladder disease, thrombembolism, headache, breast tenderness.
NOTES: See WHI (www.whi.org); use lowest dose/timeframe possible.

ESTROGEN, CONJUGATED SYNTHETIC (CENESTIN, ENUUVIA)

WARNING: 1 Risk endometrial cancer: Do not use to prevent CV disease or dementia; ↑ risk MI, stroke, breast cancer, PE, and DVT in postmenopausal (50–79 yr). 2 Dementia risk in postmenopausal (≥70 yr).

USES: Vaginosis, perineal swelling, vulvovaginal atrophy.

ACTIONS: Multiple estrogen replacement.

DOSE: For all w/ intact uterus: Prempro = 10–14 days/28-day cycle; Premphase: Tabs 0.625–1.25 mg (Enjuvia vasomotor: 10–14 days/28-day cycle; 50–79 yr). 2 Dementia risk in postmenopause (≥50 yr).

DOSE: [C, ?/L].

SE: Headache, hyperuricemia, acute gout, abdominal pain, ↑ BP; risk MI, stroke, dementia.

DOSE: 0.3 mg/d.

ETOPOSIDE [VP-16] (ETOPOPHOS, GENERIC)

WARNING: Should be administered under the supervision of a qualified physician experienced in the use of chemotherapy. Severe myelosuppression with resulting infection or bleeding may occur.

USES: Small cell lung cancer; testicular cancer; Hodgkin disease; NHLs, peds ALL, & BMT in high dose.

ACTIONS: Topoisomerase II inhibitor.

DOSE: 50–150 mg/m² IV 3–5 days; 50 mg/m² PO for 21 days (PO availability = 50% of IV; ≥ 46 gm² or 25–20 mg/kg in IM (per protocol); ↑ in renal/hepatic impairment.
W/P: [K, L].
CI: ↑ blood pressure.

EVEROLIMUS (AFINITOR, AFINITOR DISPERZ)

USES: 1 Afinitor: Hormone receptor positive, HER2-negative breast cancer w/ or without an endocrine therapy; unresectable progressive neuroendocrine tumors of pulmonary origin (PNET); advanced renal cell carcinoma (RCC) after failure of targeted therapy; adult patients w/ angiosarcoma, or lobular breast cancer, and tuberous sclerosis complex (TSC), not requiring immediate surgery, Afinitor and Afinitor Disperz: Pediatric and adult w/ tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be resected.

ACTIONS: mTOR inhibitor.

DOSE: 10 mg PO daily, ↓ to 5 mg w/ or without a decrease in risk of death (see also everolimus)
W/P: [K, L].

SE: Hypertension, creatinine, ↑ serum cholesterol, ↑ triglycerides, ↑ diabetes, ↑ lab tests; ↑ AMI, stroke, MI.

EVEROLIMUS (ZORTRESS)

USES: Prevent renal and liver transplant rejection; combo w/ basiliximab w/ ↓ incidence of transfusions due to chronic rejection.

ACTIONS: mTOR inhibitor (mammalian target of rapamycin).
**FENTANYL, TRANSDERMAL (DURAGESIC, GENERIC) [C-II]**

**WARNING:** Potential for abuse and fatal OD; resp depression possible; use w/ CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) to prevent initial titration. Initiation of CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal OD; avoid use in application site, can cause OD.

**USES:** Persistent mod-severe chronic pain in pts already tolerant to opioids.

**DOSE:** Apply patch to upper torso ≥24h; dose based on narcotic requirements in previous 24 h; start 25 μg patch of 20; ↓ in renal impairment.

**W/P:** [B, ↑] w/ CYP3A4 inhibitor or CV CYP3A4 inducer may ↑ fentanyl effect, w/ Hx substance abuse.

**Cl:** Not topical tolerant, short term pain management, postoperative pain in outpatient surgery, mild pain, PONV use, ↑ 1CYP; resp depression, severe renal/hepatic impairment, pediatrics; ↓ 2–3 yrs.

**DISP:** Patches 12.5, 25, 50, 75, 100 μg/h.

**SE:** Head press (can be fatal), sedation, ↓ BP, ↓ HR, constipation, N/V.

**NOTES:** 0.1 mg fentanyl = 10 mg IM morphine. Do not cut patch; peak level in PREGNANCY 24–72 h.

---

**FERRIC CARBOXYMALTOSE (INJECTAFER)**

**USES:** Use of deficiency anaemia.*

**ACTIONS:** Fe Supl.

**DOSE:**
- **Adults:** 500–1000 mg elemental Fe or 7.5 mg/kg over 30 min after inf.
- **Children:** 2.25 mg/kg over 15–30 min after inf.

**Cl:** Component hypersensitivity; Fe absorption w/ vit C; Fe absorption w/ tetracycline, fluoroquinolones, antacids, H2 blockers, proton pump inhibitors.

**SE:** Head press, flushing, hypophosphatemia, dizziness, HTN.

---

**FERRIC GLUCONATE (FERGON, OTHERS)**

**WARNING:** Accidental OD of iron-containing products is a leading cause of fatal poisoning in children ≤6 yr. Keep out of reach of children.

**USES:** Use of deficiency anaemia & Fe suppl.*

**CI:** Hemochromatosis, hemolytic anemia.

**DISP:** IV 30 mg/mL. (510 mg elemental Fe/kg/d) max. 2 doses daily–TID; on empty stomach.

**SE:** Head press, flushing, hypophosphatemia, dizziness, HTN.

---

**FERROUS SULFATE (OTC)**

**USES:** Use of deficiency anaemia & Fe suppl.*

**ACTIONS:** Dietary suppl.

**DOSE:**
- **Adults:** 510 mg IV × 1, then 510 mg IV × 1 3–8 days later; give 1 ML/s.
- **Children:** 2.25 mg/kg over 15–30 min after inf.

**Cl:** Monitor for hypersens & Fe BP for 30 min after dose, may alter MRI studies.

**SE:** Head press, flushing, hypophosphatemia, dizziness, HTN.

---

**FESOTERODINE (TOVIAZ)**

**USES:** Overactive bladder w/ urge urinary incontinence, urgency, frequency.*

**ACTIONS:** Competitive muscarinic receptor antagonist; w/ bladder muscle contractions.

**DOSE:** 4 mg PO qd, ↑ to 8 mg PO daily PRN.

**Cl:** [C, ↑] Avoid in prnl w/ severe renal insufficiency or w/ CV CYP3A4 inducer (eg, ketoconazole, clarithromycin); w/ bladder outlet obstruction, ↓ GI motility/constriction, narrow-angle glaucoma, myasthenia gravis.

**Cl:** Urinary retention, or uncontrolled narrow-angle glaucoma, hypersens to class.

**DISP:** Tabs 4, 8 mg.

**SE:** Dry mouth, constipation, ↓ sweating may cause heat prostration.

---

**FIDACOMICIN (DIFIDIC)**

**USES:** Gram-positive infection-associated diarrhea.*

**ACTIONS:** Marizole antibiotic.

**DOSE:** 200 mg PO BID × 10 days.

**W/P:** [B, ↓] Not for systemic infection or <14 yr; to ↑ resistance, use only when diagnosis suspected/ proven.
FINASTERIDE (PROSCAR, GENERIC, PROPECIA)

USES: 
- HHM & androgenetic alopecia.

ACTIONS: 
- 5α-reductase.

DOSE: 
- PB: 5 mg PO. 
- Allopase: 1 mg PO; food increases absorption.

W/P: 
- [X, ] — Hepatic impairment.

Cl: 
- Pregnant women should avoid handling pills, lest estrogen-to-mask feil.

DISP: 
- Tabs 1 mg (Propecia), 5 mg (Proscar).

Cl: 
- libido, wt ejaculate, erectile dysfunction, gynecomastia; may slightly ↑ risk of high-grade prostate cancer.

NOTES: 
- Both 5 PSA by ~50%; receiveable PSA baseline 6 mo (double PSA to "true" reading).
- 3–6 mo for effect on urinary flow; continue to maintain new flow; clot for use in women.

FLAVOXATE (GENERIC)

USES: 
- Relief of sx of biliary, urinary, rectal, postoperative pain, urinary frequency, incontinence.

ACTIONS: 
- Antispasmodic.

USES: 
- Relief of Sx of dysuria, urgency, nocturia, suprapubic pain, urinary frequency, incontinence.

DOSE: 
- Adult: 50–100 mg PO 1–2 mo.

W/P: 
- [B, ] — Irritant chemotherapy, W/P: [X, ]

CI: 
- [D, ?] Irritant chemotherapy, W/P: [X, ]

DISP: 
- Cream 0.5, 1, 5%; soln 1%, 2%, 5%.

CI: 
- Indications: pregnancy, serious infection, biliary, thrombocytopenia, major surgery w/in past mo, G6PD, infections, MAOI.

NOTES: 
- Spontaneous abortions in peds.

FLUCONAZOLE (DIFLUCAN, GENERIC)

USES: 
- Candidiasis (oral, cutaneous), actinomycosis, oral thrush, tinea, tinea versicolor.

ACTIONS: 
- Antifungal; 1, cytochrome P-450 steroid metabolism.

USES: 
- Basal cell carcinoma (when standard therapy impractical), actinomycosis keratitis; carcinoma in situ (CIS) of the penis.

ACTIONS: 
- Inhibits thymidylate synthetase (7, DNA synthesis).

NOTES: 
- Healing may not be evident for 1–2 mo; wash hands thoroughly, avoid occlusive dressings; do not overuse; typical penile regimen describes: apply 12 hr every 48 hr for 28 days.

FLUCORTOLONE ACETATE (GENERIC)

USES: 
- Adrenocortical insufficiency, Addison disease, self-feeding adrenocortical syndrome.*

ACTIONS: 
- Mineralocorticoid.

DOSE: 
- Adult: 0.1–0.2 mg PO.

W/P: 
- [C, ] — ↑ risk of high-grade prostate cancer.

Fluocortolone: 
- 0.05–0.1 mg/d PO.

Flucortolone: 
- 0.1–0.2 mg/d PO.

Cl: 
- Systemic fungal infections; known hypersensitivity.

DISP: 
- Tabs 0.1 mg.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 0.1 mg.

SE: 
- HTN, edema, CCF, headache, dizziness, convulsions, acne, rash, bruising, hyperglycemia.

DISP: 
- Cream 0.5, 1, 5%; soln 1%, 2%, 5%.

Cl: 
- Men with carcinomas of the breast or with overt carcinoma in situ, male hypogonadism, prostatectomy, delayed puberty in males; postmenopausal metastatic breast cancer.

USES: 
- Synthetic androgen; 
- 5α-reductase inhibitor.

ACTIONS: 
- Inhibits thymidylate synthetase (7, DNA synthesis).

NOTES: 
- Closely monitor for worsening depression or emergence of suicidality, particularly in ped.

FLUXOXYMESTERONE (GENERIC) (C-I, III)

USES: 
- Hypogonadism (primary, hypogonadotropic), delayed puberty in males, postmenopausal metastatic breast cancer.*

ACTIONS: 
- Synthetic androgen; ↓ secretion of LH & FSH (feedback inhibition).

DOSE: 
- Breast cancer: 10–40 mg/d × 1–3 mo. 
- Hypogonadism: 2–30 mg/d.

W/P: 
- [X, ] — ↑ risk of high-grade prostate cancer.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 10 mg.

W/P: 
- [C, ] — ↑ risk of high-grade prostate cancer.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Cl: 
- Men with carcinomas of the breast or with known/unexpected prostate cancer; women who are/are becoming pregnant.

DISP: 
- Tablets 100, 150, 200 mg: susp 10, 20 mL; 250 mg PO TID (750 mg total).

Cl: 
- Common: 0.5, 1, 5%; rarer: 1%, 2%, 5%.

Cl: 
- Abrupt discontinuation.

SIDE EFFECTS: 
- N/V, abdominal pain, GI bleed, anemia, reticulocytosis.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 0.1 mg.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 0.1 mg.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 0.1 mg.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 10 mg.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.

Flucortolone: 
- Flucortolone: 
- Flucortolone: 
- Tabs 20 mg/d.
FONDAPARINUX (ARIXTRA)  

**USES:** Thromboprophylaxis in hip replacement, abdominal surgery; w/ DVT or PE in cardiothoracic surgery.

**DOSE:** Po: 5 mg SQ daily; in renal impairment.

**ACTIONS:** Protein cross-linking.

**CI:** Severe hepatic impairment.

**DISP:** Caps 125 mg.

FOSFOMYCIN (MONUROL, GENERIC)  

**USES:** Uncomplicated UTI in women.

**DOSE:** 1 mg/kg PO q6–12h or 2 mg/kg PO q24h (max. 6 mg/kg/dose).

**ACTIONS:** ACE inhibitor.

**CI:** Hypotension, peritonitis, ileus.

**DISP:** Caps 250, 500 mg; soln 250 mg/5 mL; TID, 50 mg/kg/d max.

FOSYNA (GENERIC)  

**USES:** Intraocular implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg.

GANCICLOVIR (CYTOVENE, VITRASERT, GENERIC)  

**USES:** Herpes, CMV, adenovirus.

**DOSE:** 5 mg/kg IV q8h; 2 mg/kg dose PO q3–24h (max. 6 mg/kg/dose), ↓ dose in renal impairment.

**ACTIONS:** Antiviral.

**CI:** Hypocalcemia, ↑ K+.

**DISP:** Tablets 20, 40, 80 mg; soln 10 mg/mL.

GEMICITABINE (GENMAR, GENERIC)  

**USES:** Plasmocytic cancer (single agent), breast cancer w/ paclitaxel, WSCD w/ cisplatin, ovarian cancer w/ carboplatin, gastric cancer, urothelial carcinoma (systemic and intravesical).

**DOSE:** 1,000–2,500 mg/m² over 30–60 min–1/hr IV infusion × 3–4 wk or 4–6 wk, ↓ dose based on hematologic function (per protocol).

**ACTIONS:** Antineoplastic, nucleoside metabolic inhibitor, ↓ ribonucleotide reductase, produces false nucleoside base-inhibiting RNA synth.

**CI:** ↓ renal/cisplatin, gastric cancer, hepatic impairment.

**DISP:** Tablets 3–12 yr: 0–15 mg/kg/d × 10; over 3 days, 3–4 yr: 15 mg/kg/d × 3; ≥ 5 yr: 25–35 mg/kg/d × 10; 50 mg/kg/d max, ↓ in renal impairment.

GEPACTIN (NERVENTIN, GENERIC)  

**USES:** Postoperative neuroaplasia (PNAH) adjacent in partial seizure; chronic pain synds.

**DOSE:** Anticonvulsant; GABA analog.

**ACTIONS:** Sodium channel blocker; ↓ seizure frequency.

**DISP:** Tablets & Peds: > 12 yr: Anticonvulsant: 300 mg PO TID; ≥ max. 600 mg, Peds: 300 mg/day, 300 mg BID day 1, 330 mg BID day 2, 300 mg TID day 3, intrave 1,800–3,600 mg/d.

GEMSA (OSO/OSYO)  

**ACTIONS:** Cough, dizziness, angioedema, rash.

**CI:** Hereditary/idiopathic angioedema or angioedema w/ C1 esterase deficiency.

**DISP:** Tablets 10, 20, 40 mg.

GENERIC)  

**USES:** Hypertension, diabetic nephropathy.

**DOSE:** 10 mg PO initial, max. 40 mg PO/d; ↓ in elderly, ↓ in renal impairment.

**ACTIONS:** Bladder fibrosis, skin irritation with contact, reflux resulting in azotemia, vesical fibrosis or obstruction or papillary necrosis; extravesical causation perineal fistulas.

**CI:** Severe hepatic impairment.

**DISP:** Caps 100, 300, 400 mg; soln 250 mg/5 mL; scored tabs 600, 800 mg.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic; ↓ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**CI:** Renal dysfunction.

**DISP:** Tablets 20, 40, 80 mg.

GENERIC)  

**USES:** CMV retinitis in patients w/ AIDS.

**DOSE:** Following induction, 1,000 mg PO TID.

**ACTIONS:** ↑ BP , hyperglycemia,↑ K+.

**CI:** Components sensitive.

**DISP:** Caps 250, 500 mg; oral tablet 4.5 mg.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Intravesical treatment.

**DOSE:** 5 mg/kg IV q8h; 2 mg/kg dose PO q3–24h (max. 6 mg/kg/dose).

**ACTIONS:** Antiviral.

**CI:** Hypocalcemia, ↑ K+.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic; ↓ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.

GENERIC)  

**USES:** Prevention: intravitreal implant.

**DOSE:** 4.5 mg.

**ACTIONS:** Loop diuretic.

**CI:** Hypovolemia, diuretics; ↑ Na & Cl reabsorption in ascending loop of Henle & distal tubule.

**DISP:** Tablets 20, 40, 80 mg; solns 10 mg/mL.
q3mo; usually upper abdominal wall.

NOTES:

SE:

SQ implant 3.6 (1 mo), 10.8 mg (3 mo).

DISP:

[\(X, W/P:\)]

LHRH agonist, transient

Nephro/oto/neurotox.

SE:

DISP:

Premixed Inf 40, 60, 70, 80, 90, 100, 120 mg;

CI:

Infants

Adults:

↓

↓

Adults:

↓

↓

Infants

kg/dose q12–18h.

kg/dose q18–24h.

↓

\(\ast\) palliative treatment of advanced carcinoma of the

locally confined carcinoma of the prostate and

endometriosis, breast cancer.

Testosterone.

Adults:

Testosterone.

Infants

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:

↓

↓

Adults:
HYDROCHLOROTHIAZIDE/AMILORIDE (MODURETIC, GENERIC)

W/P: (D, +) Idiosyncratic reaction, resulting in acute transient myelopen and acute angioedema plasma; latent ID may become manifest.
CI: Asthma, sulfonamide allergy, renal insufficiency.
DISP: Tabs 25, 50, mg; caps 1.25 mg PO q4–6h Mg/mL.
SE: ↓ K+; ↓ hypercalcinemia, hyperuricinemia, ↓ Na+; sun sensitivity.
NOTES: Follow K+, may need supplementation.

HYDROCHLOROTHIAZIDE/AMILORIDE (MODURETIC, GENERIC)

USES: *HTN.

ACTIONS: Combined thiazide & K+- sparing diuretic.
DOSE: 1–2 tabs PO. W/P: (D, +). CI: Renal failure, sulfonamide allergy.
DISP: Tabs (amiloride/HCTZ) 5 mg/50 mg. SE: ↓ BP, photosensitivity, ↓ K+; ↓ Na+; ↓ hypercalcinemia, hyperlipidemia, hyperuricemia.

HYDROCHLOROTHIAZIDE/SPIRONOLACTONE (ALDACTAZIDE, GENERIC)

USES: *HTN.

ACTIONS: Thiazide & K+-sparing diuretic.
DOSE: 25–200 mg each component q4–6h. W/P: (D, +) CI: Sulfonamide allergy.

HYDROCHLOROTHIAZIDE/TRIAMTERENE (DYAZIDE, MAXZIDE, GENERIC)

USES: *HTN.

ACTIONS: Combo thiazide & K+-sparing diuretic.
DOSE: Dyazide 1–2 caps PO daily–BID. Maxzide: 1 tab PO. W/P: (D, +). CI: Sulfonamide allergy.
DISP: Tabs (HCTZ/triamterene) 37.5/25, 75/50 mg. SE: Photosensitivity, ↓ BP, ↑ ↓ ↓ ↓ Na+, hypercalcinemia, hyperlipidemia, hyperuricemia.
NOTES: HCTZ component in Maxzide more bioavailable than in Dyazide.

HYDROCODONE (ZONEHYDRO ER)

WARNING: Addiction, abuse, misuse, overdose and death risk. Fatal respiratory depression: overdose especially in children can be fatal. With pregnancy maternal opioid withdrawal syndrome possible. Do not consume alcohol.
USES: *Pain severe enough to require daily, around-the-clock, long-term opioid.

HYDROCODONE/ACETAMINOPHEN (HYCET, LORCET, GENERIC) [C-III]

WARNING: Acetaminophen has been associated with acute liver failure (liver transplant and death possible). Most cases associated with doses ≥4,000 mg/d and often involve more than 1 acetaminophen-containing product.
USES: *Mod–severe pain.
ACTIONS: Narcotic analgesic w/ nonnarcotic analgesic.
DOSE: Adults: 1–2 caps or tabs PO q4–6h PRN. W/P: (C, M). SE: CNS depression, severe resp depression. Disp: Many formulations; specify hydrocodone/acetaminophen dose; caps 5/50 mg, tabs 2, 5/50, 5/100, 5/200, 7.5/100, 7.5/250, 7.5/500, 7.5/1000, 10/250, 10/325, 10/500, 10/650, 10/900, 10/1500, 10/1700 mg. SE: GI upset, sedation, fatigue. NOTES: Do not exceed 4–5 acetaminophen; see Acetaminophen note.

HYDROCODONE/IBUPROFEN (REPREXAN, VICOPROFEN, GENERIC) [C-III]

USES: *Mod–severe pain (≤10 days).
ACTIONS: Narcotic, w/ NSAID.
DOSE: 1–2 tabs q4–6h PRN. W/P: (C, M) renal insufficiency, ↓ effect w/ ACE inhibitors & diuretics; ↑ effect w/ CNS depressants, EDDH, MAOI, ASA, tricyclic antidepressants, anticoagulants. CI: Component sensitivity.
DISP: Tabs 2.5/7.5, 5/10 mg hydrocodone/ibuprofen.

SE: Sedation, fatigue, GI upset.
NOTES: Not for arthritis.

HYDROCORTISONE, RECTAL (ANISOL-UC SUPOSITORY, CORTIFOMO RECTAL, PROCTOCORT, OTHERS, GENERIC)

USES: *Thermal annecia conditions, radiation proctitis, dermatoic. CI:

ACTIONS: Anti-inflammatory, steroid.
DISP: Hydrocortisone acetate. Rectal aerosol 90 mg/applicator; supp 25 mg. Hydrocortisone base. Rectal 0.5%, 1%, 2.5%, rectal sup 100 mg/BY mL. SE: Minimal systemic effect.

HYDROCORTISONE, SYSTEMIC (CORTEF, SOLU-CORTEF, GENERIC) [C-II]

See also Steroids Systemic and Topical.
USE: Adrenal insufficiency.
ACTIONS: Glucocorticoid.
DOSE: 2 mg/kg IV/ID weekly; max. dose 100 mg. W/P: (B, +). CI: Viral, fungal, or tubercular skin lesions; serious infections (except septic shock or TB meningitis).
SE: Systemic: ↑ Appetite, insomnia, hyperglycemia, bruising.
NOTES: May cause hypothalamic-pituitary-adrenal axis suppression.

HYDROMORPHONE (DILAUDID, DILAUDID HP, GENERIC) [C-II]

WARNING: A potent Schedule II opioid agonist, highest potential for abuse and risk of resp depression. HP formula is highly concentrated; do not confuse w/ standard formulations; OD and death could result. Alcohol, other opioids, CNS depressants ↓ resp depression effects.
USES: *Mod–severe pain.
ACTIONS: Narcotic analgesic. DOSE: 1–4 mg PO, IM, IV or PR q4–6h PRN; max PR q4–6h PRN; w/ hepatic failure.
W/P: (B) if prolonged use or high doses near term, ↑ resp depression and CNS effects. CI: CNS leuko w/ ↑ ICP, CO2, cor pulmonale, emphyema, hydrocortisone, status asthmaticus, HP-mg form in OB anaesthesia.
DISP: Tabs 2, 4, 8 mg scored; 20 mg 5 mL or 1 mg/mL; by 1, 4 mg, Oral/Ap/10 mg/mL; sup 3 mg.
SE: Sedation, nausea, GI upset.
NOTES: Morphine 10 mg IM = Hydromorphone 1.5 mg IV.

948
**HYDROXYZINE (ATARAX, VISTARIL, GENERIC)**

**USES:** Anxiety, sedation, itching.

**ACTIONS:** Anticholinergic, antihistamine.

**DOSE:**
- Adults: 10–25 mg PO q8h;
- SE, heat prostration w/ hot weather.

**W/P:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 10, 25, 50 mg; sup 10 mg/g (inj 100 mg/mL).

**ACTIONS:** Anticholinergic, antispasmodic.

**USES:** Irritable bowel, spastic colitis, peptic ulcer ulcers.

**NOTES:**
- After 3–5 yr.
- 15–30 s q3mo; w/ low risk for fracture, consider D/C day (do not lie down for 60 min after); 3 mg IV over 30 min q6h.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Bactericidal; d/t susceptible bacteria.

**USES:** Lower respiratory, UTI, intra-abdominal, gen, saphenous, bone and joint, skin and skin structure, endocarditis, polymicrobial infections.

**NOTES:**
- D after 30 wk, D after 30 wk, ?/↓.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Anticholinergic, antispasmodic.

**USES:** Irritable bowel, spastic colitis, peptic ulcer ulcers.

**NOTES:**
- After 3–5 yr.
- 15–30 s q3mo; w/ low risk for fracture, consider D/C day (do not lie down for 60 min after); 3 mg IV over 30 min q6h.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Bactericidal; d/t susceptible bacteria.

**USES:** Lower respiratory, UTI, intra-abdominal, gen, saphenous, bone and joint, skin and skin structure, endocarditis, polymicrobial infections.

**NOTES:**
- D after 30 wk, D after 30 wk, ?/↓.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Bactericidal; d/t susceptible bacteria.

**USES:** Lower respiratory, UTI, intra-abdominal, gen, saphenous, bone and joint, skin and skin structure, endocarditis, polymicrobial infections.

**NOTES:**
- D after 30 wk, D after 30 wk, ?/↓.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Bactericidal; d/t susceptible bacteria.

**USES:** Lower respiratory, UTI, intra-abdominal, gen, saphenous, bone and joint, skin and skin structure, endocarditis, polymicrobial infections.

**NOTES:**
- D after 30 wk, D after 30 wk, ?/↓.

**DOSE:**
- 

**CI:**
- Nephrogenic.

**DISP:** Tablets 100, 200, 400, 600, 800 mg; chew tabs 250, 500 mg; sup 250, 500 mg/mL; inj 200 mg/mL.

**ACTIONS:** Bactericidal; d/t susceptible bacteria.

**USES:** Lower respiratory, UTI, intra-abdominal, gen, saphenous, bone and joint, skin and skin structure, endocarditis, polymicrobial infections.

**NOTES:**
- D after 30 wk, D after 30 wk, ?/↓.
DOSE:
Adults: Hospitalized: Initial 100 mg/24 h PO in 4 doses; 
Max: 500 mg/24 h max. 
Pediatrics: See adult dosages. 
PTM: (Aldara): 5% (250-mg cream) single-dose packets 5% (250-mg cream). 

INDIGO CARMINE, INJECTION (INDIGOTINDISULFONATE) (GENERIC) 
ACTION: IC: Extracted and appears in urine as blue color usually within 10 min of injection. 
DOSE: 1 ml (prefered) or IV. 
PTM: [C, 1]. 
Cl: Allergy to compound. 
DOS: 1 mg/kg max. for injection; do not dilute or inject with other solutions. 
PTM: Pseudocyesis, rarely idiopathic reaction. 
NOTE: May transiently alter pulse oximetry; originally used as a renal function test. Label is not officially approved by the FDA. 

IMIDOMETHICIN (INDOCIN, TIVOREX, GENERIC) 
WARNING: May risk of CV events & GI bleeding; not post-CABG pain. 
USES: "Arthritis (osteo, rheumatoid); ankylosing spondylitis; close ductus arteriosus, *" 
ACTION: [J] Prostaglandins. 
Adults: 25–50 mg PO BID–TID. 
Pediatrics: 0.2–0.25 mg/kg/24 h; may ingest 1–2 mg/d. 
PTM: [C +]. 
Cl: ASA/NSAID sensitivity, peptic ulcerativeGI bleed. 

INTERFERON ALFA-2B (INTRON-A) 
WARNING: Can cause or aggravate or fatal disease, myocarditis, or other serious disorder. 
USES: Primary: 
Adults: Per protocols. 
Pediatrics: Per protocols. 
DOSE: 1 mg/vial; caps 25, 50; susp 25 mg/5 mL; vials 20, 40 mg caps. 
PTM: [J] bleeding or ulcer, dizziness, edema. 
Cl: Monitor renal function. 

ISONIAZID (INH) 
WARNING: Severe and sometimes fatal hep may occur usually within 1–2 mo of therapy, although may develop after mo of therapy. 
USES: "Neat & prophylaxis of TB. 
ACTION: Bacterial: interferes w/ mycolic acid synth, disrupts cell wall. 
DOSE: Adults: Active TB: 5 mg/kg/24 h PO or IM usually (300 mg/d) or 207: 15 mg/kg (max 1000 mg) x/wk. 
Prophylaxis: 300 mg PO xt 6–12 mo or 900 mg 2x/wk. 
Pediatrics: Active TB: 10–15 mg/kg daily PO or IM (300 mg max). 
Prophylaxis: 10 mg/kg/24 h PO; in hepatolental dysfunction. 
PTM: [C, +] Liver disease, dialysis; avoid INH. 
Cl: Acute liver disease, Hep INH hep. 

ITRACONAZOLE (ONEMEL, SORANOX, GENERIC) 
WARNING: GI side effects, pruritis, palmar, xerosis, dermatitis, or scleatorrhematitis. 
USES: "Systemic antifungal used in fungal infections (aspergillosis, blastomycosis, histoplasmosis, candidiasis, onychomycosis, or " 
ACTION: Acute antifungal, J. ergosterol synth. 
DOSE: Dose based on indication. 200 mg PO daily, 150 mg 3 doses for intramuscular use. 200 mg orally, 8–12 h and 600 mg (40 mg/kg) 3 doses for intramuscular use. 
PTM: [C, +] Hypersensitivity, pruritis, xerosis, dermatitis, onychomycosis, or " 

IRBSERANT (AVAPRO) 
WARNING: D/C immediately if hypertension develops. 
USES: "HTN, diabetic nephropathy*, CHF 
ACTION: Angiotensin II receptor antagonist. 
DOSE: 150 mg PO, may tit to 300 mg. 
PTM: [C 11b, 24d, 1; J 1, 2; K, 1]. 

ISOTONIC solutions (Lactated Ringers, PlasmaLyte, Saline) 
Uses: "Surgical infections (periapical, blastomycosis, histoplasmosis, candidiasis, onychomycosis, or " 
ACTION: Acute antifungal, J. ergosterol synth. 
DOSE: Dose based on indication. 200 mg PO daily, 150 mg for oral diazepam, 1875 mg (40 mg/kg) 3 doses for intramuscular use. 
PTM: [C, +] Hypersensitivity, pruritis, xerosis, dermatitis, onychomycosis, or " 

ISSUES: "Hep, peripheral neuropathy, GI upset, anorexia, dizziness, skin reaction. 
NOTE: Use w–2–3 other drugs for active TB, based on INH resistance patterns when TB acquired & sensitivity results; prophylaxis usually w/INH alone. IM rarely used. 
Cl: Peripheral neuropathy w/ pyridoxine 50–100 mg. 
See CDC guidelines (http://www.cdc.gov/ty/ for current TB recommendations. 

ITALIAN HERBS (LAUREL, BAY, MARJORAM, OREGANO) 
USING: "Spices, flavor, condiments. 
PTM: [C, +] Hypersensitivity, pruritis, xerosis, dermatitis, onychomycosis, or " 

ITALIAN WALNUT (JUGLANS REGIA) (GENERIC) 
USING: "Walnuts, an excellent source of protein and zinc. 
PTM: [C, +] Hypersensitivity, pruritis, xerosis, dermatitis, onychomycosis, or " 

ITALIAN YARROW (AUSTRIACUM) (GENERIC) 
USING: "An edible herb, used in the treatment of digestive disorders and as a diuretic. 
PTM: [C, +] Hypersensitivity, pruritis, xerosis, dermatitis, onychomycosis, or "
KETOCONAZOLE, ORAL (NIZORAL, GENERIC)
WARNING: (Oral use) Risk of total hepatoctye. Concomitant deliabetes, deont, pricline, ciapride, metabolites, DPD and DMD, DMD and maltose, antacid production. USES: - Systemic fungal infections (Candida, dimethicone, itraconazol, etc.), refractory topical dermatophytes, infection; P:ca when rapid, testosterone needed or hormone refractory. Cushings disease medical therapy when surgery not possible. ACTIONS: Adult, a fungal cell wall synth; high dose boosts P450, too, testosterone production. DOSE: PO: 200 mg PO daily, 1 to 400 mg PO daily for serious infection. PO: 400 mg PO TID w/ hydrocortisone 20–40 mg divided BID; best on empty stomach. W/P: [C, I], io any agent that a gastric pH (absorption), may enhance antacids; an EIN (Bisulfate-like reaction); numerous interactions including statins, niacin; do not use w/ hypophosphatemia. NSAIDs may cause insufficiency, bleeding diathesis, L&D, nursing, and w/ mod–severe acute pain; CI w/ PUD, GI bleed, post surgery/L&D, w/ Hx allergy to other NSAIDs recent or of GI block or perfusion. DISP: Oral tablets 200 mg. SE: N. nausea, hair loss, headache, t PS gain, dizziness, delirium, fatigue, impotence, hepatitis, adrenal suppression, acquired cutaneous adherence ("sticky skin syndrome"). NOTES: Monitor LFTs; can rapidly ↓ testosterone levels at high dose.

KETOROLAC NASAL (SPIRX)
WARNING: For short-term (≤5 days) use; CI w/ PUD, GI bleed, suspended bleeding risk, postop CABS, advanced renal disease or risk of renal failure w/ vol depletion, risk CV thrombotic events (MI, stroke). Not indicated for use in children. USES: - Short-term (≤5 days) treat pain requiring opioid level analgesia. ACTIONS: NSAIDs, i postpartum. DOSE: - 65 yr: 31.5 mg (one 17.5 mg spray each q6h), max. 126 mg/d; ↓ 65 yr, w/ renal impairment or ↓ < 50 kg: 15.75 mg (one 17.5 mg spray in only 1 nostril) q6h, max. 63 mg/d. W/P: [C (D 3rd tri), I] do not use w/ other NSAIDs can cause severe skin reactions; do not use w/ critical bleeding risk, w/ CHF. CI: See "Warning" (prophylactic to major surgery), CI w/ allergy to other NSAIDs recent or of GI block or perfusion. DISP: Nasal spray 15.75–mg ketorolac/100 μl spray (8 sprays/bottle). SE: Nasal desensitization, t sneezing, throat irritation, oliguria, rash, ↑ AR, ↑ urine output. ↓ ↑ ALT/AST, ↑ TP. NOTES: Discard open bottle after 2 hr.

KUNECATECHINS (SINECATECHINS) (VEREGEN)
USES: - External gentianviolet warts. ACTIONS: Unknown; green tea extract. DOSE: Apply 0.5%-cm ribbon to each wart 3 x/d until all warts clear, not > 16 wk. W/P: [C, I], ↓ Dose Clear 15%. SE: Erythema, pruritus, burning, pain, lesion/crateration, edema, induction, rash, phlebitis. NOTES: Youth hands beforehand use, not necessary to scale off prior to next user, avoid on open wounds, may weaken condoms & Vag diaphragms, use in comb is not recommended.

LACTOBACILLUS (LACTINEX GRANULINES) (OTC)
USES: - Control of diarrhea, especially after antibiotic treat. ACTIONS: Repairs normal intestinal flora, lactase production, (Lactobacillus acidophilus) and Lactobacillus helveticus. DOSE: Adults: [C] or Pediatric (≤10 yr), 1 packet, 1–2 caps, or 4 to 6 tabs PO–QD. W/P: [C, I]; ↓ Some products may contain whey. CI: Milk/lactose allergy. DISP: Tabs, caps, granules in packets (all OTC). SE: Flatulence, Dyspepsia. NOTES: May take granules on food.

LANTHANUM CARBONATE (FOSFENOL)
USES: - Hyperphosphatemia in end-stage renal disease. ACTIONS: Phosphate binders. DOSE: 750–1,500 mg PO daily in —, obese, w/ or immediately after meal; (tablete I) – I I-bound on PO, levels. W/P: [C, I] — No data in GI disease, not for peds. CI: Bowel obstruction, fecal impaction, ileus. DISP: Chew tabs 500, 750, 1,000 mg. SE: ↑ Gastro occlusion, headache, ↑ TP. NOTES: Chew tabs before swallowing, separate from meds that interact w/ antibiotics by 2 hr.

LEUPROLIDE (ELIGARD, LUPRON, LUPRON DEPOT, LUPRON DEPOT-PED, GENERIC)
USES: - Advanced PCA (all except Depot-Ped), endometriosis (Lupron), urethral fibrosis (Lupron), & precocious puberty (Lupron-Ped). ACTIONS: LHRH agonist, paradoxically, release of GnRH w/ Gn from anterior pituitary; in men ↓ testosterone, in women ↓ estrogen. DOSE: Adults: PCA: LUPRON DEPOT: 7.5 mg IM q4wk or 22.5 mg IM q8w or 45 mg IM q4mo. Eligard: 7.5 mg SQ q4wk or 22.5 mg SQ q6w or 45 mg SQ q2mo or 45 mg SQ q1mo. Endometriosis (LUPRON DEPOT): 3.5 mg IM q4w × 1 or 21.5 mg q2w × 1. Lupron for PCa: 25–35.75 mg IM q4wk; ↓ 37.5 mg IM q8w; ↓ 30 mg IM q4mo; ↓ 57.5 mg IM q2mo; ↓ 57.5 mg IM q1mo. Lupron-Ped: 50 μg/kg SQ q4wk; ↓ 10 μg/kg until annual downregulation achieved. Lupron DEPOT: 25 mg 3.75 mg IM q4wk. W/P: [K, I] ↓ Impending cord compression in PCA, I ↓ w/ meds or pre-existing CV disease; postmarketing reports of seizures. CI: AUB, implant in nonmen/peds, pregnancy. DISP: Inj 5 mg/mlmL, LUPRON DEPOT: 7.35 mg 1 mL for fibrinol, endometriosis; LUPRON DEPOT for PCa: 7.35 mg (1 mL), 11.25 (3 mL), 22.5 (10 mL), 45 mg (14 mL), 45 mg (16 mL). Eligard depot for PCA: 7.5 mg (1 mL), 22.5 (3 mL), 30 (4 mL), 45 mg (6 mL), LUPRON DEPOT-Ped: 7.5, 11.25, 15, 30 mg. SE: Hot flashes, gynecomasia, NV, diplopia, anorexia, dizziness, headache, insomnia, panthothenics, depression, depression, peripheral edema, & bone pain (transient "false reaction" 7–14 days after the 1st dose/3[hypercalcemia supress before suspension]); ↓ BMI w/ ≤ 8–6–8–6 use, bone loss possible, abnormal bone density, hypercalcemia. NOTES: Nonsteroidal antiinflammatory (Ig, bicarbamid) may block function in men w/ PCa, Viadur 12 mo form unavailable to new patients.
**LEVOFLOXACIN (LEVAQUIN, GENERIC)**

### Uses:
- Topical anesthetic for venipuncture and dermatologic procedures.
- Local anesthetic, epidural/caudal anesthesia.
- Regional nerve blocks, topical on mucous membranes.
- Inhibits ionic fluxes required for initiation and conduction.

### Dosage:
- Adults: Inj: 200 mg/mL; tabs 250, 750 mg, Inj 1 g (amp); Pronto 2.5 g thick layer 2–2.5 g to intact skin over 20–25 cm² of skin surface; cover with occlusive dressing (eg, Tegaderm) for at least 1 hr. Peds: Max. 30 mL to dry hair, develop a lather; wash off for 4–5 min, comb-out rins.

### Side Effects:
- Erythema, blanching, and edema.
- Component sensitivity (PABA or local anesthetics).

### Notes:
- Use on skin only; avoid eyes; use sparingly.
- Apply 30 mL to dry hair, develop a lather; wash off for 4–5 min, comb-out rins.

### LIDOCAINE/P RILOCaine (EMLA, ORAq IX)

### Uses:
- Topical anesthetic for intact skin or genital mucous membranes; adjust to physeology or dermal procedures.

### Actions:
- Local anesthetics.

### Dosage:
- Adults: EMLA cream, thin layer 2–2.5 g to intact skin over 20–25 cm² of skin surface; cover with occlusive dressing (eg, Tegaderm) for at least 1 hr.
- Peds: Max. dose: 3–3 mg/kg or 5 kg: 1 g/10 cm² for 1 hr. 3–12 mo & > 5 kg: 2 g/20 cm² for 4 hr.

### Side Effects:
- Dizziness, paresthesias, & seizures associated w/ depression.

### Notes:
- Longer contact time ↑ effect.

### LIDOCAINE/TETRACAINE, PATCH (SYNERA) CREAM (PLIAGLIS)

### Uses:
- Topical anesthetic for venipuncture and dermatologic procedures (Synera). dermatologic procedures (Patchy).

### Actions:
- Combi anest and anest local anesthetic.

### Dosage:
- Adults & Peds: Synera: Apply patch 20–30 min before procedure.
- Peds: Apply cream 25–40 min before procedure, volume based on site surface (use label).

### Side Effects:
- Erythema, blanching, and edema.

### LINDANE (GENERIC)

### Warning:
- Only for proximoinferior 1st line treat for sebaceous agents.

### Uses:
- Skin irritant.

### Actions:
- Ectoparasiticide & ovicide.

### Dosage:
- Adults & Peds: Cream on lesion: Thin layer to dry skin after curing, leave for 8–12 hr; may also use on laundry. Shampoo: Apply 30 mL to dry hair, develop a lather; wash off for 4–5 min, comb-out rins.

### Side Effects:
- Erythema, blanching, and edema.
W/P: [C (troleandomycin)]

**LYMPHOCYTE IMMUNE GLOBULIN (ANTITHYMOCYTE GLOBULIN, ATG) (ATGAM)**

**WARNING:** Should only be used by physician experienced in immunosuppressive therapy or management of solid organ and/or BMT pts. Adequate lab and supportive resources must be readily available.

**USES:** Anti-thymocyte globulin if not candidates for BMT.

**DISP:**
- **Premix Inj:** 10, 20, 40, 80 mg/mL; Inj 125, 250, 500, 600 mg; tabs 400 mg (OTC).
- **Cream:** 1%; 30/60 g.

**SE:** Anaphylactoid reaction (rare), dizziness, headache, edema, skin rash.

**W/P:**
- **GI:** abdominal pain, vomiting, diarrhea, anorexia, cramps, constipation, nausea, ileus.
- **Respiratory:** wheezing, bronchospasm, dyspnea.
- **Skin:** rash, pruritus, urticaria.
- **Other:** fever, chills, myalgia, systemic reaction precludes use; give via central line; site reaction, rare.

**NOTES:**
- **INJECTABLE** (Genentech, San Francisco, CA).
- **Ophthalmic** (Alcon Laboratories, Fort Worth, TX).
- **Rheumatic** (Mepha, Neuss, Germany).
- **Transplant** (Lilly).
MEGESTOL ACETATE (MEGACE, MEGACE-ES)

USES: “Anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS; palliative treatment of advanced carcinoma of the breast or anovulatory." 

ACTIONS: Hormone; anti-lueticizing; progestogenic analog.

DOSE: 40–320 mg/d divided doses.

NOTES: Do not D/C abruptly; Megace-ES not equivalent to others in mg.

W/P: [C, –] risk for dependency, j seizure threshold, adrenal insufficiency, head injury. 1 ICP, hepatic impairment, not OK in sickle cell disease.

CI: no MADDs.

DISP: Tabs 50, 100 mg; intracut 50 mg/mL; inj 25, 50, 75, 100 mg/mL.

SE: Rare CNS depression, seizures, adenocarcinoma; j BP; rash; N/V; bilirubin and urea spures, dyspnea.

NOTES: None.

MEPHALAN (L-PAM) (ALKERAN, GENERIC)

WARNING: Administer under the supervision of a qualified physician experienced in the use of chemotherapy. Multiple myeloma and mantle cancer*, breast & testicular cancer, melanoma; allergic & ABMT (high dose), neutropenia, thrombocytopenia.

ACTIONS: Ablating agent, nitrogen mustards.

DOSE: Alkylating multiple myeloma: 16 mg/m² IV qIVq: 4 d then at 4-wk intervals after tumor reduces; w/ or without pred. j BP, j RR allergic reaction, rash, j Ca, j glucose, j protein, j Mg, ethanol, hyoscines, j BM, j FP CT, palpitations.

NOTES: Do not D/C abruptly; Mephalan ES not equivalent to others in mg.

Peds: 2 mg/m² IV qIVq.

W/P: [D, –] r rigors from amphotericin B.

NOTES:

MEGETROL ACETATE (MEGACE, MEGACE-ES)

USES: “Anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS; palliative treatment of advanced carcinoma of the breast or anovulatory." 

ACTIONS: Hormone; anti-lueticizing; progestogenic analog.

DOSE: Apertan. Megestrol ES 825 mg/dly (35 mL or 1 teaspoon), breast cancer: 160 mg/dQD (40 mg QOD), Endometrial cancer: 40–130 mg/dly divided doses.

Peds: 1–15 mg/kg/day PO in 2–4 divided doses.

W/P: [D, –] r thromboembolitis; handle w/ care.

CI: Pregnancy.

DISP: Tabs 20, 40, 45 mg; inj 50 mg/mL, Megestrol ES 135 mg/mL.

SE: Ovarian, breast, hepatic, intestinal bleeding, photosensitivity, N/V diarrhea, headache, mastodynia, j Ca, j glucose, j protein.

MELPHALAN (L-PAM) (ALKERAN, GENERIC)

WARNING: Administer under the supervision of a qualified physician experienced in the use of chemotherapy. Multiple myeloma and mantle cancer*, breast & testicular cancer, melanoma; allergic & ABMT (high dose), neutropenia, thrombocytopenia.

ACTIONS: Ablating agent, nitrogen mustards.

DOSE: Alkylating multiple myeloma: 16 mg/m² IV qIVq: 4 d then at 4-wk intervals after tumor reduces; w/ or without pred. j BP, j RR allergic reaction, rash, j Ca, j glucose, j protein, j Mg, ethanol, hyoscines, j BM, j FP CT, palpitations.

NOTES: Do not D/C abruptly; Mephalan ES not equivalent to others in mg.

Peds: 2 mg/m² IV qIVq.

W/P: [D, –] r rigors from amphotericin B.

NOTES:

MEGETROL ACETATE (MEGACE, MEGACE-ES)

USES: “Anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS; palliative treatment of advanced carcinoma of the breast or anovulatory." 

ACTIONS: Hormone; anti-lueticizing; progestogenic analog.

DOSE: Apertan. Megestrol ES 825 mg/dly (35 mL or 1 teaspoon), breast cancer: 160 mg/dQD (40 mg QOD), Endometrial cancer: 40–130 mg/dly divided doses.

Peds: 1–15 mg/kg/day PO in 2–4 divided doses.

W/P: [D, –] r thromboembolitis; handle w/ care.

CI: Pregnancy.

DISP: Tabs 20, 40, 45 mg; inj 50 mg/mL, Megestrol ES 135 mg/mL.

SE: Ovarian, breast, hepatic, intestinal bleeding, photosensitivity, N/V diarrhea, headache, mastodynia, j Ca, j glucose, j protein.

MELPHALAN (L-PAM) (ALKERAN, GENERIC)

WARNING: Administer under the supervision of a qualified physician experienced in the use of chemotherapy. Multiple myeloma and mantle cancer*, breast & testicular cancer, melanoma; allergic & ABMT (high dose), neutropenia, thrombocytopenia.

ACTIONS: Ablating agent, nitrogen mustards.

DOSE: Alkylating multiple myeloma: 16 mg/m² IV qIVq: 4 d then at 4-wk intervals after tumor reduces; w/ or without pred. j BP, j RR allergic reaction, rash, j Ca, j glucose, j protein, j Mg, ethanol, hyoscines, j BM, j FP CT, palpitations.

NOTES: Do not D/C abruptly; Mephalan ES not equivalent to others in mg.

Peds: 2 mg/m² IV qIVq.

W/P: [D, –] r rigors from amphotericin B.

NOTES:

MEGETROL ACETATE (MEGACE, MEGACE-ES)

USES: “Anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS; palliative treatment of advanced carcinoma of the breast or anovulatory." 

ACTIONS: Hormone; anti-lueticizing; progestogenic analog.

DOSE: Apertan. Megestrol ES 825 mg/dly (35 mL or 1 teaspoon), breast cancer: 160 mg/dQD (40 mg QOD), Endometrial cancer: 40–130 mg/dly divided doses.

Peds: 1–15 mg/kg/day PO in 2–4 divided doses.

W/P: [D, –] r thromboembolitis; handle w/ care.

CI: Pregnancy.

DISP: Tabs 20, 40, 45 mg; inj 50 mg/mL, Megestrol ES 135 mg/mL.

SE: Ovarian, breast, hepatic, intestinal bleeding, photosensitivity, N/V diarrhea, headache, mastodynia, j Ca, j glucose, j protein.

MELPHALAN (L-PAM) (ALKERAN, GENERIC)

WARNING: Administer under the supervision of a qualified physician experienced in the use of chemotherapy. Multiple myeloma and mantle cancer*, breast & testicular cancer, melanoma; allergic & ABMT (high dose), neutropenia, thrombocytopenia.

ACTIONS: Ablating agent, nitrogen mustards.

DOSE: Alkylating multiple myeloma: 16 mg/m² IV qIVq: 4 d then at 4-wk intervals after tumor reduces; w/ or without pred. j BP, j RR allergic reaction, rash, j Ca, j glucose, j protein, j Mg, ethanol, hyoscines, j BM, j FP CT, palpitations.

NOTES: Do not D/C abruptly; Mephalan ES not equivalent to others in mg.

Peds: 2 mg/m² IV qIVq.

W/P: [D, –] r rigors from amphotericin B.

NOTES:

MEGETROL ACETATE (MEGACE, MEGACE-ES)

USES: “Anorexia, cachexia, or an unexplained significant weight loss in patients with AIDS; palliative treatment of advanced carcinoma of the breast or anovulatory." 

ACTIONS: Hormone; anti-lueticizing; progestogenic analog.

DOSE: Apertan. Megestrol ES 825 mg/dly (35 mL or 1 teaspoon), breast cancer: 160 mg/dQD (40 mg QOD), Endometrial cancer: 40–130 mg/dly divided doses.

Peds: 1–15 mg/kg/day PO in 2–4 divided doses.

W/P: [D, –] r thromboembolitis; handle w/ care.

CI: Pregnancy.

DISP: Tabs 20, 40, 45 mg; inj 50 mg/mL, Megestrol ES 135 mg/mL.

SE: Ovarian, breast, hepatic, intestinal bleeding, photosensitivity, N/V diarrhea, headache, mastodynia, j Ca, j glucose, j protein.

MELPHALAN (L-PAM) (ALKERAN, GENERIC)

WARNING: Administer under the supervision of a qualified physician experienced in the use of chemotherapy. Multiple myeloma and mantle cancer*, breast & testicular cancer, melanoma; allergic & ABMT (high dose), neutropenia, thrombocytopenia.

ACTIONS: Ablating agent, nitrogen mustards.

DOSE: Alkylating multiple myeloma: 16 mg/m² IV qIVq: 4 d then at 4-wk intervals after tumor reduces; w/ or without pred. j BP, j RR allergic reaction, rash, j Ca, j glucose, j protein, j Mg, ethanol, hyoscines, j BM, j FP CT, palpitations.

NOTES: Do not D/C abruptly; Mephalan ES not equivalent to others in mg.

Peds: 2 mg/m² IV qIVq.

W/P: [D, –] r rigors from amphotericin B.

NOTES:
METRONIDAZOLE (FLAGYL, FLAGYL ER, METOCREEM, METROGEL, METROLATION)

WARNING: Carcinogenic in rats.

USES: Metronidazole: flagelate (Trichomonas vaginalis, anaerobic bacteria, Helicobacter pylori), protozoa (Giardia lamblia), Trichomonas vaginalis, Giardia lamblia, anaerobic bacteria, especially in infections such as peptic ulcer disease, intra-abdominal infections, pelvic inflammatory disease, and intrauterine device infections. Metronidazole is a nitroimidazole derivative that inhibits bacterial and protozoal DNA synthesis by acting as a DNA alkylating agent. It is active against a wide range of aerobic and anaerobic bacteria and protozoa.

DOSE: Adults: 2 g/d; PO: 300 mg PO q4h or 500 mg PO q8h or 750 mg PO q12h for 7–10 days (PO preferred); IV: only if oral is not possible. IV: 1–2 mg/kg/dose IV as adults. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults: 2 g/d; PO: 300 mg PO q4h or 500 mg PO q8h or 750 mg PO q12h for 7–10 days (PO preferred); IV: only if oral is not possible. IV: 1–2 mg/kg/dose IV as adults. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

METHYLENE BLUE (UROLENE, GENERIC)

DOSE: Adults: 2 g/d; PO: 300 mg PO q4h or 500 mg PO q8h or 750 mg PO q12h for 7–10 days (PO preferred); IV: only if oral is not possible. IV: 1–2 mg/kg/dose IV as adults. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.

WARNING: CHLORAMPHENICOL (METAZOLV, REGLAN, GENERIC)

DOSE: Adults & Peds: >14 yr: intravenous: 10 mg IV 1 over 1–2 min. Peds: Repeat: 1–2 mg/kg/dose PO 30 min ac & hs. Chemo antiemetic: 1–2 mg/kg/dose IV as adults. Adults: 0.25 mg PO q4–8 h. Pediatric: 0.1–0.2 mg/kg/dose PO 30 min ac & hs.
MICAFUNGIN (MYCAMINE)

**USES:** Candidemia, acute disseminated candidiasis, Candida peritonitis & abscesses; prophylaxis Candida infection w/ HCT.

**ACTIONS:** Echinocandin, fungal cell wall synth.

**DOSE:** A. Con: 15–45 mg PO PRN. Fecal inspection after barium: 118 mL rectally × 1.

**WARNING:** Do not crush/ chew. keep away from children, throat dissection in < 1 yr or use last half of pill.

**MICONAZOLE (MONISTAT 1 COMBO, MONISTAT 3, MONISTAT 7 (OTC))

**USES:** Candital infections, dermatomycoses (tinea pedis/tinea cruris/candidiasis).

**ACTIONS:** Local antifungal, alters fungal membrane permeability.

**DOSE:** 150 mg IV daily; ↓ dosage adj may be necessary.

**SE:** Sepsis, Clostridium difficile, colitis, cholestasis, shock, hypotension.

**MICONAZOLE/ZINC OXIDE/PETROLATUM (TUCKS MINERAL OIL [OTC])

**USES:** Acute burning; on skin contact dermatitis, irritation, hydrate well.

**ACTIONS:** Temporary relief of anorectal disorders (first 7 days).

**DOSE:** Apply at each diaper change (2–12 yr); 50–60 mg/m2, N/V, diarrhea, headache, fever, rash, joint pain, fatigue, distension, photosensitivity, hyperpigmentation, 5L syndrome, pseudomembranous colitis.

**NOTES:** Do not cut/throw, keep away from children, tooth discoloration in <1 yr or use last half of pill.

**MINERAL OIL (OTC)

**USES:** Constipation, bowel irritation, fecal impaction.

**ACTIONS:** Lubricant laxative.

**DOSE:** Adults: 15–45 mL PO PRN. Fecal inspection after barium: 118 mL rectally × 1.

**WARNING:** Do not use PO in peds < 1 yr; do not use PO in peds > 1 yr.

**SE:** Lipid pneumonia (aspiration of PO mineral oil), ↑ protein, ↑ lipid phospholipids.

**MINERAL OIL/PRAMOXINE HCL/ZINC OXIDE (TUCKS OINTMENT (OTC))

**USES:** First 7 days.

**ACTIONS:** Topical anesthetic.

**DOSE:** Adults & Peds: ≥ 12 yr: Cleanse, rinse, & dry, apply externally or into anus canal w/ tip 3 × /12 h.

**SE:** No placement into rectum.

**MITOMYCIN (GENERIC)

**ACTIONS:** Alkylating agent; generates oxygen-free radicals,↑ protein synthesis.

**DOSE:** 1.7 mg/dL/↓ serum digoxin when starting both together.

**SE:** Colitis, vomiting, nausea, diarrhea, bloody diarrhea, anorexia, dizziness, fatigue.

**MIRABEGRON (MYRBETRIQ)

**USES:** Overactive bladder (OAB) w/ symptoms of urge urinary incontinence, urgency, and urinary frequency.

**ACTIONS:** 0–3 adrenergic agonist; relaxes smooth muscle.

**DOSE:** Start 25 mg PO daily; ↑ to 50 mg daily after 8 wk. PRN: 25 mg. daily w/ severe renal or mild hepatic impairment; swallow whole, do not cut/chew.

**SE:** [D, –] Severe uncontrolled HTN, urinary retention w/ bladder outlet obstruction & antimuscarinic drugs; w/ drugs metabolized by CYP2D6 (e.g., thioridazine, flecainide, propafenone); do not use w/ ESRD or severe hepatic impairment; monitor serum digoxin when starting both together.

**MITOMYCIN (GENERIC)

**ACTIONS:** Alkylating agent, generates oxygen-free radicals,↑ protein synthesis.

**DOSE:** 1.7 mg/dL/↑ protein synthesis.

**SE:** Colitis, vomiting, nausea, diarrhea, bloody diarrhea, anorexia, dizziness, fatigue.

**MIRABEGRON (MYRBETRIQ)

**USES:** Overactive bladder (OAB) w/ symptoms of urge urinary incontinence, urgency, and urinary frequency.

**ACTIONS:** 0–3 adrenergic agonist; relaxes smooth muscle.

**DOSE:** Start 25 mg PO daily; ↑ to 50 mg daily after 8 wk. PRN: 25 mg. daily w/ severe renal or mild hepatic impairment; swallow whole, do not cut/chew.

**SE:** [D, –] Severe uncontrolled HTN, urinary retention w/ bladder outlet obstruction & antimuscarinic drugs; w/ drugs metabolized by CYP2D6 (e.g., thioridazine, flecainide, propafenone); do not use w/ ESRD or severe hepatic impairment; monitor serum digoxin when starting both together.

**MITOMYCIN (GENERIC)

**ACTIONS:** Alkylating agent; generates oxygen-free radicals,↑ protein synthesis.

**DOSE:** 1.7 mg/dL/↑ protein synthesis.

**SE:** Colitis, vomiting, nausea, diarrhea, bloody diarrhea, anorexia, dizziness, fatigue.
**MITOTANE (LYSODREN)**

**WARNING:** Administer only by physician experienced in chemotherapy, discontinue temporarily immediately following shock or severe trauma since adrenal suppression is its prime action. Exogenous steroids should be administered in such circumstances.

**USES:** Adjuvant chemotherapeutic agent, suppresses corticosteroid production by inhibiting 11β-Hydroxylase (aromatase OC).

**DOSE:** 2–6 g/d in divided dose TID–QID; increase as tolerated up to max. tolerated dose (generally 2–10 g/d); decrease dose with side effects; administer with glucocorticoids and if needed mineralocorticoid replacement.

**W/P:** [C, I]; increases warfarin metabolism.

**CI:** Hypersensitivity to compound.

**DISP:** Tablets 500 mg.

**SE:** Adrenal insufficiency, GI distress, depression, lethargy, somnolence, dizziness, vertigo, orthostasis.

**NOTES:** Neurapraxic testing with use ≥2 yr; higher doses of glucocorticoids required due to metabolism; treat until there is no clinical benefit.

**MITOXANTRONE (GENERIC)**

**WARNING:** Administer only by physician experienced in chemotherapy, except for acute leukemia, do not use in WBC count of <1,500 cells/mm<sup>3</sup>; severe neutropenia can result in infection, follow CBC; cardiotoxic (CHF); secondary analysis, ARB recommended.

**USES:** Combination for myelogenous, promyelocytic, monocytic, and erythroid acute leukemias, progressive relapsing MS; pain related to inoperable adrenocortical carcinoma; discontinue temporarily in LVEF .

**ACTIONS:** Anthracycline; DNA-intercalating agent; pDNA synth by attacking topoisomerase II.

**DOSE:** IV prop, Cap 12–14 mg/kg ext 3–5 mg PO BID; ↓ dose w/ hepatic impairment, leukopenia, thrombocytopenia.

**W/P:** [B, D–I]; reports of secondary AML, w/ MS.

**CI:** Hypersensitivity, kidney disease, head injury; chewing delayed release forms can cause severe tissue reaction.

**SE:** Moderate to severe neutropenia, thrombocytopenia, anemia, leukopenia, GI distress, nausea, vomiting, diarrhea, abdominal pain, edema, fever, chills, headache, arthralgia, myalgia, hypotension, rash, urticaria, hypoadrenalinemia.

**NOTES:** May require chelated dosing to relieve severe tissue pain.

**MOXIFLOXACIN (AVELOX)**

**WARNING:** Risk Achilles tendon rupture and tendinitis. 1 in pts >60 yr; on steroids or with organ transplant; avoid w/ myelophthemia, may cause muscle weakness.

**USES:** Acute sinusitis & bronchitis, skin/tissue/bone/tendon/dental infections, conjunctivitis, community-acquired pneumonia 1B, anthrax, endocarditis.

**ACTIONS:** 4th-gen quinolone; pDNA synth. Spectrum: Excellent gram < except MRSA & S. aureus; good gram < except P. aeruginosa, Stenotrophomonas maltophilia, V. acnes, Enterococcus spp; good aerobic.

**DOSE:** 400 mg PO/TIV daily; avoid cation products, reduce 1B.

**W/P:** [D, C]; ↓ quinolone sensitivity, interactions w/ maj <, CYP1A2, 2C9, 3A4-containing products, & class III & IV antiarrhythmic agents.

**CI:** Quinolone component sensitivity.

**DISP:** Tablets 400 mg, ABC Pak 5 tabs, inj.

**SE:** Diarrhea, N, QT prolongation, sepsis, photosensitization, peripheral neuropathy risk.

**MUPIROCIN (BACTROBAN, BACTROBAN NASAL)**

**USES:** Impetigo (cont); skin lesion infection w/ S. aureus or S. pyogenes; eradicates NRP in nasal carriage.

**ACTIONS:** Bacterial protein synth.

**DOSE:** Topical: Apply small amount 3–5 x 5–14 days. Nasal: Apply 1/2 single-use tube BID in nostril 5–14 days.

**W/P:** [B, I, M]; do not use w/ other nasal products.

**DISP:** Oral 2%, cream: 2%; nasal unit 2% 1-g single-use tube.

**SE:** Nasal irritation, rash.

**NOTES:** Pt to contact healthcare provider if no improvement in 3–5 days.

**MYCOPHENOLATE MOFETIL (CELLCEPT, GENERIC)**

**WARNING:** Risk of infections, lymphoma, other cancer, progressive multifocal leukoencephalopathy (PML); risk of pneumonia loss and inflammation; female of child-bearing potential must use contraception.

**USES:** Prevent organ rejection after transplant.

**ACTIONS:** Cytosine to lymphocytes.

**DOSE:** Adults: 1 g PO BID, dose differ based on transplant.

**W/P:** [D, A-C]; 1 or 1.5 or 2 mg; 750 mg PO BID, [D, A-C]; 2–7.5 mg; 1 g PO used w/ steroids or prednisone or tacrolimus; ↓ in renal insufficiency in neutropenia.

**SE:** Infusion over ≥ 2 hr. PO: Take on empty stomach, do not open caps.

**DISP:** Caps 250, 500 mg; susp 200 mg/mL, inj 550 mg.

**CI:** Hypersensitivity, pain, fever, headache, infection, HTN, anemia, leukopenia, edema.

**NOTES:** CellGard & Myfico are not interchangeable.

**NALOXONE (GENERIC, EVZIO)**

**USES:** Opioid addiction (diagnosis) & OD.

**ACTIONS:** Competitive opioid antagonist.

**DOSE:** Oral: Apply small amount 3–10 x 5–14 days. Nasal: Apply 1/2 single-use tube BID in nostril 5–14 days.

**W/P:** [B, I, M]; do not use w/ other nasal products.

**DISP:** Oral 2%, cream: 2%; nasal unit 2% 1-g single-use tube.

**SE:** Nasal irritation, rash.

**NOTES:** Pt to contact healthcare provider if no improvement in 3–5 days.
**NAPROXEN (ALEVE [OTC]), ANAPROX, ANAPROX DS, EC-NAPROSYN, NAPRELAN, NAPROSYN, GENERIC**

**WARNING:** May ↑ risk of CV events & GI bleeding.

**USES:** Arthritis & pain.

**ACTIONS:** NSAID, prostaglandins.

**DOSE:** 
- Adults & Peds: > 12 yr: 200–500 mg BID to 1,500 mg/d max.
- > 2 yr: 245–510 mg/d PO, ↓ in hepatic impairment.

**W/P:** PO; ↓ in 3–4 doses.

**CI:** NSAID or ASA triad sensitivity, peptic ulcer, tox; also topical 

**Peds:** 0.01–0.1 mg/kg/dose IV, IM, or SQ; repeat IV 1–2 h ra co r2h rp c.

**SE:** Headache common on initial Treat; reflex sympathetic dystrophy; peripheral neuropathy, muscle 

**DISP:** PO soln may ↓ absorption; may ↑ with foods; GI upset; ↑ in pts with renal impairment.

**NEOMYCIN (NEO-FRADIN)

**WARNING:** Systemic absorption of oral route may cause neurotoxicity; rash; opportune infections. 

**USES:** Neutropenic colitis; ophthalmic w/ other topical agents; ear aminoglycoside; interstitial pneumonitis possible; most cases in 1st 3 mo; may require alternative CS for refractory cases.

**W/P:** PO; ↓ in 3–4 doses; 12 g max.

**DOSE:** PO: 50–100 mg/kg/d PO in 3–4 doses; 12 g max.

**CI:** Renal failure, neuromuscular disease, hoarseness, hearing loss.

**DISP:** Tabs 500 mg; Afl急Furadantin 200,000 U/mL; amp 1, 20 mL.

**NOTES:** Avoid w/ CrCl < 50 mL/min; use 400 mg qd.

**NEOMYCIN-POLYMIXYN BLADDER IRRITANT [NEOSPORIN GU IRRIGANT]

**USES:** ↓ Bladder irritant in the urinary bladder of albinistic patients to help prevent bacteria and gram-negative rod sepsis associated with the use of indwelling catheters.

**ACTIONS:** Bactericidal; do not for Senita or streptococc.

**DOSE:** 1 mL irrigant in 1 L of 0.9% NaCl; contain 640,000 U/mL; amp 1, 20 mL.

**CI:** Component allergy, anti-pseudomonal allergy.

**DISP:** Sodium neomycin sulfate 40 mg & polymyxin B 200,000 U/mL; amp 1, 20 mL.

**SE:** Rash, neomycin ophthalmic (rare).

**NOTES:** Potential for bacterial/fungal super-infection; not for IV use only 3-way catheter for irrigation.

**NIFEDIPINE (ADALAT CC, AFEITAB CR, PROCARDIA, PROCARDIA XL, GENERIC)

**USES:** HTN; tocolytic.

**ACTIONS:** Calcium channel blocker.

**DOSE:** 
- Adults: SR tabs 30–90 mg/d.
- PO: 0.25–0.5 mg/kg q24h + 0.6–4 y/d.

**W/P:** PO; ↓ in hepatic impairment.

**CI:** NSAID, aminoglycoside allergy.

**DISP:** Caps 10, 20 mg; SR tabs 30, 60, 90 mg.

**SE:** Headache common on initial Treat; reflex sympathetic dystrophy; peripheral neuropathy; ↑ BP, flushing, dizziness.

**NOTES:** Adalat CC & Procardia XL not interchangeable; used for medical expulsive therapy of ureteral stone; consider to IV w/ 1 blockers such as tamsulosin.

**NITROFURANTOIN (FURADANTIN, MACROBID, MACRODANTIN, GENERIC)

**USES:** Prophylaxis & treat UTI.

**ACTIONS:** Interferes w/ metabolism & cell wall synthesis. Spectrum: Some gram (+) & (-) Bacteria; Proteus, Enterococcus, Salmonella, & some Pseudomonas resistant.

**DOSE:** 
- Adults: Prophylaxis: 50–100 mg PO; Treat: 50–100 mg PO QID × 7 days; Macrolid 100 mg PO BID × 7 days.
- Peds: Prophylaxis: 1–2 mg/kg/d PO × 1–2 doses; max 100 mg/d. Treat: 5–7 mg/kg/d in 4–6 doses (as needed/failure).

**W/P:** PO; ↓ in OK if child < 1 mo) avoid w/ CR1 < 40 mL/min.

**CI:** Anuria, diaphoresis, or significant impairment of renal function (CrCl < 60 mL/min). Infants < 1 mo; pregnancy at term; history of cholestatic jaundice/hyperbilirubinemia associated w/ nitrofurantoin.

**DISP:** Caps 25, 50, 100 mg. Vodantoin susp 25 mg/mL.

**SE:** GI effects, depigmentation, various autonomic/pulmonary reactions, peripheral neuropathy, hemolytic anemia w/ G6PD deficiency, rare aplastic anemia.

**NOTES:** Macrolides (eg, Macrodantin) > neosporin than other forms; not for comp UTI; may turn urine brown (reflective of piperacillin or cephalosporin).

**NORFLOXACIN (NOROXIN)

**WARNING:** Risk Achilles tendon rupture and tendinitis, ~ 1 yr pts > 60 yr; on steroids or with organ transplant; avoid w/ myasthenia gravis, may ↑ muscle weakness.

**USES:** Cmp & uncomp UTI; prototaxis due to E. coli, gonorrhea, inflammatory diarrhea, conjunctivitis.

**ACTIONS:** Quinolone, J, DNA gyrase, bacteriostatic. Spectrum: Broad gram (+) and (-) E. coli, cef, k. pneumoniae, F. meningitidis, F. urethritis, S. epidermidis, S. aureus.

**DOSE:** 
- Uncomp UTI (E. coli, K. pneumoniae, P. aeruginosa): 400 mg PO BD × 3 doses; other uncomp UTI Treat: 7–10 days. Comp UTI: 400 mg PO q8h for 10–31 days. Gonorhea: 800 mg × 1 dose. Prostatitis: 400 mg PO BID × 28 days. Cysticfibrosis, traveler’s diarrhea: 400 mg PO BID × 1–3 days; take 1 h ac or 2 h pc.

**W/P:** PO; ↓ in Quinolone sensitivity, w/ some antibiotics ↓ QT.

**CI:** ↑ in left ventricular ejection fraction due to paroxysm.

**DISP:** Tabs 400 mg; ciprofloxacin 3 mg/mL.

**SE:** Phototoxicity, headache, dizziness, asthenia, GI upset, pseudomembranous colitis, ocular burning w/ ophthal., peripheral neuropathy risk w/ PO only.

**NOTES:** Interactions w/ antacids, theophylline, caffeine, good conc in the kidney & urine, poor blood levels; not for uspseps, CJD, suggests do not use for GC.
OXYBUTYNIN TRANSDERMAL SYSTEM (OXYTROL, OXYTROL FOR WOMEN [OTC])

OXYBUTYNIN (GENERIC)

USES: *Microsporum Canis infections (oral, skin, scalp).*


DOSE: Adults & Peds: PO: 400, 200–400, 600 U PO “wash & swallow” QID. Vag: 1 tab Vag hs 2 or hs, Topical: Apply BID–TID to area.

Ped Infants: 200,000 U PO q6h.

W/P: [B, ?/L, ?/O].

DISP: PO susp 100,000 U/mL; PO tabs 500,000 U; capsules 200,000 U; Vag tabs 100,000 U; topical ointment 100,000 U/g. Powder 100,000 U/g.

SE: GI upset, 5%. Not for systemic infections; see also transepidermal forms.

NFLOXACIN (FLOXIN)

WARNING: *Risk Achilles tendon rupture and tendinitis. 3 yr or pts >60 yr, on steroids or with organ transplant; avoid w/ myasthenia gravis, may ↑ weakness.

USES: *Lower resp tract, skin, skin structure, & UTI, prostatitis, uncomp mononucleosis, & Chlamydia infections.*


DOSE: Adults: 200–400 mg PO BID or tr q12h. ↓ in renal impairment, take on empty stomach.

W/P: [B, ?/L, ?/O]. Absorption w/ antacids, sucralfate, H2, CYP3A4 inhibit, CYP2C9, and CYP2C19; highly protein bound, ↑ by antacids, sucralfate, H2, CYP3A4, CYP2C9, and CYP2C19; highly protein bound, may be displaced by other highly bound drugs. Risk of CVA, QT interval, memory impairment; ER form empty shell expelled in stool.

SE: Diarrhea, headache, constipation, dizziness. NOTES: ODT contains phenylalanine. No single IV dose ≥ 8 mg.

ONDANSETRON, ORAL SOLUBLE FILM (ZUPLENZ)

USES: Prevent chemotherapy-induced & postop N/V.

ACTIONS: Serotonin receptor (5-HT3) antagonist.

DOSE: Adults: Highly emetogenic chemo: 24 mg 8 mg film 30 min prechemo; HT all IV: 8 mg film 10D. Adults & Peds: ≥ 32 yr: Mod emetogenic chemo: 8 mg film 30 min prechemo, then 8 mg in 8 hr; 8 mg film 900 mg × 1–2 days after chemo.

Adults: Postop: 1 mg 8 mg film 30 min × 2 hr preop; ↑ w/ hepatic impairment.

W/P: (B, ?/L, ?/O).

C: Apomorphine.

DISP: Oral soluble film 4, 8 mg.

SE: Use w/ dry hands, do not chew/swallow, place on tongue, dissolve in 4–20 s. peppermint flavored.

OSPEMIFENE (OSPHENA)

WARNING: *Risk endometrial Ca, ↑ risk of CVA, DVT.*

USES: *Treatment of moderate–severe dyspareunia.*

ACTIONS: Estrogen agonist/antagonist.

DOSE: Adults: 1 tab daily.

W/P: [B, ?/L, ?/O]. Do not use w/ estrogens and estrogen agonist/antagonists, fluconazole & rifampin ↑ effect, ketonazole ↓ effect. ↑ tab effects w/ drugs that inhibit CYP3A4 and CYP2D6. High protein bound, may be displaced by other highly bound drugs.

C: Estrogland glandular bleeding known/expected estrogen-sensitive cancer; pregnancy.

DISP: Tab 60 mg.

SE: DVT, hemorhorax or thrombotic stroke, arterial thromboembolism cl, hot flashes; vaginal discharge; hypoestrogenism, muscle cramps, metabolized by CYP3A, CYP2C9, and CYP1A2.

DOSE: Do not use w/ severe liver disease.

OXACILLIN (GENERIC)

USES: *Infections of susceptible S. aureus, Neisseria & other organisms.*

ACTIONS: Bactericidal, 100% wall synth. Spectrum: Excellent gram (+ –), poor gram (+ –).

DOSE: Adults: 250–500 mg (2 g severe) IV or q4–6h.

Ped: 25–300 mg/kg IV q4–6h.

W/P: [B, ?/L, ?/O].

C: FN sensitivity.

DISP: Powder for 10 500 mg, 1, 2. 10 g.

SE: GI upset, interstitial nephritis, blood dyscrasias, may ↓ DSF-effectiveness.

OXYBUTYNIN (DITROPAN, DITROPAN XL, GENERIC)

USES: Relief of symptoms of bladder instability associated with voiding in patients with unobstructed neurogenic or reflex neurogenic bladder (4x, urgency, frequency, urinary leakage, urge incontinence, dysuria). DITROPAN: Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency; pediatric patients <6 yr w/ symptoms of detrusor overactivity associated w/ a neurologic condition (e.g., spina bifida).

ACTIONS: Anticholinergic, relaxes bladder smooth muscle, ↑ bladder capacity.

DOSE: Adults: 5 mg BD-TID; 5 mg every 12hr max. 5–10 mg, 30 mg max.

Ped: ≥ 5 yr: 5 mg PO BD-TID; 15 mg max.

Ped: 1–5 yr: 0.2 mg/kg/day 2–4 mg (group 5 mg/5 mL); 15 mg max.; ↓ to 1 mg in elderly; periodic drug holidays OK.

W/P: [B, ?/L, ?/O].

C: Naurone–angle glaucoma, myasthenia gravis, G6PD, allergic colitis, myoglobin, megaloblastosis.

DISP: Tabs 5 mg; XL tabs 10, 15 mg group 5 mg/5 mL.

SE: Anticholinergic (drowsiness, xerostomia, constipation, tachycardia), QT interval, memory impairment; ER form empty shell expelled in stool.

NOTES: See topical forms of oxybutynin.

OXYBUTYNIN, TOPICAL (GELIQUE)

USES: *Overactive bladder with symptoms of urge urinary incontinence, urgency, frequency.*

ACTIONS: Anticholinergic, relaxes bladder smooth muscle, ↑ bladder capacity.

DOSE: 1 g cadet gel to dry skin (submucosal/urethral/rectal/genera arms).

W/P: [B, ?/L, ?/O].

C: Gastric or urinary retention; narrow–angle glaucoma.

DISP: Gel 10%, 1-g sachets (100 mg oxybutynin).

SE: Anticholinergic (drowsiness, xerostomia, constipation, blurred vision, T HR rise, pruritus, redness, pain at site; UTI).

NOTES: Cover w/ clothing, skin-to-skin transfer can occur; gel is flammable, after applying wait 1 hr before showering.

OXYBUTYNIN TRANSDERMAL SYSTEM (OXYTROL, OXYTROL FOR WOMEN [OTC])

USES: *Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.*

ACTIONS: Anticholinergic, muscarinic antagonist; relaxes bladder smooth muscle, ↑ bladder capacity.

DOSE: One 3.9 mg system apply 2×/wk (q3–4d) to abdomen, hip, or buttock.

W/P: [B, ?/L, ?/O].
OXYCODONE/ACETAMINOPHEN ER (XARTEMIS XR) [CII]

**ACNE**: Acute pain that requires opioids where alternatives are inadequate.

**USES**: Acute pain.

**NOTES**: Do not apply to same site w/in 7 days.

**PACKAGE**: OxyContin 10, 15, 20, 30, 40, 60, 80, 160 mg; liq 4.83 mg oxycodone hydrochloride, 325 mg aspirin; soln 5 mg oxycodone & 325 mg acetaminophen/5 mL.

**INDICATIONS**: Narcotic analgesic w/ NSAID.

**USES**: Mod–severe pain.

**NOTES**: Check renal function; abuse potential w/ oxycodone.

**PACLITAXEL (ABRAXANE, TAXOL, GENERIC)**

**ACNE**: Administration only by physician experienced in chemotherapy; fatal anaphylaxis and hypersensitivity possible; severe myelosuppression possible.

**USES**: Chemoreduction chemotherapeutic agent, non-clear cell lung cancer.

**NOTES**: Myelosuppression.

**OXYCODONE/ACETAMINOPHEN PERCOCET, TYLEX [C-II]

**WARNING**: Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4,000 mg/d, and often involve more than 1 acetaminophen-containing product.

**USES**:Mod–severe pain.

**ACTIIONS**: Narcotic analgesic.

**DOSE**: Adults: 1–2 tablets/caps PO q4–6h PRN (pergadine hydrochloride, 4 mg; oxycodone hydrochloride, 5 mg; aspirin, 325 mg).

**SE**: Allergy, paralytic ileus, resp depression.

**DISP**: Peroral tablets/capsules, extended-release.

**ANNEX**: Component allergy. Relative hepatic and renal impairment. Acute maalaise, dizziness, constipation, abdominal pain.

**NOTES**: Check renal function, abuse potential w/ oxycodone.

**OXYCODONE/ACETAMINOPHEN COMBUNOX [C-II]

**ACNE**: Acute pain that requires opioids where alternatives are inadequate.

**USES**: Acute pain.

**NOTES**: Do not apply to same site w/in 7 days.
**PENICILLIN G BENZATHINE (BICILLIN)**

**USES:** Single-dose regimen for streptococcal pharyngitis, rheumatic fever, gono/borreliosis, syphilis.

**DOSE:** Based on indication range 0.6–24 MU in – doses q4h.

**Pharmacodynamics:**
- Bactericidal; + / †; less effective against meningococci.
- Spectrum: + / †.
- Spectrum: + / † / ††.
- Spectrum: + / † / †† / †††.
- Spectrum: + / † / †† / ††† / ††††.
- Spectrum: + / † / †† / ††† / †††† / †††††.
- Spectrum: + / † / †† / ††† / †††† / †††††.

**Side Effects:**
- Allergic reactions: rash, urticaria, angioedema.
- Cardiovascular: hypotension, bradycardia.
- Gastrointestinal: nausea, vomiting, diarrhea.
- Hematologic: anemia, leukopenia, thrombocytopenia.
- Hepatic: jaundice, cholestasis.
- Renal: acute tubular necrosis.
- Respiratory: wheezing, bronchospasm.
- Skin: rashes, urticaria, angioedema.
- Ophthalmic: photophobia, blurring of vision.

**Precautions:**
- Strict adherence to dosing schedule is essential.
- Pregnancy: Category B.
- Lactation: Generally accepted as safe.
- Children: Doses should be adjusted based on body weight.
- Adolescents: No specific dosage recommendations.
- Elderly: No dose adjustment usually required.
- Renal impairment: No dose adjustment generally required.
- Hepatic impairment: No dose adjustment generally required.
- Allergic reactions: Preceding dose with antihistamines and/or corticosteroids is recommended.
- Drug interactions: Beta-lactamase inhibitors (e.g., clavulanate) may enhance bactericidal activity.

**Pharmacokinetics:**
- Absorption: Rapid intramuscular injection.
- Distribution: Widely distributed in body tissues and fluids.
- Metabolism: Mostly by metabolism in the liver.
- Excretion: Primarily by renal excretion.

**Interactions:**
- OTC: Tylenol, Motrin, Advil, ibuprofen, aspirin.
- Rx: Nonsteroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants.

**Contraindications:**
- Hypersensitivity to penicillins.
- History of anaphylaxis.
- Severe renal or hepatic dysfunction.
- Pregnancy (Category B).
- Lactation.

**Dosage:**
- Adults: 6–9 MU SQ 1–2×/wk; Children: 0.9–1.8 MU/kg/dose q4h.
DOSE: Adults: 1.2–2.4 mg/L, deep 8 lg/mL q–4h.
Ped: 50,000 U/kg/dose, 2.4 mg/dose max.; deep IM q–4 wk.
W/P: [B, M].
CI: Allergy.
DISP: [I] 300,000, 600,000 U/mL; [B] 2–4 mL of benzathine or procaine (300,000 U procaine or 300,000 U benzathine w/ 300,000 U procaine [2 mL]).
SE: [I] oral pain, acute interstitial nephritis, anaphylaxis.
NOTES: IM can only sustain a dosage, w/ levels up to 4 wk; drug of choice for noncongenital syphilis.

PENTASAN POLYSULFATE SODIUM (ELMIRON)

USES: "False paincomfort w/ interstitial cystitis."

ACTIONS: Bladder wall buffer.
K20 mEq/h, max. 40 mEq/h & 150 mEq/d (monitor when the urine pH is >6.5). Use w/ caution in renal insufficiency; metabolic alkalosis. Rule out bowel obstructions before use.

Commonly Used Potassium Supplements

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Salt</th>
<th>Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glu-K</td>
<td>Gluconate</td>
<td>Tablet</td>
</tr>
<tr>
<td>Karon Cl 10</td>
<td>KCI</td>
<td>Tablet, SR</td>
</tr>
<tr>
<td>Karon Cl 20%</td>
<td>KCI</td>
<td>Liquid</td>
</tr>
<tr>
<td>KayCell</td>
<td>KCI</td>
<td>Liquid</td>
</tr>
<tr>
<td>K-lok</td>
<td>K-Cl</td>
<td>Powder</td>
</tr>
<tr>
<td>K-Max Cl</td>
<td>KCl</td>
<td>Effervescent tablet</td>
</tr>
<tr>
<td>Klorveiss</td>
<td>K-Cl</td>
<td>Effervescent tablet</td>
</tr>
<tr>
<td>Micro K</td>
<td>KCI</td>
<td>Tablet, SR</td>
</tr>
<tr>
<td>Micro KCI</td>
<td>KCI</td>
<td>Capsule, SR</td>
</tr>
<tr>
<td>Potassium Chloride 10%</td>
<td>KCI</td>
<td>Liquid</td>
</tr>
<tr>
<td>Potassium Chloride 20%</td>
<td>KCI</td>
<td>Liquid</td>
</tr>
<tr>
<td>Twin K</td>
<td>Chloride</td>
<td>Effervescent tablet</td>
</tr>
</tbody>
</table>

**PROBENECID (PROBANAL, GENERIC)**

**DOSE:**
- Adults: 500 mg PO TID, 1 to 3 wk based on response, 350 mg max, renal impairment (90–100 mg/d or 150 mg PO QID for 3 wk max).
- Initial dose: 500 mg PO QID for 1 wk; then 250 mg PO QID for the remainder of therapy.

**USAGES:**
- Malignant hyperthermia, acute gout.

**ACTIONS:**
- Inhibits urate reabsorption in proximal tubules, competes with urate for renal tubule transport sites.

**SIDE EFFECTS:**
- Headache, GI upset, rash, pruritus, dizziness, palpitations, edema, uric acid kidney stones.

**NOTES:**
- Reduce dose in renal impairment or elderly.

**PROPRANOLOL (INDERAL LA, COMPASS) (PRO-BANTHINE, GENERIC) (GENERIC)**

**DOSE:**
- Adults: 80–220 mg PO QD, 1–2 wk, then 160–240 mg PO QD in 3–4 wk.
- Prophylaxis for migraine headache: 150 mg PO QD for 1 wk, then 100 mg PO bid to 600 mg/day based on response.

**USAGES:**
- Migraine prophylaxis.

**ACTIONS:**
- β-Antagonist.

**SIDE EFFECTS:**
- Headache, GI upset, rash, pruritus, dizziness, palpitations, edema, uric acid kidney stones.

**NOTES:**
- Reduce dose in renal impairment or elderly.

**PROLONGED-RELEASE FORMULATIONS**

**DOSE:**
- Adults: 80 mg PO bid or 160 mg PO qd, titrate to 120–240 mg PO qd max.

**USAGES:**
- Blood pressure control.

**ACTIONS:**
- Increases diastolic pressure.

**SIDE EFFECTS:**
- Headache, palpitations, edema, uric acid kidney stones.

**NOTES:**
- Reduce dose in renal impairment or elderly.

**PYRAZINAMIDE (GENERIC)**

**DOSE:**
- Adults: 250 mg PO QD for 1–2 wk; then 500 mg PO QD for 1–2 wk; then 1,500 mg PO QD for 3 wk max.

**USAGES:**
- Anti-tuberculosis.

**ACTIONS:**
- Bacteriostatic; unknown mechanism.

**SIDE EFFECTS:**
- Headache, GI upset, rash, pruritus, dizziness, blood dyscrasias.

**USES:**
- Anti-tuberculosis.

**NOTES:**
- Reduce dose in renal impairment or elderly.

**PSEUDOSPEHEDRINE (MANY OTC MONO AND COMBINATION BRANDS)**

**DOSE:**
- Adults: Up to 3 mg IV bolus q10min

**USAGES:**
- Retrograde ejaculation.

**ACTIONS:**
- Non-selective α-1 and β-1 blockers.

**SIDE EFFECTS:**
- Headache, palpitations, edema, uric acid kidney stones.

**NOTES:**
- Reduce dose in renal impairment or elderly.
RISEDORANE, DELAYED RELEASE (ATELVIA)

USEs: *Piglet disease; Treatment prevention pneumococci-induced postsurgical osteoporosis, 1 bone mass in osteoporotic men; w/ calcium only FDA approved for female osteoporosis.*

ACTIONS: Bisphosphonate, 1 osteoclast-mediated bone resorption.

DOSE: Piglet disease: 30 mg PO for 2 mo. Osteoporosis Pneumococcal 5 mg daily or 35 mg qwk or 150 mg qtr 30 min before 1st food/drink of the day. pig weight for least 30 min after dose.


NOTES: Desloratadine, as strontium.

RIFAMPIN (RIFADIN, RIMACTANE, GENERIC)

USEs: *TB & treat & prophylaxis of N. meningitidis, H. influenzae, S. aureus, S. pyogenes; adjunct w/ severe infection.*

ACTIONS: *Ribosomal protein synth.*

DOSE: Adults: N. meningitidis & H. influenzae carrier: 600 mg PO for 4 d. ER 600 mg PO or IV daily or 2 × 300 mg w/ combo regimen.

W/P: [C, X+] −; [Fosamprenavir, multiple drug interaction.*

WARNING: Allergy, active fl. meningococcal infection, w/ saquinavir/ritonavir.

DISP: Caps 150, 300 mg; [R, B] +; [S, Y] −.

NOTES:从未 use as single agent w/ active TB.

RISEDORANE, DELAYED RELEASE (ATELVIA)

USEs: *TB & treat & prophylaxis of N. meningitidis, H. influenzae, S. aureus, S. pyogenes; adjunct w/ severe infection.*

ACTIONS: *Ribosomal protein synth.*

DOSE: Adults: N. meningitidis & H. influenzae carrier: 600 mg PO for 4 d. ER 600 mg PO or IV daily or 2 × 300 mg w/ combo regimen.

W/P: [C, X+] −; [Fosamprenavir, multiple drug interaction.*

WARNING: Allergy, active fl. meningococcal infection, w/ saquinavir/ritonavir.

DISP: Caps 150, 300 mg; [R, B] +; [S, Y] −.

NOTES:从未 use as single agent w/ active TB.
Rivaroxaban (Xarelto)

USES:
- Reduces the risk of pulmonary embolism (PE) and deep vein thrombosis (DVT) in patients with medical conditions associated with an increased risk of venous thromboembolism (VTE) who are candidates for thromboprophylaxis in the setting of acute medical illness (AMI), including medical surgery, medical illness, and medical conditions (eg, prolonged immobilization, major medical illness, or major surgery) that require hospitalization.

NOTES: Consider the risk of bleeding vs the benefits of using rivaroxaban, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sirolimus (Rapamune, Zortress)

WARNING:
- May increase the risk of aortic regurgitation and decrease arterial compliance.

USES:
- Used as an immunosuppressant to prevent rejection following organ transplantation.

NOTES: Consider the risk of bleeding vs the benefits of using sirolimus, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silodosin (Rapaflo)

USES:
- Used as a 5-alpha reductase inhibitor to treat benign prostatic hyperplasia (BPH).

NOTES: Consider the risk of bleeding vs the benefits of using silodosin, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sevelamer Hydrochloride (Renagel)

USES:
- Used to bind phosphate in the gut and lower serum phosphorus levels in patients with renal failure to prevent the development of secondary hyperparathyroidism.

NOTES: Consider the risk of bleeding vs the benefits of using sevelamer hydrochloride, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silver Nitrate (Generic)

USES:
- Used to remove granulation tissue and warts, treat prostatitis, and prevent urinary tract infection.

NOTES: Consider the risk of bleeding vs the benefits of using silver nitrate, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silver Sulphadiazine (Silvadene, Generic)

USES:
- Used as a topical antiseptic to prevent and treat infection in 2nd- and 3rd-degree burns.

NOTES: Consider the risk of bleeding vs the benefits of using silver sulphadiazine, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sipuleucel-T (Provenge)

USES:
- Used to treat asymptomatic or minimally symptomatic metastatic castrate-resistant PCa.

NOTES: Consider the risk of bleeding vs the benefits of using sipuleucel-T, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sildenafil (Viagra, Revatio)

USES:
- Used to treat erectile dysfunction in men who have vardenafil or tadalafil intolerance.

NOTES: Consider the risk of bleeding vs the benefits of using sildenafil, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sargramostim (GM-CSF, Leukine)

USES:
- Used to stimulate myeloid recovery following bone marrow transplantation.

NOTES: Consider the risk of bleeding vs the benefits of using sargramostim, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silodosin (Rapaflo)

USES:
- Used as a 5-alpha reductase inhibitor to treat benign prostatic hyperplasia (BPH).

NOTES: Consider the risk of bleeding vs the benefits of using silodosin, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sevelamer Hydrochloride (Renagel)

USES:
- Used to bind phosphate in the gut and lower serum phosphorus levels in patients with renal failure to prevent the development of secondary hyperparathyroidism.

NOTES: Consider the risk of bleeding vs the benefits of using sevelamer hydrochloride, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silver Nitrate (Generic)

USES:
- Used to remove granulation tissue and warts, treat prostatitis, and prevent urinary tract infection.

NOTES: Consider the risk of bleeding vs the benefits of using silver nitrate, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Silver Sulphadiazine (Silvadene, Generic)

USES:
- Used as a topical antiseptic to prevent and treat infection in 2nd- and 3rd-degree burns.

NOTES: Consider the risk of bleeding vs the benefits of using silver sulphadiazine, especially in patients with a bleeding tendency or those at increased risk for bleeding.

Sipuleucel-T (Provenge)

USES:
- Used to treat asymptomatic or minimally symptomatic metastatic castrate-resistant PCa.

NOTES: Consider the risk of bleeding vs the benefits of using sipuleucel-T, especially in patients with a bleeding tendency or those at increased risk for bleeding.
SODIUM BICARBONATE

USES: Alkalization of urine, RTA, metabolic acidosis, \( \text{K}^{+} \), \( \text{H}^{+} \), tricyclic antidepressants OD, alkalize bladder prior to transcatheter retrograde ejaculation.

ACTIONS: Alkalizing agent.

DOSE: Adults: EICC 2010: Cardiac arrest w/ good ventilation, hydration, O2 of TCA, ASA, ouabain, diphosphopyridine: 1 mEq/kg IV bolus; repeat 1/2 dose q15min PHN. Metabolic acidosis: 2–5 mEq/kg IV over 6 hr & PHN based on acid-base status. 
- \( \text{K}^{+} \): 50 mEq IV over 5 min. Alkalize urine: 4.4 mEq/kg PO, then 12–24 mEq q6h. Adjust based on urine pH. 2 amp (100 mEq) IV IV at 100–250 mL/h. Monitor urine pH & serum bicarbonate. chronic renal failure: 1–3 mEq/l. D5W: 0.5–2 mEq/1 in 4–5 doses.
- Peds: Severe metabolic acidosis, hyperkalemia: 1 mEq/kg IV slow bolus. 4.2% in Infusion: 1–1.5 m. Chronic renal failure: See Adult dosage. D5W: TMA: 2–3 mEq/kg PO. Proximal RTA: 5–10 mEq/kg. titrate based on serum bicarbonate. urine alkalization: 84–840 mEq (10–100 mEq) in – dosing. Adjust based on urine pH.
- W/P: [C, 7].
- CI: Alkalosis, \( \text{Na}^{+} \), severe pruritus (using \( \text{Ca}^{2+} \)).
- DISP: PO: tablets: 325 mg = 3.8 mEq; 810 mg = 7.6 mEq IV (1 mEq/l IV), 4.2 (5 mEq/10 mL). 5.5 (8.85 mEq/10 mL). 8.4 (10 mEq/5 mL) vial or amp.
- SE: Nausea, vomiting, diarrhea, rash, \( \text{Na}^{+} \), metabolic alkalis.
- NOTES: \( 1 \text{g neutralizes} 12 \text{mEq of acid} \), \( 50 \text{mEq bicarbonate} = 50 \text{mEq} \text{KCl} \), can make 3 amp 1 L D5W w/ 150 mEq bicarbonate.

SODIUM CITRATE/CITRIC ACID (ORACIT)

USES: Chronic metabolic acidosis, alkalize urine; dissolve acid urolithiasis urine.

ACTIONS: Urinary alkalinization.

DOSE: Adults: 10–30 mL in 1–3 oz H2O q8–12 h & hs or by mouth. 
- Peds: 5–15 mL in 1–3 oz H2O q8–12 h & hs; best after meals.
- W/P: [C, 7].
- CI: Severe renal impairment, oliguria or azotemia, uncontrolled Addison’s disease, adynamia episodic hernia, acute dehydration, heat cramps, anuria, severe myocardial damage, and hypokalemia.
- DISP: 15–30 mL unit dose: 16 (673 mL) or 4 oz.
- SE: Tasting, metabolic alkalinosis, \( \text{K}^{+} \). Gluconate, avoid use of multiple 35 mL amp; can cause ↑ \( \text{Na}^{+} \) hyperosmolality.
- NOTES: \( 1 \text{mL} = 1 \text{mEq Na} \& 1 \text{mEq bicarbonate.} \)

SODIUM PHOSPHATE (OSMOPREP, VISICOL)

WARNING: Acute phosphate nephropathy reported w/ permanent renal impairment risk; \( \text{K}^{+} \), hyperkalemia, bowel obstruction, baseline kidney disease, w/ meds that affect renal perfusion/function (eg, diuretics, ACE inhibitor, ARB, NSAIDs).

USES: Bowel prep prior to colonoscopy in adults, short-term constipation.

ACTIONS: Hypo-osmotic laxative.

DOSE: Peds: PO w/ at least 8–10 oz H2O q6h. 15–20 mL for 6 doses; then 2 additional tabs in 15 min, 3–5 hr prior to colonoscopy. 1 tab q6h for 6 doses, then 2 additional tabs in 15 min.
- W/P: [C, ] renal impairment, electrolyte disturbances.
- CI: Megacolon, bowel obstr.
- DISP: Tabs: 0.388, 1.02 g (32/16 tablets).
- SE: QT \( \uparrow \), PMI, 4–6 cardiac arrest, delirium, hallucinations, convulsions, abdominal bloating/ cramping.
- NOTES: Acute phosphate nephropathy is associated w/ calcium phosphate crystal deposits in the renal tubules and may result in permanent renal dysfunction. Risk factors for acute phosphate nephropathy: Age <55 yr, hyperkalemia, pre-existing renal impairment, bowel obstruction, or acute colitis; \( \text{K}^{+} \) meds that may affect renal perfusion/function (eg, diuretics, ACE inhibitors, ARBs and possibly NOX).
- SE: Hypokalemia, paralytic ileus, constipation, severe electrolyte disturbances, abdominal pain, nausea, vomiting, diarrhea.
- NOTES: Monitor BP 1st 6 hr; may require \( \text{K}^{2+} \) dose (daily or no other day). Severe hypophosphatemia (\( \leq 1.5 \text{mEq/l} \)), \( \text{Na}^{+} \), alkalosis, \( \text{K}^{+} \), hyperkalaemia.
- DISEASES: Balkan dialysis, \( \uparrow \) AKI.

SODIUM POLYSTYRENE SULFONATE (KAYEXALATE, KONEX, GENERIC)

USES: Treat of \( \uparrow \text{K}^{2+} \).

ACTIONS: Na\( ^{+} \text{K}^{2+} \) ion-exchange resin.

DOSE: Adults: 15–60 g PO or 30–50 g PR q8h based on serum \( \text{K}^{+} \).
STARCH, TOPICAL, RECTAL (TUCKS SUPPOSITORIES [OTC])

USING: Temporary relief of itching, pruritus, rash

DOSE: Topical protectant

W/P: [?, ?]

STEROIDS, SYSTEMIC (SEE TABLE AT BOTTOM OF PAGE)

The following relates only to the commonly used systemic glucocorticoids.

DOSE: Varies w/ use & institutional protocols.

• Adrenal insufficiency, acute: Adults: Hydrocortisone: 100 mg IV then 300 mg/d — q8h for 48 hr then convert to 50 mg PO q8h = 6 doses, taper to 30–50 mg — BID. Peds: Hydrocortisone: 1–2 mg/kg daily then 150–250 mg daily — q6–8h.

• Adrenal insufficiency, chronic (physiologic replacement): May need mineralocorticoid supplement such as Florinef: Adults: Hydrocortisone: 20 mg PO q a.m., 10 mg PO p.m.; cortisone: 25–35 mg PO daily. Dexamethasone: 0.3–0.5 mg/d or 0.6–0.75 mg q14–q16 hr; 4–12 mg PO, IM, IV. Peds: Hydrocortisone: 8–10 mg/m2/d — q6h; some may require up to 12 mg/m2/d. Hydrocortisone succinate: 0.25–0.35 mg/kg/d.

• Adrenal, acute: Adults: Methylprednisolone 40–80 mg/d IV in 1–2 doses PO or IV over 30–60 min — q8h. Peds: Prednisolone 1–2 mg/kg/d or prednisone 1–2 mg/kg/d — daily – BID for up to 5 days. methylprednisolone 12 mg IV q8h — BID; dexamethasone 0.1–0.3 mg/kg — q6h.

• Congenital adrenal hyperplasia: Peds: Initial hydrocortisone 10–30 mg/m2/d in 3–4 doses.

• Status asthmaticus: Adults: Dexamethasone: 0.5–2 mg/kg IV (M, q12h — q8h, then 0.5–1 mg/kg/d IV or IM — BID (if tolerated). Peds: Dexamethasone: 0.5–2 mg/kg — q6h (start 24 hr before & cont for 4–6 doses after extubation).

• Immunosuppressant—corticosteroids:
  • Adults: Prednisone: 50–60 mg PO q24h (start at 0.5–1 mg/kg/d — BID (if tolerated).
  • Adults: Hydrocortisone: 15–240 mg PO q6h (M, q12h — q8h, then 0.5–1 mg/kg/d IV — BID (if tolerated).

• Rheumatic disease: Adults: Prednisone: Prednisolone: 2–4 mg/kg/d PO or IV — q6h. Peds: Hydrocortisone: 1–2 mg/kg/d intermittent or continuous inf. may thrice up to 50 mg/h.

• Status asthmaticus: Adults & Peds: Hydrocortisone: 1–2 mg/kg IV q4h for 24 hr; then q6h (start at 0.5–1 mg/kg/d). Dexamethasone: 0.5–2 mg/kg IV q8h (start 24 hr before & cont for 4–6 doses after extubation).

• Hydrocortisone: Use lowest potency product for shortest period for effect (see Table next page)

Commonly Used Systemic Steroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Relative Equivalent</th>
<th>Relative Mineralocorticoid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose (mg)</td>
<td>Activity</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>0.75</td>
<td>0</td>
</tr>
<tr>
<td>Beclomethasone (Decadron)</td>
<td>0.75</td>
<td>0</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Methylprednisolone succinate (Depo-Medrol)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Prednisolone (Deltasone)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Prednisolone (Deltas-Cort)</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

neuromuscular blockage w/ respiratory paralysis. Administer or application may cause adrenal suppression or hyperglycemia. 

USES: * Neuro/oto/renal toxicity possible; Skin atrophy w/ chronic use; chronic

SE: * Monitor levels: Peak: 20–30 μg/mL, trough: <5 μg/mL, TAC peak: >50, TAC: 

DOSE: Adults: 1 g, max 3 g/weight (max: 1 g). PO: 15 mg/kg/dose w/ CYP3A4 inhibitor, 

STRONTIUM-89 CHLORIDE (METASTRON) 

USES: Bone pain in patients with various metastatic.

ACTIONS: Ca\(^{2+}\) analogues taken up by bone in areas of active osteogenesis with selective radiation of metastasis.

DOSE: 148 MBq (4 mCi) IV slowly, or 15–22 MBq/kg. W/P [D, −].

DISP: Intrathecally.

SE: Patients nadir about 12–16 wk after treatment.

DOSE: Adults: Chew 500 mg TD w/ meals; may 1 dose weekly to target phos <5 mg/dL; max. dose studied 3,000 mg/d.

W/P: [D, −].

DISP: Tab 500 mg.

SE: None. 

REFERENCES: None. 

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose.

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose.

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.

DOSE: Adults: 50 mg PO daily, = 4 wk, followed by 2 wk holiday. 1 to 37.5 mg or 5.5 mg/dL; max. dose studied 20–30 mg/kg/dose. 

DISP: Caps 12.5, 25, 50 mg.

SE: None. 

W/P: PO, −. Multiple interactions require dose modification (eg, St. John’s wort), TNF and S15 reported.
TACROLIMUS, EXTENDED RELEASE (ASTAGRAF XL)

NOTES: Monitor left ventricular ejection fraction, CO, CBC, CMP, chemistry (K, Hg, Na, PO₄, glucose), TSH & TFTs periodically; ↓ dose in 2.5 mg increments if not tolerated.

TACROLIMUS, EXTENDED RELEASE (ASTAGRAF XL)

WARNING: Only physicians experienced in immunosuppression should prescribe. ↑ Risk of malignancy; use in heart transplant not recommended for frailty in female patients. USES: "To kidney transplant rejection w/ MMF and steroids, w/ or w/o basiliximab induction."

ACTIONS: Calcineurin inhibitor/immunosuppressant.

DOSE: → w/ basiliximab induction: 0.15 mg/kg/day (target level day 1–6: 5–17 ng/mL; Mon 3–12: 4–12 ng/mL). w/o induction: Peak 0.1 mg/mL; postop 0.2 mg/mL (target level Day 1–6: 6–20 ng/mL; Mon 3–12: 6–14 ng/mL). Take daily a.m.; empty stomach; do not take w/ alcohol or grapefruit juice; take whole.

W/P: [C, -] → not interchangeable w/ immediate release; follow glucose, Cs, K*, can ± BP can ± QT interval; do not use w/ sirolimus, CYP3A4 inhibitors, avoid live vaccines, monitor for red cell aplasia w/ Cytoxan; avoid topical if <2 yr; Neuro & nephrotoxic, ↑ risk opportunistic infections; avoid grapefruit juice.

Cl: Component allergy, castor oil allergy w/ IV form.

DISP: ER Caps 0.5, 1, 5 mg.

SE: N, constipation, edema, tremor, anemia.

NOTES: Monitor levels; African Americans may need ↓ dose; use tacrolimus immediate release.

TACROLIMUS, IMMEDIATE RELEASE (PROGRAF, GENERIC)

WARNING: ↑ Risk of infection and lymphoma. Only physicians experienced in immunosuppression should prescribe.

USES: "Prevent organ rejection (kidney/heart/liver)."

ACTIONS: Calcineurin inhibitor/immunosuppressant.

DOSE: Adults: IV: 0.03–0.05 mg/kg in kidney and liver, 0.03 mg/kg in heart or liver. Peds: IV: 0.03–0.05 mg/kg as cont inf. PO: 0.15–0.2 mg PO = 0.18. Adults & Peds: Femoral → empty stomach; ↓ w/ hepatic impairment.

W/P: [C, -] → w/ Cytoxan; avoid topical if <2 yr; Neuro & nephrotoxic, ↑ risk opportunistic infections; avoid grapefruit juice.

Cl: Component allergy, castor oil allergy w/ IV form.

DISP: Caps 0.5, 1, 5 mg, 10 mg.

SE: HTN, edema, headache, insomnia, fever, pruritus, ↑2 K*, hyperglycemia, GI upset, anemia, leukopenia, tremors, pancreatitis, pleural effusion, seizures, lymphoma, PPIs, GI nephrotoxicity, PNH.

NOTES: Monitor levels; ↑ glucose, 5–12 ng/mL, based on indication and time since transplant.

TADALAFIL (CIALIS)

USES: Erectile dysfunction, BPH, alone or together.

ACTIONS: PDE5 inhibitors, ↑ cyclic guanosine monophosphate (cGMP) & NO levels; relax smooth muscles, dilates coronary arteries, 15–120 min, duration 24–36 hr.

DOSE: Adults: IV: 10 mg PO before sexual activity (5–20 mg max. based on response). 1 dose/24 h. Daily dosing: 2.5 mg PO, may ↑ to 5 mg PO, w/o regard to meals. BP therapy related with tadalafil and fosfomorphate, nadalid dose is 5 mg for up to 26 wk; ↓ w/ renal/hypertensive dysfunction, 5 mg not more than once in every 72 hr or ↓ O(2) <30 mmHg/ERD on dialysis.

W/P: [B, -] → w/ Blockers (except tamsulosin), use w/ CYP3A4 inhibitor 2.5 mg/day dose or 5 mg PNU dose; ClO = 0 mL/min; HTN/diabetes/severe hepatic impairment, do not use daily dosing.

Cl: Therapeutic.

DISP: Tabs: 2.5, 5, 10, 20 mg.

SE: Headache, flushing, dyspnea, back/limb pain, myalgia, nasal congestion, urticaria, SJS, dermatitis, angioedema, intraoperative floppy iris syndrome.

NOTES: Longest acting of class (36 hr); daily dosing may ↑ drug interactions; excessive EOD may ↑ orthostasis, transient global amnesia report; not recommended in combo w/ α-blocker for BPH.

TAMSULOSIN (FLOMAX, GENERIC)

USES: "BPH: medical therapy for urinary stenosis.

ACTIONS: Antagonist of prostatic α-receptors.

DOSE: 0.4 mg/day, may ↑ 0.8 mg PO daily.

W/P: [B, ?] [↑] Flapcy's syndrome w/ cataract surgery. DISP: Caps 0.4 mg.

SE: Headache, dizziness, syncope, somnolence, ↓ BP; ↓ renal, metabolic, cardiovascular, orthostatic hypotension (OHN), sudden, ↓ loss of hearing, retention.

NOTES: Longest acting of class (36 hr); daily dosing may ↑ drug interactions; excessive EOD may ↑ orthostasis, transient global amnesia reports; not recommended in combo w/ α-blocker for BPH.

TERBINAFINE (TORISEL, GENERIC)

USES: "Antifungal agent.

ACTIONS: Multikinase inhibitor, ↓ mTOR (maximum target of rapamycin), ↓ hypoxic-induced factors, ↓ VEGF.

DOSE: 25 mg IV 30–60 min 1 x/wk. Hold w/ ANC <1,000 cells/uL, ↓ ph = 75–700 cells/uL, or NC1 grade 3. Revise when tox grade 2 or less, restart w/ dose ↓ 2.5 mg not <15 mg/kg w/ CYP3A4 inhibition; ↓ 12.5 mg/kg w/ CYP3A4 inhibitors; ↓ 50 mg/kg.

Cl: [B, -] → Avoid live vaccines, ↓ wound healing, avoid psoralen.
TESTOSTERONE, IMPLANT (TESTOPEL) [C-II]

USES: "Male hypogonadism (congenital/acquired)."

ACTIONS: Testosterone replacement.

DOSE: 150-450 mg (2-6 pellets) SQ implant (implant two 75-mg pellets for each 25-mg testosterone required weekly, eg, for 75-mg pellets, implant 450 mg of 6 pellets).

W/P: [X, — May cause polyuria, worsening of BPH Sx, prostate cancer: patients may use O2, CrF; may use O2, increased glucose and insulin requirements; venous thrombosis risk.

Cl: PSA, male breast CA, PRG woman.

DISP: 75 mg implant (3.2 mm × 9 mm).

SE: Pain/Inflamm at site, gynecomastia, excessive sweating, dizziness, hirsutism, male pattern baldness, acne, retention of sodium and edema, suppression of clotting factors, polyuria, Na, jaundice, T 4/Thyroxine, anterior pituitary hormones, NE, hypothyroidism, and pelvis hepatitis, 11β lipoid, sleep apnea, T PSA.

NOTES: Check levels and adjust PRN (500–1,000 ng/dL testosterone range). Follow periodic DPT and CBC; typical site upper outer posterior gluteal region using sterile technique. Local anesthesia. 4 mm stab wound and provided 166 insertion trocar.

TESTOSTERONE, NASAL GEL (NATESTO) [C-II]

WARNING: Utilization reported in children exposed to topical testosterone products. Children to avoid contact w/ unwashed or unclothed application sites.

USES: "Adult male hypogonadism (congenital/acquired)."

ACTIONS: Testosterone replacement.

DOSE: 2 pumps each nostril (11 mg testosterone) in each nostril; T/D (total 33 mg/3); blow nose before use; avoid bleaching for 1 hr after.

W/P: [X, — Avoid with nasal pathology, monitor BPH Sx and for DVT, may cause azoospermia, edema, sleep apnea; not rec if < 19 yr, venous thrombosis risk.

CI: Prostate cancer, male breast cancer, women.

DISP: Metered-dose pump; 1 pump = 5.5 mg of testosterone.

SE: 1 PSA, headache, rhinorrhea, epistaxis, nasal discomfort, nasal polyps, broken, OI, CrF, nausea, nasal scale; 1 pump = 5.5 mg of testosterone.

NOTES: Previously known as Complexx/RT, may minimize exposure of testosterone to women or children; check testosterone, PSA, Hgb, LFTs, and lipids periodically.

TESTOSTERONE, TOPICAL (ANDROGEL 1%, ANDROGEL 1.62%: ANDRODERM, AXIRON, FORTESTA, STRIANT, TESTIM, VOGELXO) [C-III]

WARNING: Utilization reported in children exposed to topical testosterone products. Children to avoid contact w/ unwashed or unclothed application sites.

USES: "Male hypogonadism (congenital/acquired)."

ACTIONS: Testosterone replacement; 1 lean body mass, libido.

DOSE: [X, — 1,250 mg IM (glucose) initially, at 4 wk, every 10 wk thereafter; observe for 30 min for POME or anaphylaxis.

W/P: [X, — May worsen BPH Sx, azoospermia possible, edema with pre-existing cardiac/hepatic/renal Dz, sleep apnea with other risk factors, monitor PSA, headache; lifespan periodically, monitor Hb if on warfarin; we sendees may ↑ fluid retention; venous thrombosis risk.

Cl: PSA, male breast cancer, women, component unsuitability.

SE: Acne, injection-site pain, T PSA and estradiol, hypertension, fatigue, irregularity, T hemoglobin, insomnia, mood swings.

NOTES: Available only through a restricted program (Evident REMS); other ftms do not commonly used; testosterone enanthate (Delatestryl, Genrin) / testosterone cypionate (Depo-T, Testoderm) dose 144-288 w/ variable serum levels.

TETRACYCLINE (GENERIC)

USES: "Broad-spectrum antibiotic."


DOSE: Adults: 250–500 mg PO BID–QID.

PE: [X, — 8 yr; 25–50 mg/kg/24 h PO Q6–12h; w/ renal/hepatic impairment, no food preferred.

W/P: [X, —]

Cl: PREGNANCY, children < 8 yr.

DISP: Caps 100, 250, 500 mg; tabs 250, 500 mg; PO susp 250 mg/mL.

SE: Photosensitizy, GI upset, renal failure, pseudomembranous colitis, hepatic impairment.

NOTES: May cause some rash, if not severe, severe dose formation in children; do not administer w/ antacids or milk products.

TICAGRELOR (BRILINTA)

WARNING: Bleeding risk; can be fatal, daily aspirin > 700 mg may ↓ effectiveness; do not start w/ active bleeding. He intracranial bleed, planned CABG, if hypersensitive and recent procedure, suspect bleeding manage any bleed w/ DVT of eczepel.

USES: "J. CV death and heart attack in ACS."

ACTIONS: Oral antiplatelet; reversibly binding ADP receptor antagonists in GPIb.

DOSE: Initial 180 mg PO w/ ASA 325, then 90 mg BID w/ ASA 75–100 mg.

W/P: [X, —] w/ Mod hepatic impairment; w/ strong CYP3A inhibitors or CYP3A inducers.

Cl: pH extracranial bleed, active pathologic bleeding, severe hepatic impairment.

DISP: Tab 90 mg.

SE: Bleeding, SOB.

NOTES: REMS; D/C 5 days prepro.
**TICARCILLIN/POTASSIUM CLAVULANATE (TIMENTIN)**

**USES:** Infections of the skin, bone, resp & urinary tract.

**ACTIONS:** Carbapenem; β-lactamase inhibitor; Gram-negative; anaerobic; Gram-positive; susceptible to β-lactamase.

**DOSE:**
- **Adults:** PO 3.1 g IV q4–6h max. 24 g ticarcillin/2 g clavulanate.
- **Children:** PO 100 mg/kg/dose IV q8h; max. 24 g ticarcillin/2 g clavulanate.
- **Infants:** PO 50–100 mg q6h–q8h.

**NOTES:**
- Elderly: ↑ dose w/ renal insufficiency.
- GI upset; rash; angioedema; urticaria; anaphylactic; anaphylactic shock; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia.

**TRAMODOL (RYBIX ODT, RYZOLT ER, ULTRAM, ULTRAM GENERIC) (C-IV)**

**USES:** Mod–severe pain.

**ACTIONS:** Centrally acting synthetic opioid analgesic.

**DOSE:** Adults: 50–100 mg PO q4–6h PRN; start 25 mg PO q6–8h; 1–2 tab to 25 mg PO QD, 1–50 mg Q4–6h (max 400 mg/d 100 mg q4–8h); 0.625 mg–5 mg/mL; 1–2 tab q4–8h; max. 400 mg/d.

**NOTES:**
- Elderly: ↓ dose w/ renal insufficiency.
- GI upset; rash; angioedema; anaphylaxis.
- Avoid EtOH; do not cut, chew ODT tabs.
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants);
- Seizures risk w/ psychotropic drugs.
- Seizures risk w/ anticonvulsants; GI upset; rash; angioedema; anaphylaxis.

**TROMBAYCIN (NEBCIN)**

**USES:** Serious gram − infections.

**ACTIONS:** Aminoglycoside; β-protein synth. Spectrum: β-lactamase.

**DOSE:**
- **Adults:** Conventional dosing: 1–2.5 mg/kg/dose IV q8h–q12h. Once-daily dosing: 5–7 mg/kg/dose q24h.
- **Pediatrics:** 1 mg/kg/dose IV q8h or q12h.

**NOTES:**
- ↑ dose w/ renal insufficiency.
- GI upset; rash; angioedema; anaphylaxis.
- Avoid EtOH; use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants).
- Use cautiously in hepatic/renal insufficiency (w/ anticonvulsants; GI upset; rash; angioedema; anaphylaxis).

**TOBRAMYCIN (THIOLA)**

**USES:** Infections.

**ACTIONS:** Aminoglycoside; β-protein synth. Spectrum: β-lactamase.

**DOSE:**
- **Adults & Peds:** 1 mg/kg dose IV q4–6h max. 2 tab PO q4–6h max. 100 mg w/ renal insufficiency.

**NOTES:**
- ↑ dose w/ renal insufficiency.
- GI upset; rash; angioedema; anaphylaxis.
- Avoid EtOH; use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis).

**TIOCONAZOLE (NERITIN) (OTC)**

**USES:** Vaginal fungal infections.

**ACTIONS:** Topical antifungal.

**DOSE:**
- **Adults:** PO 250–500 mg.
- **Children:** PO 50 mg; ER 100, 200, 300 mg; Rybix ODT 100 mg.

**NOTES:**
- Avoid EtOH; abuse potential d/t prodrug.
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants).
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis).

**TICARCILLIN/POTASSIUM CLAVULANATE (TIMENTIN)**

**USES:** Infections of the skin, bone, resp & urinary tract.

**ACTIONS:** Carbapenem; β-lactamase inhibitor; Gram-negative; anaerobic; Gram-positive; susceptible to β-lactamase.

**DOSE:**
- **Adults:** PO 3.1 g IV q4–6h max. 24 g ticarcillin/2 g clavulanate.
- **Children:** PO 100 mg/kg/dose IV q8h; max. 24 g ticarcillin/2 g clavulanate.
- **Infants:** PO 50–100 mg q6h–q8h.

**NOTES:**
- Elderly: ↑ dose w/ renal insufficiency.
- GI upset; rash; angioedema; anaphylactic; anaphylactic shock; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia; hypocalcemia; hypomagnesemia; hypophosphatemia; hyperkalemia.

**TRAMODAL/ACETAMINOPHEN (ULTRACET) (C-IV)**

**USES:** Short-term treat acute pain (<5 days).

**ACTIONS:** Centrally acting synthetic opioid analgesic.

**DOSE:** 2 tabs PO q4–6h PRN; 1 tab max.

**NOTES:**
- Avoid EtOH; use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants).
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis).

**TOLERODINE (DETROL, DETROL LA, GENERIC)**

**USES:** Overactive bladder with symptoms of urgency, urinary incontinence, urge, and frequency.

**ACTIONS:** Anticholinergic; muscarinic receptor antagonist.

**DOSE:**
- Detrol: 1–2 mg PO BID, Detrol LA: 2–4 mg LA.
- ER, GENERIC: 1–2 mg LA PO q24h.

**NOTES:**
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis)

**TIOCONFLOX (THIOLA)**

**USES:** Prevent cystine urolithiasis in patients with severe homozygous cystinuria with urinary cystine >500 mg/dl, who are resistant to conservative measures. High fluid intake, alkali and diet modification, or have adverse reactions to β-lactam.

**ACTIONS:** Prevents cystine urolithiasis in patients with severe homozygous cystinuria with urinary cystine >500 mg/dl, who are resistant to conservative measures. High fluid intake, alkali and diet modification, or have adverse reactions to β-lactam.

**DOSE:**
- **Children:** PO once-daily dosing: 1–2 mg/kg/dose IV q8h (at least 15 mg/kg/dxl divided 4 doses); 1 mg/kg/dose IV q12h (at least 15 mg/kg/dxl divided 2 doses).
- **Adults & Peds:** 50 mg PO q6h; 25 mg PO q4h.

**NOTES:**
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis).
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
- Use cautiously in chronic pain (w/ tranquilizers or antidepressants; GI upset; rash; angioedema; anaphylaxis).

**TRIMETHOPRIM/SULFAMETHOXAZOLE (TRIMOPRIM/SULFADIAZINE)**

**USES:** Antifungal & anti-inflammatory.

**DOSE:** Apply lightly to area BID; max. 25 mg/d.

**NOTES:**
- Variants: systemic fungal infections.
- Use cautiously in hepatic/renal insufficiency; severe renal insufficiency.
SE: Local irritation, hypertrophic, pigment changes.
NOTES: For short-term use (~7 days). See also nystatin.

TRIAMTERENE (OXYBENNUM)
WARNING: Hyperkalemia can occur.
USES: Edema associated w/ CHF, cirrhosis.
ACTIONS: K⁺ sparing diuretic.
DOSE: Adults: 50–100 mg PO QD – 2×4 wk; q1–4 wk.
W/P: [C (expert opinion), 1].
CI: K⁺, renal impairment; caution w/ other K⁺ sparing diuretics.
DISP: Caps 50, 100 mg.
SE: —.

TRIETHYLENETHIOPHOSPHORAMIDE (THIOPETA)
USES: Breast, ovarian cancer, lymphomas (cholecyturic used) prophylactic regimen for alliegenic & ABMT w/ high doses, intravesical for bladder cancer, Intravesical effusions.
ACTIONS: Polyfunctional antithymic agent.
DOSE: For protocol typical 0.3–0.4 mg/kg IV q1–4 wk. Eflornithine: Intravesical 0.6–0.6 mg/kg 60 mg into the bladder & retained 2 hr q1–4wk; 900–125 mg; in ABMT regimen (highest dose w/o ABMT is 160 mg/kg), 4 in renal failure.
W/P: [D, —] w/ IF suppression, renal and hepatic impairment.
CI: Component allergy.
DISP: Hg 15 mg.
SE: —.

TRIETHYLMETHOXAZOLE & SULFAMETHOXAZOLE (SMX) [CO-TRIMOXAZOLE, TMP-SMX] (BACTRIM, BACTRIM DS, SEPTRAS, DS, GENERIC)
USES: U/TI, Trichomoniasis, Chlamydia, Shigellosis, Pneumonia by gram +, – organisms; PO Treat w/ dapsone & ABMT w/ high doses, Intravesical for bladder cancer, Synergistic combo, interacts w/ warfarin.
ACTIONS: Synthetase inhibitors. Close monitoring required for patients w/ preexisting renal impairment.
DOSE: Adults: 60 mg PO SID or 20 mg/kg/24 h IV in 1–2 doses; PCP: 15–20 mg/kg IV or PO (TMP) in 4 doses; Nocardia: 10–15 mg/kg IV fr PO (TMP) in 4 doses; IV, prophylactic; 1 g PO SID.
W/P: [C (D if near term), —].
CI: —.
SE: —.

TRIHYDROXALIC ACID, SULFUR 
USES: Synergistic action, interacts w/ warfarin.
ACTIONS: Synergistic combo, interacts w/ warfarin.
DOSE: All doses based on TMP.
W/P: [C (D if near term), —].
SE: —.

VALACYCLOVIR (VALTREX, GENERIC)
USES: VZV, herpes zoster, genital herpes, herpes labialis.
DOSE: Zostavax: 1 g PO TID × 3 days. Genvar/Apovir (initial episode): 1 g BD × 7–10 days; Recurrence: 500 mg PO BID × 3 days. Herpes prophylaxis: 500–1,000 mg/d. Herpes labialis: 2 g PO q2h × 1 day w/ renal failure.
W/P: [B, ±] CYP3A4 effects in elderly.
DISP: Caps 500, 1,000 mg. Tab 500, 1,000 mg.
SE: Headache, GI upset, ↑ LFTs, dizziness, pruritus, photophobia.

VALMISURON (VALSTAR)
USES: Intravenous therapy of BCG refractory bladder CIS in patients for whom immediate cystectomy would be associated with unacceptable morbidity or mortality.
ACTIONS: An anthracycline, alkylating agent.
DOSE: 500 mg intravenously 1 wk for 6 wk (4 wk shrinkage in 55 mg/d, total volume of 75 mL).
W/P: [C] — do not administer w/ perfusion-related bladder.
CI: Hypersensitivity to anthracyclines or piperazine castor oil, U/I, bladder capacity > 75 mL.
DISP: 5 mL single-use vials (200 mg/mL).
SE: Frequency, dysuria, urgency, spasm, hematuria, pain, incontinence.
NOTES: Monitor closely for disease recurrence or progression; if there is not a complete response of CIS to treatment after 3 mo or if CIS recurs, cystectomy must be reconsidered. Procedures for proper handling and disposal of antitumor drugs should be used. Spills should be cleaned up w/ unlabeled chlorine bleach.

VANCOMYCIN (VANCOCIN, GENERIC)
USES: Serious MMA infections, Enterococcal infections; PO treat of S. aureus and C. difficile pseudomembranous colitis.
ACTIONS: Synthetase inhibitors.
DOSE: 20 mg PO BID; 60 mg ER caps PO daily a.m., 1 hr ac or on empty stomach. ↓ w/ CrCl <30 ml/min in elderly.
W/P: [C, ±, —] w/ ESR use, in hot environments, ulcerative colitis, myasthenia gravis, renal/hepatic impairment.
CI: Slower gastric retention, narrow-angle glaucoma.
DISP: Tabs 20 mg. Caps 80–60 mg.
SE: Dry mouth, constipation, headache, rash.

VANCOYMYCIN (VANCOCIN, GENERIC)
USES: S. aureus w/ or w/o endocarditis, infection, meningitis.
ACTIONS: Muscarinic antagonist. ↓ bladder smooth muscle tone.
DOSE: 20 mg PO SID; 60 mg ER caps PO daily a.m., 1 hr ac or on empty stomach. ↓ w/ CCl <30 ml/min in elderly.
W/P: [C, ±, —] w/ ESR use, in hot environments, ulcerative colitis, myasthenia gravis, renal/hepatic impairment.
CI: Slower gastric retention, narrow-angle glaucoma.
DISP: Tabs 20 mg. Caps 80–60 mg.
SE: Dry mouth, constipation, headache, rash.

VANOCOYMYCIN (VANCOCIN, GENERIC)
USES: S. aureus w/ or w/o endocarditis, infection, meningitis.
ACTIONS: Muscarinic antagonist. ↓ bladder smooth muscle tone.
DOSE: 20 mg PO SID; 60 mg ER caps PO daily a.m., 1 hr ac or on empty stomach. ↓ w/ CCl <30 ml/min in elderly.
W/P: [C, ±, —] w/ ESR use, in hot environments, ulcerative colitis, myasthenia gravis, renal/hepatic impairment.
CI: Slower gastric retention, narrow-angle glaucoma.
DISP: Tabs 20 mg. Caps 80–60 mg.
SE: Dry mouth, constipation, headache, rash.

VANOCOYMYCIN (VANCOCIN, GENERIC)
USES: S. aureus w/ or w/o endocarditis, infection, meningitis.
ACTIONS: Muscarinic antagonist. ↓ bladder smooth muscle tone.
DOSE: 20 mg PO SID; 60 mg ER caps PO daily a.m., 1 hr ac or on empty stomach. ↓ w/ CCl <30 ml/min in elderly.
W/P: [C, ±, —] w/ ESR use, in hot environments, ulcerative colitis, myasthenia gravis, renal/hepatic impairment.
CI: Slower gastric retention, narrow-angle glaucoma.
DISP: Tabs 20 mg. Caps 80–60 mg.
SE: Dry mouth, constipation, headache, rash.
VARDENAFIL (LEVITRA, STAXYN, GENERIC)

**USE:** Erectile dysfunction.

**DOSE:** PO: 10 mg, 20 mg, 40 mg; PDE5 inhibitor, increases cGMP and NO.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNING:** Can cause major/fatal bleeding.

**USES:** Prophylaxis & Treat of PE & DVT, AF w/ embolization, other postop indications.

**DOSAGE:** PO: 5 mg, 10 mg, 20 mg; 2.5 mg w/ CV, hepatic, or renal disease or if sex not rec (toxic > μg dose; use w/ caution in patients with bleeding risk). Remember: If you stop the drug, the effect is permanent.

**NOTES:** Monitor vit K intake; use w/ caution in patients w/ bleeding risk.

**VINCRISTINE (MARQIBO, GENERIC)

**USE:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.

**WARNINGS:** Can cause major/fatal bleeding.

**USES:** Hodgkin’s disease, non-Hodgkin’s malignant lymphomas, thymomas, neuroblastomas, Wilms’ tumor, acute leukemia.

**DOSE:** IV: 1–5 mg/m²; IV over 1 hr or continuous infusion (1 mg/min). Inhibited by: Barbiturates, carbamazepine, cholestyramine, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline.

**ACTIONS:** Promotes disassembly of mitotic spindle, causing metaphase arrest, early exit.
ZALEDRONIC ACID (RECLAST, ZOMETA, GENERIC)

USES:
- Hypercalcemia of malignancy (HCM), skeletal-related events in community-acquired pneumonia, multiple myeloma, & metastatic bone lesions (Zometasetm); treatment/radiation dose of postmenopausal osteoporosis, Paget disease, bone mass in men w/ osteoporosis,人事-induced osteoporosis (RDI).

ACTIONS:
- Bisphosphonate; ↓ osteoclastic bone resorption.

DOSE: Zometa: HCM: 4 mg IV q 24 hrs; may retreat in 7 days w/ adequate renal function. Postmenopausal osteoporosis: 5 mg IV q 4 wk; Paget: 5 mg IV x 1.

W/P: [ ]; w/ Olcegepant, angioedema; ASA-sensitive asthmatics; avoid invasive dental procedures.

NOTES: Requires vigorous prehydration; do not exceed 30 minutes of infusion; give Ca²⁺- and vit D sups; may ↓ atypical subtrochanteric femur fractures.

Cytochrome P-450 enzymes and common medication interactions

CYP1A2
- Substrates: Acetaminophen, caffeine, cyclobenzaprine, clonazepam, imipramine, medazepam, nisoldipine, phenobarbital, theophylline
- Inhibitors: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, fluvoxamine, ketonazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Most NSAIDs (including COX-2), glipizide, thiabendazole, indinavir, tamoxifen, warfarin

CYP2A6
- Substrates: Aripiprazole, clozapine, haloperidol, risperidone, thioridazine

CYP2C9
- Substrates: Carvedilol, metoprolol, propafenone, tamsulosin

CYP2C19
- Substrates: Aripiprazole, clozapine, haloperidol, risperidone, thioridazine

CYP3A
- Substrates: Ketoconazole, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2D6
- Substrates: Aripiprazole, clozapine, haloperidol, risperidone, thioridazine

CYP2D6
- Substrates: Aripiprazole, clozapine, haloperidol, risperidone, thioridazine

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, fluvoxamine, ketonazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
- Inducers: Carbamazepine, charcoal-broiled foods, cruciferous vegetables, omeprazole, midazolam, smoking

CYP2C19
- Substrates: Amiodarone, clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice (in high ingestion), indinavir, itraconazole, ketocnazole, nefazodone, nefazodone, nelfi,
SECTION VII
Reference Tables
Aging Male Survey (AMS)
(See also Section II: Aging Male Survey)

AMS Questionnaire

Which of the following symptoms apply to you at this time? Please mark the appropriate box for each symptom. For symptoms that do not apply, please mark "none."

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Decline in your feeling of general well-being (general state of health, subjective feeling)</td>
<td></td>
</tr>
<tr>
<td>2. Joint pain and muscular ache (lower back pain, joint pain, pain in a limb, general back ache)</td>
<td></td>
</tr>
<tr>
<td>3. Excessive sweating (unexpected/sudden episodes of sweating, hot flashes independent of strain)</td>
<td></td>
</tr>
<tr>
<td>4. Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early and feeling tired, poor sleep, sleeplessness)</td>
<td></td>
</tr>
<tr>
<td>5. Increased need for sleep, often feeling tired</td>
<td></td>
</tr>
<tr>
<td>6. Irritability (feeling aggressive, easily upset about little things, moody)</td>
<td></td>
</tr>
<tr>
<td>7. Nervousness (inner tension, restlessness, feeling fidgety)</td>
<td></td>
</tr>
<tr>
<td>8. Anxiety (feeling panicky)</td>
<td></td>
</tr>
<tr>
<td>9. Physical exhaustion/lacking vitality (general decrease in performance, reduced activity, feeling of getting less done, of achieving less, of having to force oneself to undertake activities)</td>
<td></td>
</tr>
<tr>
<td>10. Decrease in muscular strength</td>
<td></td>
</tr>
<tr>
<td>11. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings, feeling nothing is of any use)</td>
<td></td>
</tr>
<tr>
<td>12. Feeling that you have passed your peak</td>
<td></td>
</tr>
<tr>
<td>13. Feeling burnt out, having hit rock-bottom</td>
<td></td>
</tr>
<tr>
<td>14. Decrease in beard growth</td>
<td></td>
</tr>
<tr>
<td>15. Decrease in ability/frequency to perform sexuality</td>
<td></td>
</tr>
<tr>
<td>16. Decrease in the number of morning erections</td>
<td></td>
</tr>
<tr>
<td>17. Decrease in sexual desire/libido (lacking pleasure in sex, lacking desire for sexual intercourse)</td>
<td></td>
</tr>
</tbody>
</table>

Have you got any other major symptoms?  Yes  No

If Yes, please describe...

Score = None 1 2 3 4 5

Thank you very much for your cooperation.

Antibiotic Prophylaxis: AUA Guidelines

Patients undergoing urologic surgery should be considered for appropriate antibiotic prophylaxis. The American Urological Association (AUA) has made the following recommendations to help with decisions regarding use of antimicrobial prophylaxis in urologic surgery based on upper or lower urinary tract surgery. The selection of agent and determination of appropriate dosage should always consider the patient's specific circumstances (e.g., age, etc.).

Key points in the AUA guidelines:

- The duration of surgical prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.
- Begin infusion of the 1st dose within 60 minutes of the incision (except 120 min for IV fluoroquinolones and vancomycin).
- Do not extend prophylaxis beyond 24 h after a procedure except with prophylactic materials, if a urinary catheter is present prior to or is placed at the time of the procedure in patients with risk factors, or in the presence of documented bacteriuria.
- For surgical prophylaxis, all agents should be administered IV (except for oral medications for fluorquinolones,trimethoprim-sulfamethoxazole, bowel preparation agents, and some agents given at catheter removal); in addition, intramuscular administration for antimicrobials for transurethral prostate biopsy is acceptable.
- With an existing infection, a therapeutic course of antimicrobials should be given in an attempt to sterilize the field or suppress the bacterial count.
- Prophylaxis can be omitted if urine culture shows no growth.
- Standard dosing regimens are noted. Dose adjustments based on body weight. Additional intraoperative doses are required intraoperatively if the procedure extends beyond 2 half-lives of the initial dose.
- Use agents with appropriate post-procedure endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.

The duration of surgical prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.

- Begin infusion of the 1st dose within 60 minutes of the incision (except 120 min for IV fluoroquinolones and vancomycin).
- Do not extend prophylaxis beyond 24 h after a procedure except with prophylactic materials, if a urinary catheter is present prior to or is placed at the time of the procedure in patients with risk factors, or in the presence of documented bacteriuria.
- For surgical prophylaxis, all agents should be administered IV (except for oral medications for fluorquinolones, trimethoprim-sulfamethoxazole, bowel preparation agents, and some agents given at catheter removal); in addition, intramuscular administration for antimicrobials for transurethral prostate biopsy is acceptable.
- With an existing infection, a therapeutic course of antimicrobials should be given in an attempt to sterilize the field or suppress the bacterial count.
- Prophylaxis can be omitted if urine culture shows no growth.
- Standard dosing regimens are noted. Dose adjustments based on body weight. Additional intraoperative doses are required intraoperatively if the procedure extends beyond 2 half-lives of the initial dose.
- Use agents with appropriate post-procedure endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.

The duration of surgical prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.

- Begin infusion of the 1st dose within 60 minutes of the incision (except 120 min for IV fluoroquinolones and vancomycin).
- Do not extend prophylaxis beyond 24 h after a procedure except with prophylactic materials, if a urinary catheter is present prior to or is placed at the time of the procedure in patients with risk factors, or in the presence of documented bacteriuria.
- For surgical prophylaxis, all agents should be administered IV (except for oral medications for fluorquinolones, trimethoprim-sulfamethoxazole, bowel preparation agents, and some agents given at catheter removal); in addition, intramuscular administration for antimicrobials for transurethral prostate biopsy is acceptable.
- With an existing infection, a therapeutic course of antimicrobials should be given in an attempt to sterilize the field or suppress the bacterial count.
- Prophylaxis can be omitted if urine culture shows no growth.
- Standard dosing regimens are noted. Dose adjustments based on body weight. Additional intraoperative doses are required intraoperatively if the procedure extends beyond 2 half-lives of the initial dose.
- Use agents with appropriate post-procedure endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.

The duration of surgical prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.

- Begin infusion of the 1st dose within 60 minutes of the incision (except 120 min for IV fluoroquinolones and vancomycin).
- Do not extend prophylaxis beyond 24 h after a procedure except with prophylactic materials, if a urinary catheter is present prior to or is placed at the time of the procedure in patients with risk factors, or in the presence of documented bacteriuria.
- For surgical prophylaxis, all agents should be administered IV (except for oral medications for fluorquinolones, trimethoprim-sulfamethoxazole, bowel preparation agents, and some agents given at catheter removal); in addition, intramuscular administration for antimicrobials for transurethral prostate biopsy is acceptable.
- With an existing infection, a therapeutic course of antimicrobials should be given in an attempt to sterilize the field or suppress the bacterial count.
- Prophylaxis can be omitted if urine culture shows no growth.
- Standard dosing regimens are noted. Dose adjustments based on body weight. Additional intraoperative doses are required intraoperatively if the procedure extends beyond 2 half-lives of the initial dose.
- Use agents with appropriate post-procedure endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.

The duration of surgical prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.

- Begin infusion of the 1st dose within 60 minutes of the incision (except 120 min for IV fluoroquinolones and vancomycin).
- Do not extend prophylaxis beyond 24 h after a procedure except with prophylactic materials, if a urinary catheter is present prior to or is placed at the time of the procedure in patients with risk factors, or in the presence of documented bacteriuria.
- For surgical prophylaxis, all agents should be administered IV (except for oral medications for fluorquinolones, trimethoprim-sulfamethoxazole, bowel preparation agents, and some agents given at catheter removal); in addition, intramuscular administration for antimicrobials for transurethral prostate biopsy is acceptable.
- With an existing infection, a therapeutic course of antimicrobials should be given in an attempt to sterilize the field or suppress the bacterial count.
- Prophylaxis can be omitted if urine culture shows no growth.
- Standard dosing regimens are noted. Dose adjustments based on body weight. Additional intraoperative doses are required intraoperatively if the procedure extends beyond 2 half-lives of the initial dose.
- Use agents with appropriate post-procedure endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.
## Antibiotic Prophylaxis: AUA Guidelines (Continued)

### PROPHYLAXIS FOR UPPER URINARY TRACT INSTRUMENTATION

<table>
<thead>
<tr>
<th>Procedure (Organisms)</th>
<th>Prophylaxis Indicated</th>
<th>Antimicrobial(s) of Choice</th>
<th>Alternative Antimicrobial(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock-wave lithotripsy (GU tract)</td>
<td>All patients</td>
<td>Fluoroquinolones: Levofloxacin: 500 mg PO single dose Ofloxacin: 400 mg PO (q12h)</td>
<td>Amoxycillin plus clavulanate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMP-SMX (Trimethoprim-sulfamethoxazole): 1 double-strength tablet PO (q12h)</td>
<td></td>
</tr>
<tr>
<td>Ureteroscopy (GU tract)</td>
<td>All patients</td>
<td>Fluoroquinolones: Levofloxacin: 500 mg PO single dose Ofloxacin: 400 mg PO (q12h)</td>
<td>Amoxycillin plus clavulanate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole: 1 g IV (q12h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Clindamycin: 600 mg IV (q8h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Ampicillin/sulbactam: 1.5–3 g IV (q6h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Fluoroquinolones: Levofloxacin: 500 mg PO single dose Ofloxacin: 400 mg PO (q12h)</td>
<td></td>
</tr>
<tr>
<td>Percutaneous renal surgery (GU tract and skin)</td>
<td>All patients</td>
<td>Aminoglycosides: Gentamicin: 5 mg/kg IV single dose Tobramycin: 7.5 mg/kg IV single dose Amikacin: 15 mg/kg IV single dose</td>
<td>Amoxycillin plus clavulanate</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Metronidazole: 1 g IV (q12h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Clindamycin: 600 mg IV (q8h)</td>
<td></td>
</tr>
<tr>
<td>Vaginal surgery (GU tract, skin, and Group B Strept.)</td>
<td>All patients</td>
<td>Aminoglycosides: Gentamicin: 5 mg/kg IV single dose Tobramycin: 7.5 mg/kg IV single dose Amikacin: 15 mg/kg IV single dose</td>
<td>Amoxycillin plus clavulanate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole: 1 g IV (q12h)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Clindamycin: 600 mg IV (q8h)</td>
<td></td>
</tr>
</tbody>
</table>

### Key:
- gen. = generation
- GU = genitourinary


2. Order of agents is not indicative of preference.


4. For surgery involving colon, bowel preparation with oral neomycin plus either erythromycin base or metronidazole can be added to or substituted for systemic agents.
**Antibiotic Prophylaxis: AUA Guidelines (Continued)**

**PROPHYLAXIS FOR UPPER URINARY TRACT INSTRUMENTATION (Continued)**

<table>
<thead>
<tr>
<th>Without entering urinary tract (skin)</th>
<th>With risk factors</th>
<th>Without entering urinary tract (skin)</th>
<th>With risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin: 600 mg IV single dose</td>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>Ampicillin/sulbactam: 1.5–3 g IV (q6h)</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
</tr>
<tr>
<td>Ampicillin/sulbactam: 1.5–3 g IV (q6h)</td>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>Ciprofloxacin: 500 mg PO (q12h)</td>
<td>Piperacillin/tazobactam: 3.375 g IV (q6h)</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin: 500 mg PO (q12h)</td>
<td>Levofloxacin: 500 mg PO single dose</td>
<td>Fluoroquinolones:</td>
<td></td>
</tr>
<tr>
<td>Levofloxacin: 500 mg PO (q12h)</td>
<td>Ciprofloxacin: 500 mg PO (q12h)</td>
<td>Levoftoxacin: 500 mg PO single dose</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin: 500 mg PO (q12h)</td>
<td>Aminoglycosides:</td>
<td>Amikacin: 15 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td>Amikacin: 15 mg/kg IV single dose</td>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>Tobramycin: 5 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>Tobramycin: 5 mg/kg IV single dose</td>
<td>OR Amikacin: 15 mg/kg IV single dose</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>Amikacin: 15 mg/kg IV single dose</td>
<td>Ciprofloxacin: 500 mg PO (q12h)</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>Piperacillin/tazobactam: 3.375 g IV (q6h)</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Gentamicin: 5 mg/kg IV single dose</td>
<td>OR Clindamycin: 600 mg IV (q8h)</td>
<td>OR</td>
<td></td>
</tr>
</tbody>
</table>
Anticoagulation and Antiplatelet Therapy in Urologic Practice

The following is based on Anticoagulation and Antiplatelet Therapy in Urologic Practice: ICUD and AUA Review Paper. The American Urologic Association (AUA) and the International Consultation on Urological Disease (ICUD) collaborated on this review.


Patients often have multiple comorbidities and require urologic surgical intervention. Conditions can include coronary arterial disease requiring percutaneous coronary artery intervention with angioplasty, bare metal coronary stents, drug eluting coronary stent, cardiac dysrhythmias (such as atrial fibrillation, others), valvular heart disease, deep venous thrombosis, and inferior vena cava filters. This table provides guidelines on the management of anticoagulation and antiplatelet (AP) therapy in urologic practice. These are only general guidelines with the most effective approach for an individual patient best determined by the patient’s clinical conditions and in collaboration with a multidisciplinary medical team that may include internists, cardiologists, or neurologists where appropriate.

- **Anticoagulant (AC)**
  - Heparins
  - Warfarin
  - New oral anticoagulants (NOACs) include thrombin inhibitor, dabigatran, and the factor Xa inhibitors, rivaroxaban, and apixaban

- **Oral Anti Platelet (AP)**
  - AP medications: aspirin, clopidogrel, ticagrelor, ticlopidine, dipyridamole

1. **Deep venous thrombosis and pulmonary embolism** are discussed in Section I: “Deep Venous Thrombosis and Pulmonary Embolus, Urologic Considerations” and Section II: “Deep Venous Thrombosis, Prophylaxis, AUA Guidelines.”

2. For patients on clopidogrel or aspirin for secondary stroke prevention: continue aspirin through the perioperative period.

3. **Coronary artery stents:** Dual AP therapy should not be stopped before urologic surgery within 12 mo of drug eluding stent or within 3 mo of a bare metal stent. For urologic procedures outside of these limits discontinuation of the clop idogrel, prasugrel, or ticagrelor, and continuation of aspirin, is recommended if procedural bleeding risks are acceptable.

4. **Mechanical heart valves:** AC bridge therapy is recommended.

5. **Cardiac risk factors on low-dose aspirin monotherapy:** continue in perioperative period without increased risk of major bleeding.

6. **Low-dose aspirin without specific indication:** may be scheduled electively, discontinuing the aspirin until directed by the team.

7. **Patients on NOACs (apixaban, dabigatran, rivaroxaban), with nonvalvular atrial fibrillation should be risk stratified:**
   - **Minor bleeding risk:** these agents do not have to be modified, similar to the management with warfarin or low-molecular-weight heparin.
   - **Urgent procedure:** delay for 24–36 hr and obtain consultation.
   - **Emergency procedure:** if bleeding risk increased, expert consultation and avoid spinal/epidural anesthesia.
   - **With operative loss of nephrons** determine renal function post-op and adjust these agents.

8. **Atrial fibrillation in high-risk procedure:** stop warfarin 5 days before surgery; restart 12–24 hr post-op if bleeding risk acceptable.

9. **Higher risk of thromboembolic events (eg, mechanical valves) on warfarin:** bridging anticoagulation with unfractionated heparin or low-molecular-weight heparin. The NOACs apixaban, dabigatran, or rivaroxaban, would be stopped 3–5 days before elective surgery based on the bleeding risk of the procedure. Rivaroxaban may increase stroke risk if stopped; bridging with some other AC such as heparin is recommended.
Anticoagulation and Antiplatelet Therapy in Urologic Practice (continued)

10. **Prosthetic heart valves:** follow standard guidelines (ie, the American College of Cardiology, American Heart Association, etc.):
   - **Low risk of thrombosis:** bileaflet mechanical AVR and no risk factors (eg, atrial fib, previous thromboembolism, left ventricular dysfunction, hypercoagulable conditions, older generation thrombogenic valves, mechanical tricuspid valves or more than one mechanical valve). Stop warfarin 48–72 hr pre-op and restarted within 24 hr post-op. Heparin is usually unnecessary. Check INR immediately pre-op to ensure that the INR is >1.5.
   - **High risk of thrombosis:** (any mechanical mitral valve replacement or a mechanical aortic valve with any risk factor [see above for risk factors]) begin bridging when the INR <2 (usually 48 hr pre-op): dose adjust aPTT 2–3 times the control. Unfractionated heparin is stopped 4–6 hours pre-op and restarted post-op based on bleeding stability. Restart warfarin as soon as possible postoperatively; unfractionated heparin is continued until the INR is therapeutic for at least 48 hr.

11. **Bridging regimens:** As recommended by the American College of Chest Physicians:
   - A high-dose (therapeutic-dose) heparin bridging (eg, LMW heparin: enoxaparin 1 mg/kg BID or 1.5 mg/kg daily, dalteparin 100 IU/kg BID or 200 IU/kg daily, tinzaparin 175 IU/kg daily, or IV unfractionated heparin to keep aPTT 1.5–2 times control).
   - A low-dose (prophylactic-dose) heparin regimen (eg, enoxaparin 30 mg BID or 40 mg daily, dalteparin 5,000 IU daily, unfractionated Heparin 5,000–7,500 IU BID).
   - An intermediate-dose regimen (eg, enoxaparin 40 mg BID).

12. **ESWL:** oral ACs and APs agents should be stopped and or reversed. Coordinate with multidisciplinary team.

13. **Ureteroscopy:** can be performed with continuing oral ACs and APs agents.

14. **Percutaneous nephrolithotomy (PCNL):** oral ACs and APs agents discontinued prior to PCNL and patients bridged where deemed necessary.

15. **Laser prostatectomy:** In appropriately selected patients can be safely accomplished with a therapeutic INR who has a significant risk of thrombosis without stopping oral ACs and APs agents.

16. **Standard electro surgical TURP:** The use of oral ACs and APs agents in patients undergoing TURP is associated with an increased risk of bleeding. Anticoagulation should be carefully assessed and managed; alternative treatment of the bladder outlet may be preferable.

17. **Prostate biopsy:** safe on low-dose aspirin. With oral ACs small studies suggest this can be performed without significant major bleeding risk. Stopping APs agents before biopsy, when medical evaluation demonstrates a low risk of thromboembolic complications, is associated with a lower rate of minor complications.

18. **Perioperative continuation of aspirin:** this may be associated with a minor risk of increased bleeding, but the transfusion rate is not increased and the consequences of bleeding are minor. The exception is with transurethral resection of the prostate.
AUA Symptom Index/International Prostate Symptom Score (I-PSS)

(See also Section II: AUA (American Urologic Association) Symptom Index for BPH and International Prostate Symptom Score (IPSS))

American Urological Association (AUA) Symptom Index for BPH

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. INCOMPLETE EMPTYING</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the last month or so, how often have you had a sensation of not</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>emptying your bladder completely after you finished urinating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. FREQUENCY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month or so, how often have you had to urinate again</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 hours after you finished urinating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. INTERMITTENCY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month or so, how often have you stopped and started</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>again several times when you urinated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. URGENCY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month or so, how often have you found it difficult to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>postpone urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. WEAK STREAM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month or so, how often have you had a weak urinary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stream?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. STRAINING</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month or so, how often have you had to push or strain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>to begin urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. SLEEPING</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the last month, how many times did you most typically get up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>to urinate from the time you went to bed at night until the time you</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>got up in the morning?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SCORE: (0-35)

The International Prostate Symptom Score (IPSS) uses the same 7 questions as the AUA Symptom Index, but adds a “Disease Specific Quality of Life Question” (sometimes referred to as the “bother score”) and scored on a scale from 0 to 6 points (“delighted” to “terrible”).

If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?

<table>
<thead>
<tr>
<th>Feeling</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delighted</td>
<td>0</td>
</tr>
<tr>
<td>Pleased</td>
<td>1</td>
</tr>
<tr>
<td>Mostly satisfied</td>
<td>2</td>
</tr>
<tr>
<td>Mixed</td>
<td>3</td>
</tr>
<tr>
<td>Mostly disappointed</td>
<td>4</td>
</tr>
<tr>
<td>Unhappy</td>
<td>5</td>
</tr>
<tr>
<td>Terrible</td>
<td>6</td>
</tr>
</tbody>
</table>

CATHETER GUIDE
(See also Section II: “French Catheter Scale”)

French Catheter Scale
In French Units (1 French = 1/3 mm diameter)

<table>
<thead>
<tr>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>32</td>
<td>30</td>
<td>28</td>
<td>26</td>
<td>24</td>
<td>22</td>
<td>20</td>
<td>19</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 French = 1.0 mm = .039 inches
18 French = 6 mm = .236 inches

Needle Gauge

Inches

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
</tr>
</tbody>
</table>

Centimeters

(With permission from Cook Urological, Inc., “French Catheter Scale”)

(With permission from Cook Urological, Inc., “French Catheter Scale”)
### Contrast Agents, Genitourinary

Contrast agents used in urology include intravascular (CT, excretory urography, vascular studies, etc.), gastrointestinal (oral contrast), body cavity (histogram and tube studies), uroradiological (cystogram, urethrogram, retrograde pyelography, etc.), and MRI contrast agents (gadolinium-based paramagnetic compounds). Commonly used intravascular and uroradiological agents are shown in the tables below. See also Section I: “Contrast Allergy and Reactions” and Section II: “Contrast Induced Nephropathy (CIN)” and “Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy (NSF/NFD).”

Key points:
- Intravascular contrast agents are classified as ionic or nonionic and high, low, or iso-osmolar relative to serum (290 mOsm/kg H2O).
- High-osmolar contrast media (HOCM) are the oldest intravascular agents and ionize in solution (osmolality typically >1,000). Low-osmolar contrast media (LOCM) and iso-osmolar contrast media (IOCM) are nonionic compounds (no ionization in solution). The toxicity of contrast agents generally decreases as osmolality approaches that of serum. Typical osmolality (in mOsm/kg H2O) is as follows: HOCM > 1,000, LOCM ~ 400–800, and IOCM 290.
- Uroradiologic contrast agents are not injected into the circulation so that issues relating to potential toxicity are almost nonexistent.
- MRI contrast agents: Nephrogenic systemic fibrosis (NSF) is associated with the administration of intravenous gadolinium. The primary risk factor is renal insufficiency (dialysis patient or with a GFR < 30).

#### Intravascular Contrast Agents

Agents sorted by osmolarity from highest to lowest and represent commonly used agents in the United States.

<table>
<thead>
<tr>
<th>Product</th>
<th>Chemical Structure</th>
<th>Anion</th>
<th>Cation</th>
<th>Osmolality (mOsm/kg H2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD-76(TM) (Covidien)</td>
<td>Ionic</td>
<td>Diatrizoate</td>
<td>Meglumine Sodium</td>
<td>1,551</td>
</tr>
<tr>
<td>Conray(TM) 43 (Covidien)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>1,000</td>
</tr>
<tr>
<td>Omnipaque(TM)–350 (GE Healthcare)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>1,000</td>
</tr>
<tr>
<td>Conray(TM) 43 (Covidien)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>790</td>
</tr>
<tr>
<td>Optiray(TM) 370 (Bayer Healthcare)</td>
<td>Ioversol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>702</td>
</tr>
<tr>
<td>Conray(TM) 43 (Covidien)</td>
<td>Iothalamate</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>702</td>
</tr>
<tr>
<td>Omnipaque(TM)–350 (GE Healthcare)</td>
<td>Iothalamate</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>702</td>
</tr>
<tr>
<td>Optiray(TM) 300 (Covidien)</td>
<td>Ioversol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>651</td>
</tr>
<tr>
<td>Omnipaque(TM)–300 (GE Healthcare)</td>
<td>Iohexol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>651</td>
</tr>
<tr>
<td>Cholangrafin® (Bracco)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>654</td>
</tr>
<tr>
<td>Optiray(TM) 400 (Covidien)</td>
<td>Ioversol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>601</td>
</tr>
<tr>
<td>Isovue® –300 (Bracco)</td>
<td>Nonionic</td>
<td>Iopamidol 61.2%</td>
<td>Nonionic</td>
<td>616</td>
</tr>
<tr>
<td>Omnipaque(TM)–300 (GE Healthcare)</td>
<td>Iohexol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>610</td>
</tr>
<tr>
<td>Isovue® –250 (Bracco)</td>
<td>Nonionic</td>
<td>Iopamidol 51%</td>
<td>Nonionic</td>
<td>527</td>
</tr>
<tr>
<td>Omnipaque(TM)–240 (GE Healthcare)</td>
<td>Iohexol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>527</td>
</tr>
<tr>
<td>Isovue® –200 (Bracco)</td>
<td>Nonionic</td>
<td>Iopamidol 40.8%</td>
<td>Nonionic</td>
<td>513</td>
</tr>
<tr>
<td>Ultravist® 150 (Bayer Healthcare)</td>
<td>Iopromide</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>526</td>
</tr>
<tr>
<td>Omnipaque(TM)–140 (GE Healthcare)</td>
<td>Iohexol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>527</td>
</tr>
<tr>
<td>Visipaque(TM) 270 (GE Healthcare)</td>
<td>Iodixanol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>526</td>
</tr>
<tr>
<td>Visipaque(TM)–320 (GE Healthcare)</td>
<td>Iodixanol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>522</td>
</tr>
</tbody>
</table>

#### Uroradiologic Contrast Agents

<table>
<thead>
<tr>
<th>Product</th>
<th>Chemical Structure</th>
<th>Anion</th>
<th>Cation</th>
<th>Osmolality (mOsm/kg H2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystografin® (Bracco)</td>
<td>Ionic</td>
<td>Diatrizoate</td>
<td>Meglumine</td>
<td>156</td>
</tr>
<tr>
<td>Cystopaque® 15 (Bracco)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>140</td>
</tr>
<tr>
<td>Conray(TM) 43 (Covidien)</td>
<td>Ionic</td>
<td>Iothalamate</td>
<td>Meglumine</td>
<td>1000</td>
</tr>
<tr>
<td>Omnipaque(TM)–300 (GE Healthcare)</td>
<td>Iothalamate</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>1000</td>
</tr>
<tr>
<td>Omnipaque(TM)–350 (GE Healthcare)</td>
<td>Iothalamate</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>844</td>
</tr>
<tr>
<td>Visipaque(TM) 270 (GE Healthcare)</td>
<td>Iodixanol</td>
<td>Nonionic</td>
<td>Nonionic</td>
<td>100</td>
</tr>
</tbody>
</table>

INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF) 
Patient Questionnaire 

These questions ask about the effects that your erection problems have had on your sex life over the last four weeks. Please try to answer the questions as honestly and as clearly as you are able. Your answers will help your doctor to choose the most effective treatment suited to your condition. In answering the questions, the following definitions apply:

- **Sexual activity** includes intercourse, caressing, foreplay, and masturbation
- **Sexual intercourse** is defined as sexual penetration of your partner
- **Sexual stimulation** includes situation such as foreplay, erotic pictures etc.
- **Ejaculation** is the ejection of semen from the penis (or the feeling of this)
- **Orgasm** is the fulfillment or climax following sexual stimulation or intercourse

**Over the past 4 weeks:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Please check one box only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 How often were you able to get an erection during sexual activity?</td>
<td></td>
</tr>
<tr>
<td>Q2 When you had erections with sexual stimulation, how often were your erections hard enough for penetration?</td>
<td></td>
</tr>
<tr>
<td>Q3 When you attempted intercourse, how often were you able to penetrate (enter) your partner?</td>
<td></td>
</tr>
<tr>
<td>Q4 During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?</td>
<td></td>
</tr>
<tr>
<td>Q5 During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?</td>
<td></td>
</tr>
<tr>
<td>Q6 How many times have you attempted sexual intercourse?</td>
<td></td>
</tr>
<tr>
<td>Q7 When you attempted sexual intercourse, how often was it satisfactory for you?</td>
<td></td>
</tr>
<tr>
<td>Q8 How much have you enjoyed sexual intercourse?</td>
<td></td>
</tr>
<tr>
<td>Q9 When you had sexual stimulation or intercourse, how often did you ejaculate?</td>
<td></td>
</tr>
</tbody>
</table>

(Continued on next page)
Q10 When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?

1. Almost never or never
2. A few times (less than half the time)
3. Sometimes (about half the time)
4. Most times (more than half the time)
5. Almost always or always

Q11 How often have you felt sexual desire?

1. Almost never or never
2. A few times (less than half the time)
3. Sometimes (about half the time)
4. Most times (more than half the time)
5. Almost always or always

Q12 How would you rate your level of sexual desire?

1. Very low or none at all
2. Low
3. Moderate
4. High
5. Very high

Q13 How satisfied have you been with your overall sex life?

1. Very dissatisfied
2. Moderately dissatisfied
3. Equally satisfied and dissatisfied
4. Moderately satisfied
5. Very satisfied

Q14 How satisfied have you been with your sexual relationship with your partner?

1. Very dissatisfied
2. Moderately dissatisfied
3. Equally satisfied & dissatisfied
4. Moderately satisfied
5. Very satisfied

Q15 How do you rate your confidence that you could get and keep an erection?

1. Very low
2. Low
3. Moderate
4. High
5. Very high

Total Score ___________

Interpretation of IIEF

<table>
<thead>
<tr>
<th>IIEF Domains</th>
<th>Maximum Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Erectile Function (Questions 1, 2, 3, 4, 5, 15)</td>
<td>30</td>
</tr>
<tr>
<td>B. Orgasmic Function (Questions 9, 10)</td>
<td>10</td>
</tr>
<tr>
<td>C. Sexual Desire (Questions 11, 12)</td>
<td>10</td>
</tr>
<tr>
<td>D. Intercourse Satisfaction (Questions 6, 7, 8)</td>
<td>15</td>
</tr>
<tr>
<td>E. Overall Satisfaction (Questions 13, 14)</td>
<td>10</td>
</tr>
</tbody>
</table>

A score of 0–5 is awarded to each of the 15 questions that examine the 4 main domains of male sexual function: erectile function, orgasmic function, sexual desire, and intercourse satisfaction.

Analysis of the questionnaire should, therefore, be viewed as an adjunct to, rather than a substitute for, a detailed sexual history and examination. The following guidelines are typical based on the IIEF scores and are based on the recommendations of the British Association of Urologic Surgeons:

1. Low IIEF scores (<14 out of 30) in Domain A (Erectile Function) may be considered for a trial course of therapy with Sildenafil unless contraindicated. Specialist referral is indicated if this is unsuccessful.
2. Patients demonstrating primary orgasmic or ejaculatory dysfunction (Domain B) should be referred for specialist investigation.
3. Patients with reduced sexual desire (Domain C) require testing of blood levels of androgen and prolactin.
4. Psychosexual counselling should be considered if low scores are recorded in Domains D and E but there is only a moderately lowered score (14 to 25) in Domain A.

Male Sexual Health Questionnaire (MSHQ) Short Form


A modified form, known as the MSHQ Short Form is commonly used for assessing ejaculatory dysfunction (also called the MSHQ-EjD). See also Section II: Male Sexual Health Questionnaire (MSHQ) and the MSHQ short form.

In the past month:

<table>
<thead>
<tr>
<th>Ejaculatory Function</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often have you been able to ejaculate or &quot;cum&quot; when having sexual activity?</td>
<td>All the time (5)</td>
<td>Most of the time (4)</td>
<td>About half the time (3)</td>
<td>Less than half the time (2)</td>
<td>None of the time/could not ejaculate (1)</td>
</tr>
<tr>
<td>2. How would you rate the strength or force of your ejaculation?</td>
<td>As strong as it always was (5)</td>
<td>A little less strong than it used to be (4)</td>
<td>Somewhat less strong than it used to be (3)</td>
<td>Much less strong than it used to be (2)</td>
<td>Very much less strong than it used to be (1)</td>
</tr>
<tr>
<td>3. How would you rate the amount or volume of semen or fluid when you ejaculate?</td>
<td>As much as it always was (5)</td>
<td>A little less than it used to be (4)</td>
<td>Somewhat less than it used to be (3)</td>
<td>Much less than it used to be (2)</td>
<td>Very much less than it used to be (1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bother/Satisfaction</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>4. If you have had any ejaculation difficulties or have been unable to ejaculate, have you been bothered by this?</td>
<td>No problem with ejaculation (0)</td>
<td>Not at all bothered (1)</td>
<td>A little bothered (2)</td>
<td>Moderately bothered (3)</td>
<td>Very bothered (4)</td>
</tr>
</tbody>
</table>

National Institutes of Health (NIH) Chronic Prostatitis Symptom Index (CPSI)
(See also Section II: National Institutes of Health (NIH) Chronic Prostatitis Symptom Index. Form is to be filled out by patient.)

Pain or Discomfort
1. In the last week, have you experienced any pain or discomfort in the following areas?
   - Area between rectum and testicles (perineum) [Yes] [No]
   - Testicles [Yes] [No]
   - Tip of the penis (related to urination) [Yes] [No]
   - Below your waist, in your pubic or bladder area [Yes] [No]

2. In the last week, have you experienced:
   - Pain or burning during urination [Yes] [No]
   - Pain discomfort during or after sexual climax (ejaculation) [Yes] [No]

3. How often have you had pain or discomfort in any of these areas over the last week?
   - Never [ ]
   - Rarely [ ]
   - Sometimes [ ]
   - Often [ ]
   - Usually [ ]
   - Always [ ]

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?
   0 = Not at all
   1 = Less than 1 time in 5
   2 = Less than half the time
   3 = About half the time
   4 = More than half the time
   5 = Almost always

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?
   - Not at all [ ]
   - Only a little [ ]
   - Some [ ]
   - A lot [ ]

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?
   - Not at all [ ]
   - Less than 1 time in 5 [ ]
   - Less than half the time [ ]
   - About half the time [ ]
   - More than half the time [ ]
   - Almost always [ ]

Impact of Symptoms
7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?
   - None [ ]
   - Only a little [ ]
   - Some [ ]
   - A lot [ ]

Quality of Life
8. How much did you think about your symptoms, over the last weeks?
   - None [ ]
   - Only a little [ ]
   - Some [ ]
   - A lot [ ]

Scoring the NIH-Chronic Prostatitis Symptom Index Domains
Pain: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, and 4 =___________
Urinary Symptoms: Total of items 5 and 6 =___________
Quality of Life Impact: Total of items 7, 8, and 9 =___________

Prostate Cancer Screening Guidelines

Screening for prostate cancer is highly controversial. This table summarizes some of the major US and international medical groups recommendations in this area.

<table>
<thead>
<tr>
<th>Organization (Year)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>American Cancer Society (ACS)</strong> (2010)</td>
<td>1. No routine screening; after informed discussion of risk and benefits for those who wish to be screened 2. No screening with &lt;10-yr life expectancy 3. Screen with PSA, w/ or w/o DRE, at age 50 with &gt;10 yr life expectancy; if PSA &gt;2.5 ng/mL, screen yearly, otherwise screen every 2 yr 4. Beginning screening discussions at age 40-45 if at high risk of developing prostate cancer (eg, black man, or with a first-degree relative with prostate cancer diagnosed before age 65). 5. Biopsy referral threshold is 4 ng/mL. With PSA 2.5-4 ng/mL, encourage individualized decision making and assessment (<a href="http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp">http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp</a>), which can include age, race, family history, DRE, previous biopsy results, and use of 5α-reductase inhibitors.</td>
</tr>
<tr>
<td><strong>American College of Physicians</strong> (2013)</td>
<td>1. Inform men age 50-69 about limited benefits and harms; screen only if patient wants it 2. Do not screen &lt;age 50 if average risk, over 69, or &lt;10-15-yr life expectancy</td>
</tr>
<tr>
<td><strong>American Urological Association</strong> (2013)</td>
<td>1. No screening under 40; not recommended if average risk 40-54; individualize if high risk* 2. Shared decision making for men age 55-69 3. No screening over age 75 or any man &lt;10-15-yr life expectancy some men over age 70 in excellent health might benefit from screening. 4. Reduce the harms of screening, a screening interval of 2 yr or more may be preferred. 5. Lack of evidence for using any tests (eg, PSA derivatives, PSA kinetics, PSA molecular markers, urinary markers, imaging, or risk calculators) other than PSA for triggering a biopsy referral. 6. No specific threshold for biopsy referral.</td>
</tr>
<tr>
<td><strong>Australian Cancer Council (2011)</strong></td>
<td>1. Does not support population-based screening 2. Recommends a patient-centered approach that individualizes the decision</td>
</tr>
<tr>
<td><strong>Canadian Task Force on Preventive Health Care (2006; 2014 Update pending)</strong></td>
<td>1. Recommends against screening for prostate cancer with PSA or TRUS 2. Insufficient evidence to recommend for or against screening with DRE</td>
</tr>
<tr>
<td><strong>European Society for Medical Oncology (ESMO)</strong> (2013)</td>
<td>1. Recommends against population-based screening; favors individualized shared decision making 2. There is inconsistent evidence screening men &lt;55 and 70-75 yr of age; evidence that the harms of screening outweigh the benefits for men over age 75.</td>
</tr>
<tr>
<td><strong>National Comprehensive Cancer Network (NCCN)</strong> (2014)</td>
<td>1. Informed discussion with all 2. Baseline DRE and PSA age 45; if PSA &lt;1, repeat every age 50; if PSA &gt;1, repeat every 1-2 yr 3. Age 50-70 with normal DRE and PSA &lt;3, repeat every 1-2 yr 4. Use caution screening if &gt; age 70 and only if very healthy; few &gt; age 75 benefit from screening</td>
</tr>
<tr>
<td><strong>United Kingdom National Screening Committee (2010)</strong></td>
<td>1. Does not recommend screening for prostate cancer</td>
</tr>
<tr>
<td><strong>United States Preventive Services Task Force (USPSTF)</strong> (2012)</td>
<td>1. No role in any man unless symptoms (grade D) 2. Men requesting screening be supported in making an informed decision.</td>
</tr>
</tbody>
</table>

All PSA values are ng/mL
* African American or have a 1st-degree relative diagnosed with PCa at <65 yr of age.
* Several 1st-degree relatives diagnosed with PCa at <65 yr of age.
* Positive family history or African American race.

SEXUAL HEALTH INVENTORY FOR MEN
IIEF-5

PATIENT INSTRUCTIONS
Sexual health is an important part of an individual’s overall physical and emotional well-being. Erectile dysfunction is one type of very common sexual complaint. There are many different treatment options for erectile dysfunction. This questionnaire is designed to help you and your physician identify if you may be experiencing erectile dysfunction and to potentially discuss treatment options.

Each question has several responses from which you are asked to choose the one that best describes your own situation. Please be sure that you select at least one but only one response by circling the number that best fits your answer.

Over the past six months:

<table>
<thead>
<tr>
<th>Question</th>
<th>Very low</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
<th>Very high</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do you rate your confidence that you could get and keep an erection?</td>
<td>No sexual activity</td>
<td>Almost/never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than half the time)</td>
</tr>
<tr>
<td>When you had erections with sexual stimulation, how often were your erections hard enough for penetration?</td>
<td>No sexual activity</td>
<td>Almost/never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than half the time)</td>
</tr>
<tr>
<td>During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?</td>
<td>Did not attempt intercourse</td>
<td>Almost/never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than half the time)</td>
</tr>
<tr>
<td>During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?</td>
<td>Did not attempt intercourse</td>
<td>Extremely difficult</td>
<td>Very difficult</td>
<td>Difficult</td>
<td>Slightly difficult</td>
</tr>
<tr>
<td>When you attempted sexual intercourse, how often was it satisfactory for you?</td>
<td>Did not attempt intercourse</td>
<td>Almost/never</td>
<td>A few times (much less than half the time)</td>
<td>Sometimes (about half the time)</td>
<td>Most times (much more than half the time)</td>
</tr>
</tbody>
</table>

Score:_____

If your score is 21 or less, you show signs of erectile dysfunction, and your doctor can suggest treatment options that can improve your condition.

Sexual Health Inventory for Men. An abridged 5-item version of the 15-item International Index of Erectile Function (IIEF-5) was developed to diagnose the presence and severity of erectile dysfunction (ED). Reprinted with permission from Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Peria BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999;11:319–326.
**TNM Classification: Cervix Cancer**

**DEFINITION OF TNM**

**T1**
- Cervical carcinoma confined to uterus (T1a) Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5 mm measured from the base of the epithelium and a horizontal spread of ≤7 mm. Vascular space involvement, venous or lymphatic, does not affect classification. (T1a1) Measured stromal invasion ≤3 mm in depth and ≤7 mm in horizontal spread (T1a2) Measured stromal invasion >3 mm and not >5 mm with a horizontal spread ≤7 mm

**IA1/A2**
- IA1: Clinically visible lesion confined to cervix or microscopic lesion greater than T1a/IA2 (T1b1) Clinically visible lesion >4 cm in greatest dimension (T1b2) Clinically visible lesion >4 cm in greatest dimension
- A2: No regional lymph node metastasis

**IB1/B2**
- IB1: Clinically visible lesion confined to cervix or microscopic lesion greater than T1a/IA2 (T1b1) Clinically visible lesion >4 cm in greatest dimension (T1b2) Clinically visible lesion >4 cm in greatest dimension
- B2: No regional lymph node metastasis

**IIB**
- IIB: Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2 (T1b1) Clinically visible lesion >4 cm in greatest dimension (T1b2) Clinically visible lesion >4 cm in greatest dimension
- B2: No regional lymph node metastasis

**IIIA**
- Tumor extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or nonfunctioning kidney (T3a) Tumor involves lower third of vagina, no extension to pelvic wall (T3b) Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney
- N1: Regional lymph node metastasis

**IIIB**
- T4: Tumor invades mucosa of bladder or rectum, and/or extends beyond true pelvis (bulbous edema is not sufficient to classify a tumor as T4)
- M0: No distant metastasis

**IVA**
- M1: Distant metastasis (including peritoneal spread, involvement of supraclavicular, mediastinal, or paraaortic lymph nodes, lung, liver, or bone)

**IVB**
- M1: Any T, Any N, M1

**TNM Classification: Colon Cancer**

**DEFINITION OF TNM**

- **T1**: Tumor invades submucosa
- **T2**: Tumor invades muscularis propria
- **T3**: Tumor invades through the muscularis propria into perirectal tissues
- **T4**: Tumor directly invades other organs or structures, and/or perforates visceral peritoneum

- **N0**: No regional lymph node metastasis
- **N1a**: Metastasis in 1 regional lymph node
- **N1b**: Metastasis in 2–3 regional lymph nodes
- **N1c**: Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized paricolic or pararectal tissues without regional nodal metastasis
- **N2a**: Metastasis in 4–6 regional lymph nodes
- **N2b**: Metastasis in 7 or more regional lymph nodes

- **M1a**: Metastasis confined to 1 organ or site (eg, liver, lung, ovary, nonregional node)
- **M1b**: Metastases in more than 1 organ/site or the peritoneum

**STAGE GROUPINGS**

- **Stage I**
  - **T1 N0 M0**
  - **T2 N0 M0**

- **Stage II**
  - **T3 N0 M0**
  - **T4 N0 M0**

- **Stage III**
  - **T3 N1 M0**
  - **T2 N2a M0**

- **Stage IV**
  - **Any T Any N M1a**
  - **Any T Any N M1b**

**Stage IIIA**

- **T1–T2 N1a–N1c M0**
- **T1 N2a M0**

**Stage IIIB**

- **T3 T4a N1a–N1c M0**
- **T2 T3 N2a M0**
- **T1 T2 N2b M0**

**Stage IIIC**

- **T4b N0 M0**

**Stage IVA**

- **Any T Any N M1a**

**Stage IVB**

- **Any T Any N M1b**

---

*Note: Tumor directly invades or is adherent to other organs or structures, and/or perforates visceral peritoneum include invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (eg, invasion of the sigmoid colon by a carcinoma of the cecum or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria). Invasion of the sigmoid colon by a carcinoma of the cecum or colon, for example, is classified as Dukes’ A1, whereas invasion of an adjacent organ (eg, bladder, ovary, other pelvic organ) by direct extension (without perforation of the visera) is classified as T4a. Invasion of the sigmoid colon by a carcinoma of the cecum or colon, for example, is classified as Dukes’ A1, whereas invasion of an adjacent organ (eg, bladder, ovary, other pelvic organ) by direct extension (without perforation of the visera) is classified as T4a. The V and L classifications should be used to identify the presence or absence of vascular or lymphatic invasion, whereas the PN site-specific factor should be used for perineural invasion.*

---

TNM Classification: Kidney Cancer

DEFINITION OF TNM

Stage I
- T1: Tumor ≤ 7 cm in greatest dimension, limited to the kidney
- T1a: Tumor ≤ 4 cm in greatest dimension, limited to the kidney
- T1b: Tumor > 4 cm but not > 7 cm in greatest dimension, limited to the kidney
- N0: No regional lymph node metastasis

Stage II
- T2: Tumor > 7 cm in greatest dimension, limited to the kidney
- T2a: Tumor > 7 cm but ≤ 10 cm in greatest dimension, limited to the kidney
- T2b: Tumor > 10 cm, limited to the kidney
- N0: No regional lymph node metastasis

Stage III
- T3: Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota’s fascia
- T3a: Tumor grossly extends into the renal vein or its segmental (muscle containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota’s fascia
- T3b: Tumor grossly extends into the vena cava below the diaphragm
- T3c: Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
- N1: Metastasis in a single regional lymph node

Stage IV
- T4: Tumor invades beyond Gerota’s fascia (including contiguous extension into the ipsilateral adrenal gland)
- M0: No distant metastasis
- M1: Distant metastasis

Stage Groupings

- Stage I: T1 N0 M0
- Stage II: T2 N0 M0
- Stage III: T1 or T2 N1 M0*
- Stage IV: T3 N0 or N1 M0*
- Stage IV: T4 Any N M0*
- Stage IV: Any T Any N M1

* not illustrated

TNM Classification: Penis Cancer

**DEFINITION OF TNM**

- **T1**: Noninvasive verrucous carcinoma
  - T1a: Tumor invades subepithelial connective tissue without lymph vascular invasion and is not poorly differentiated (ie, grade 3–4)
  - T1b: Tumor invades subepithelial connective tissue with lymph vascular invasion or is poorly differentiated
- **cN0**: No palpable or visibly enlarged inguinal lymph nodes
- **cN1**: Palpable mobile unilateral inguinal lymph node

**STAGE GROUPINGS**

- **Stage I**
  - T1a  N0  M0
- **Stage II**
  - T1b  N0  M0
  - T2  N0  M0
- **Stage IIIA**
  - T1a  N1  M0
  - T1b  N1  M0
  - T2  N1  M0
- **Stage IIIB**
  - T1a  N2  M0
  - T1b  N2  M0
  - T2  N2  M0
- **Stage IV**
  - T4       Any N  M0
  - Any T  N3       M0
  - Any T  Any N  M1

*Note: Lymph node metastases outside of the true pelvis in addition to visceral or bone sites.*

TNM Classification: Prostate Cancer

Note: Prostate cancer can be staged clinically (eg: cT1b) or pathologically (eg: pT2b). Pathologic and clinical staging are similar except that there is no pathological T1 stage.

<table>
<thead>
<tr>
<th>TNM Classification: Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEFINITION OF TNM</td>
</tr>
</tbody>
</table>

**Stage I**
- T1: Clinically inapparent tumor neither palpable nor visible by imaging (T1a: Tumor incidental histologic finding in less than 5% of tissue resected; T1b: Tumor incidental histologic finding in more than 5% of tissue resected; T1c: Tumor identified by needle biopsy eg, because of elevated PSA)
- N0: No regional lymph node metastasis
- G1: Well differentiated (Gleason 2-4)

**Stage IIA**
- T2: Tumor confined within prostate* (T2a: Tumor involves one-half of one lobe or less; T2b: Tumor involves more than one-half of one lobe but not both lobes; T2c: Tumor involves both lobes)
- N0: No regional lymph node metastasis
- G2: Moderately differentiated (moderate anaplasia Gleason 5-6)

**Stage IIB**
- T3: Tumor extends through the prostate capsule** (T3a: Extracapsular extension (unilateral or bilateral); T3b: Tumor invades seminal vesicle(s))
- N0: No regional lymph node metastasis
- G3–4: Poorly differentiated/undifferentiated (marked anaplasia Gleason 7-10)

**Stage III**
- T4: Tumor is fixed or invades adjacent structures other than central vessels, muscularis of urethra, bladder, levator muscles, or pelvic wall
- N0: No regional lymph node metastasis
- N1: Metastasis in regional lymph node(s)
- M0: No distant metastasis

**Stage IV**
- M1: Distant metastasis (M1a: Nonregional lymph node(s); M1b: Bone(s); M1c: Other site(s) with or without bone disease)

*Note: when more than 1 site of metastasis is present, the most advanced site category is used (M1c is most advanced).

**Stage 1**
- T1a–c: N0 M0 G1
- T1a: N0 M0 G1
- T1b: N0 M0 G1
- T1c: N0 M0 G1

**Stage II**
- T2a: N0 M0 G1
- T2b: N0 M0 G1

**Stage III**
- T3a: N0 M0 G1
- T3b: N0 M0 G1

**Stage IV**
- T4: N0 M0 G1
- N0 T1: N0 M0 G1
- N0 T2: N0 M0 G1
- N0 T3: N0 M0 G1
- N0 T4: N0 M0 G1

**TNM Classification: Rectal Cancer**

**DEFINITION OF TNM**

<table>
<thead>
<tr>
<th>T Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into perirectal/fascial tissues</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor penetrates to the surface of the visceral peritoneum*</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor directly invades or is adherent to other organs or structures <strong>,</strong>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis in 1 regional lymph node</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastasis in 2-3 regional lymph nodes</td>
</tr>
<tr>
<td>N1c</td>
<td>Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in 1 organ or site (eg, liver, lung, ovary, nonregional node)</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in 2-3 organs or sites</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in ≥4 organs or sites</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in ≥5 organs or sites</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Metastasis confined to 1 organ or site (eg, liver, lung, ovary, nonregional node)</td>
</tr>
<tr>
<td>M1b</td>
<td>Metastasis in ≥2 organs or sites</td>
</tr>
</tbody>
</table>

**STAGE GROUPINGS**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Stage</th>
<th>N Stage</th>
<th>M Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1–T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0–N1c</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T3</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td>IIC</td>
<td>T3–T4a</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td>IIBc</td>
<td>T4b</td>
<td>N1–2</td>
<td>M0, M1b</td>
</tr>
</tbody>
</table>

*Note: Direct invasion in T4 includes invasion of other organs or structures of the colon/rectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the left colon by a carcinoma of the transverse colon). If invasion is due to spread through lymph nodes (eg, invasion of the left colon by a carcinoma of the cecum), it should be classified T3 or T4a.***

***Note: Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1–4a depending on the anatomical depth of wall invasion. The V and L classifications should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN site-specific factor should be used for perineural invasion.***

### TNM Classification: Renal Pelvis and Ureter Cancer

**DEFINITION OF TNM**

**T**
- **T1**: Tumor invades subepithelial connective tissue
- **T2**: Tumor invades the muscularis
- **T3**: (For renal pelvis only) Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma.
- **T4**: Tumor invades adjacent organs, or through the kidney into the perinephric fat

**N**
- **N0**: No regional lymph node metastasis
- **N1**: Metastasis in a single lymph node, ≤2 cm in greatest dimension
- **N2**: Metastasis in a single lymph node, >2 cm but not >5 cm in greatest dimension; or multiple lymph nodes, none >5 cm in greatest dimension
- **N3**: Metastasis in lymph node, >5 cm in greatest dimension

**M**
- **M0**: No distant metastasis
- **M1**: Distant metastasis

**STAGE GROUPINGS**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>V</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
</tbody>
</table>

**Stage IVb**: Any N, M0

---

**TNM Classification: Testis Cancer**

**DEFINITION OF TNM**
- **pT1** - Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis
- **pT2** - Tumor limited to the testis and epididymis with vascular/lymphatic invasion of tumor extending through the tunica albuginea with involvement of the tunica vaginalis
- **pT3** - Tumor involves the spermatic cord with or without vascular/lymphatic invasion
- **pT4** - Tumor involves the scrotum with or without vascular/lymphatic invasion

**STAGE GROUPINGS**

**Stage I**
- pT1 N0 M0 Sx*

**Stage IA**
- pT1 N0 M0 S0

**Stage IB**
- pT2 N0 M0 S0
- pT3 N0 M0 S0
- pT4 N0 M0 S0

**Stage II**
- Any pT/Nx M0 S0
- Any pT/Nx N1–3 M0 S0
- Any pT/Nx N1–3 M0 S1

**Stage III**
- Any pT/Nx M1 S0
- Any pT/Nx M1 S1
- Any pT/Nx M1 S2
- Any pT/Nx M1 S3

**Stage IV**
- Any pT/Nx S1–3

---

TNM Classification: Urethral Cancer

DEFINITION OF TNM

Stage I

T1
Tumor invades subepithelial connective tissue
N0
No regional lymph node metastasis

Stage II

T2
Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
N1
Metastasis in a single lymph node ≤ 2 cm in greatest dimension

Stage III

T3
Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck
N1
Metastasis in a single lymph node ≤ 2 cm in greatest dimension

Stage IV

T4
Tumor invades other adjacent structures
N2
Metastasis in a single node more than 2 cm in greatest dimension, or in multiple nodes

Stage IV

M1
Distant metastasis

STAGE GROUPINGS

T1  N0  M0
T2  N1  M0*
T2  N0  M0*
T2  N1  M0
T3  N0  M0*
T3  N1  M0*
T3  N2  M0
T4  Any N  M0
Any T  N3  M0
Any T  Any N  M1
**TNM Classification: Urinary Bladder Cancer**

**DEFINITION OF TNM**

**T1**
- Tumor invades subepithelial connective tissue
- No regional lymph node metastasis

**T2**
- Tumor invades muscularis propria
- N0: No regional lymph node metastasis

**T3**
- Tumor invades perivesical tissue (pT3a) Microscopically (pT3b) Macroscopically
- N0: No regional lymph node metastasis

**T4**
- Tumor invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvis wall, abdominal wall
- N1: Single regional lymph node metastasis in the true pelvis (hypogastric, obturator, external iliac, or presacral lymph node)
- N2: Multiple regional lymph node metastasis in the true pelvis (hypogastric, obturator, external iliac, or presacral lymph node metastasis)
- N3: Lymph node metastasis to the common iliac lymph nodes

**N0**
- No regional lymph node metastasis

**M0**
- No distant metastasis

**Stage I**
- T1
- N0
- M0

**Stage II**
- T2a
- N0
- M0
- T2b
- N0
- M0

**Stage III**
- T3a
- N0
- M0
- T3b
- N0
- M0
- T4a
- N0
- M0

**Stage IV**
- T4b
- N0
- M0
- Any T
- N1
- M0
- Any T
- N2
- M0
- Any T
- N3
- M0
- Any T
- Any N
- M1

**Uroradiology Signs** (See also Section II: “Uroradiology Signs”)

<table>
<thead>
<tr>
<th>Sign (Typical Modality)</th>
<th>Description</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial cut-off sign (CT or MRI w/contrast)</td>
<td>Abrupt termination of contrast material within the renal artery</td>
<td>Renal artery obstruction from thrombosis, embolus or dissection from trauma</td>
</tr>
<tr>
<td>Ball-on-Tea, Lobster Claw, signet ring (XR, retrograde urography)</td>
<td>Patterns of renal papillary excavation; signet ring occurs when the necrotic papillary tip remains in the pelvis and then it is filled with contrast material (acts as the “stone” for the ring)</td>
<td>Papillary necrosis (nonsteroidal anti-inflammatory drugs [NSAIDs], sickle cell anemia, analgesic nephropathy, infection-TB, and diabetes mellitus)</td>
</tr>
<tr>
<td>Balloon on a string (XR)</td>
<td>High exit point of ureter from a dilated renal pelvis (can be seen with hydronephrotic rim sign, crescent sign, or on its own)</td>
<td>Ureteropelvic junction obstruction</td>
</tr>
<tr>
<td>Bear’s paw (CT)</td>
<td>Dilated multiloculated appearing renal calyces with contracted renal pelvis (in setting of obstructing stone)</td>
<td>Diffuse xanthogranulomatous pyelonephritis</td>
</tr>
<tr>
<td>Bullet on a Bodkin (XR, CT)</td>
<td>Encasement of the ureter; dilated ureter (the bullet) on top of the smaller encased ureter (the bodkin)</td>
<td>Metastatic disease; extension from an adjacent tumor, lymphoma, or retroperitoneal fibrosis</td>
</tr>
<tr>
<td>Cobra head sign (XR)</td>
<td>Dilatation of the distal ureter that is surrounded by a thin lucent line</td>
<td>Orthotopic ureteroceles</td>
</tr>
<tr>
<td>Codweb (CT)</td>
<td>Exaggerated appearance of perirenal septa</td>
<td>Multiple disease processes but commonly seen in acute ureteral obstruction from stones</td>
</tr>
<tr>
<td>Coiled catheter sign (XR)</td>
<td>Related to goblet sign: Dilated ureteral segment provides a space for catheter to coil within</td>
<td>Urothelial carcinoma</td>
</tr>
<tr>
<td>Comet sign (CT)</td>
<td>Focal density with adjacent, tapering, noncalcified “tail”</td>
<td>Phlebolith</td>
</tr>
<tr>
<td>Concentric ring sign—aka Target sign (MR, best T1 weighted)</td>
<td>Rings of hyper and hypointensity within a hematoma (inner bright ring signifies hemoglobin degradation)</td>
<td>Renal hematoma present for greater than 3 wk</td>
</tr>
<tr>
<td>Corkscrew ureter (XR)</td>
<td>Healing stages of tuberculosis involving the ureter</td>
<td>Late ureteral tuberculosis</td>
</tr>
<tr>
<td>Crescent sign (CT w/contrast)</td>
<td>Concentrated contrast material in collecting tubules, parallel to a dilated calyx</td>
<td>Prolonged, incomplete obstruction of collecting system. (Typically indicates that renal function is still recoverable upon relief of the obstruction)</td>
</tr>
<tr>
<td>Dromedary hump (any modality)</td>
<td>A pseudomass appearing in the left kidney, that is drained by a normal collecting system element</td>
<td>Normal variant of kidney is molded by the adjacent spicula creating a protrusion that can be mistakenly identified as a mass</td>
</tr>
<tr>
<td>Drooping lily sign (XR)</td>
<td>Dilated upper moiety ureter in a duplicated system that places downward and/or lateral pressure on the functional lower moiety</td>
<td>Completely duplicated system with an obstructed upper moiety</td>
</tr>
</tbody>
</table>

Angio, angiography; CT, computed tomography; MRI, magnetic resonance imaging; XR, plain x-ray; IVP or retrograde pyelogram.
**URORADIOLOGY SIGNS (Continued)**

<table>
<thead>
<tr>
<th>Sign (Typical Modality)</th>
<th>Description</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faceless kidney (any modality)</td>
<td>Normal renal parenchyma, lacking central renal sinus structures (duplicated system) or any edema that eliminates the typical appearance of the kidney</td>
<td>Renal duplication (slice in between duplicated systems); edema obliterating normal kidney appearance can signify any inflammatory condition or infiltrative condition such as lymphoma or renal cell carcinoma</td>
</tr>
<tr>
<td>Fragmented staghorn (XR)</td>
<td>Disrupted densities following the outline of the renal pelvis; usually associated with renal enlargement</td>
<td>Pyonephrosis or Xanthogranulomatous pyelonephritis</td>
</tr>
<tr>
<td>Goblet sign (Retrograde XR)</td>
<td>Ureteral dilatation below an intraluminal filling defect; usually a chronic process</td>
<td>Urothelial cell carcinoma; less likely metastatic disease or endometriosis</td>
</tr>
<tr>
<td>Growing calculus sign (XR)</td>
<td>Apparent enlargement of medullary califications contained in acritic tubules pre- and postcontrast administration</td>
<td>Medullary nephrocalcinosis caused by medullary sponge kidney</td>
</tr>
<tr>
<td>Horseshoe</td>
<td>Kidneys joined by a lower pole isthmus that crosses anterior to the aorta, just inferior to the inferior mesenteric artery</td>
<td>Most common congenital fusion abnormality of the kidney (Horseshoe kidney)</td>
</tr>
<tr>
<td>Hydronephrotic rim sign (CT or MR w/contrast)</td>
<td>Variable enhancement of residual but atrophic renal parenchyma surrounding dilated renal pelvis and calyces (inner margin of rim is concave toward hilum, can also have enhancement of cortical columns)</td>
<td>Chronic hydronephrosis</td>
</tr>
<tr>
<td>Keyhole sign (US)</td>
<td>Thick bladder wall and dilated posterior urethra</td>
<td>Posterior urethral valves</td>
</tr>
<tr>
<td>Kidney sweat (US, CT, MR)</td>
<td>Extracapsular hypoechoic rim of fluid around kidney (perirenal edema)</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Loop-to-loop colon</td>
<td>Transverse colon extends lateral to abdominal wall, descending colon then courses medially to fill renal fossa creating a loop of colon</td>
<td>Renal agenesis</td>
</tr>
<tr>
<td>Lying down (pancake) adrenal gland</td>
<td>Typical shape of adrenal gland is dependent on kidney; when kidney absent, the adrenal gland (when present) can assume a flattened appearance</td>
<td>Renal agenesis</td>
</tr>
<tr>
<td>Maiden waist deformity (XR)</td>
<td>Medial deviation of bilateral ureters; ureters are drawn toward each other in the lumbosacral region</td>
<td>Retroperitoneal fibrosis</td>
</tr>
<tr>
<td>Mulberry (XR)</td>
<td>Density in the urinary system with less developed spikes (mamillated appearance)</td>
<td>Calcium oxalate dihydrate stone</td>
</tr>
<tr>
<td>Pear sign (XR, CT)</td>
<td>Symmetric compression of the bladder</td>
<td>Pelvic fluid (hematoma, lymphocele, urinoma, abscess), pelvic hypomacia, vascular distalation from aneurysms or collateral vessels, lymph node enlargement or psoas hypertrophy</td>
</tr>
<tr>
<td>Phantom calyx sign (XR)</td>
<td>No identifiable collecting system element where one should be seen</td>
<td>Inflammation (tuberculosis, acute pyelonephritis), neoplasm, stricture from trauma and/or stone passage, ischemia, congenital anomaly, renal contusion or technical error of underfilling</td>
</tr>
</tbody>
</table>

Angio, angiography; CT, computed tomography; MR, magnetic resonance imaging; XR, plain x-ray; IVP or retrograde pyelogram.
**URORADIOLOGY SIGNS (Continued)**

<table>
<thead>
<tr>
<th>Sign (Typical Modality)</th>
<th>Description</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pie-in-the-sky sign (XR)</td>
<td>High position of contrast opacified bladder in pelvis</td>
<td>Pelvic hematoma from pelvic trauma; high suspicion of urethral injury</td>
</tr>
<tr>
<td>Pipestem ureter</td>
<td>Ureter is straight and rigid</td>
<td>Ureteral tuberculosis</td>
</tr>
<tr>
<td>Putty kidney</td>
<td>Calcifications outlining the entire, or close to the entire kidney</td>
<td>Genitourinary tuberculosis (end-stage finding in kidney)</td>
</tr>
<tr>
<td>Reverse rim sign (CT or MR w/contrast)</td>
<td>Hypoattenuating renal cortex with medullary enhancement</td>
<td>Disruption of cortical blood flow with development of cortical necrosis. Can be caused by shock, intravascular hemolysis, toxins, and rejection in transplanted kidney</td>
</tr>
<tr>
<td>Rim sign of vascular compromise (CT or MR w/contrast)</td>
<td>Rim of subcapsular enhancement</td>
<td>Renal artery obstruction from thrombosis, embolus or dissection from trauma (most commonly). Renal vein thrombosis and acute tubular necrosis (less commonly)</td>
</tr>
<tr>
<td>Sawtooth ureter</td>
<td>Dilatation and ragged irregularity of the ureter</td>
<td>Early ureteral tuberculosis</td>
</tr>
<tr>
<td>Soft-tissue rim sign (CT)</td>
<td>Focal density with surrounding edema of ureteral wall</td>
<td>Unilateral stone; usually impacted; may be absent with stones &gt;4 mm or when at UVJ. Can help distinguish stone from phlebolith as it is uncommon for phlebolith to have soft tissue rim</td>
</tr>
<tr>
<td>Spaghetti sign (XR, CT)</td>
<td>Linear filling defect within the bladder</td>
<td>Gross hematuria; this sign implies blood has come from above the bladder (ureter acts as a mold for the blood clot)</td>
</tr>
<tr>
<td>Spoked wheel pattern (US, CT, MR)</td>
<td>Peripheral “rim” vessel branching into centripetal “spoke” vessels within a mass; can have a central area of decreased perfusion (central scar)</td>
<td>Renal cell carcinoma; oncocytoma</td>
</tr>
<tr>
<td>Spotted nephrogram (CT or MR w/contrast, renal angiography)</td>
<td>Patchy irregular enhancement of the renal parenchyma</td>
<td>Small vessel occlusion, caused by scleroderma, hypertensive nephrosclerosis, or periarteritis nodosa</td>
</tr>
<tr>
<td>Staghorn (XR)</td>
<td>Branching radiopaque densities following the outline of the renal pelvis</td>
<td>Renal calculus that fills the entire renal collecting system, forming a cast of the renal pelvis</td>
</tr>
<tr>
<td>Stipple sign (Angio)</td>
<td>Contrast material trapped between the papillary projections of urothelial cell carcinoma</td>
<td>Urothelial cell carcinoma, best seen in large papillary bladder tumors</td>
</tr>
<tr>
<td>String of pearls (Angio)</td>
<td>Arteries with thickened ridges, alternating with wall thinning and aneurysm formation</td>
<td>Fibromuscular dysplasia</td>
</tr>
<tr>
<td>Thimble bladder</td>
<td>Thick wall of calcification in the bladder that reduces its capacity</td>
<td>Tuberculosis of the bladder</td>
</tr>
<tr>
<td>Threads and streaks sign (Angio, CT, MR)</td>
<td>Linear string/thread-like vessels supplying the intravascular tumor in the affected vasculature</td>
<td>Vascularized tumor thrombus extending into the renal vein or IVC</td>
</tr>
<tr>
<td>Toy jacks (XR)</td>
<td>Spiked density in the urinary system</td>
<td>Calcium oxalate diphylate stone</td>
</tr>
<tr>
<td>Tramline or railroad track calcifications</td>
<td>Thin rims of dystrophic calcifications on both sides of renal cortex</td>
<td>Renal cortical necrosis (most commonly). Glomerulonephritis, hyperparathyroidism, Aport syndrome (less common)</td>
</tr>
</tbody>
</table>

Angio, angiography; CT, computed tomography; MR, magnetic resonance imaging; XR, plain x-ray; IVP or retrograde pyelogram.

Voiding Diary

(See also Section II: “Voiding Diary (Frequency Volume Chart (FVC)).” This form is meant to be completed by the patient.)

This voiding diary records your amount of fluid intake, amount you void and if there is any leakage of urine. It should be completed for an entire 24-hr period. For the most useful results, it should be done over 2 or 3 separate 24-hr periods. You must measure and complete this form every time you void or experience urinary leakage. Please bring these voiding diary records to your next Urology office visit. Copy additional pages if needed.

How to complete this form:
1. Begin the record with your first morning void after you wake up for the day.
2. Measure all fluid intake and the amount voided in mL or ounces. Ladies can measure the amount of urine by placing a plastic bowl or collection container that we can provide to you on the toilet seat. Men can void into a suitable collection jar or other container.
3. If you experience sudden leakage of urine, note the activity you were doing at the time of leakage (laughing, coughing, sneezing, lifting, etc.).
4. If you experience urinary leakage, use the following scale to estimate the amount of urine that you leaked:
   1 = Dampness
   2 = Wet underwear or pad
   3 = Soaked through or emptied bladder
5. Indicate by Yes/No if when you leaked you had an urge to void. FVC

Your Name: __________________________ Date: __________________________
Your Physician’s Name: __________________________

<table>
<thead>
<tr>
<th>Time</th>
<th>Fluid Intake</th>
<th>Amount Voided</th>
<th>Leak Volume</th>
<th>Did you have an urge with leakage?</th>
<th>Physical activity at time of leakage</th>
</tr>
</thead>
<tbody>
<tr>
<td>(AM or PM)</td>
<td>(Type and amount in ounces or mL)</td>
<td>(In ounces or mL)</td>
<td>(See above for estimate)</td>
<td>(Yes/No)</td>
<td></td>
</tr>
</tbody>
</table>
INDEX

Acute adrenal insufficiency, 14–15, 22–23
Acute bacterial prostatitis (NHLI), 354–355
Acute cortical necrosis, 71
Acute gluteal neuropathy, 806
Acute inflammatory demyelinating polyneuropathy, 699
Acute kidney injury (AKI), 6–7, 643, 742, 775
Acute lymphocytic leukemia (ALL), 791
Acute myoclonic encephalopathy, in
Acute polycystic kidney disease, 765–766
Acute tubular necrosis (ATN), 6, 12–13
Acute gouty nephropathy, 806
Acute myelogenous leukemia, 250
Acute nephritic syndrome, 162–163
Acute perinephric abscess, 2
Adenosquamous prostate cancer, 759
Adenomatous polyps, 804
Adenoma sebaceum, 796
Adenomatoid metaplasia, 803
Adenomatoid tumors, 803
Adenopathy, paratesticular, 16–17, 530–531
Adrenal, 18–19
Adrenal cavity, 759
Adrenal cancer, with pelvic lymphadenopathy, 223
Adrenal cortical carcinoma, 20–21
Adrenal crisis, 22–23
Adrenal cysts, 644
Adrenal cytomegaly, 644
Adrenal gland metastases, 644–645
Adrenalectomy, 2
Adrenocortical carcinoma (ACC), 20–21
Adrenocorticotropin (ACTH) deficiency, 24–25
Adrenocortical insufficiency, 14–15, 22–23
Adrenocortical insufficiency, algorithm for, 825
Adrenocortical insufficiency, general considerations in, 24–25
Adrenocortical metastases, 232
Adrenocortical tumor, 24–25
Adrenocorticotropin (ACTH) deficiency, 24–25
Adrenocorticotropic hormone (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropic hormone (ACTH), 825
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenalectomy, 24
Adrenal gland metastases, 644–645
Adrenals, in children, 6
Adrenal hypoplasia, 643
Adrenal incidentalomas, 24, 644
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenal mass, 62
Adrenal mass, 232
Adrenocortical carcinoma (ACC), 24
Adrenocortical disease, primary pigmented
Adrenocortical insufficiency, algorithm for, 825
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
Adrenocorticotropin (ACTH), in congenital adrenal hyperplasia, 644
P1: OSO/OVY

P2: OSO/OVY

LWBK1391-Index

QC: OSO/OVY

LWBK1391-Gomella

1010

r r r

T1: OSO

September 19, 2014

13:12

Index

Bladder cancer and tumors (Contd.)
lymphangioma, 720
metastases, 658
metastatic, 58–59
neurofibroma, 659
non-muscle-invasive bladder cancer, 54–55
paraganglioma, 659
rhabdomyosarcoma, 659–660
small cell carcinoma, 660
squamous cell carcinoma, 56–57
staging of, 52
urothelial, micropapillary, 657
urothelial invasive (T2/3/4), 62–63
Bladder contractility index (BCI), 657
Bladder exstrophy, 146–147
Bladder injury, intraoperative, 66–67
Bladder mass, differential diagnosis, 658
Bladder outlet obstruction (BOO), 68–69, 228
hesitancy and intermittency from, 184
Bladder outlet obstruction index (BOOI), 659
Bladder overactivity, 217
Bladder pain/interstitial cystitis symptom score
(BPIC-SS), 659
Bladder stones. See Bladder calculi; Calculi
(stones)
dysuria from, 124
filling defect from, 152–153
Bladder TB, 526–527
Bladder trabeculation and cellules, 660
Bladder trauma, 70–71. See also Bladder
injury, intraoperative
combined EBR/IBR, 70
extraperitoneal (EBR), 70
intraperitoneal (IBR), 70
Bladder trauma, algorithm for, 829
Bladder wall calcification, differential diagnosis,
660
Bladder wall thickening, differential diagnosis,
660
Blastomyces dermatitidis, 660
Blastomycosis, genitourinary, 660
Bleomycin sulfate, 929
Bleomycin toxicity, 661
α-Blockers
for autonomic dysreflexia, 38
for bladder outlet obstruction, 69
Blood, in urinalysis, 912
“Blue balls”, 152
Blue diaper syndrome, 661
Blue dot sign, 650, 661
Blue nevus, 661
β 2 microglobulin, spot urine for, 913
Boari-Ockerblad flap, 661
Body mass index (BMI), urologic
considerations, 661
Bolande disease, 242–243
Bone lesions, 58
Bone marrow/stem cell transplantation,
urologic considerations, 661
Bone metastasis, urologic considerations,
661–662
Bone mineral density, urologic considerations,
662
Bone scan, urologic considerations, 662
Bonney test, 662
BOO. See Bladder outlet obstruction (BOO)
Borrelia burgdorferi, 720

Bors-Comarr classification of voiding
dysfunction, 662
Bosniak classification of renal cysts, 662
Bother score, 712
Botox, 929–930
Bottle Operation, 648
Botulinum toxin injection
for autonomic dysreflexia, 38
Botulinum toxin type A, 929–930
Bourne test, 662
Bowen Disease (BD), 74–75, 744
Bowenoid papulosis (BP), 74, 662–663,
744
Bowenoid papulosis of penis, 745
Boyarsky Guidelines, for BPH, 663
Boyce nephrotomy, 663
BPH symptom index, 652
Brachytherapy, for prostate cancer
antibiotic prophylaxis for, 979
Brachytherapy seed embolus, 663
Brain metastasis, urologic considerations,
663
Breast cancer
with gynecomastia, 171
Breast development, 790
Brenner tumors, 663
Bricker ureteral anastomosis, 663
Brigham sling, 663
Brink score, 663
British testicular tumor classification, 663
Broccoli seed extract, 917
Bromocriptine, 930
Bronchogenic cyst, retroperitoneal, 663
Brunn buds and nests, 663–664
Brushite stones, 664
BTA stat test, 664
BTA test, 664
Bulbocavernosus reflex (BCR), 647, 664
Bulbourethral gland duct ectasia, 674–675
Bulking agents, injectable, 664
Bulletus, 745
Bullous pemphigoid, 664–665
Bumetanide (Bumex), 930
BUN (Blood urea nitrogen),
increased/decreased, 665
Bupivacaine, 930
Bupivacaine, liposome, 930
Buprenorphine, 930
Burch colposuspension, 665
Buried penis, 745
Burns
chemical, 76
classification of, 76
electrical, 76
external genitalia, 76–77
perineum, 76–77
thermal, 76
Buschke–Lowenstein tumor, 665, 748
Butabarbital, hyoscyamine, hydrobromide, +
phenazopyridine, 930
Butorphanol, 930
BXO. See Balanitis xerotica obliterans (BXO)
Byars flaps, 665
C
Cabazitaxel (Jevtana), 930
Cadmium, 24-hour urine study of, 914

Calcifications
abdominal, 665
adrenal, 643
bladder, 665
pelvic, 665
prostate, 665
prostatic utricle, 761
renal, 665
of vas deferens, 782
Calcific uremic arteriolopathy, 665–666
Calcinosis, idiopathic scrotal, 665
Calcionate, 931
Calciphylaxis, 665–666
Calcitonin, 930–931
Calcitriol, 931
Calcium, 24-hour urine study, 914
Calcium acetate (Phoslo), 931
Calcium carbonate, 931
Calcium citrate (Citracal), 666
Calcium glubionate, 931
Calcium load and fast studies, 666
Calcium monohydrogen phosphate, 664
Calcium oxalate, 254–255
Calcium phosphate, 254–255
Calcium salts, 931
Calcium stones, 600
Calcium supplementation and urolithiasis, 666
Calculi (stones)
bladder
filling defect from, 152–153
calcium oxalate, 254–255
calcium phosphate, 254–255
prostate, 348–349
renal, drug-induced, 809
seminal vesicle, 782
staghorn, 695
urethral, 802
algorithm for, 904
uric acid, 600
Calluna vulgaris, 918
Calyceal diverticulum, 78–79
Camey I and II orthotopic urinary diversion, 666
Canal of Nuck hydrocele and cyst, 666
Cancidas (Caspofungin), 931
Candida albicans, 666
Candidal balanitis, 75
Candidal infection, 42, 43
Candidiasis, cutaneous, of external genitalia,
666
Candiduria, algorithm for, 831
Capsaicin, 917
Capsicum, 917
Captopril, 931
Captopril test, 666
Carboplatin, 931
Carcinoid tumors
genitourinary, 666
of testis, 790–791
Carcinoma. See specific orgran
Carcinoma in situ (CIS), 52
bladder
general considerations in, 72
of bladder, 64–65
penis, Bowen disease and erythroplasia of
Queyrat, 74
of testis, 791
Carcinoma of urethral diverticulum, 802


Index
Index
Pyelitis cystica, 766
Pyelonephritis, 590
Pyelogenic cyst, 767
Pyelitis glandularis, 766–767
Pyelitis cystica, 766
Purple urine bag syndrome (PUBS), 766
Punica granatum, 718
Pumpkin seed, 918
Quakel corporal shunt, 767
Q-tip test, 767
Pyuria, 40–41, 386–387
Pyridoxine (vitamin B6), 705
Pyridoxine, 965
Pyridium plus, 930
Pyrazinamide, 964–965
Pyospermia, 767, 781
Pyonephrosis, 384–385, 767
Pyoderma gangrenosum, 714
Pygeum africanum,

Pyelonephritis, 590.
See also

Pyelogenic cyst, 767
Pyelitis glandularis, 766–767
Pyelitis cystica, 766
Purple urine bag syndrome (PUBS), 766
Punica granatum,

Pumpkin seed, 918
Quakel corporal shunt, 767
Q-tip test, 767
Pyuria, 40–41, 386–387
Pyridoxine (vitamin B6), 705
Pyridoxine, 965
Pyridium plus, 930
Pyrazinamide, 964–965
Pyospermia, 767, 781
Pyonephrosis, 384–385, 767
Pyoderma gangrenosum, 714
Pygeum africanum,
Senior-Loken syndrome (SLS), 774
Serosa retna, 778, 918, 919
Serious cell only syndrome, 694
Serotic cells, 504
Serotic cell tumors, 500, 502–503, 504
Serum creatinine, increased/decreased, 675
Sevelamer carbonate, 966
Sevelamer hydrochloride, 966
Sex cord-stromal tumor, 504
of testis, 792
Sex hormone binding globulin (SHBG), 26, 783
Sex reversal syndrome, 784
Sexsomnia, 783
Sexual abuse, pediatric, 462–463
Sexual development disorders, 116–117
Sexual anhedonia, 783–784
Sexual activity, 675
Sexually transmitted disease (STD), 466–467
gonorrhea, 166–167
infant hydronephrosis, 196
in spinal dysraphism, 252
masses, 470–471
liposarcoma of, 786
denervation of, 503
sores of, 790
tumors, 470–471, 530–531
Spermatic cord hydrocele, 703
Spermatic cord hydrocele, 703
Spermatoceles, 472–473, 685
Spermatozoa, in urine, 912
Sperm granulomas, 785
Strontium-89 chloride, 969
Streptomycin, 969
Strickler ureteral anastomosis, 788
Squamous cell carcinoma (SCC), 72
Squamous cell carcinoma (SCC)
of bladder, 56–57
bladder, 72
do not hallucinate.
of penis, 748
Squamous cell carcinoma (SCC), 542–543
do not hallucinate.
of penis, algorithm for, 874
ureter, 542–543
urethra, 560–561, 570–571
Sphalerite nephrolithiasis, 803
bladder, 72
gout, 784
St. Joseph’s aspirin, 927
Stalod, 930
Staghorn calculi, 695
Stamey test, 788
Stanhope, 292
Stents, prostatic, 761
Sterile pyuria, 40
Steroid, systemic, 968, 969, 979
Stevens-Johnson syndrome, 686
Steroid-induced, 239
Straddle injury, 749
Staungaria, 788
Streptococcus pyogenes, 719
Streptomycin, 969
Stress urinary incontinence (SUI), 210
Streptococcus pyogenes, 719
Stricture, 210
Stenosis in pregnancy, 600
Strophanthin, 979
Streptococcus pyogenes, 719
Stokes, catheterizable, 80–81
Stone disease, 679
Stone passage statistics, of ureter, 800
Stoma, 560
Structured, 784
Stoses, catheterizable, 80–81
Stones in pregnancy, 600
Strobini, 979
Stomach, 964
Stomach, 560
Stomach, 560–561
Stow, 788
Strontium-89 chloride, 969
Streptomycin, 969
Stress urinary incontinence (SUI), 210
ureter, 800
urethra, 572–573
dysuria from, 124
Stroke (CVA), 480–481
Strontium-89 chloride, 969
Stout, 800
Stout, 800
Stout’s disease, 788
Subcutaneous angioblastic hyperplasia with eosinophilia, 649
Subcutaneous hemangiomata, 746
Suburethral (SUT), 787
Sural nerve, 572
Superficial basal cell carcinoma, 74

Index
P1: OSO/OVY

P2: OSO/OVY

LWBK1391-Index

QC: OSO/OVY

LWBK1391-Gomella

T1: OSO

September 19, 2014

13:12

Index
Transurethral resection of bladder tumor
(TURBT), 53, 55, 64
hemorrhage after, 180–181
Transurethral resection of prostate (TURP)
hemorrhage after, 180–181
incontinence after, with myasthenia gravis,
250
Transurethral resection (TUR) syndrome,
522–523
fluid overload in, 522–523
hypervolemia in, 522–523
Transverse myelitis syndrome, 699
Transvestic fetishism, 740
Trapped penis, 745
Trauma
bladder, 70–71. See also Bladder injury,
intraoperative
combined EBR/IBR, 70
extraperitoneal (EBR), 70
intraperitoneal (IBR), 70
penis, algorithm for, 875
perineal, 749
renal
adult, 430–431
hemodynamically stable,algorithm for, 892
pediatric, 432–433
scrotal, 456–457
algorithm for, 894
ureter, 550–551
intraoperative, 546–547
urethral, 546–547, 550–551, 574–575
Triad
Carney, 667
Currarino, 30
Lenk, 817
Prune belly syndrome, 366–367
reactive arthritis, 768
Triamcinolone-nystatin, 972–973
Triamterene, 973
Trichomoniasis, 795
Trichophyton rubrum, 680
Trichotemnomania, pubic, 795
Trichotillomania, pubic, 795
Triethylenethiophosphoramide, 973
Trigonitis, 795
Trimethoprim (TMP), 973
Trimix, 961
TRI-MIX, 794
Triple X syndrome, 817
Triplo-X, 817
Triptorelin, 973
Trisomy 8, 795
Trisomy 9, 795
Trisomy 13, 795
Trisomy 18, 683, 795
Trisomy 21, 682, 796
Trisomy 22, 796
Trisomy 4 P, 795
Trisomy 9 P, 795
Trisomy 20 P, 796
Trisomy 10 Q, 795
Trisomy 11 Q, 795
Trisomy syndrome, 796
Trocar injury, during laparoscopy,
524–525
Trospium, 973
True hermaphroditism, 796

Tryptophan malabsorption, 661
Testicular cystic lymphangiomas, 791
Tuberculosis (TB)
and abdominal mass, 2
bladder and urethra, 796
genitourinary, 526–527
male external genitalia, 796
prostate and epididymis, 796
steroids for, 529
Tuberculosis (TB), epididymitis from, 138
Tuberous sclerosis (TS), 504, 796
Tubular ectasia, of rete testis, 776
Tubular metaplasia, 803
Tubulocystic carcinoma of kidney (TCCK), 771
Tumor lysis syndrome (TLS), 734, 796–797
Tumors of dysgenetic gonads, 697
Tunica albuginea, 530–531
Tunica vaginalis mesothelioma, 507
Tunica vaginalis tumors, 797
TURBT. See Transurethral resection of bladder
tumor (TURBT)
Turner syndrome, 797
Turner-Warwick inlay urethroplasty, 797
TURP syndrome, 522–523
Tylenol, 923
U
UISS-UCLA International Kidney Cancer
Staging System, 797
Ulcer, Hunner, 703
Ulcerative colitis, 710
Ulcers, genital, 694
Ultracet, 972
Umbilical abnormalities, 532–533
Umbilical artery, 532–533
Umbilical drainage, 532–533
Umbilical granuloma, 532–533
Umbilical infection, 532–533
Umbilical mass, 532–533
Umbilical polyps, 532–533
Umbilical sinus, 532–533
Unasyn, 927
Underactive bladder, 534–535
α-adrenergic blockers for, 535
choline esterase inhibitors for, 535
muscarinic receptor agonists for, 535
Undervirilized male syndrome, 797
Undescended testes. See Cryptorchidism
Undescended testicle, algorithm for, 898
Unilateral Horner’s syndrome, in
neuroblastoma, 258
Uninhibited detrusor contraction, 797
Upper genitourinary anomalies, cloacal
exstrophy with, 148
Upper urinary tract filling defect, 152–153
Upper urinary tract instrumentation, antibiotic
prophylaxis for, 980–981
Urachal abnormalities, 797–798
Urachal adenocarcinoma, 50–51
Urachal carcinoma, 526–527, 533, 538–539,
798
staging systems, 798t
Urachal cyst, 532–533, 797
infected, 532
Urachal diverticulum, of bladder, 797
Urachal sinus, 532, 797
Urachal tissue, persistent, 532–533

r r r

1029

Urachus, 532
Urachus, patent, 532–533
Urate, dietary, 798
Urate nephropathy, 733–734
Urea nitrogen, 24-hour urine study of, 914
Ureaplasma urealyticum, 798
Urecholine, 929
Uremia, algorithm for, 899
Uremic medullary cystic disease, 724
Uremic sponge kidney, 724
Ureter
agenesis/atresia of, 798
deviation, 798
diverticulum, 798
duplicated and bifid, 798–799
ectopic, 799
fibroepithelial polyps of, 799
fish hook (reverse J), 799
hemangiomas of, 799
J hooking of, 799
leiomyomas of, 799
leiomyosarcomas of, 799
metastasis to, 799
neurofibromas of, 799–800
pipe-stem, 800
radiation injury to, 800
retrocaval, 800
shepherd’s crook, 800
spiral, 800
stone passage statistics, 800
strictures, 800
and tuberculosis, 528–529
valves, 800
Ureteral bud theory, 246
Ureteral calculi, algorithm for, 904
Ureteral cancer
squamous cell carcinoma, 542–543
urothelial carcinoma, 544–545
Ureteral ectopia, 799
Ureteral jets, 801
Ureteral obstruction, 548–549
Ureteral perfusion test, 815
Ureteral stent, encrusted, 685
Ureteral strictures, urinary diversion and, 801
Ureteral TB, 526–527, 528–529
Ureteral valves, 800
Ureter cancer
TNM classification, 999
Ureteritis, 801
Ureteritis cystica, 801
Ureteroarterial fistula, 690
Ureterocele, 552–553
hydronephrosis from, 196
Ureteroenteric anastomotic stricture (UE),
554–555
Ureteroneocystostomy, 801
Ureteropelvic junction obstruction (UPJO),
556–557
Whitaker test for, 556
Ureteropelvic junction (UPJ) obstruction,
Anderson-Hynes pyeloplasty for, 647
Ureteropelvic junction (UPJ) obstruction,
hydronephrosis from, 196
Ureteroscopy, antibiotic prophylaxis for,
980
Ureterovesical junction (UVJ) obstruction,
hydronephrosis from, 196


Urethral trauma, 550–551
Urethral tumors, general considerations in, 540–541
Urethral adenocarcinoma of accessory glands, 803
adenomatous polyps, 801
bleeding, 801
calcium, 802
condyloma, 802
diverticuloma, 802
diverticula, male, 802
duplication of, 802
foreign body, 802
hemangiomata, 802
hypermobility, 803
lymphoma, 803
malacia, 803
malignant melanoma, 803
metastasis to, 803
meatus, normal caliber, 803
malignant neoplasms, 72–73
malignant melanoma, 803
nephrogenic metaplasia, 803
metastasis to, 803
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
malignant neoplasms, general considerations, 72–73
TNM classification, 1002
Urethral papilloma, 740
Urethral tear, 689–690
Uropatia, 924
Urethroscopy, 919
Urine analysis, 919
Uterus, 919
Uterine hyperplasia, 514

V
Vaccinium macrocarpon, 917
VACTERL/VATER association, 810
VACTERL/VATER syndrome, 810
Vasectomy reversal, general considerations, 812
and postvasectomy pain syndrome, 812
obstruction, 812
congenital absence, 628–629
algorithm for, 909
pediatric, 626–627
adult, 624–625

Vasovasostomy, 812
Vasomotor instability, in males, 188–189
Vasography, 812
Vasectomy, 812
Vasculitis, 812
Varicocele, 780
Vardenafil, 974
Vaprisol, 936
Vanishing UDT, 536–537
Vanishing testis syndrome, 811
Vanillylmandelic acid (VMA), 24-hour urine
Vanderbilt cystectomy index (VCI), 811
Vancomycin, 973–974
Valacyclovir, 973
Vaginosis, 811
Vaginitis, 622–623
Vaginal wall masses, 741
Vaginal wall cyst, 568–569
Vaginal surgery, antibiotic prophylaxis for, 980
Vaginal prolapse, 811
Vaginal mesh erosion, 620–621
Vaginal mass, newborn, 811
Vaginal fusion, 811
Vaginal dyspareunia, 122
Vaginal duplication, 810
Vaginal discharge, 810
Vaginal bleeding, abnormal, algorithm for, 907
Vaginal agenesis, 810
Vacuum-assisted closure therapy, 694
VATER syndrome, 810
Varicocele, 780
Vardenafil, 974
Vaprisol, 936
Vanishing UDT, 536–537
Vanishing testis syndrome, 811
Vanillylmandelic acid (VMA), 24-hour urine
Vanderbilt cystectomy index (VCI), 811
Vancomycin, 973–974
Valacyclovir, 973
Vaginosis, 811
Vaginitis, 622–623
Vaginal wall masses, 741
Vaginal wall cyst, 568–569
Vaginal surgery, antibiotic prophylaxis for, 980
Vaginal prolapse, 811
Vaginal mesh erosion, 620–621
Vaginal mass, newborn, 811
Vaginal fusion, 811
Vaginal dyspareunia, 122
Vaginal duplication, 810
Vaginal discharge, 810
Vaginal bleeding, abnormal, algorithm for, 907
Vaginal agenesis, 810
Vacuum-assisted closure therapy, 694
VATER syndrome, 810
Varicocele, 780
Vardenafil, 974
Vaprisol, 936
Vanishing UDT, 536–537
Vanishing testis syndrome, 811
Vanillylmandelic acid (VMA), 24-hour urine
Vanderbilt cystectomy index (VCI), 811
Vancomycin, 973–974
Valacyclovir, 973
Vaginosis, 811
Vaginitis, 622–623
Vaginal wall masses, 741
Vaginal wall cyst, 568–569
Vaginal surgery, antibiotic prophylaxis for, 980
Vaginal prolapse, 811
Vaginal mesh erosion, 620–621
Vaginal mass, newborn, 811
Vaginal fusion, 811
Vaginal dyspareunia, 122
Vaginal duplication, 810
Vaginal discharge, 810
Vaginal bleeding, abnormal, algorithm for, 907
Vaginal agenesis, 810
Vacuum-assisted closure therapy, 694
Yohimbine, 919
Yohimex, 919
Yolk sac tumors, 492–493, 508, 510
 Bladder, 818
 Prostate, 818
 Young classification of posterior urethral valves, 818
 Young-Dees-Leadbetter bladder reconstruction, 818
 Young syndrome, 818

Z
 Zellweger syndrome, 818
 Zemas, 936
 Zinner syndrome, 818
 Zipper entrapment, 818–819
 Zithromax, 928
 Zoladex, 947
 Zoledronic acid, 692, 975
 Zometa, 692

Zona pellucida binding assay, 819
 Zoon balanitis, 75
 Zosyn, 902
 Zovirax, 923–924
 Zyflamend, 919
 Zygotale intrafallopian transfer (ZIFT), 651
 Zylogepim, 924
 Zylogap, 923
 Zymir, 952