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SECOND EDITION

THE 5-MINUTE UROLOGY CONSULT

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Leonard G. Gomella, MD, FACS

The Bernard W. Godwin, Jr. Professor of Prostate Cancer

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and

Associate Director, Kimmel Cancer Center

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To Tricia, Leonard, Patrick, Andrew, and
Michael, for their understanding and
encouragement.

“En tierra de los ciegos el tuerto es rey.”

SPANISH PROVERB

PREFACE

I am very pleased to present the second edition of The 5-Minute Urology Consult. The first edition was released almost 10 years ago in 2000 and has steadily grown in popularity. 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. Urologic diseases and conditions are common problems that are seen by health care providers. Almost one third of all congenital 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 and residents and fellows preparing for oral and written in-service and practicing urologists preparing for certification exams will find the book a useful study aid. This second edition has undergone extensive editing and updating to reflect the most current data possible at the time of publication.

So much information is available today on the Internet, many are asking why medical books such as this are even necessary as a reference. 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. 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. It also represents a core of essential “must know” information specifically written for the field of urology.

The broad array of topics addressed in this book are based on reviews of published literature, major textbooks, grand rounds case presentations, validated internet resources, and actual patient consultations. Coverage includes adult and pediatric urology, as well as subspecialty areas of urology such as urologic oncology, endourology, female urology, neurourology, andrology, infectious diseases, and renal transplantation. While primarily written for practitioners in the United States, the table of contents has been reviewed by our international editorial board, who represent over two dozen countries, in an attempt to capture as many diseases and conditions as possible for international readers.

This book, a member of the popular “5-Minute Consult” series published by Wolters Kluwer Health/LWW, generally follows the organizational formatting of the other books in the series. However, there are notable exceptions as this book is focused on a surgical subspecialty. Section I: Urologic Diseases and Conditions provides information on over 270 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. Further, evidence based medicine references, standard fare in the “5-Minute Consult” series, are new to

this urology edition. This addition is representative of the popular 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 cannot be found or is insufficient to perform this level of evidence analysis. The reader will note in this second edition the introduction of evidence-based medicine references in some of the chapters as appropriate. Many topics are further supported by algorithms and an enhanced online image library.

Section II: Short Topics: A to Z consists of over 1,200 key concepts, diseases, presenting complaints or conditions in the field that the practitioner must be aware of but may not be worthy of a complete two page chapter. Section III features over 35 visual algorithms to enhance specific topics in Section I. Section IV is dedicated exclusively to a core discipline in our field, Urine Studies. Section V: Alternative Urologic Therapies (Phytotherapy) is a focused review that is of interest to patients and caregivers alike. Section VII: 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 based on published literature with additional input and the personal observations of the authors and editors. Lastly, Section VII: Appendix is a collection of useful reference tables and forms. An online image library, available as a supplement to the text, can be found at www.5minurologyconsult.com.

In any project of this magnitude, there are many individuals responsible for its success. I would like to acknowledge the following individuals who provided the initial encouragement and guidance in 1996 to develop the first urology version of the 5-Minute Consult: Lippincott Williams & Wilkins editors Carroll Cann and Craig Percy and Dr. Mark Dambro. Thanks to my former assistant Denise Tropea who provided key administrative support to keep the contributors and this second edition organized. A special thanks to the over 280 authors and editors who took the time to contribute to this edition. Ryan Shaw, Julia Seto, Brian Brown, Jeri Litteral, Erika Kors and the staff at Lippincott Williams & Wilkins went to extraordinary measures to move the publishing process along to meet certain critical deadlines, and for these efforts, I am very grateful. On a sad note, our good friend Dr. John Stein who was to assume the Chair at the Department of Urology at the University of Southern California in Los Angeles, died suddenly at a very young age in 2008. He was serving as a member of our editorial board at the time and will be missed by all of us in the field. We extend our condolences to his family. Most importantly, I would like to thank my wife, Tricia, and our children, Leonard, Patrick, Andrew, and Michael, for allowing me to sacrifice many nights, weekends, and holidays over the

last 2 years to complete this book.

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
editor@urologyquestion.com
www.urologyquestion.com

EVIDENCE-BASED MEDICINE

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 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 30 years ago, there has been increased emphasis on this concept in daily patient care. While there are currently many different systems of evidence-based medicine, 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 below. 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 primary 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. (5)[A]"

The A designation, as noted in the algorithm below, 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 is 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 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 het “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.

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EDITOR-IN-CHIEF

Leonard G. Gomella, MD, FACS

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Assistant Professor
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Chief
Urologic Oncology Branch
National Institutes of Health
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Taha Abo-Almagd
Abdel-Meguid, MD
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Department of Urology
El-Minia University, Faculty of Medicine
El-Minia, Egypt
Consultant and Associate Professor
Department of Urology
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Resident Physician
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Medical University of South Carolina
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Assistant Professor
Department of Urologic Oncolog
Fox Chase Cancer Center
Philadelphia, Pennsylvania
Jeffrey D. Branch, MD
Assistant Professor
Department of Urology
Loyola University Medical Center
Maywood, Illinois
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Associate Professor of Urologic Surgery
Division of Urologic Surgery
Washington University School of Medicine
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Department of Urology
Hackensack University Medical Center
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Associate Professor
Head, Section of Urologic Oncology
Division of Urology, Department of Surgery
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Augusta, Georgia
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University of Pennsylvania
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Daniel J. Canter, MD
Clinical Instructor
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Division of Urology
Hopsital of the University of Pennsylvania
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Department of Urology
University of North Carolina at Chapel Hill
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Brett S. Carver, MD
Assistant Attending and Assistant Member
Department of Surgery, Division of Urology
Memorial Sloan Kettering Cancer Center
New York, New York
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Professor and Chairman
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Department of Urology
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A.I. duPont Hospital for Children
Wilmington, Delaware
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Associate Professor
Section of Surgery
Sackler Faculty of Medicine, Tel-Aviv University
Associate Professor, Attending Urologist
Department of Urology
Tel-Aviv Sourasky Medical Center
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Cory A. Chevalier, BS, MSII
SUNY Upstate Medical University
Syracuse, New York
Edmund Chiong, MBBS, FRCSEd, FRCSI, FAMS
Assistant Professor
Department of Surgery, Yong Loo Lin School of Medicine
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Fellow
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Resident
Department of Urology
Arthur Smith Institute for Urology

North Shore/Long Island Jewish
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Resident
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SUNY Downstate Medical School
Brooklyn, New York
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Division of Urology
Oregon Health & Sciences University
Portland, Oregon
Michael S. Cookson, MD
Professor
Department of Urologic Surgery
Vanderbilt Universtiy
Nashville, Tennessee
Douglas E. Coplen, MD
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Washington University School of Medicine
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The Royal Melbourne Hospital
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Massachusetts General Hospital
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Department of Urology
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Resident
Department of Urology
Penn State Milton S. Hershey Medical Center
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Resident
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Michael J. Erhard, MD
Assistant Professor
Department of Urology
Mayo Clinic
Chairman
Department of Surgery
Nemours Children’s Clinic
Jacksonville, Florida
Deborah R. Erickson, MD
Professor
Department of Surgery, Division of Urology
University of Kentucky

Lexington, Kentucky
Matthew R. Eskridge, MD
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Gordon L. Fifer, MD
Resident
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana
Robert S. Figenshau, MD
Associate Professor
Department of Surgery, Division of Urology
Washington University School of Medicine
St. Louis, Missouri
T. Ernesto Figueroa, MD
Clinical Associate Professor
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Chief
Division of Pediatric Urology
Alfred I. duPont Hospital for Children
Wilmington, Delaware
John M. Fitzpatrick, MCh, FRSCI, FRCSGlas, FRCS
Professor
Department of Surgery
University College, Dublin
Chief
Department of Surgery
Mater Misercordiae Hospital
Dublin, Ireland
Robert C. Flanigan, MD, FACS
Albert J. Jr. and Claire R. Speh Professor and Chair
Department of Urology

Loyola University Medical Center
Maywood, Illinois
Neil E. Fleshner, MD, MPH, FRCSC
Professor
Department of Surgery
University of Toronto
Head
Division of Urology
University Health Network
Toronto, Ontario
Debra L. Fromer, MD
Chief
Center for Bladder, Prostate and Pelvic Floor Health
Department of Urology
Hackensack University Medical Center
Hackensack, New Jersey
Clifford Georges, MD
Resident
Department of Urology
SUNY Downstate Medical School
Brooklyn, New York
Jason P. Gilleran, MD
Assistant Professor
Department of Urology
The Ohio State University
Ohio State Medical Center
Columbus, Ohio
Jordan Gitlin, MD
Resident
Department of Surgery
Division of Urology
University of Alabama at Birmingham
Birmingham, Alabama
Paul Gittens, MD
Fellow Male Reproductive Medicine and Surgery

Baylor College of Medicine
Houston, Texas
Deborah T. Glassman, MD
Clinical Assistant Professor of Urology
Department of Urology
Thomas Jefferson University
Attending Staff
Department of Urology
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania
Manlio A. Goetzl, MD
Resident
Department of Urology
University of Kansas Medical Center
Kansas City, Kansas
Tricia Lacy Gomella, MD
Part-time Assistant Professor of Pediatrics
The Johns Hopkins University School of Medicine
Baltimore, Maryland
Neil H. Grafstein, MD
Assistant Professor
Department of Urology
Mount Sinai School of Medicine
Director of Reconstructive Urology
Department of Urology
Mount Sinai Medical Center
New York, NY
H. Barton Grossman, MD
Professor
Department of Urology
University of Texas M. D. Anderson Cancer Center
Houston, Texas
Robert L. Grubb, III, MD
Associate Professor
Department of Surgery, Division of Urology

Washington University School of Medicine
Chief
Department of Urology
St. Louis VA Medical Center
St. Louis, Missouri
Narmada P. Gupta, MD, MCh
Professor and Chairman
Department of Urology
All India Institute of Medical Sciences
New Delhi, India
Justin Gyorfi, MD
Resident
Division of Urology, Department of Surgery
West Virginia University
Morgantown, West Virginia
Gabriel P. Haas, MD, FACS
Professor
Department of Urology
SUNY Upstate Medical University
Syracuse, New York
Ethan J. Halpern, MD
Professor
Department of Radiology and Urology
Thomas Jefferson Medical College
Co-Director, Jefferson Prostate Diagnostic Center
Department of Radiology and Urology
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania
J. Nathaniel Hamilton, MD
Resident
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Lindsay A. Hampton
Resident Physician

Department of Urology
University of Carlifornia
San Francisco, California
David A. Hatch, MD
Professor of Urology and Pediatrics
Department of Urology
Loyola University Stritch School of Medicine
Chief, Pediatric Urology
Department of Urology
Loyola University Medical Center
Maywood, Illinois
Jason C. Hedges, MD, PhD
Chief Resident
Department of Urology and Renal Transplantation
Oregon Health & Science University
Portland, Oregon
C. D. Anthony Herndon, MD, FAAP, FACS
Associate Professor
Department of Surgery/Pediatrics
Division of Urology/Section Pediatric Urology
University of Alabama at Birmingham
Birmingham, Alabama
Irvin H. Hirsch, MD
Clinical Professor
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Steve J. Hodges, MD
Assistant Professor
Department of Urology
Wake Forest University School of Medicine
Winston-Salem, North Carolina
Mark Horowitz, MD, FAAP, FACS
Associate Professor of Pediatric Urology
Chief of Pediatric Urology

SUNY Downstate Medical Center, Brooklyn, New York
Staten Island University Hospital
Staten Island, New York
William C. Huang, MD
Assistant Professor
Department of Urology
New York University School of Medicine
Attending
Department of Urology
New York University Langone Medical Center
New York, New York
Scott G. Hubosky, MD
Assistant Professor
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Chad P. Huckabay, MD
Attending Urologist
Arthur Smith Institute of Urology
New Hyde Park, New York
Cory M. Hugen, MD
Resident
Department of Urology
Loyola University Stritch School of Medicine
Loyala University Medical Center
Maywood, Illinois
Taro Iguchi, MD, PhD
Assistant Professor
Department of Urology
Osaka City University School of Medicine
Osaka City Urniversity Hospital
Osaka, Japan
Serge A. Jabbour, MD, FACP, FACE
Associate Professor of Clinical Medicine, Interim Director
Department of Medicine, Divison of Endocrinology

Jefferson Medical College, Thomas Jefferson University
Philadelphia, Pennsylvania
Richard H. Jadick, DO
CDR USN
Medical College of Georgia
Augusta, Georgia
Thomas W. Jarrett, MD
Professor and Chairman
Department of Urology
George Washington University
Chief
Department of Urology
George Washington University Hospital
Washington, DC
James R. Johannes, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Hubert John, MD
PD Dr. Med
Zentrum für Urologie
Klinik Hirslanden
Zürich, Switzerland
David J. Kaplan, MD
Resident
Department of Urology
Temple University School of Medicine
Philadelphia, Pennsylvania
Steven A. Kaplan, MD
Professor of Urology
Chief, Institute Bladder and Prostate Health
Weill Medical College, Cornell University
New York, New York
Nicholas T. Karanikolas, MD

Director of Urologic Oncology
Staten Island University Hospital
Assistant Professor
State University Health Sciences Center at Brooklyn
Staten Island University Hospital
Nalitt Cancer Center
Staten Island, New York
Michael W. Kattan, PhD
Chair
Department of Quantitative Health Sciences
Cleveland Clinic
Cleveland, Ohio
Matthew D. Katz, MD
Minimally Invasive Urologic Oncology Fellow
Division of Urologic Surgery
Washington University School of Medicine
St. Louis, Missouri
Melissa R. Kaufman, MD, PhD
Assistant Professor
Department of Urologic Surgery
Vanderbilt University
Nashville, Tennesse
Thomas E. Keane, MBBCh, FRCSI, FACS
Professor and Chief
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Francis X. Keeley, Jr., MD, FRCS
Consultant Urologist
Bristol Urological Institute
Southmead Hospital
Bristol, England
Adam S. Kibel, MD
Professor
Department of Surgery, Division of Urologic Surgery

Washington University School of Medicine
Attending Physician
Department of Surgery, Division of Urology
Barnes Jewish Hospital
St. Louis, Missouri
Michelle J. Kim, MD
Assistant Professor
Department of Urology
Touro University College of Medicine
Hackensack University Medical Center
Hackensack, New Jersey
Ashley B. King, MD
Resident
Division of Urology
Virginia Commonwealth University School of Medicine
Richmond, Virginia
Eric A. Klein, MD, FACS
Professor of Surgery
Cleveland Clinic Lerner College of Medicine
Chairman
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio
Joseph C. Klink, MD
Urology Resident
Division of Urology, Department of Surgery
Duke University
Durham, North Carolina
Michael O. Koch, MD, FACS
Chairman
Department of Urology
Indiana University School of Medicine
Indianapolis, Indiana
Harry P. Koo, MD, FAAP, FACS
Barbara and William Thalhimer Professor and Chairman

Division of Urology
Virginia Commonwealth University School of Medicine
Richmond, Virginia
Helen J. Kuo, MD
Resident
Department of Urology
Indiana University
Indianapolis, Indiana
Alexander Kutikov, MD
Urological Oncology Fellow
Division of Urological Oncology, Departement of Surgical Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania
H. Henry Lai, MD
Assistant Professor of Surgery
Department of Surgery, Division of Urologic Surgery
Washington University School of Medicine
Attending Physician
Department of Surgery
Barnes-Jewish Hospital
St. Louis, Missouri
Costas D. Lallas, MD, FACS
Assistant Professor
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Benjamin R. Lee, MD
Professor
Department of Urology
Tulane University School of Medicine
Director, Endourology, Robotics and Laparoscopy Fellowship
Department of Urology
Tulane University Hospital and Clinic
New Orleans, Louisiana
Nicholas T. Leone, MD

Bard Fellow in Endourology
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Herbert Lepor, MD
Professor and Martin Spatz Chairman
Department of Urology
New York University School of Medicine
Director of Urology
Department of Urology
New York University Medical Center
New York, New York
Timothy J. LeRoy, MD
Resident
Department of Urology
Mayo Clinic
Jacksonville, Florida
Aihua Li, MD, PhD
Chairman and Professor
Department of Urology
Branch of Xinhua Hospital, Shangai Jiatong University
Chairman and Chief Urologist
Department of Urology
Yangpu District Central Hospital
Shanghai, China
Evangelos N. Liatsikos, MD, PhD
Associate Professor
Department of Urology
Universary of Patras
Head of Endoscopy and Laparoscopy
Department of Urology
University Hospital of Patras
Patras, Greece
Robert Linden, MD
Chief Resident

Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
W. Marston Linehan, MD, FACS
Chief, Urologic Oncology Branch
National Institutes of Health
National Cancer Institute
Bethesda, Maryland
Kevin R. Loughlin, MD, MBA
Professor
Department of Surgery (Urology)
Harvard Medical School
Senior Surgeon
Department of Surgery
Brigham and Women’s Hospital
Boston, Massachusetts
Franklin C. Lowe, MD, MPH
Professor of Clinical Urology
Department of Urology
Columbia University College of Physicians and Surgeons
Associate Director
Department of Urology
St. Luke’s/Roosevelt Hospital
New York, New York
M. Scott Lucia, MD
Associate Professor of Pathology
Department of Pathology
Urniversity of Colorado Dever School of Medicine
Director, Prostate Diagnostic Lab
University Hospital
University of Colorado
Denver, Colorado
John H. Lynch, MD
Professor and Chairman
Department of Urology

Georgetown University Hospital
Washington, DC
Richard J. Macchia, MD
Chair and SUNY Distinguished Teaching Professor
Department of Urology
SUNY Downstate Medical School
University Hospital Brooklyn
Kings County Hospital Center
Brooklyn, New York
John M. Mai, MD
Resident
Department of Urology
Temple University Hospital
Philadelphia, Pennsylvania
S. Bruce Malkowicz, MD
Professor of Urology
Department of Surgery
University of Pennsylvania
Attending Surgeon
Department of Surgery, Divsion of Urology
Hospital of the University of Pennsylvania
Philadelphia, Pennsylvania
Michael J. Marberger, MD, FRCS(ed)
Professor and Chairman
Department of Urology
Medical University of Vienna
Vienna, Austria
Tracy P. Marien, MD
Resident
Department of Urology
New York University School of Medicine
New York, New York
Brian K. Marks, MD
Clinical Assistant Instructor
Department of Urology

SUNY Downstate Medical School
Brooklyn, New York
Matthew G. McIntyre, MD
Resident
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
J. William McRoberts, MD
Emeritus Chief of Urology & Professor of Surgery
Unviersity of Kentucky College of Medicine
Lexington, Kentucky
Jamie C. Messer, MD
Resident
Department of Surgery
Penn State Milton S. Hershey Medical Center
Hershey, Pennsylvania
Peter D. Metcalfe, MD, FRCSC
Assistant Professor
Department of Surgery
University of Alberta
Pediatric Urologist
Department of Surgery
Stollery Children’s Hospital
Alberta, Canada
Adam R. Metwalli, MD
Consultant
Urologic Oncology Branch
National Cancer Institute
Bethesda, Maryland
Chesapeake Urology Associates
Division of Minimally Invasive Surgery and Robotics
Fulton, Maryland
Monica M. Metzdorf, MD
Pediatric Urologist
Department of Urology

Kaiser Permanente Medical Group
Los Angeles, California
Douglas F. Milam, MD
Associate Professor
Department of Urologic Surgery
Vanderbilt University
Nashville, Tennesse
Rosalia Misseri, MD
Assistant Professor
Department of Urology
Indiana University School of Medicine
Staff Physician
J.W. Riley Hospital for Children
Indianapolis, Indiana
Atsushi Mizokami, MD, PhD
Lecturer
Department of Integrative Cancer Therapy and Urology
Kanazawa University Graduate School of Medical Sciences
Kanazawa, Japan
Robert M. Moldwin, MD
Associate Professor of Clinical Urology
The Arthur Smith Institute for Urology
Hofstra University School of Medicine
Director, Pelvic Pain Center
The Smith Institute for Urology
Long Island Jewish Medical Center
New Hyde Park, New York
Francesco Montorsi, MD
Professor
Department of Urology
Universita Vita Salute San Raffaele
Milan, Italy
Guillermo Montoya, MD
Associate Professor
Department of Urology

Universidad Nacional Autonoma de México
Hospital de Especialildades
Mexico City, Mexico
Rocco A. Morabito, MD
Resident
Division of Urology, Department of Surgery
West Virginia University
Morgantown, West Virginia
Judd W. Moul, MD, FACS
James H. Semans, MD Professor of Surgery
Department of Surgery
Duke University
Chief
Department of Surgery, Division of Urologic Surgery
Duke University Medical Center
Durham, North Carolina
Mark A. Moyad, MD, MPH
Director of Preventive and Alternative Medicine
Department of Urology
University of Michigan Medical Center
Ann Arbor, Michigan
Phillip Mucksavage, MD
Resident
Department of Surgery, Division of Urology
Hospital of the University of Pennsylvania
Philadelphia, Pennsylvania
John Patrick Mulhall, MD
Director, Sexual Medicine Program
Division of Urology
Memorial Sloan Kettering Cancer Center
New York, New York
Ravi Munver, MD
Associate Professor
Department of Urology
Touro University College of Medicine

Vice Chairman/Chief, Minimally Invasive and Robotic Urologic Surgery
Hackensack University Medical Center
Hackensack, New Jersey
Jack H. Mydlo, MD
Professor and Chairman
Department of Urology
Temple University
Philadelphia, Pennsylvania
Richard Natale, II, MD
Chief Resident
Department of Urology
University of Florida
Shands Hospital
Jacksonville, Florida
Christian J. Nelson, PhD
Assistant Attending Psychologist
Department of Psychiatry and Behavioral Sciences
Memorial Sloan-Kettering Cancer Center
New York, New York
Eric Nelson, MD
Fellow in Pediatric Urology
Department of Urology
Baylor College of Medicine
Houston, Texas
Joel B. Nelson, MD
Frederic N. Schwentker Professor and Chairman
Department of Urology
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania
Craig S. Niederberger, MD, FACS
Professor
Department of Urology
University of Illinois
Chief
Department of Urology

University of Illinois Medical Center
Chicago, Illinois
Paul H. Noh, MD
Assistant Professor
Department of Surgery
University of Cincinnati
Assistant Professor
Division of Pediatric Urology
Cincinnati Children’s Hospital Medical Center
Cincinnati, Ohio
Alejandro Ramon Nolazco, MD
Especialista Consultor En Urologia
Chief of Department
Hospital Britanico De Buenos Aires and Hospital Universitario Austral
Buenos Aires, Argentina
Raymond W. Pak, MD
Staff Urologist
Department of Urology
Malizia Clinic
Urologist
Department of Urology
Emory University Hopital - Midtown
Atlanta, Georgia
John M. Park, MD
The Cheng-Yang Chang Endowed Professor of Pediatric Urology
Chief, Division of Pediatric Urology
Department of Urology
University of Michigan Health System
Ann Arbor, Michigan
Amit R. Patel, MD
Chief Resident
Glickman Urologic & Kidney Institute
The Cleveland Clinic
Cleveland, Ohio
Jitesh Patel, MD

Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Nick A. Pavona, MD
Chairman Department of Urology
Benjamin Franklin University Medical Center
Chadds Ford, Pennsylvania
Mark L. Pe, MD
Chief Resident
Department of Urology
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania
Margaret S. Pearle, MD, PhD
Professor
Department of Urology and Internal Medicine
University of Texas Southwestern Medical Center
Dallas, Texas
David F. Penson, MD, MPH, FACS
Professor
Department of Urologic Surgery
Vanderbilt University
Director
Center for Surgical Quality and Outcomes Research
Vanderbilt University Medical Center
Nashville, Tennessee
Michael Perrotti, MD, FACS
Clinical Associate Professor
Department of Surgery
Albany Medical College
Director of Urologic Oncology
Department of Surgery
Saint Peter’s Cancer Care Center
Albany, New York
Steven P. Petrou, MD, FACS

Professor
Department of Urology
Mayo Clinic College of Medicine
Consultant
Department of Urology
Mayo Clinic Hospital
Jacksonville, Florida
Daniel P. Petrylak, MD
Associate Professor of Medicine
Department of Medicine
Columbia University Medical Center
New York, New York
Joel Picus, MD
Associate Professor of Medicine
Department of Medicine, Oncology Division
Medical Oncology Section
Washington University School of Medicine
St. Louis, Missouri
Hector Pimentel, MD
Physician
Department of Urology
University of Illinois at Chicago
Chicago, Illinois
Peter A. Pinto, MD
Staff Clinician
Director of the Urologic Oncology Fellowship Program
Urologic Oncology Branch
National Cancer Institute
Bethesda, Maryland
Michel A. Pontari, MD
Professor
Department of Urology
Temple University School of Medicine
Philadelphia, Pennsylvania
Glenn M. Preminger, MD, FACS

Professor, Urologic Surgery
Director, Comprehensive Kidney Stone Center
Department of Urologic Surgery
Duke University Medical Center
Durham, North Carolina
Juan Miguel Proano, MD
Clinical Fellow
Urologic Oncology Branch
National Intitutes of Health
National Cancer Institute
Bethesda, Maryland
Dmitri Pushkar, MD, FEBU
Professor and Chairman, General Scientific Secretary, Russian Society of Urology, Urologist General
Department of Urology
MSMSU
Moscow, Russia
Marcus L. Quek, MD
Assistant Professor
Department of Urology
Loyola University Stritch School of Medicine
Loyola Univeristy Medical Center
Maywood, Illinois
Ganesh V. Raj, MD, PhD
Assistant Professor of Urology
Department of Urology
University of Texas Southwestern Medical Center
Dallas, Texas
Matthew C. Raynor, MD
Resident
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana
Matthew J. Resnick, MD
Resident

Department of Urology
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania
Audrey C. Rhee, MD
Division of Urology
Medical College of Georgia
Augusta, Georgia
Stephen B. Riggs, MD
Assistant Professor
Department of Urology
Eastern Virginia Medical School
Norfolk, Virginia
Roger S. Rittmaster, MD
Executive Director
Oncology Clinical Development
GlaxoSmithKline, Inc.
Research Triangle Park, North Carolina
Wilmer B. Roberts, MD, PhD
Chief Resident Department of Urology
James Buchanan Brady Urological Institute
Johns Hopkins Medical Institutions
Johns Hopkins Hospital
Baltimore, Maryland
Alexandra E. Rogers, MD
Resident
Department of Urology
Mayo Clinic
Jacksonville, Florida
Inger Rosner, MD
Clinical Fellow
Urologic Oncology Branch
National Institutes of Health
National Cancer Institute
Bethesda, Maryland
Ashley E. Ross, MD, PhD

Resident/Research Fellow
Department of Urology
Brady Urological Institute
Johns Hopkins University School of Medicine
Johns Hopkins Hospital
Baltimore, Maryland
Mohamad W. Salkini, MD
Assistant Professor of Surgery
Department of Surgery/Urology
West Virgina University
Cosultant/Staff Urologist
Department of Surgery/Urology
West Virginia University Hospital
Morgantown, West Virgina
Susan E. Saunders
Senior Resident
Division of Urology/Department of Surgery
West Virginia University
Morgantown, West Virginia
Ihor S. Sawczuk, MD
Professor and Chairman of Urology
Hackensack University Medical Center
Touro University College of Medicine
Hackensack, New Jersey
Charles D. Scales, Jr., MD
Resident in Urologic Surgery
Division of Urology, Department of Surgery
Duke University Medical Center
Durham, North Carolina
Anthony John Schaeffer, MD
Resident
The James Buchanan Brady Urological Institute
Johns Hopkins Medical Institutions
Baltimore, Maryland
Anthony J. Schaeffer, M, FACS

Herman L. Kretschmer Professor and Chairman
Department of Urology
Northwester University Feinberg School of Medicine
Northwestern Memorial Hospital
Chicago, Illinois
Bruce J. Schlomer, MD
Resident
Department of Urology
University of Texas Southwestern
Resident Physcian
Department of Urology
Parkland Hospital
Dallas, Texas
Francis X. Schneck, MD
Associate Professor
Department of Urology
University of Pittsburgh Medical Center
Clinical Director
Department of Urology
Children’s Hospital of Pittsburgh
Pittsburgh, Pennsylvania
Florian R. Schroeck, MD
Resident
Department of Surgery, Divison of Urology
Duke University Medical Center
Durham, North Carolina
Stacy M. Scofield, BS
Research Associate
Department of Urology
New York Presyterian Hospital
New York, New York
Benjamin J. Scoll, MD
Resident
Department of Urology
Temple University Hospital

Philadelphia, Pennsylvania
Ahma Shabsigh, MD, FACS
Assistant Professor
Department of Urology
Ohio State University
Ohio State University Medical Center
Columbus, Ohio
Kelly E. Shaffer, MD
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
David S. Sharp, MD
Assistant Professor
Department of Urology
The Ohio State University Medical Center
Columbus, Ohio
Travis Shaw, DO
Urology Resident
Department of Urology
Albert Einstein Medical Center
Philadelphia, Pennsylvania
Joel Sheinfeld, MD
Professor
Department of Urology
Weill College of Medicine, Cornell University
Deputy Chief
Department of Urology Service
Memorial Sloan-Kettering Cancer Center
New York, New York
Patrick J. Shenot, MD
Assistant Professor
Vice Chair for Academic Affairs
Residency Program Director
Department of Urology
Jefferson Medical College

Thomas Jefferson University
Philadelphia, Pennsylvania
Kashif Siddqi, MD
Section of Urology, Department of Surgery
Medical College of Georgia
Augusta, Georgia
Jaspreet Singh, DO
Fellow in Urologic Oncology
Department of Urology
Kimmel Cancer Center
Tomas Jefferson University
Philadelphia, Pennsylvania
Craig B. Slotoroff, MD
Chief Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Marc C. Smaldone, MD
Chief Resident
Department of Urology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania
Alex Sokol, MD
Chief Resident
Department of Urology
SUNY Downstate Medical School
Brooklyn, New York
Gregory Spana, MD
Resident
Department of Urology
SUNY Upstate Medical School
Syracuse, New York
Arun K. Srinivasan, MD, MRCS
Arthur Smith Institute for Urology
North Shore/Long Island Jewish

New Hyde Park, New York
Danielle A. Stackhouse, MD
Resident
Department of Surgery, Division of Urology
Duke University Medical Center
Durham, North Carolina
Doron S. Stember, MD
Fellow
Urology Service, Department of Surgery
Memorial Sloan-Kettering Cancer Center
New York, New York
Carsten Stephan, MD
Privatdozent Dr. Med
Department of Urology
Charité – Universitätsmedizin Berlin
Urologist
Department of Urology
Charité Campus Mitte
Berlin, Germany
Aaron B. Stike, MD
Resident
Division of Urology
Viginia Commonwealth University School of Medicine
Richmond, Virginia
Stephen E. Strup, MD
William S. Farish Professor and Chief of Urology
Department of Surgery, Division of Urology
University of Kentucky
Lexington, Kentucky
Douglas E. Sutherland, MD
Attending Urologist
Department of Urology
MultiCare Urology of Tacoma
Tacoma, WA
Can Talug, MD

Chief Resident
Division of Urology/Department of Surgery
West Virginia University
Morgantown, West Virginia
Teuvo Tammela, MD, PhD
Professor and Chief of Urology
Department of Urology
Tampere University Hospital
Tampere, Finland
Aisha K. Taylor, MD
Resident
Department of Urology
Feinberg School of Medicine
Northwestern University
Chicago, Illinois
Claudio Teloken, MD, PhD
Professor of Urology
Department of Urology
UCSPA–Federal University of Medical Sciences
Porto Alegre, Brazil
Patrick E. Teloken, MD
Collaborator
Department of Urology
Universidade Federal de Ciencias da Saude de Portol Alegre
Porto Alegre, Brazil
Dan Theodorescu, MD, PhD
Professor
Department of Urology
University of Virginia Health System
Charlottesville, Virginia
David D. Thiel, MD
Assistant Professor of Urology
Department of Urology
Mayo Clinic
Jacksonville, Florida

Anil A. Thomas, MD
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio
Raju Thomas, MD, FACS, MHA
Professor and Chairman
Department of Urology
Tulane University School of Medicine
New Orleans, Louisiana
J. Brantley Thrasher, MD, FACS
Professor and William L. Valk Chair
Department of Urology
University of Kansas Medical Center
University of Kansas Hospital
Kansas City, Kansas
Adeep Thumar, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Edouard J. Trabulsi, MD
Associate Professor
Department of Urology
Co-Director, Jefferson Prostate Diagnostic Center
Kimmel Cancer Center
Thomas Jefferson University
Philadelphia, Pennsylvania
Erica J. Traxel, MD
Assistant Professor
Division of Urology, Department of Surgery
Washington University School of Medicine
Assisant Professor
Division of Pediatric Urology
St. Louis Children’s Hospital
St. Louis, Missouri

Olivier Traxer, MD
Professor of Urology
Department of Urology
University of Pierre et Marie Curie Paris 6
Tenon Hospital
Paris, France
JC Trussell, MD
Clinical Investigator of Urology
Department of Urology
SUNY Upstate Medical University
Syracuse, New York
Eric C. Umbreit, MD
Resident
Department of Urology
Mayo Clinic
Rochester, Minnessotta
Robert G. Uzzo, MD
Professor and Chairman
Department of Surgery
Fox Chase Cancer Center
Philadelphia, Pennsylvania
Richard Valicenti, MD
Professor and Chair
Department of Radiation Oncology
UC Davis School of Medicine
Sacramento, California
Hendrik Van Poppel, MD, PhD
Chairman
Department of Urology
University Hospitals Leuven, Campus Gasthuisberg Herestraat
Leuven, Belgium
Sandip P. Vasavada, MD
Associate Professor of Surgery
Center for Female Pelvic Medicine and Reconstructive Surgery
Cleveland Clinic Lerner College of Medicine

Glickman Urological Institute
Cleveland, Ohio
Goutham Vemana, MD
Resident
Department of Urology
University of Cincinnati
University Hospital
Cincinnati, Ohio
Humberto Villavicencio, MD
Presidente de la Asociación Española de Urología
Director del servicio de Urologia
Fundacic n Puigvert
Barcelona, Spain
Ilan Waldman, MD
Chief Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Julian Wan, MD
Clinical Associate Professor of Urology
Department of Urology
University of Michigan Medical School
Ann Arbor, Michigan
Bradley W. Warner, MD
Chief Resident
Department of Urology
Univeristy of Kentucky
Lexington, Kentucky
Michael J. Wehle, MD
Assistant Professor
Department of Urology
Mayo Clinic
Jacksonville, Florida
Perry R. Weiner, DO
Clinical Assistant Professor

Vice Chair for Clinical Affairs
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania
Avi C. Weiss, MD
Chief Resident
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Shawn E. White, MD
Resident
Division of Urology
University of Pennsylvania
Philadelphia, Pennsylvania
Benajmin M. Whittam, MD
Resident
Department of Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennesse
J. Stuart Wolf, Jr., MD
The David A. Bloom Professor of Urology
Director, Division of Minimally Invasive Urology
University of Michigan
Ann Arbor, Michigan
Paul R. Womble, MD
Resident
Department of Urology
The University of Kansas Medical Center
Kansas City, Kansas
Michael Wong, MBBS, MMED
Senior Consultant
Department of Urology
Singapore General Hospital
Medical Director
Singapore Urology and Fertility Centre

Mount Elizabeth Hospital
Sinapore
Timothy R. Yoost, MD
Resident Physician
Department of Urology
Medical University of South Carolina
Charleston, South Carolina
Paul R. Young, MD
Assistant Professor
Department of Urology
Mayo Clinic
Jacksonville, Florida
Stanley Zaslau, MD, MBA, FACS
Urology Residency Program Director and Associate Professor
Division of Urology
West Virginia University
Morgantown, West Virginia
Joseph R. Zola, MD
Resident
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Contents

SECTION I

Urologic Diseases and Conditions

ABDOMINAL MASS, ADULT, UROLOGIC CONSIDERATIONS

Taro Iguchi, MD, PhD

Gabriel Haas, MD

BASICS

DESCRIPTION

Urologic abdominal masses are mostly retroperitoneal. They are generally:

- Renal in origin
- Adrenal in origin
- Germ cell origin
- Metastic origin

RISK FACTORS

- Infection: Predisposes to abscess formation
- Trauma: May lead to hematoma
- Renal and adrenal cancer risk factors: See Section I, “Renal Masses” and “Adrenal Cortical Carcinoma”

PATHOPHYSIOLOGY

Various urologic pathologic conditions may present with a mass:

- Primary renal neoplasms:
  - Malignant: RCC, renal sarcoma, adult Wilms tumor, urothelial carcinoma, lymphoma
  - Benign: Renal cortical adenoma, renal oncocytoma, renal hemartoma (angiomyolipoma) fibroma
- Primary adrenal neoplasms: Adrenal cortical carcinoma, pheochromocytoma, adrenal adenoma, paraganglioma
- Hydronephrosis
- Primary and metastatic GCT: Are composed of seminoma, embryonal cell carcinoma, yolk sac tumor, teratoma, and choriocarcinoma.
- Primary extra-gonadal GCTs can occur intraperitoneally.
- Metastatic GCTs are associated with retroperitoneal lymphadenopathy:
  - Renal abscesses: Usually follow insufficient treatment of lobar nephronia; needle aspiration may be needed to make a diagnosis.
- TB can cause cold abscess formation. Pus developing from a renal source may track alongside psoas muscle and appears in the groin, where it must be distinguished from hernia.
- Perinephric abscess: Usually arises as a result of pre-existing renal factors such as renal calculi, ureteral calculi, hydronephrotic changes, renal cystic disease, or infected carcinoma.

- Hematomas: May be caused by a ruptured kidney or ureteral avulsion. Blood in the retroperitoneal space may track to the corresponding iliac fossa.
- Renal cysts
- Bladder-related: Retention, tumors and urachal abnormality, or cancer
- Metastatic tumors to the adrenal glands and kidney

DIAGNOSIS

HISTORY

- Weight loss, cachexia, night sweats may be associated with chronic septic disease, such as TB or malignancy.
- Spiking fever and throbbing pain are usually associated with abscess formation.
- Pain may be due to spontaneous renal hemorrhage, invasion by a tumor of neighboring tissues, clot colic with gross hematuria, or distant metastatic disease to bone or brain.
- Classic triad of hematuria, flank pain, and a flank mass is only seen in few cases of RCC.
- Medical history is significant for TB, lobar nephronia, upper tract stones, or infection.
- History of recent trauma

PHYSICAL EXAM

- General exam may reveal lymphadenopathy or leg edema due to compression of lymphatics by the mass.
- Abdominal/pelvic exam:
  - Bimanual exam of the flank and upper abdomen may reveal a palpable mass.
  - In the male patient, a varicocele may be present and seen more often on the right side when renal tumor clot forms and extends from the right renal vein into vena cava.
  - Scrotal exam for testicular masses is indicated since they may be associated with retroperitoneal lymphadenopathy.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood tests:
  - A full lab work-up for renal cancer should include CBC, calcium, urea and creatinine, and liver function tests to exclude metastasis.
  - Adrenal metabolic work-up if adrenal mass is suspected
  - Tumor markers: AFP, -hCG, and LDH if testicular tumor is suspected. AFP may be produced by pure embryonal carcinoma, teratocarcinoma, yolk sac tumor, but not by pure choriocarcinoma or pure seminoma. Among patients with nonseminomatous testis tumors, ~50–70% have elevated levels of AFP and ~40–60% have elevated levels of -hCG. LDH may be elevated, but is not specific to testicular tumors.

- Urine tests:
  - U/A and culture if abscess is suspected
  - Culture to exclude TB may be needed.

Imaging

- US: Probably best for detecting cystic lesions and should be used as an initial work-up. Doppler US is useful to reveal blood flow of the mass.
- CT: Best for solid abdominal masses. Contrast-enhanced CT may be useful for solid tumor and lymphadenopathy. CT is useful for estimate of development range to circumference and search for lung and liver metastases.
- Multirow detector CT makes multiplanar reconstruction images or 3D images available to recognize the relationship to surrounding tissues and vascular structures.
- MRI: May have less advantage over CT initially, but is useful to diagnose adrenal gland tumors. MR urography may be useful for patients with obstructive uropathy, chronic renal failure, or iodine hypersensitivity, but multirow detector CT can substitute MR urography.
- IVU: Generally replaced by enhanced CT and/or MRI
- Renal arteriography and venacavography have been largely replaced by multislice CT angiography.
- PET: Alone or combination with CT (PET-CT) is approved to diagnose metastases for kidney but not for testicular tumors. PET-CT is also useful for assessment of response after chemotherapy or radiation therapy.
- MIBG scintigraphy: Useful in diagnosing pheochromocytoma

Diagnostic Procedures/Surgery

Needle biopsy of indeterminant retroperitoneal mass

Pathological Findings

Depend on histologic nature of the mass

DIFFERENTIAL DIAGNOSIS

- GI tract tumors
- Metastatic tumors
- Hematoma (nonurologic): Spine fracture, leaking abdominal aneurysm, acute pancreatitis
- Gynecologic causes: Pregnancy, uterine fibroids, ovarian cysts and tumors
- Vascular: Aneurysm
- Retroperitoneal cysts
- Primary retroperitoneal neoplasm arising from connective tissue: Retroperitoneal lipoma, retroperitoneal sarcoma

- Retroperitoneal lymph nodes and nervous tissue tumors
- Hernia

TREATMENT

- Initial management may vary by primary disease.
- Urologic tumors: Early-stage renal and adrenal tumors are usually managed surgically.
- Immunotherapy or chemotherapy may be used in the high stage.
- Retroperitoneal lymphadenopathy associated with testicular cancer: RPLND and/or chemotherapy may be used, depending on the degree of node involvement.
- Hydronephrosis: Management for releasing obstruction. If renal dysfunction is caused, drainage is necessary (eg, double-J catheter, nephrostomy).
- Renal abscesses: Drainage of pus (or surgical removal) and administration of antibiotics
- Cysts: Asymptomatic benign renal and adrenal cysts are usually left alone. Large symptomatic cysts may be treated by percutaneous aspiration under US guidance. Ethanol injection into an emptied renal cyst was shown to decrease cyst refill.

SURGERY/OTHER PROCEDURES

Depends on clinical diagnosis

ADDITIONAL TREATMENT

May be indicated based on tumor type

ONGOING CARE

PROGNOSIS

Based on the primary cause

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Abdominal Mass Newborn/Child
- Hydronephrosis/Hydroureteronephrosis (adult and pediatric) and specific tumor types

- Newborn/Child Retroperitoneal Mass and Cysts
- Renal Masses

CODES

ICD9

- 255.9 Unspecified disorder of adrenal glands
- 593.9 Unspecified disorder of kidney and ureter
- 789.30 Abdominal or pelvic swelling, mass, or lump, unspecified site

ABBREVIATIONS

- AFP: -fetoprotein
- -hCG: -subunit of human chorionic gonadotropin
- CT: Computed tomography
- GCTs: Germ-cell tumors
- IVU: IV urogram
- LDH: Lactic acid dehydrogenase
- MIBG: 131l-metaiodobenzylguanidine
- MRI: Magnetic resonance imaging
- PET: Positron emission tomography
- RCC: Renal cell carcinoma
- TB: Tuberculosis
- US: Ultrasonography

ABDOMINAL MASS, NEWBORN/CHILD, UROLOGIC CONSIDERATIONS

Job K. Chacko, MD

T. Ernesto Figueroa, MD

BASICS

DESCRIPTION

- Traditional presentation was palpable mass in the newborn/child abdomen.
- Current presentation is usually by prenatal US.
- Most masses are nonsurgical; 87% of surgical lesions are benign.
- 2/3 of abdominal masses in 1st mo of life arise from the genitourinary tract.

EPIDEMIOLOGY

- Newborn abdominal mass in 1 per 1,000 live births
- Incidence of hydronephrosis: 1:100
- Incidence of hydronephrosis that requires surgery: 1:500

RISK FACTORS

None

Genetics

Disease-specific

GENERAL PREVENTION

Prenatal US can screen for anomalies

PATHOPHYSIOLOGY

Disease-specific, related to organ of origin

COMMONLY ASSOCIATED CONDITIONS

Disease-specific

DIAGNOSIS

HISTORY

- Prenatal US:
  - Oligohydramnios: Associated with PUV, bilateral UPJ, urethral atresia, polycystic or multicystic dysplastic kidneys, renal agenesis
  - Polyhydramnios: Associated with high GI obstructions
- Postnatal history:
  - Initial discovery
  - Duration from detection of mass
  - Location: Midline, side, upper/lower abdomen

- Rapidity of growth
- Constitutional symptoms: Fever, pain, weight loss, UTI, dysuria, hematuria, melena, anorexia, bilious vomiting

PHYSICAL EXAM

- Perform thorough abdominal exam:
  - Size/location
  - Solid/cystic
  - Tender/nontender
  - Smooth/irregular
  - Fixed/mobile
  - Indurated/soft
  - Auscultation/percussion/transillumination
- Additional exam:
  - Nasogastric tube for intestinal decompression
  - Foley catheter for urinary decompression
  - Rectal/introital exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Labs should be tailored to clinical suspicion
- CBC:
  - Anemia, neutropenia, thrombocytopenia may suggest bone marrow involvement.
  - Leukocytosis suggests possible infection/obstruction.
- BUN/creatinine/electrolytes
  - Elevated BUN/creatinine suggest renal compromise, dehydration
- Urinalysis:
  - Hematuria seen in Wilms tumor, renal vein thrombosis, UPJ obstruction after trauma
- 24-hr urine:
  - Elevated homovanillic acid and vanillylmandelic acid seen in neuroblastoma or pheochromocytoma
- Serum -hCG and -fetoprotein:
  - Used in tumors such as teratoma, liver, and germ-cell tumors
- Uric acid and lactate dehydrogenase:
  - Elevated in tumor lysis syndromes/rapid cell turnover

Imaging

- Plain abdominal x-rays:
  - Can check for obstruction/ileus; air–fluid levels on upright and lateral; absence of air in rectum
  - Ground-glass appearance can be seen with displacement of intestinal gas by mass.
  - Calcifications can suggest neuroblastoma, teratoma, hepatoblastoma, meconium peritonitis, urinary or biliary stones.
- Abdominal US:
  - Used to establish location and size, organ of origin
  - Can determine cystic vs. solid
  - Inexpensive and noninvasive; rarely requires sedation
- CT:
  - Used to enhance findings on US
  - Good anatomic detail
  - Useful in older children and suspected malignancies
- MRI:
  - Good for vascular involvement, adrenal origin
  - Good anatomic detail
  - May require sedation/anesthesia
- Radionuclide scans:
  - Renal scans: Used to determine renal function, scarring, infection, and obstruction
  - Biliary scans: Evaluate for choledochal cysts
  - Liver-spleen scans: Used for diagnosis of liver tumors or splenic enlargement
- VCUG:
  - Used to rule out lower urinary tract pathology (PUV, VUR, ureterocele)

Pathological Findings

Disease-specific

DIFFERENTIAL DIAGNOSIS

- Renal masses:
  - Hydronephrosis: Most common cause of neonatal abdominal mass:

    UPJ obstruction: Most common cause of hydronephrotic abdominal mass

    Other causes: UVJ obstruction, PUV, VUR, megaureter, and ureteroceles

    30–50% diagnosed prenatally

    <15% of neonates present with mass

    Later presentation: UTI, flank pain, hematuria after trauma, Dietl crisis

Workup with US, VCUG, and renal scan

– Multicystic dysplastic kidney:

2nd most common cause; together with UPJ constitute 40% of all neonatal abdominal masses

Unilateral flank mass; more common on left, and in boys; noted within 1st mo of life

US shows cluster of grapes; nuclear scan shows nonfunction on affected side

Nephrectomy if increasing in size, hypertensive, vomiting due to compression

Evaluate contralateral side; UPJ and VUR common; 25% VUR so VCUG necessary

– Multilocular cystic nephroma:

Spectrum from benign cyst to cystic Wilms tumor

Present in males <5 yr and females >30 yr

Diagnosis by surgical excision

– Renal vein thrombosis:

Most common cause of neonatal hematuria; 65% occur in neonatal period, 30% after age 1; male predominance

Classic features: Abdominal mass, hematuria, thrombocytopenia, leukocytosis, proteinuria, anemia, coagulopathy

Occurs in conditions associated with dehydration, maternal diabetes, sepsis, diarrhea, congenital heart disease, or sickle cell disease

– Polycystic kidney disease:

Autosomal recessive; diagnosed in neonatal period; 50% die in 1st few hours or days; of survivors, only 50% alive at 10 yr

Autosomal dominant; usually present in 3rd–5th decade; neonatal cases occur with renomegaly

– Congenital mesoblastic nephroma:

Most common solid renal tumor in 1st yr of life

Mean age 3.5 mo

Surgery is curative.

– Wilms tumor:

Most common childhood abdominal malignancy; most common malignant renal neoplasm in children

Usually presents as smooth, nontender, unilateral abdominal mass.

Rare >10 yr and <6 mo

Median age 3.5 yr

80% of cases occur in age <5 yr

Increased frequency in WAGR, Beckwith-Wiedemann, hemihypertrophy, and Denys-Drash syndromes

Combination surgery, chemotherapy, and radiation yields success rates >90% in favorable histology; lower in unfavorable (anaplasia) histology

- Retroperitoneal masses:
  - Neuroblastoma:

    Most common solid neonatal abdominal mass

    Most common malignancy of newborn

    50% of all malignant tumors in children; 50% before age 2

    Fixed, painful, irregular mass that often crosses midline; hepatic mass in stage VI-S

    Fever, malaise, weight loss; ill-appearing compared to Wilms tumor

    90% have catecholamine excess.
  - Adrenal hemorrhage:

    1–2% of healthy infants

    Predisposing factors: Birth trauma, prolonged labor, large birth weight

    Supportive care, rare intervention
- Genital masses:
  - Hydrocolpos:

    Enlarged fluid-filled uterus due to obstruction from vaginal atresia, imperforate hymen, or cloacal anomaly

    Pelvic midline mass; US shows fluid-filled mass between bladder and rectum
  - Ovarian cyst:

    1:3,000 girls

    Most common cause of abdominal cystic tumor in female fetus

    Presents as large mobile midabdomen mass

    Cysts and tumors: 17% neonatal to age 4; 28% from 59 yr; 55% 9–18 yr; prepuberty 50% are malignant, teratoma most common
  - Rhabdomyosarcoma:

    15–20% arise from genitourinary system: Prostate, bladder, paratesticular, vulvar/vaginal, uterine

    2 subtypes: Embryonal (most common) and alveolar (worse prognosis)

    Treatment involves chemotherapy and/or radiation followed by surgery

- GI masses:
  - 12% of neonatal abdominal masses
  - Intestinal duplication:
    Most common; congenital cystic abnormalities
    Ileum most common, followed by esophageal, duodenum
  - Lymphoma:
    Common in boys >5 yr
    60% non-Hodgkin; 1/3 involve abdomen; can present as intussusception
  - Hypertrophic pyloric stenosis
  - Intestinal cysts (meconium, omental, duplication, mesenteric)
- Hepatobiliary masses:
  - Primary liver tumors are 3rd most common solid abdominal mass in childhood (15% total)
  - Benign lesions: 1/3 (hemangioendothelioma, mesenchymal hamartoma, adenoma, focal nodular hyperplasia, congenital cysts)
  - Malignant: 2/3 (hepatoblastoma most common <5 yr; hepatocellular carcinoma present ages 12–15)
  - Hemolytic anemias
  - Congestive heart failure
  - Choledochal cyst
  - Infection
  - Glycogen storage diseases
  - Metastatic disease
- Splenic masses:
  - Infections
  - Congenital splenic cysts
  - Congenital hemolytic anemias:
    Hemoglobinopathies
    Thalassemias
    Hereditary spherocytosis

TREATMENT

Stabilize patient as necessary. Treatment is based on diagnosis.

SURGERY/OTHER PROCEDURES

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

ONGOING CARE

PROGNOSIS

Disease-specific

COMPLICATIONS

Treatment-specific

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Disease-specific

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See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass and Hemorrhage
- Hydrocolpos
- Hydronephrosis/Hydroureteronephrosis (dilated ureter/renal pelvis), pediatric and prenatal
- Neuroblastoma
- Polycystic Kidney Disease
- Wilms Tumor

CODES

ICD9

- 591 Hydronephrosis
- 761.2 Oligohydramnios affecting fetus or newborn
- 789.30 Abdominal or pelvic swelling, mass, or lump, unspecified site

ABBREVIATIONS

- -hCG: Human chorionic gonadotropin
- PUV: Posterior urethral valves
- RUS: Renal ultrasound
- UPJ: Ureteropelvic junction

- US: Ultrasound
- UVJ: Ureterovesical junction
- VCUG: Voiding cytourethrogram
- VUR: Vesicoureteral reflux
- WAGR: Wilms, aniridia, genital anomalies, retardation

ACUTE TUBULAR NECROSIS (ATN)

Costas D. Lallas, MD

BASICS

DESCRIPTION

- Most common type of intrarenal ARF, usually due to prolonged ischemia or administration of nephrotoxins
- A syndrome of intrinsic renal failure secondary to ischemic or toxic insults
- Histopathologic findings of ATN variable
- Decreased urine output:
  - Can be nonoliguric, oliguric >500 mL/d, or anuric. Mortality increases from 20–60% to 80% if the patient is oliguric or anuric.
- Signs of underlying disorder:
  - Signs of sepsis or of hypotensive events secondary to trauma, cardiac disease, surgery with excessive blood loss, or interruption of blood supply to kidneys

EPIDEMIOLOGY

- ARF is present in 209 per million population.
- ARF may affect 2–5% of patients in a tertiary care hospital, and the incidence of ARF in the surgical or medical ICU may exceed 20–30%.
- Breakdown of ARF: ATN, 45%; prerenal causes, 21%; acute or chronic renal failure, 13%; urinary tract obstruction, 10%; glomerulonephritis or vasculitis, 4%; acute interstitial nephritis, 2%; atheroemboli, 1%

RISK FACTORS

- Decreased renal perfusion from:
  - Prolonged hypotension, surgical interruption of blood flow, NSAIDs, ACE inhibitors, cyclosporine
- Nephrotoxic agents:
  - Radiocontrast media (low osmolality is safer), aminoglycosides, cisplatinum, amphotericin, drug intoxications with acetaminophen or ethylene glycol
  - The most commonly seen nephrotoxins in the hospitalized patient include radiographic contrast material, antibiotics (especially aminoglycosides and amphotericin B), chemotherapeutic agents, NSAIDs, and ACE inhibitors.

Genetics

No known genetic link

GENERAL PREVENTION

- Avoid severe renal hypoperfusion.

- Proper drug dosing
- Prompt recognition and management of conditions such as rhabdomyolysis

PATHOPHYSIOLOGY

- Acute tubular injury
- Renal hypoperfusion and renal ischemia are the most common causes of ATN.
- The ischemic form is due to the reductions in GFR secondary to vascular and tubular factors:
  - Ischemia from reductions in GFR from decreased renal plasma flow or dilatation of the efferent arteriole. After return of normal blood flow, ATN persists secondary to tubular changes.
  - Additionally, both exogenous and endogenous nephrotoxic compounds exist.
  - Tubular factors: Back-leak and tubular obstruction. Tubular obstruction secondary to a sloughed brush border, cellular debris, Tamm-Horsfall protein, and decreased filtration pressure contribute to obstruction and maintenance of ATN.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes mellitus
- Renal artery stenosis
- Renal insufficiency

DIAGNOSIS

HISTORY

- Specific attention to:
  - Hypotensive episodes, blood transfusions, IV contrast exposure
- Meticulous listing of medications to include dosage to assure appropriate dosing for level of renal function
- Make sure other medications that depend on renal metabolism are also given at appropriate doses to avoid side effects.

PHYSICAL EXAM

- Vital signs and hemodynamic parameters should be critically assessed.
- A patient's weight is helpful information, and its daily measurement is important in the diagnosis and management of ARF.
- Evaluate the volume status of the patient:
  - Evaluate neck veins and auscultation of heart and lungs; assess extremities and the presacral area for edema.
- General exam:
  - Evaluate for bladder distention and assess for signs of vasculitis or cutaneous rashes.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum tests:
  - BUN/plasma creatinine ratio: The ratio is normal at 10–15:1 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 tetracycline.
  - Rate of rise of plasma creatinine: Rise of >0.3–0.5 mg/dL in ATN vs. slower rise with fluctuations with prerenal disease
- Urine tests:
  - Urinalysis: Muddy brown granular and epithelial cell casts and free epithelial cells secondary to sloughing of the tubular epithelium vs. near-normal in prerenal disease
  - The classic sediment of ATN includes pigmented (muddy brown) granular casts and renal tubular epithelial cells, which may be seen in nearly 80% of cases of oliguric ARF.
  - Urine sodium concentration: High; >40 mEq/L due to tubular injury vs. <20 mEq/L in prerenal disease in an attempt to conserve sodium (Na)
  - Fractional excretion of sodium: >2% in ATN but <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 fractional excretion of Na are IV contrast material, rhabdomyolysis, sepsis, and multisystem organ failure.
  - Urine osmolality: Urine osmolality <450 mOsmol/kg in ATN secondary to loss of concentrating ability; >500 mOsmol/kg in prerenal disease
  - Urine creatinine concentration divided by plasma creatinine concentration: Ratio is <20 in ATN but >40 in prerenal disease, reflecting loss of tubular water reabsorption

Imaging

- Renal US:
  - Sensitive test to determine obstruction
  - Doppler can detect blood flow in different vessels.
- 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.

DIFFERENTIAL DIAGNOSIS

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

TREATMENT

- 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 + insensible losses.

MEDICATION

- High-dose loop diuretics such as furosemide (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. Dopamine 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.

SURGERY/OTHER PROCEDURES

Consideration for dialysis access if renal failure severe

ADDITIONAL TREATMENT

HD, PD, and CAVH:

- CAVH: Need ICU, limited mobility; need anticoagulation, removes fluid well but slow correction of electrolyte abnormalities
- PD: No anticoagulation needed but slower correction of electrolyte abnormalities
- HD: Expensive, anticoagulation necessary, vascular access necessary but allows rapid correction of fluid and electrolyte abnormalities

ONGOING CARE

PROGNOSIS

- Slight improvements in survival in those patients with ATN requiring dialysis in an ICU setting:
  - The Mayo Clinic report comparing 1977–1979 with 1991–1992 showed high survival both in hospital (52% 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 hypotension
- Major causes of death are infection and underlying disease, not renal failure:
  - Patients at risk are generally very ill, with evidence of multiorgan dysfunction.
  - Of patients who survive ATN, nearly 50% will have a complete recovery of renal function and the majority of the remainder have an incomplete recovery; ~5% of all ARF patients require chronic maintenance dialysis.

COMPLICATIONS

Fluid overload, electrolyte disturbances, metabolic acidosis:

- Hypertension, edema, acute pulmonary edema, hyponatremia, hyperkalemia, hypermagnesemia, hypercalcemia, hyperphosphatemia, hyperuricemia
- Uremic signs and symptoms:
  - GI: Nausea, vomiting, GI bleed
  - Neurologic: Encephalopathy, coma, seizures, peripheral neuropathy
  - Cardiac: Pericarditis, uremic pneumonitis
  - Hematologic: Bleeding, anemia
  - Immunologic: Impaired granulocyte/lymphocyte function

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Duration:
  - Renal failure phase usually lasts 7–21 d 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 preexisting renal disease and prolonged ARF secondary to repeat ischemic insults and/or nephrotoxin administration
  - If the patient survives, baseline CR is usually only 1–2 mg/dL above baseline.
  - Those patients who need dialysis and have bioincompatibility with the dialysis membrane or have repeat episodes of hypotension have a worse prognosis.

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See Also (Topic, Algorithm, Electronic Media Element)

- Acute Renal Failure
- Acute Kidney Injury
- Anuria and Oliguria

CODES

ICD9

584.5 Acute renal failure with lesion of tubular necrosis

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ARF: Acute renal failure
- ATN: Acute tubular necrosis
- CAVH: Continuous arteriovenous hemofiltration
- Cr: Creatinine
- GFR: Glomerular filtration rate
- HD: Hemodialysis
- NSAIDS: Nonsteroidal anti-inflammatory drugs
- PD: Peritoneal dialysis
- US: Ultrasonography

ADDISON DISEASE

Miguel Proano, MD

Gennady Bratslavsky, MD

BASICS

DESCRIPTION

- Primary adrenal insufficiency
- Differentiated from secondary (pituitary failure) and tertiary (hypothalamic failure) causes of adrenocortical insufficiency.
- Mineralocorticoid function usually remains intact in secondary and tertiary adrenal insufficiency.

ALERT

Acute adrenal insufficiency (Addisonian crisis):

- Life-threatening hypotensive shock
- Most common cause is acute withdrawal of chronic steroid
- Acute stress (ie, surgery) without an adequate stress dose of steroids

EPIDEMIOLOGY

- 1–4 per 100,000
- Male = Female
- TB (20%): Most common cause in underdeveloped nations
- Autoimmune (70%): Most common cause in modern nations
- 110–140 per million
- Death rate 0.3 per 100,000

RISK FACTORS

- Chronic steroid use
- Head trauma
- Endemic infections
- Anticoagulation
- Severe stress or sepsis
- Genetic factors
- HLA DR3-DQ2, DR4-DQ8
- Infections: TB, AIDS

Genetics

- 40% of patients have a 1st/2nd-degree relative with associated disorder.
- APS 1:
  - Autosomal dominant; presents in childhood

  - Chronic mucocutaneous candidiasis, hypoparathyroidism, adrenal insufficiency
  - Most common in Iranian Jews, Finns, and Sardinians
- APS 2:
  - Presents in adulthood
  - Adrenal insufficiency, autoimmune hypothyroidism and/or immune-mediated diabetes (type 1)
- Congenital adrenal hypoplasia (CAH):
  - Rare familial condition, 1/12,500 births
  - Mutation of DAX-1 gene
- Contiguous gene deletion syndrome:
  - X-linked, retardation, muscular dystrophy, characteristic facies
- Familial glucocorticoid deficiency (FGD):
  - Rare, autosomal recessive trait
  - Cortisol and androgen secretion is unresponsive to ACTH.
  - Aldosterone secretion normal
- Allgrove (triple A) syndrome:
  - Rare, gene unknown; achalasia, alacrima, and adrenal insufficiency
- ALD:
  - Defect in metabolism of very-long fatty acid chain; 1/20,000
  - Progressive demyelination and adrenal insufficiency
- CAH:
  - Deficiency in enzyme involved in steroid metabolism (see “Pathophysiology”)

PATHOPHYSIOLOGY

- Multiple etiologies for primary adrenal insufficiency
- Autoimmune is most common cause (80% of the cases), followed by TB; AIDS is becoming a more frequent cause.
- Partial or complete T-cell–mediated destruction of adrenal cells:
  - 90% of adrenal gland needs to be destroyed to cause insufficiency
  - Decreased production of cortisol, aldosterone and adrenal androgens
  - Hypovolemia and prerenal azotemia leads to orthostatic hypotension, dizziness, and lethargy
  - Adrenal crisis is mostly attributable to mineralocorticoid deficiency
  - Pituitary compensation with increased ACTH production as well as pro-opiomelanocortin and melanocyte-stimulating hormone, which causes hyperpigmentation
- Adrenal dysgenesis or hypoplasia:

- AHC, triple A syndrome (see “Genetics”)

- Adrenal destruction:
  - APS 1, APS 2, ALD (see “Genetics”)
  - Infectious destruction:
  - TB, histoplasmosis (South America), blastomycosis, paracoccidioidomycosis, syphilis, African trypanosomiasis, AIDS, CMV necrotizing adrenalitis
  - Acute adrenal hemorrhage:
    Meningococcemia
    Disseminated intravascular coagulation
    Anticoagulant therapy
  - Surgical adrenalectomy
- Adrenal infiltration:
  - Adrenal metastasis; rare cause
  - Amyloidosis
  - Sarcoidosis
  - Lymphoma
  - Hemochromatosis
- CAH:
  - 21-hydroxylase deficiency (95% cases)
  - 3-hydroxysteroid dehydrogenase deficiency
  - 11 -hydroxylase deficiency
  - 17 -hydroxylase deficiency
  - Lipoid adrenal hyperplasia
  - Aldosterone synthase deficiency

Pediatric Considerations

- Early detection may prevent salt wasting adrenal crisis in CAH (21-OH).
- Female infants:
  - Ambiguous or virilized genitals
- Male infants:
  - Hyperpigmentation of labioscrotal fold
- Evaluate for CAH with any ambiguous genitalia.

ALERT

Therapeutic drugs that decrease steroid production or accelerate metabolism may place a compromised patient into adrenal insufficiency.

- Drugs that inhibit cortisol biosynthesis:

- Aminoglutethimide, etomidate, ketoconazole, metyrapone, suramin
- Drugs that accelerate cortisol metabolism:
  - Phenytoin, barbiturates, rifampin

COMMONLY ASSOCIATED CONDITIONS

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

DIAGNOSIS

HISTORY

Vague symptoms; requires high index of suspicion:

- Fatigue, weight loss, anorexia, vomiting, GI complaints, abdominal pain, diarrhea, muscle aches, salt craving, hypotension, behavior changes, headaches, sweating, depression, decreased libido, lethargy

PHYSICAL EXAM

- Vitals: Orthostatic hypotension
- Documented weight loss
- Generalized pigmentation, darkened skin
- Pigmented buccal mucosa and nail beds
- Loss of axillary or pubic hair
- Vitiligo
- Goiter

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Electrolytes disturbances:

- Classic triad: Hyponatremia, hyperkalemia, azotemia (60%)
- Hypercalcemia
- Lymphocytosis
- Hypoglycemia
- Metabolic acidosis

Imaging

- In TB, adrenal calcifications in 50% of cases
- If adrenal infarct or hemorrhage suspected, then CT or MRI is appropriate

Diagnostic Procedures/Surgery

- Screening in chronic (nonacute) patients:

- Measure morning total serum cortisol, ACTH, aldosterone, renin levels.
- Adrenal insufficiency (1)[C]:
  Low cortisol (<3 g/dL)
  High ACTH levels (>100 pg/mL)
  Low aldosterone levels
  Elevated renin levels

- Stimulation tests used to confirm or evaluate abnormal screening results:
  - Infuse 0.25 mg of cosyntropin, then measure serum cortisol at 60 min
    Cortisol >20 g/dL excludes primary but not secondary adrenal insufficiency (1)[C].
  - CRH stimulation test may be used to further evaluate secondary and tertiary causes.

Pathological Findings

Atrophic adrenals in autoimmune adrenalitis

DIFFERENTIAL DIAGNOSIS

- Primary adrenal insufficiency (Addison)
- Secondary adrenal insufficiency (ACTH deficiency/pituitary failure):
  - No hyperpigmentation
  - Chronic steroids
  - Pituitary failure:
    Panhypopituitarism
    Sheehan syndrome (postpartum necrosis)
    Pituitary apoplexy
    Brain trauma
    Pituitary or hypothalamus surgery
    Tertiary adrenocortical insufficiency (hypothalamic failure)

TREATMENT

ALERT

- Acute adrenal crisis (Addisonian crisis)
- The 5 S's: Salt, sugar, steroids, support, and search for a precipitating cause:
  - Infusion of normal saline and 5% glucose
  - 100 mg hydrocortisone IV or 4 mg dexamethasone IV (3)[C]
  - Obtain stat electrolytes, cortisol, and ACTH
  - Treat; do not wait for lab results.

MEDICATION

- Corticosteroid replacement:

- Hydrocortisone 15–20 mg/d (3)[C]
  b.i.d. dosing: 20 mg, 10 mg
  t.i.d. dosing: 10 mg, 5 mg, 5 mg
- Cortisone acetate 20–30 mg/d (3)[C]
  25 mg A.M., 12.5 mg P.M.

- Mineralocorticoid replacement:
  - Fludrocortisone 0.05–0.20 mg/d (3)[C]
- Major stress: Surgery, trauma, sepsis:
  - IV hydrocortisone 100–300 mg/d (t.i.d. dosing) then taper (3)[C]
- Minor stress: Illness, fever:
  - Increase steroid dose 2–3-fold then taper over several days

Pediatric Considerations

Hydrocortisone 10–12 mg/m2/d (divided t.i.d.) (3)[C] Synthetic glucocorticoids less suitable:

- Prednisolone, dexamethasone
- Undesirable long-term side effects

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 d.

Pregnancy Considerations

- Serum cortisol increases 8-fold during pregnancy secondary to estrogen levels but not because of adrenal production
- ACTH levels are lower than normal
- Successful pregnancies reported
- Continue unchanged dose of glucocorticoids during pregnancy; give stress doses of IV hydrocortisone 100–300 mg during labor
- Fludrocortisone dose monitored and adjusted according to BP, electrolytes, and edema

ADDITIONAL TREATMENT

- Some recommend salt loading prior to major stress (3)[C]
- Future therapies in trials: DHEA replacement therapy (controversial); modified-release hydrocortisone tablets; continuous SC hydrocortisone infusion

ONGOING CARE

PROGNOSIS

- Adrenal crisis may be lethal.

• Recommended dosages for glucocorticoid and mineralocorticoid replacement rarely cause significant side effects; close 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, hypernatremia, congestive heart failure, suppressed renin levels, growth retardation
• Acute withdrawal of chronic steroid replacement may precipitate acute adrenal crisis.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Medic-Alert bracelet to be worn at all times
• Instruct patients on proper use of emergency hydrocortisone injections.
• Mineralocorticoid replacement:
  – BP orthostatic hypotension
  – Electrolyte monitoring:
    Sodium and potassium
  – Plasma renin activity (PRA):
    Goal: PRA slightly above upper limit of normal
• Glucocorticoid replacement:
  – Evaluate signs and symptoms of hypo- or hypercortisolism.
  – Measuring cortisol levels is neither efficient nor effective.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Addison Disease (Adrenocortical Insufficiency Algorithm)
• Waterhouse-Friderichsen Syndrome

CODES

ICD9

255.41 Glucocorticoid deficiency

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- AIRE: Autoimmune regulator gene
- ALD: Adrenoleukodystrophy
- APS: Polyglandular autoimmune syndrome
- CAH: Congenital adrenal hyperplasia
- CRH:
- DAX-1: Dosage-sensitive sex reversal adrenal hypoplasia gene 1
- DHEA: Dehydroepiandrosterone
- FGD: Familial glucocorticoid deficiency
- PRA: Plasma renin activity (PRA)

ADENOMATOID TUMORS, PARATESTICULAR

Florian R. Schroeck, MD
Judd W. Moul, MD

BASICS

DESCRIPTION

- Benign, most often paratesticular tumor of likely mesothelial origin
- In men, can be located in the spermatic cord, tunica albuginea, ejaculatory ducts, prostate, and suprarenal recess

EPIDEMIOLOGY

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)[C]

- Adenomatoid tumor of the epididymis is the most common paratesticular tumor in adults.

)[C]

)[C]

RISK FACTORS

None reported

Genetics

None described; however, 1 form of papillary cystadenoma can be associated with von Hippel-Lindau syndrome.

PATHOPHYSIOLOGY

Based on the presence of microvilli on the free surface of the cells and the presence of mucopolysaccharides, likely of mesothelial origin

DIAGNOSIS

HISTORY

- Duration of scrotal mass, change in size over time
- Prior malignancy or scrotal surgery
- Symptoms:
  - Pain or aching sensation
  - Radiation of pain
  - Conditions that ameliorate or exacerbate discomfort

PHYSICAL EXAM

- Scrotum and scrotal contents:
  - Inspection: Symmetry, varicocele
  - Palpation: Localization of the mass outside of the testes and within the epididymis; fluctuance (hydrocele, spermatocele); exam of the cord structures with and without Valsalva

to rule out hernia, or extension to the cord

– Transillumination: To identify the presence of a clear, fluid-filled mass (hydrocele, spermatocele)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No specific laboratory tests
- If suspicious for testicular tumor, -hCG, AFP, and LDH should be obtained prior to inguinal exploration.

Imaging

- US:

)[C]

- MRI:
  - Demonstrates low signal intensity relative to the testicular parenchyma on T2-weighted images.
  - Can aid in determining the paratesticular origin of the lesion
  - Adenomatoid tumors typically enhance after administration of gadolinium contrast.

Diagnostic Procedures/Surgery

Inguinal exploration, tumor resection with frozen section

Pathological Findings

- Gross:
  - May arise anywhere within the epididymis, but most commonly involves the distal epididymis, adjacent to the lower pole of the testes
  - Sometimes found in tunica albuginea of the testes and spermatic cord
  - Small and well circumscribed
- Microscopic:
  - Uniformly benign: None has ever been reported to metastasize; local invasion of adjacent structures has occasionally been observed.
  - Mixed epithelial and stromal elements
  - The epithelial element is eosinophilic and has a vacuolated cytoplasm.

)[C]

DIFFERENTIAL DIAGNOSIS

- Benign tumors of the epididymis:
  - Leiomyoma
  - Papillary cystadenoma (associated with von Hippel-Lindau syndrome)
  - Embryomas

  - Cholesteatomas
  - Teratomas
  - Lipomas
  - Hamartomas
  - Dermoid cyst
  - 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 tumors of the epididymis:
  - Urologic (prostate, kidney)
  - GI (stomach, colon, carcinoid, pancreas)
- Other lesions of the epididymis:
  - Granuloma (sperm, TB)
  - Spermatocele
  - Epididymitis
  - Sarcoid
  - Epidermoid inclusion cyst
  - Epididymal abscess

TREATMENT

The primary approach is surgical.

SURGERY/OTHER PROCEDURES

- Can be performed as outpatient surgery in most cases
- Because testicular or epididymal malignancy cannot be ruled out prior to exploration, an inguinal approach with proximal vascular control is the standard of care.
- Once the testis is delivered, the surgeon may elect to perform biopsy with frozen section to confirm the diagnosis of adenomatoid tumor.

)[C]

- If there is any doubt regarding the benign nature of the mass, then radical orchiectomy is the prudent treatment.

ONGOING CARE

PROGNOSIS

)[C]

COMPLICATIONS

Scrotal hematoma, infections

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Instruct in testicular self-exam

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ADDITIONAL READING

http://www.webpathology.com/case.asp?case=86

See Also (Topic, Algorithm, Electronic Media Element)

- Epididymis, Mass (Epididymal Tumor and Cysts) (Chief Complaint)
- Paratesticular Tumors, General
- Testis, Tumor and Mass, Adult, General

CODES

ICD9

- 222.0 Benign neoplasm of testis
- 222.2 Benign neoplasm of prostate
- 222.3 Benign neoplasm of epididymis

ABBREVIATIONS

- AFP: Alpha-fetoprotein
- -hCG: Human chorionic gonadotropin
- GI: Gastrointestinal
- LDH: Lactate dehydrogenase
- MRI: Magnetic resonance imaging
- TB: Tuberculosis
- US: Ultrasound

ADRENAL ADENOMA

Matthew R. Eskridge, MD

Matthew G. McIntyre, MD

BASICS

DESCRIPTION

- A benign adrenal cortical neoplasm that may or may not have endocrine activity
- Up to 80% nonfunctioning and benign; the other 20% require further evaluation and therapy:
  - Generally <4 cm in size and often discovered during evaluation for another reason

EPIDEMIOLOGY

- Found in 1.4–8.7% of autopsies
- Incidental adrenalomas found on 0.5–5% of abdominal CTs (82% nonfunctioning, 5% Cushing, 1% Conn):
  - Usually occurs between 20 and 60 yr

Incidence

~1% if <30 yr and 7% if >70 yr

RISK FACTORS

Slightly more common in females

Genetics

More common in multiple endocrine neoplasia type I, Beckwith-Wiedemann syndrome, and the Carney complex

PATHOPHYSIOLOGY

- Primary hyperaldosteronism (Conn syndrome) caused by excess production of aldosterone from the zona glomerulosa causes hypernatremia, hypokalemia, alkalosis
- Cushing syndrome caused by excess production of cortisol from the zona fasciculata, which suppresses ACTH from the pituitary

COMMONLY ASSOCIATED CONDITIONS

- Hypertension
- Diabetes mellitus
- MEN1 syndrome
- Subclinical Cushing syndrome (obesity, HTN, type 2 diabetes, hypercholesterolemia)

DIAGNOSIS

HISTORY

- Often asymptomatic and incidentally detected
- Hirsutism

- Oligomenorrhea
- Easy bruising
- Personality changes
- Excessive acne
- Polyuria/polydipsia
- Muscle weakness
- Fatigue
- Headache
- Uncontrolled hypertension
- Diabetes mellitus
- History of anticoagulation may increase risk of adrenal hemorrhage

PHYSICAL EXAM

- Hypertension
- Truncal obesity, buffalo hump
- Muscle weakness
- Purple striae, thin skin

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Conn syndrome:
  - Hypernatremia, hypokalemia, alkalosis
  - Elevated serum aldosterone (>15 ng/mL)
  - Suppressed serum renin activity (<2 ng/mL)
  - Serum aldosterone-to-renin ratio is 20:1.
  - Confirm with 3-day high-sodium diet (>200 mEq/d) followed by 24-hr urine:
    Urine aldosterone >14 g/24-hr
    Urine potassium >30 mEq/24-hr
- 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–9 AM
    Normal: Suppresses cortisol <5 ng/mL
    Cushing syndrome: Inability/resistance to cortisol suppression
  - Rule out ACTH-dependent cause (ectopic or pituitary hypersecretion of ACTH)
    Measure late-afternoon ACTH

>15 pg/mL = ACTH-dependent

<15 pg/mL = ACTH-independent (adrenal)

– Confirm with high-dose dexamethasone suppression test:

8 mg dexamethasone at 11 PM

>50% reduction: ACTH (pituitary hypersecretion of ACTH)

<50% reduction: ACTH (ectopic production of ACTH)

No reduction: ACTH-independent (adrenal)

Imaging

- Small, well-defined, homogenous
- Size criteria important (5 cm usually benign; >6 cm 90% malignant)
- May see atrophy of contralateral adrenal
- CT (triphasic adrenal scan needed):
  - <10 HU on noncontrast CT
  - >60% washout at 15 min
  - Could also contain lipid and thus have low HU but HU values are never below –20. Lower HU is associated with adrenal myelolipoma.
- MRI:
  - Hypointense on T1 and T2
  - Loss of signal between in- and out-of-phase images (microscopic fat-sensitive sequence)

Diagnostic Procedures/Surgery

Adrenal biopsy or fine-needle aspiration may be performed; may not be able to differentiate benign from malignant adrenocortical tumor.

ALERT

Rule out pheochromocytoma before performing biopsy on an adrenal mass.

Pathological Findings

- Aldosterone-producing adenoma: Eosinophilic, laminated cytoplasmic inclusions (spironolactone bodies), found after treatment with the antihypertensive drug spironolactone
- Cortisol-producing adenoma: Neoplastic cells are vacuolated due to presence of intracytoplasmic lipid with mild nuclear pleomorphism and no mitotic activity or necrosis
- Bilateral adrenal adenomas may be associated with systemic diseases that may predispose to adrenal insufficiency (fungal, TB, histoplasmosis).

DIFFERENTIAL DIAGNOSIS

- Adrenal cortical carcinoma (up to 80% functional)
- Adrenal hemorrhage, especially if bilateral lesions

- Adrenal hyperplasia (pituitary hypersecretion of ACTH)
- Adrenal myelolipoma
- Lymphoma
- Metastatic tumor (melanoma, lung, breast, kidney)
- Neuroblastoma
- Nonfunctioning adenoma
- Pheochromocytoma
- TB; other infections

TREATMENT

Based on functional status and size of lesion

MEDICATION

- For hormonally active adenomas in patients who refuse surgery or who have contraindications to surgery
- Conn syndrome:
  - Spironolactone, eplerenone; aldosterone receptor antagonists in the distal convoluted tubule
  - 2nd line: Amiloride, triamterene; inhibitors of distal convoluted tubule aldosterone sensitive sodium channels
- Cushing syndrome:
  - Aminoglutethimide: Blocks the 1st step in cortisol synthesis (cholesterol to pregnenolone)
  - Metapyrone: Blocks the final step in cortisol synthesis (11-deoxycortisol to cortisol)
  - Ketoconazole: Inhibits 1st step and to a lesser extent the last step in cortisol synthesis

SURGERY/OTHER PROCEDURES

- Indications:
  - Hormonally active masses
  - Any mass >4 cm (90% of masses >6 cm are assumed to be adrenal cortical carcinomas)
  - Masses with suspicious imaging characteristics (in homogeneous, irregular borders, HU >20) of carcinoma
- Laparoscopic adrenalectomy is preferred over open adrenalectomy due to less postoperative pain and shorter hospital stay, but may not be possible with larger masses.

ONGOING CARE

PROGNOSIS

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

COMPLICATIONS

- Hypertension
- Diabetes mellitus
- Atherosclerosis
- Poor wound healing
- Nephrolithiasis (15% of patients with Cushing due to hypercalciuria)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Routine BP monitoring

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Adrenal Mass, Solid Algorithm
- Adrenal Angiomyelolipoma
- Adrenal Cortical Carcinoma
- Adrenal Hemorrhage
- Adrenal Incidentaloma

CODES

ICD9

227.0 Benign neoplasm of adrenal gland

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- BP: Blood pressure
- CT: Computed tomography

- HU: Hounsfield units

ADRENAL ANGIOMYELOLIPOMA (AML)

Michael S. Cookson, MD

Benjamin M. Whittam, MD

BASICS

DESCRIPTION

- Adrenal angiomyelolipoma (AML) is a rare and benign tumor
- Hormonally inactive
- Contains adipose, hematopoietic tissue
- Unilateral
- Adrenal gland most common site for AML

EPIDEMIOLOGY

)

- 3% of all adrenal tumors

)

- Average age 50 yr
- Uncommon <30 yr
- 85% Caucasian

PATHOPHYSIOLOGY

Metaplasia of reticuloendothelial cells of blood capillaries in adrenal gland in response to necrosis, infection, or stress

COMMONLY ASSOCIATED CONDITIONS

Sometimes can exist with hormone-secreting adrenal adenoma

DIAGNOSIS

HISTORY

- Often asymptomatic
- Incidental finding on radiographic exam
- Unspecific flank or abdominal pain:
  - Intratumor, peritumoral hemorrhage can rarely present as a significant bleed with hypotension
  - Tumor necrosis
  - Mechanical compression from tumor bulk
- Rarely hematuria and abdominal mass

PHYSICAL EXAM

- Flank or abdominal pain
- Hypertension (compression of renal artery)

- Nonspecific

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[C]

- Endocrine evaluation: Renin, aldosterone, cortisone, ACTH

Imaging

- Often diagnostic

)[B]:

  - Suprarenal
  - Well-circumcised, capsulated
  - Fat: HU 20, sometimes as low as –100
  - 20% with calcifications
  - Enhance with contrast
  - Diagnostic if fatty component present
  - If high quantity of myeloid tissue or very large may be difficult to diagnose with CT
  - Heterogenous appearance could look more like liposarcoma

- Abdominal US:
  - Typically large >5 cm
  - Hyperechoic tumor
  - Not as specific as MRI or CT
  - Not typically used to characterize AML

)[B]:

  - High signal intensity on T1 and T2
  - Heterogenous appearance on T2
  - Enhance with gadolinium
  - Used to confirm adrenal origin in large AML

Diagnostic Procedures/Surgery

ALERT

- Rule out pheochromocytoma before biopsy of any adrenal mass.

)[C]:

  - Risk of rupture or bleeding
  - Last resort if unable to diagnose with imaging

Pathological Findings

Variable amounts of adipose and hematopoietic stem cells

DIFFERENTIAL DIAGNOSIS

- Retroperitoneal lipoma
- Liposarcoma
- Renal AML
- Retroperitoneal teratoma
- Adrenal cortical adenoma
- Adrenal cortical carcinoma
- Adrenal metastasis

TREATMENT

- With hemorrhage stabilize patient
- Treatment based on symptomatic vs. asymptomatic and size

SURGERY/OTHER PROCEDURES

)[C]

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- Laparoscopic approach if possible

ONGOING CARE

PROGNOSIS

- No death rate reported
- Does not undergo malignant transformation

COMPLICATIONS

- Spontaneous rupture causing retroperitoneal hemorrhage
- Rupture may occur post trauma.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Require lifelong follow-up to assess for interval growth and monitor contralateral adrenal gland

REFERENCES

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Adrenal Mass Algorithm
- Adrenal Myelolipoma

CODES

ICD9

227.0 Benign neoplasm of adrenal gland

SNOMED

91967007 benign neoplasm of adrenal gland (disorder)

ABBREVIATIONS

- ACTH, adrenocorticotropic hormone
- AML, angiomyelolipoma
- CT, computed tomography
- HU, Hounsfield units
- MRI, magnetic resonance imaging
- US, ultrasound

ADRENAL CORTICAL CARCINOMA

Michael O. Koch, MD
Helen J. Kuo, MD

BASICS

DESCRIPTION

Primary malignancy arising in the adrenal cortex

EPIDEMIOLOGY

- Rare: Incidence is ~2.0 per million people per year
- Bimodal occurrence: Initial peak in children <5; 2nd peak in adults 30–40
- Slight predominance in women and on left side, but of little diagnostic significance
- ~80–130 cases in the US annually

RISK FACTORS

Genetic associations (see below)

Genetics

- Familial syndromes associated with adrenocortical neoplasms:
  - Li-Fraumeni (loss of p53 on 17q13)
  - Carney complex (PRKARIA on 17q22-24)
  - MEN-1 (Menin product of MEN1 gene on 11q13)
  - Beckwith-Wiedemann:
    Overexpression of IGFII and loss of p57(kip2) tumor suppressor gene
    Loss of 11q15
- Activating mutations of G-protein genes

PATHOPHYSIOLOGY

- Extremely difficult to distinguish benign from malignant adrenal tumors in absence of metastatic disease
- Role of percutaneous needle biopsy limited for this reason
- Pathologic features such as mitotic activity, grade, vascular invasion, various architectural features, and tumor size have not consistently correlated with prognosis.
- Most (60–70%) ACCs are functioning, although this is related to the extent of work-up (cortisol producing most common).

COMMONLY ASSOCIATED CONDITIONS

- Cushing syndrome (functioning tumors)
- Beckwith-Wiedemann is linked in 15% of ACC

DIAGNOSIS

HISTORY

- Most common symptoms are related to excess cortisol production (Cushing syndrome) in 50–60%, then virilization (20%), or mixed syndromes (20–30%)
- Average time between onset of symptoms and diagnosis of ACC: 9 mo
- Constitutional symptoms:
  - Weight loss, malaise, weakness, nausea or vomiting usually associated with poor prognosis
- Cushing syndrome:
  - Moon facies, truncal obesity, buffalo hump, glucose intolerance or diabetes (polyuria, polydipsia), muscle wasting, HTN, acne, hirsutism
  - In children suggested by generalized weight gain and delayed growth
- Nonfunctional tumors:
  - Pain or palpable mass in upper quadrant are often seen at presentation
- Mass effect:
  - Painful or palpable mass
  - Lower extremity edema
  - Urinary obstruction
  - Budd-Chiari syndrome
  - GI symptoms
- Hyperaldosteronism (rare):
  - Hypertension
  - Hypokalemic alkalosis
- Feminization (rare)

PHYSICAL EXAM

- Palpable abdominal mass
- Signs of Cushing syndrome (functional ACCs): Violaceous striae, moon facies, truncal obesity, buffalo hump, glucose intolerance, hyperpigmentation
- Signs of virilization (oligomenorrhea, hirsutism, cystic acne, excessive muscle mass, voice deepening, temporal balding, clitoromegaly)
- Signs of feminization: Gynecomastia

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- The initial screen for function in an adrenal mass should include serum electrolytes, serum catecholamines, and a 24-hr urinary free cortisol.
- 24-hr urinary free cortisol: Most sensitive measure of excess cortisol production; obtain 2 or 3 consecutive specimens

• Urine levels of cortisol metabolites including 17-hydroxycorticosteroids and 17-ketosteroids may be elevated.

• Excess 17-ketosteroid levels suggest a malignant tumor vs. benign functioning tumor.

• Adrenal-induced virilization confirmed by plasma testosterone, adrenal androgens (DHEA and DHEA-S), and 24-hr 17-ketosteroid

• Other biochemical abnormalities:

– Loss of circadian rhythm of cortisol secretion

– Loss of suppressibility of pituitary-adrenal axis

– Low levels of ACTH (due to high cortisol level)

– When an adrenal mass is present and function is demonstrated, additional tests, such as the dexamethasone suppression test, are rarely indicated.

Imaging

• CT of abdomen: Initial study in patients with suspected ACC:

– Benign tumors: Homogenous appearance, generally <4–6 cm, smooth and round or oval contour, well-delineated margins

– Primary ACCs: Irregular contour, invasion of surrounding structures, nonhomogeneous internal architecture

• MRI not proven to be more sensitive in differentiating malignant from benign tumors:

– MRI is preferred imaging modality for vena caval imaging.

– ACCs generally isodense to the liver on T1-weighted images; intermediate to high signal intensity (brighter white) on T2-weighted images. (less bright than pheochromocytoma)

– Chemical-shift MRI with in-phase and opposed-phase pulse sequences possibly helps distinguish from benign adenoma and metastases.

Pathological Findings

• Macroscopic:

– Lobulated, necrotic areas, calcifications, intratumoral hemorrhages

• Microscopic:

– Weiss criteria for malignancy includes 3 of the following: High nuclear grade, mitotic rate >5/50/hpf, atypical mitotic fevers, eosinophilic tumor cell cytoplasm, diffuse architecture in >33% of tumor, necrosis, vascular invasion, sinusoidal invasion, capsular invasion

DIFFERENTIAL DIAGNOSIS

• Functioning adrenal masses:

– Adenoma, aldosteronoma, pheochromocytoma

• Nonfunctioning adrenal masses:

– Hemorrhage, cyst, metastatic tumor, neuroblastoma

- Other: Renal cell carcinoma

TREATMENT

Inhibitors of steroid synthesis (metyrapone, aminoglutethimide, ketoconazole) may be useful in controlling symptoms of glucocorticoid excess.

MEDICATION

- Often the 1st and only treatment of ACC, due to high rate of advanced disease at presentation
- Mitotane (op-DDD), an analog of the insecticide DDT, is the treatment of choice for metastatic ACC:
  - Objective regression in tumor size in 35%
  - Dosage escalated to tolerance, which is limited
  - Late CNS toxicity, particularly depression, often significant
  - Both glucocorticoid and mineralocorticoid replacement necessary
- Cytotoxic chemotherapy trials limited by small number of cases:
  - Cisplatin and etoposide (VP 16) have shown synergistic antitumor activity against ACC.

SURGERY/OTHER PROCEDURES

- Complete surgical excision is the best chance of cure for patients with stage I and II tumors and in children.
  - High rate of unresectability
- Adrenal masses with endocrine activity should be resected.
- Adrenal masses >6 cm: High rate of malignancy and should also be resected
- Anterior approach (chevron or subcostal incision) for the rare low-stage ACC
- For more usual advanced ACCs, a thoracoabdominal incision provides optimal exposure.
- En bloc nephrectomy often necessary
- Invasion of vena cava or caval tumor thrombus managed as for renal cell carcinoma
- Extent of caval involvement often determines resectability.
- Debulking of ACC has had mixed survival benefits in the literature.
- Important to give perioperative steroid preparation for functioning ACCs to avoid adrenal crisis
- Aggressive surgical resection of locally recurrent or metastatic ACC recommended but 5-yr survival only 10–20% in these patients
- Surgical removal of metastases (concurrent or recurrent) does not seem to improve prognosis.

ADDITIONAL TREATMENT

Radiotherapy

Generally ineffective. Reserved for skeletal metastasis palliation to reduce pain or risk of fractures.

Additional Therapies

- ACC shows resistance to chemotherapy as tumor cells express high levels of multidrug-resistance protein (MDR1).
- Current ongoing trials with MDRI efflux pump inhibitor (tariquidar), epidermal growth factor inhibitors (gefitinib), antivascular endothelial growth factor (bevacizumab), and tyrosine kinase inhibitor (sunitinib)

ONGOING CARE

PROGNOSIS

- Prognosis in patients with ACC is poor. 16–37% overall survival.
- The prognosis equally poor for functioning and nonfunctioning ACCs.
- Median survival is <3 yr.
- Stage at diagnosis is the most important prognostic variable.
- 70% of patients have advanced disease at presentation.
- Mean survival of 3 mo with unresectable disease

COMPLICATIONS

- Fever due to tumor necrosis
- Anemia from hemorrhage into the tumor
- Adrenal crisis in patients who undergo surgery for functioning tumors without adequate steroid prep

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up after resection of ACC: Periodic visits for symptom screening and physical exam
- Chest x-ray and CT should be done periodically to monitor for local and pulmonary recurrences.
- Serum and urinary steroid levels appropriate for clinical presentation should also be monitored.
- Follow-up should be long-term, since late recurrence of ACC (after 10 yr) is not uncommon.

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See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Adrenal Mass Algorithm

CODES

ICD9

194.0 Malignant neoplasm of adrenal gland

ABBREVIATIONS

- ACC: Adrenal cortical carcinoma
- ACTH: Adrenocorticotropic hormone
- CT: Computed tomography
- GI: Gastrointestinal
- HTN: Hypertension
- MRI: Magnetic resonance imaging

ADRENAL INSUFFICIENCY, ACUTE

Nicholas T. Karanikolas, MD

BASICS

DESCRIPTION

- Acute adrenal insufficiency (Addisonian crisis) symptoms are attributable to mineralocorticoid deficiency, and patients usually present with hypotension and shock.
- Symptoms of the disease are difficult to recognize; often the diagnosis of Addison disease is made when patients present with an acute crisis.
- An acute crisis is often precipitated by a stressor (ie, infection or surgery).
- Patient may present in hemodynamic compromise secondary to sodium and plasma volume depletion.
- An Addisonian crisis should be treated immediately; treatment should not be delayed pending diagnostic test results and is most commonly due to Addison disease (primary adrenal insufficiency).
- 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

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

EPIDEMIOLOGY

- New cases of Addison disease: 0.6/100,000 of population per year
- Up to 0.7% of patients undergoing major surgery may experience adrenal insufficiency.
- >3/4 of patients with septic shock manifest adrenal insufficiency.
- Addison disease: 4–11/100,000 of population

RISK FACTORS

- AIDS
- Autoimmune conditions
- Anticoagulation
- TB
- Medications: Ketoconazole, aminoglutethimide, dronabinol
- Long-term steroid use with sudden discontinuation

Genetics

- Hereditary factors may influence development of autoimmune adrenal insufficiency.
- Familial glucocorticoid insufficiency may be associated with a recessive gene pattern.

- Addison disease has been associated with a variety of autoimmune diseases.

GENERAL PREVENTION

Awareness of the potential for Addisonian crisis and appropriate preventive measures (see below)

PATHOPHYSIOLOGY

- The adrenal cortex produces 3 steroid hormones: Glucocorticoids (cortisol), mineralocorticoids (aldosterone), 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 the ACTH stimulation for the cortex.
- Chronic steroid administrations results in suppression of ACTH production.
- Bilateral adrenal hemorrhage can cause acute insufficiency.

COMMONLY ASSOCIATED CONDITIONS

Nearly 50% of patients with adrenalitis have some form of autoimmune disease: Hypoparathyroidism, gonadal collapse, diabetes mellitus type I, hypothyroidism (Hashimoto), or hyperthyroidism (Graves disease).

DIAGNOSIS

HISTORY

- Prior steroid use:
  - Risk increases with least 20 mg/d prednisone or equivalent for at least 5 days within the past 12 mo.
  - Patients on normal physiologic levels require about 1 mo to recover normal adrenal function.
  - Extensive topical use of high-potency steroids or high-dose inhaled steroids over prolonged periods can also be a factor.
- Lapse in steroid therapy in a patient on chronic therapy
- Severe physiologic stress such as burn, surgery, or severe bacterial infection
- Bleeding diathesis or anticoagulant use
- Abdominal or flank pain and nausea are common
- Primary or secondary adrenal insufficiency usually present insidiously with nonspecific symptoms of chronic fatigue, weakness and lethargy, anorexia, weight loss, postural hypotension, and abdominal pain.
- 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, sur-

gery, or trauma.

– Acute adrenal insufficiency should be considered in patients presenting in the emergency room with abdominal pain, nausea, diarrhea, hypotension, and fever.

PHYSICAL EXAM

- Check BP: Extreme hypotension and/or shock refractory to fluids and pressors suggests Addisonian crisis.
- Vitiligo often coexists with Addison disease:
  – Hyperpigmentation along palmar creases, buccal mucosa, pressure points, perianal mucosa, and nipple areolas
- 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 hypothermic.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

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

- Plasma cortisol
- Serum ACTH
- Electrolyte abnormalities: Decreased sodium and chloride levels, increased potassium levels and an increased BUN/Cr ratio
- Hypercalcemia is seen during adrenal crisis.
- Hypocalcemia may be seen with associated polyglandular failure and hypoparathyroidism.
- Excess pro-opiomelanocortin and melanocyte-stimulating hormone levels may be found.

Imaging

- Abdominal x-rays may show adrenal calcifications if adrenocortical insufficiency is secondary to fungal or TB infection.
- Abdominal CT may show enlarged adrenal glands with TB infection or malignant mass.
- Adrenals may be small secondary to idiopathic atrophy, autoimmune adrenalitis, or advanced TB.
- Adrenal gland hemorrhage or thrombosis may be seen.

Diagnostic Procedures/Surgery

- Rapid (250 g) ACTH stimulation test:
  – Following collection of baseline serum cortisol, 250 g of synthetic ACTH is administered IM or IV.

– Plasma cortisol response is reassessed at 60 minutes.

– Those with no response have primary adrenal failure; if the levels increase following injection the adrenal insufficiency is secondary to pituitary dysfunction.

- Low-dose (1 g) ACTH stimulation test:

– Following the collection of baseline serum cortisol, 1 g of ACTH is administered IV or IM.

– Plasma cortisol is checked at 60 minutes.

– Those with no response have primary adrenal failure; if the levels increase following injection the adrenal insufficiency is secondary to pituitary dysfunction.

DIFFERENTIAL DIAGNOSIS

- Acute crisis:
  - Septic shock, hemorrhagic shock, cardiogenic shock, acute abdomen
- Chronic insufficiency:
  - Secondary adrenocortical insufficiency
  - Celiac disease
  - Syndrome of inappropriate ADH secretion
  - Lead exposure
  - Severe nutritional deficiencies
  - Neurofibromatosis
  - Peutz-Jeghers syndrome
  - Porphyria cutanea tarda
  - Salt-depletion nephritis
  - Bronchogenic carcinoma
  - Anorexia nervosa
  - Depression

TREATMENT

- Maintain ABCs
- Treatment instituted with fluid and dexamethasone or hydrocortisone should not be delayed in suspected adrenal crisis. Start treatment and perform more extensive tests once patient is stabilized.

MEDICATION

- IV fluids: 0.9% normal saline or 5% dextrose in normal saline
- Hydrocortisone: 100 mg bolus immediately; followed by either 100 mg q8h or 300 mg/d continuous infusion for 2–3 days
- Dexamethasone: 2–8 mg as a single dose; this may be repeated as necessary.

Pediatric Considerations

- Hydrocortisone: 1–2 mg/kg/dose bolus immediately; followed by 25–150 mg/d given in divided doses q6–8h (infants and young children)
- In older children, 150–250 mg/d in divided doses q6–8h

Geriatric Considerations

- Start dosage on the low end of dosing range:
  - Greater frequency of impaired renal and cardiac function.
- Increased susceptibility to adverse effects such as glaucoma, diabetes, and osteoporosis with long-term therapy.

Pregnancy Considerations

- During labor and delivery, IV normal saline 0.9% and 25 mg of IV hydrocortisone should be given q8h with quick tapering after delivery.
- Considered compatible with lactation: Infant must be monitored for adverse effects including hypoadrenalism.

ADDITIONAL TREATMENT

Maintenance doses of steroids:

- Hydrocortisone (oral): 15–20 mg A.M. and 5–10 mg P.M.
- Prednisone (oral): 5 mg A.M. and 2.5 mg P.M.
- Fludrocortisone (oral): 0.05–0.2 mg/d

ONGOING CARE

PROGNOSIS

- High risk of morbidity and mortality associated with unrecognized 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
- Edema
- Glaucoma
- Hirsutism
- Hyperglycemia
- Hypertension
- Immunosuppression
- Increased intraocular pressure
- Mood changes

- Peptic ulcer
- Weight gain

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Corticosteroid dose must be doubled or tripled when the patient has an episode of minor fever, infection, trauma, or physical stress.
- For a moderate-stress procedure, the patient will require a single dose of IV hydrocortisone (100 mg) before the procedure.
- For minor procedure no adjustment is needed.
- Monitor BP
- Monitor weight
- Serum electrolyte levels
- Blood glucose levels
- Monitor growth in pediatric patients
- Bone density
- Ophthalmologic exams

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Addison Disease
- Addison Disease (Adrenocortical Insufficiency) Algorithm
- Adrenal Hemorrhage

CODES

ICD9

- 255.41 Glucocorticoid deficiency
- 255.42 Mineralocorticoid deficiency

ABBREVIATIONS

ACTH: Adrenocorticotropin hormone

ADRENAL MASS

Michelle J. Kim, MD

Ihor S. Sawczuk, MD

BASICS

DESCRIPTION

- The adrenal glands are paired retroperitoneal organs that lie within the perinephric fat just anterior/superior/medial to the kidneys.
- The adrenal glands produce a number of steroid hormones and catecholamines that are essential for homeostasis.

EPIDEMIOLOGY

)[A]:

- Peak incidence at age 50–70

)[A]: 50–60% on right, 30–40% on left, 10–15% bilateral

- Female: Male 1.2–1.5: 1
- Nonfunctional adenoma: 75%
- Cortisol-producing: 8%
- PHEO: 5%
- ACC: 5%
- Metastases: 2%
- Aldosterone-producing: 1%

)[A]:

- Bimodal age distribution: age <5 yr and then 40–50 yr old
- Slightly higher incidence in females
- 2–6% are bilateral
- Slightly higher incidence on left side

)[A]:

- 6% at autopsy, 4% on imaging

RISK FACTORS

- Age: Malignancy more common at younger age than benign lesions

)[A]:

- Malignancies: Female < Male (1:2)
- Benign lesions: Female > Male (1.7:1)

- If patient has known history of primary cancer, especially melanoma, lung, breast, or kidney cancer, 50% of adrenal masses are metastases.

Genetics

)[B]

- MEN2: 40–50% have adrenal mass
- Carney complex: 30% have adrenal mass
- Li-Fraumeni Syndrome: 10–20% have adrenal mass
- VHL: 10–20% have adrenal mass

PATHOPHYSIOLOGY

- The adrenal gland is divided into the cortex and medulla.
- Adrenal cortex:
  - Zona glomerulosa: Produces mineralocorticoid aldosterone that regulates sodium and fluid homeostasis, promotes exchange of potassium for sodium in the distal tubule.
  - Zonal fasciculata: Produces glucocorticoid cortisol that regulates cellular metabolism, glucose metabolism, immune processes, and other regulatory functions.
  - Zona reticularis: Produces the adrenal androgens androstenedione, DHEA, and DHEAS.
- Adrenal medulla:
  - Produces catecholamines dopamine, norepinephrine, and epinephrine.
- Each region and zone produces specific, hormonally active products. Any of these regions can over- or underproduce secretory products with resulting signs and symptoms:
  - CUS: Excess cortisol production
  - CON: Primary hyperaldosteronism
  - PHEO: Excess catecholamine production
  - Sex steroid–secreting tumors (SEX): Excess testosterone or estradiol, androstenedione, DHEA, DHEAS; can be virilizing or feminizing
  - ADD: Adrenal insufficiency
  - Selective adrenal insufficiency is rare.

COMMONLY ASSOCIATED CONDITIONS

See “Genetics.”

DIAGNOSIS

HISTORY

- General: Weight gain (CUS, ACC), weight loss (PHEO, ADD), malaise (CUS, CON, PHEO, ADD), anorexia (PHE, ADD)
- GI: Abdominal pain (PHEO < ADD), nausea/vomiting (PHE, ADD), diarrhea (ADD), constipation (PHEO)
- Cardiovascular: Orthostatic hypotension/syncope/dizziness (PHE, ADD), palpitations (PHEO)

• Neurologic: Headache (CON, PHEO, ADD), muscle weakness (CUS, CON, PHEO < ADD), paresthesias (CON), muscle cramps (CON), personality changes (CUS, PHE, ADD), tremor (CON, PHEO)

• Skin: Diaphoresis (PHEO), acne (CUS, ACC), easy bruising (CUS), purple striae (CUS), hirsute (CUS, SEX), gynecomastia (CUS, SEX)

• Menses: Abnormal cycles (CUS, SEX)

• Genitourinary: Frequency (CON), testicular atrophy (SEX)

• Medical history: Malignancies, syndromes

• Medications: Exogenous steroids

• Family history (see “Genetics”)

PHYSICAL EXAM

• Vital signs: HTN (CUS, CON, PHEO, ACC), hypotension (ADD), orthostasis (PHE, ADD), tachycardia (PHEO, ADD)

• Skin: Acne (CUS), striae (CUS), bruising (CUS)

• HEENT: Moon facies (CUS), buffalo hump (CUS)

• Abdomen: Central obesity (ACC), cachectic (PHEO/ADD)

• Heart: Hyperdynamic (PHEO, ADD)

• Chest: Gynecomastia (CUS, SEX)

• Extremity: Edema (CUS ± CON)

• Genitourinary: Testicular atrophy (SEX)

• Musculoskeletal: Muscle wasting (ACC, CUS, PHEO, ADD), osteoporosis (CUS)

• Neurologic: Paresthesias (CON), weakness (CUS, CON, PHEO, ADD), tremors (CON, PHEO)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[A]

• CUS:

– Serum electrolytes: Hyperkalemia, hyperglycemia

– Serum cortisol AM/PM levels: Patients with CUS show higher levels with loss of diurnal variation.

– 24-hr urinary cortisol >100 g

– Low-dose dexamethasone suppression: 1 g, dexamethasone given:

Patients with CUS have a serum cortisol >5 g/dL. Cushing disease and normal patients suppress serum cortisol to <5 g/dL.

– High-dose dexamethasone suppression: 2 g dexamethasone q6h for 2 days:

>50% suppression if Cushing disease; failure of suppression if adrenal source.

- CON:
  - Serum electrolytes: Hypokalemia despite supplementation
  - Low plasma renin activity
  - High plasma aldosterone concentration
  - 24-hr urine: Potassium >40 mEq and aldosterone >15 g
  - Defined by elevated plasma or urinary aldosterone level indexed against urinary sodium excretion after sodium loading, with low plasma renin activity.
- PHEO:
  - 24-hr urine for metanephrines and catecholamines: 91–98% specific and sensitive.
  - Plasma metanephrines has 96–100% sensitivity but only 85–89% specificity.
- SEX:
  - Serum testosterone, estradiol, androstenedione, DHEA, and DHEAS
  - 24-hr urine for 17-ketosteroids; absence indicates gonadal etiology.

)[A]:

- 62% are functional
- Most commonly Cushing 30–40%
- Virilization alone in 20–30%

Imaging

- CT:
  - Hyperplasia: Diffuse thickening of the adrenals

Adenoma: Low attenuation on noncontrast CT due to high fat content, rapid washout on contrast CT.

Myelolipoma: Fatty content

ACC: Size >6 cm, necrosis, calcifications

Metastases: Often see bilateral masses

- MRI:
  - Adenoma: Low T2 signal
  - PHEO: High T2 signal
  - ACC: Intermediate to high T2 signal
- MIBG scan:
  - MIBG is concentrated in APUD (amine precur uptake and decarboxylation) cells in the medulla. Useful to identify PHEOs.

Diagnostic Procedures/Surgery

ALERT

Do not biopsy adrenal mass until PHEO ruled out.

- Adrenal vein sampling:
  - For lateralization of masses not visualized by imaging, especially aldosteronoma.
- Glucagon stimulation test:
  - 1 mg IV of glucagons stimulates catecholamine production in patients with pheochromocytomas. Must monitor BP.
- Clonidine suppression test:
  - 0.3 mg PO causes fall in serum catecholamines in patients with neurogenic HTN but not in patients with pheochromocytomas.
- Iodocholesterol scan:
  - To demonstrate increased adrenal metabolic activity, rarely useful
- Adrenal biopsies:
  - Must perform biochemical evaluation 1st to rule out pheochromocytoma.
  - Primary role is to rule out metastases
  - 2.8% complication rate

Pathological Findings

- Benign:
  - Adrenocortical adenomas
  - Adrenal hyperplasia
  - Adrenal cyst
  - Myelolipoma
  - Lipoma
  - Hemorrhage
- Neoplastic:
  - ACC
  - PHEO
  - Adrenal metastases
- Adrenal pseudotumors

DIFFERENTIAL DIAGNOSIS

- See “Pathological Findings.”
- CUS: Rule out exogenous steroids
- CON: Licorice ingestion

Pediatric Considerations

- ACC:
  - 0.002% of all childhood malignancies

- Better survival than adults
- Most are hormonally active.

• PHEO:
- Higher incidence of familial and bilateral masses

TREATMENT

)[C]

MEDICATION

• PHEO:
- Immediate -adrenergic blockade with phenoxybenzamine 10 mg PO b.i.d. up to 40–100 mg/d
- -blockade preoperatively
- Metatyrosine: Decreases catecholamine synthesis

• Mitotane for unresectable, recurrent, or metastatic ACC. No improvement in survival.

SURGERY/OTHER PROCEDURES

• All biochemically active adrenal masses should be removed.
• All masses >5 cm should be removed:
- Most ACCs are >6 cm but with underestimation of size on imaging, use 5 cm as the cutoff.

• Open adrenalectomy: Reserved for large masses with invasion into adjacent organs

)[C]

• Robotic adrenalectomy
• Partial adrenalectomy:
- For solitary adrenals, bilateral disease, familial syndromes

ADDITIONAL TREATMENT

Radiotherapy

ACC: For palliation of bone metastases

Additional Therapies

ACC: Cisplatin, etoposide, 5-flurouracil, doxorubicin, and vincristine have been used with variable results.

ONGOING CARE

PROGNOSIS

)[C]:

• Mean survival 18 mo
• 5-yr survival rate 15–47%
• Stage is most significant prognostic factor

COMPLICATIONS

Unrecognized malignancy or pheochromocytoma

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

)[B]:

- 5–25% increase in size during follow-up
- 0–11% become functional
- 0.1% risk of malignant transformation

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See Also (Topic, Algorithm, Electronic Media Element)

- Addison Disease
- Adrenal Calcifications
- Adrenal Cysts
- Adrenal Hemorrhage
- Adrenal Incidentaloma
- Adrenal Mass Algorithm
- Adrenal Myelolipoma
- Adrenal, Metastases to
- Adrenocortical Carcinoma
- Cushing Disease and Syndrome
- Pheochromocytoma

CODES

ICD9

- 194.0 Malignant neoplasm of adrenal gland
- 227.0 Benign neoplasm of adrenal gland
- 255.9 Unspecified disorder of adrenal glands

ABBREVIATIONS

- ACC: Adrenocortical carcinoma
- ADD: Addison disease
- CON: Conn syndrome
- CT: Computed tomography
- CUS: Cushing syndrome
- DHEA: Dehydroepiandrosterone
- DHEAS: Dehydroepiandrosterone sulfate
- MEN: Multiple endocrine neoplasia
- MIBG: Metaiodobenzylguanidine scan
- PHEO: Pheochromocytoma
- SEX: Sex steroid–secreting tumor

AMYLOIDOSIS, GENITOURINARY

David D. Thiel, MD

Steven P. Petrou, MD

BASICS

DESCRIPTION

- Heterogeneous group of disorders associated with extracellular deposition of protein in abnormal fibrillar form:
  - Can involve any organ system
  - Kidney, ureters, seminal vesicles, prostate, penis, and testis can be involved
  - >50% of GU cases involve the bladder
- 25 structurally unrelated proteins known to cause amyloidosis
- May be primary, secondary, or hereditary
- May be organ limited or systemic
- Cystoscopic appearance may mimic neoplasm

EPIDEMIOLOGY

- Mean age of localized GU amyloid is 55 yr (range 28–80 yr)
- Approximated incidence is 10 per 1 million
- In some Middle Eastern countries, FMF is highest worldwide:
  - The frequency of renal amyloidosis in untreated FMF is ~100%. In those countries, amyloidosis represents a significant proportion of all renal disease.

RISK FACTORS

- Chronic and recurrent mucosal and submucosal inflammation
- Hemodialysis patients get deposits in kidneys
- Chronic inflammatory disorders (TB)

Genetics

- Familial or hereditary amyloidoses exist
- Dozens of specific variants described
- Familial forms often do not present until adulthood

PATHOPHYSIOLOGY

- Extracellular deposition of protein in an abnormal fibrillar form
- Thought to be a misfolding 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 proteinuria:
  - See “Hypoalbuminemia” and “Edema.”
- The amyloidosis are classified as systemic or localized, primary, or secondary, or according to which type of amyloid is deposited. By convention, a combination of these ap-

proaches is used clinically:

- Systemic amyloidosis affect >1 body organ or system.
- Localized amyloidosis affect only 1 body organ or tissue type.
- Primary amyloidosis arise from a disease with disordered immune cell function (eg, multiple myeloma) and other immunocyte dyscrasias.
- Secondary (reactive) amyloidosis occur as a complication of some other chronic inflammatory or tissue destructive disease: Infections (TB, osteomyelitis, etc.) or inflammatory (rheumatoid arthritis, etc.)

COMMONLY ASSOCIATED CONDITIONS

- ESRD and hemo- or peritoneal dialysis
- Nephrotic syndrome
- Diabetes
- Multiple myeloma
- Renal cell carcinoma

DIAGNOSIS

HISTORY

- Patient on hemodialysis
- Family history of amyloidosis
- Chronic disease or inflammation
- Rarely, renal cell carcinoma can be associated with the development of amyloid
- Bladder: Painless hematuria (75%):
  - Irritative voiding symptoms (urgency, frequency)
  - Clinically similar to bladder cancer
- Ureter: Obstruction (flank pain):
  - Anuria if bilateral amyloidosis
  - Hematuria
- Prostate: Hematuria:
  - Outlet obstruction may be present

PHYSICAL EXAM

- Peripheral edema (nephritic syndrome)
- No specific physical findings

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Proteinuria in 50–80%
- 50% of systemic amyloid presents with renal failure

- In primary amyloidosis, elevated monoclonal proteins can be detected in the urine

Imaging

- CT or US may demonstrate hydronephrosis with obstruction (ureteral amyloid).
- MRI: T2-weighted images are suggestive of amyloid deposition; can be confused with tumor extension into seminal vesicles on MRI for prostate cancer

Diagnostic Procedures/Surgery

- Cystoscopy for hematuria.
  - Lesion difficult to distinguish from TCC without biopsy or resection
- Ureteroscopy or retrograde pyelograms for ureteral involvement
- Renal biopsy is often the primary means of diagnosis in systemic amyloidosis.

Pathological Findings

- Diagnosis requires histologic demonstration of amyloid deposits:
  - Use Congo red stain:
    Orange under light microscope
    Apple-green under polarized light
  - Electron microscope can be used to identify microfibrils.
  - Immunohistochemical analysis assists in typing:
    Diagnosis of transthyretin-type amyloidosis limits need for further evaluation as it identifies the amyloidosis as inherited
- Seminal vesical amyloidosis can be seen in radical prostatectomy specimens, but the significance is unknown.

DIFFERENTIAL DIAGNOSIS

- Bladder: Lesions difficult to distinguish from TCC without biopsy
- Ureter: May confuse with stones
- Urethral stricture: May be confused with carcinoma
- Nephrotic syndrome and glomerulonephritis

TREATMENT

Supportive care with therapy directed at primary cause if identified

MEDICATION

- Treat underlying inflammatory disease:
  - Lifelong colchicines in MFM
  - Anti-TB therapy for TB
- High-dose antiplasma cell treatment (IV melphalan) followed by stem cell transplant
- Adjuvant intravesical DMSO (10%) for 8 wks has shown success in preventing bladder recurrence:

- DMSO shown in vivo to destabilize fibrils

SURGERY/OTHER PROCEDURES

- Bladder: TUR of lesion with fulguration (laser or electrocautery):
  - Laser fulguration
  - Partial cystectomy
  - Total cystectomy is rarely needed.
- Urethra: Excision of mass
- Ureters: Excision and reimplant or ureter-ureterostomy
- Renal: Transplantation for ESRD

ADDITIONAL TREATMENT

For systemic disease, regular monitoring of serum or urine protein levels can direct therapy.

ONGOING CARE

PROGNOSIS

- Once amyloid causes renal failure, prognosis is 12–14 mo.
- Secondary amyloidosis has better prognosis:
  - Rare for isolated secondary GU amyloid to develop systemic disease if not present initially

COMPLICATIONS

- See above
- Systemic amyloid rarely presents with urinary symptoms.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Bladder or urethra: Repeat periodic surveillance cystoscopies (potentially lifelong):
  - Recurrences in >50%
- Ureters: Repeat renal US or CT to evaluate for obstruction

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Failure, Acute

- Renal Failure, Chronic

CODES

ICD9

- 277.30 Amyloidosis, unspecified
- 277.39 Other amyloidosis

ABBREVIATIONS

- CT: Computed tomography
- DMSO: Dimethyl sulfoxide
- ESRD: End-stage renal disease
- FMF: Familial Mediterranean fever
- GU: Genitourinary
- MRI: Magnetic resonance imaging
- TCC: Transitional cell caricinoma
- TUR: Transurethral resection
- US: Ultrasound

ANDROPAUSE (LATE-ONSET HYPOGONADISM)

Serkan Deveci, MD

John P. Mulhall, MD

BASICS

DESCRIPTION

- Late-onset hypogonadism (LOH):
  - A biochemical syndrome associated with advancing age and deficiency in serum T levels with or without a genomic sensitivity to androgens associated with a constellation of symptoms.
  - Results in significant alterations in the quality of life and adversely affects the function of multiple organ systems (muscle, bone, cognition, erectile tissue, glycemic control).
- Synonym(s): Androgen deficiency in the aging male (ADAM); partial androgen deficiency in the aging male (PADAM); aging-associated androgen deficiency (AAAD); andropause; male menopause; male climacteric

EPIDEMIOLOGY

- T levels decline beginning in the 3rd decade at a rate of ~10% per decade.
- 25% of men >50 yr and 50% of men >70 yr of age have T levels in the hypogonadal range.

RISK FACTORS

See “Associated Conditions.”

Genetics

- Androgen sensitivity is associated with the length of CAG repeats in the androgen receptor gene.
- Shorter CAG repeat length is associated with overall greater androgen activity.

GENERAL PREVENTION

Avoidance of anabolic steroids may help maintain T levels in aging

PATHOPHYSIOLOGY

T levels decline progressively in aging men. This decline is a result of:

- Impairment in testicular T production.
- Reduced hypothalamic secretion of GnRH, which results in inadequate stimulation of LH.
- Decreased sensitivity of Leydig cells in the testis to LH.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- Sleep apnea syndrome

- HIV
- Depression
- Metabolic syndrome
- Chronic illness
- Prior anabolic steroid use

DIAGNOSIS

HISTORY

The decline in T is associated with:

- Diminished energy
- Decreased intellectual activity
- Diminution in muscle mass and strength
- Reduced sexual desire
- Decreased erectile quality
- Increase in visceral fat
- Decrease in bone mineral density
- Sleep disturbances
- Decrease in body hair
- Depressed mood
- Poorer glycemic control and, in chronic and profound hypogonadism, insulin resistance and the metabolic syndrome are more prevalent.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- ~98% of the circulating T is bound to SHBG and albumin.
- T is bound with high affinity to SHBG and with low affinity to albumin. Only 1–2% of T is unbound or free. Albumin-bound and free T combined is known as bioavailable T.
- SHBG increases with age and results in a decline in free T and bioavailable T levels.
- Total T and SHBG levels or the reliable measurement of free T levels with equilibrium dialysis method (which is usually not available in most commercial labs) plus the presence of some symptoms (as outlined above) are needed to establish the presence of hypogonadism.
- The presence of low T should prompt a repeat measurement of T levels as well as an assessment of gonadotropins (LH, FSH in young men) and prolactin.
- Bioavailable or calculated free T are not affected by alterations in SHBG. There is great debate as to which test is most reliable (total, free bioavailable) to establish the presence of hypogonadism.
- Serum sample for T determination should be obtained before 10 AM.

- Diagnosis is made on the basis of clinical and laboratory findings.
- Generally accepted abnormal T values:
  - Total T below 300 ng/dL with symptoms and any level <200 ng/dL, OR
  - Free T <50 pg/mL
- Additional testing:
  - Assessment of LH and prolactin are required when T levels are below normal values.
  - A serum estradiol level may be helpful in defining if aromatase inhibition is indicated.
  - In patients in whom T supplementation is considered, a repeat T, CBC, and PSA levels, plus a DRE are advised.
  - Hematocrit levels >50% are generally believed to be a relative contraindication to T supplementation.

Imaging

- Hyperprolactinemia, if clinically suspected, should be evaluated with a pituitary MRI to diagnose prolactinoma.
- In men with confirmed hypogonadism assessing bone densitometry is warranted to rule out osteopenia or osteoporosis.

DIFFERENTIAL DIAGNOSIS

- Decreased libido and ED due to other causes
- Acute and chronic systemic disease
- Pituitary tumors and infarct
- Craniopharyngioma
- Hyperprolactinemia
- Hemochromatosis (with testicular involvement)
- Status post chemotherapy or testicular radiation

TREATMENT

- PDE5i can be added to the patients with no improvement in erectile function with only T replacement.
- Maximum dose of PDE5i (sildenafil 100 mg, vardenafil 20 mg, tadafil 20 mg) is optimal starting dose. Down-titrate then for side effects or efficacy.

MEDICATION

- Replacement:
  - Oral, IM, transdermal (patches, gel), subdermal, and buccal preparations are currently available for T supplementation.

– The selection should depend on patient and physician choice.

– Short-term (transdermal, oral, and buccal) forms are preferred to long-acting (IM, subdermal) preparations for 1st-line therapy because they reproduce the circadian rhythmicity of T production by testis.

– Alkylated androgens such as 17-methyl-T as an oral agent should not be used because of its potential liver toxicity

- 1st-line treatment for hypogonadism is transdermal T (gel) supplementation (AndroGel [Solvay] Testim [Auxilium]):
  - 2.5–5 g/d is usual starting dose; dosing is titrated to serum T levels and symptoms.
  - Transdermal T preparations are currently 1% compounds.
  - ~85% of men will achieve therapeutic levels on transdermal T.
  - Those who do not will require IM T supplementation.
- Starting dose of IM T is usually 200 mg IM every 2 wk.
- Absolute contraindications to T supplementation: Breast carcinoma, known untreated prostate cancer:
  - Note: Whether prostate cancer, treated or untreated, should represent a contraindication is highly controversial at this time. Increasingly, major centers are exploring the use of T supplementation in such men.
- Relative contraindications to T supplementation:
  - Urinary retention due to BPH
  - Polycythemia
  - Sleep apnea

ONGOING CARE

PROGNOSIS

T supplementation is associated with:

- Improvement in quality of life
- Restoration of sexual function
- Improvement in cognitive function
- General improved sense of well-being
- Improvement in lipids and glycemic control
- Decreased cardiovascular risk
- Possibly enhanced response to PDE5i

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Diabetes, serum lipids, and cardiac function should be evaluated in aging men.

- Cortisol, thyroid hormones, DHEA, DHEAS should be examined in complicated cases.
- Hematologic assessment should be done periodically to examine for polycythemia (usually 1–3 mo after initiating treatment).
- Bone density increases with T replacement, so should be assessed at 1–2 yearly intervals depending upon the original bone density result.
- DRE and PSA measurement should be repeated at quarterly intervals for the 1st yr; then every 6 mo.
- Transrectal US-guided biopsy is indicated when DRE and/or PSA are abnormal or the latter rises rapidly on T supplementation. The rate of rise for which a biopsy is indicated is controversial; a useful guide is anything >0.75 ng/mL rise over a 12-mo period.
- In patients on IM T, we recommend a peak and trough T evaluation, the day after the injection and day before next injection respectively. In this fashion, dose and frequency of injection can be titrated.

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CODES

ICD9

257.2 Other testicular hypofunction

ABBREVIATIONS

- AAAD: Aging-associated androgen deficiency
- ADAM: Androgen deficiency in the aging male
- CBC: Complete blood count
- DHEA: Dehydroepiandrosterone
- DHEAS: Dehydroepiandrosterone sulfate

- DRE: Digital rectal exam
- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- GnRH: Gonadotropin-releasing hormone
- HIV: Human immunodeficiency virus
- LH: Luteinizing hormone
- LOH: Late-onset hypogonadism
- PADAM: Partial androgen deficiency in the aging male
- PDE5i: Phosphodiesterase type-5 inhibitors
- PSA: Prostate-specific antigen
- SHBG: Sex hormone binding globulin
- T: Testosterone
- US: Ultrasonography

ANORECTAL MALFORMATIONS: IMPERFORATE ANUS, CLOACA, AND UROGENITAL SINUS ANOMALIES

Erica J. Traxel, MD

Paul H. Noh, MD

BASICS

DESCRIPTION

Arm's area 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 rectum and urinary tract.
- Cloaca: In females, a common channel between urinary tract, vagina, and rectum.
- Urogenital sinus (UGS): In females, a common channel between vagina and urinary tract.

EPIDEMIOLOGY

)[B]:

)[A]

)[A]

RISK FACTORS

)[A]

)[B]

Genetics

ARM found in certain congenital syndromes with associated genetic abnormalities:

- Currarino triad: ARM, sacral bony defect, presacral mass; autosomal dominant
- Townes-Brock syndrome: ARM, external ear abnormalities, hearing loss, polydactyly, renal anomalies (agenesis, horseshoe); autosomal dominant
- Pallister-Hall syndrome: ARM, hypothalamic hamartomas, hypopituitarianism, polydactyly, syndactyly, holoprosencephaly; autosomal dominant
- Cat-eye syndrome: ARM, coloboma, preauricular tag, heart defect, urinary tract abnormalities, mental retardation
- Trisomy 21: Imperforate anus without fistula

GENERAL PREVENTION

No known means of prevention

PATHOPHYSIOLOGY

- Classic theory: The urorectal septum (mesoderm), in particular its medial aspect (Tournoux fold), fails to grow caudally to meet the lateral Rathke 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 hind gut.

COMMONLY ASSOCIATED CONDITIONS

- Can occur as an isolated abnormality or as part of a syndrome:
  - VACTERL: Vertebral, anorectal, cardiac, tracheoesophageal fistula, renal, limb abnormalities
- In general, the higher the ARM, the more likely there are associated abnormalities.
- Urinary abnormalities are present in half of ARM:

)[B]
)[B]
)[B]
)[B]
)[B]

- Genital abnormalities:

)[B]
)[B]

  - Bicornuate uterus
  - Duplicated vaginas with septum
  - Ambiguous genitalia, clitoromegaly in UGS associated with CAH

)[B]:

  - Sacral agenesis the most common vertebral anomaly.

)[B]:

  - Tethered cord, thickened/fatty filum terminale, lipoma, and syringomyelia

)[B]:

  - Ventricular septal defect most common

DIAGNOSIS

HISTORY

- Diagnosis may or may not be anticipated based on prenatal US.
- 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 retention in UGS
  - Amenorrhea and abdominal distension due to hydrometrocolpos or hematocolpos at puberty in UGS

PHYSICAL EXAM

- Thoroughly examine the perineum to determine number and position of orifices:
  - Perineum flattened in higher-level ARM.
- Inspect the genitalia: Rule-out hypospadias, cryptorchidism, clitoromegaly.
- Assess vertebrae; look for sacral abnormalities.
- Palpate for an abdominal mass that may represent a distended bladder or hydrometrocolpos.
- Rule-out associated pathologies:
  - Cardiac auscultation for murmur
  - Insert nasogastric tube for tracheoesophageal fistula
  - Skeletal/limb assessment
  - Palpation of bilateral kidneys
- Generally observe for 1st 24 hr of life to stabilize and watch for passage of meconium to indicate presence of a perineal fistula.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Renal profile
- 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:
  - Wangensteen-Rice invertogram
  - Prone, cross-table lateral plain film
  - Distance between rectal gas shadow and perineum measured
- Abdominal US: Evaluate bilateral kidneys, bladder, ± Müllerian structures
- Voiding cystourethrogram (VCUG)/cloaca gram/genitogram: Evaluate presence of VUR as well as relation of urinary tract to rectum (and to Müllerian structures)
- Colostogram: Distal to mucus fistula and proximal to colostomy to evaluate colon 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

- ECG: Rule-out cardiac anomalies

- Urodynamics: Especially in cases of UTI, VUR, urinary incontinence, sacral anomalies
- Exam under anesthesia/endoscopy: Helps delineate relationships between structures and measure length of common channel and proximity of fistula/confluence to bladder neck

DIFFERENTIAL DIAGNOSIS

- Spectrum of ARMs
- High:
  - Cloaca: Further subdivided into 3 cm common channel; females only
  - Rectovesical (bladder neck) fistula
  - Rectovaginal fistula
  - Recto prostatic urethral fistula; most common ARM in males
  - Anorectal agenesis without fistula
  - Rectal atresia
- Intermediate:
  - Rectovestibular fistula; most common ARM in females
  - Recto bulbar urethral fistula
  - Anal agenesis without fistula
  - Anorectal stenosis
- Low:
  - Ano vestibular fistula
  - Anocutaneous (perineal) fistula
  - Anal stenosis
  - Covered anus
- Urogenital sinus:
  - Some associated with virilization, as in CAH
  - Some not associated with virilization
  - Can be result of congenital cloaca following isolated repair of the rectum

TREATMENT

- Newborn should not be given any enteric intake and should have nasogastric suction.
- Hydrometrocolpos (present in 50% of cloaca) and urinary retention in newborn period managed with catheter drainage until operative intervention

MEDICATION

- IV antibiotics neonatally and perioperatively
- Prophylactic antibiotics continued at least until VUR is ruled-out
- Eventual fecal incontinence may be treated with combination of enemas and antimotility agents (Loperamide).

- Eventual constipation may be treated with combination of enemas and laxatives.
- Anticholinergics may be necessary for NGB.

SURGERY/OTHER PROCEDURES

- Newborn:
  - Diverting colostomy with mucus fistula needed in all but the lowest of ARM:

Level of colostomy should be distal on descending colon; distance between stomas should be wide to minimize the length of bowel that could potentially be in contact with urine in cases of fistula, to minimize infection and metabolic abnormalities (hyperchloremic metabolic acidosis).

  - Neonatal posterior sagittal anorectoplasty (PSARP) in low ARM
  - In cases of hydrometrocolpos, vaginotomy may be necessary as newborn
  - In cases of urinary retention, cutaneous vesicostomy may be necessary as newborn
- Definitive surgery at age 2–24 mo:
  - Lower lesions can be approached through a PSARP.
  - Higher lesions typically require laparotomy as well as PSARP.
  - In cloaca with a long common channel, when vagina will not reach perineum, can perform a vaginal switch if duplicated vaginas present, or can interpose a section of bowel between vagina and perineum.
  - Genitoplasty in cases of virilized genitalia
- Colostomy take-down a few months after definitive reconstruction, once anal dilations satisfactory
- Further urologic surgery later as indicated (ureteral reimplantation for VUR, bladder neck reconstruction for incontinence, augmentation for small capacity, poorly compliant bladder, etc.)

ADDITIONAL TREATMENT

Clean intermittent catheterization may be necessary in cases of NGB.

ONGOING CARE

PROGNOSIS

)[B]:

  - Voluntary bowel movements in 74% of ARM
  - Fecal soiling occurs in 57% of ARM (in absence of a bowel management program)
  - Total fecal continence (voluntary bowel movements, no soiling) in 41% of ARM; the lower the ARM, the better the likelihood of fecal continence.
  - Constipation in 43% of ARM; the lower the ARM, the more likely to have constipation.

)[B]:

- Present overall in 9% of ARM
- Highest probability in cloaca (19% if common channel <3 cm, 69% if >3 cm)

COMPLICATIONS

- Ongoing problems usually due to underlying congenital abnormality, not iatrogenic causes
- NGB in many ARM, but rarely due to surgery

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- 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/hematocolpos, infertility, ectopic pregnancy, delivery issues

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See Also (Topic, Algorithm, Electronic Media Element)

Exstrophy, Cloacal

CODES

ICD9

- 751.2 Congenital atresia and stenosis of large intestine, rectum, and anal canal
- 751.5 Other congenital anomalies of intestine

ABBREVIATIONS

- ARM: Anorectal malformation
- CAH: Congenital adrenal hyperplasia
- ECG: Echocardiogram
- MRI: Magnetic resonance imaging
- NGB: Neurogenic bladder
- PSARP: Posterior sagittal anorectoplasty
- US: Ultrasound
- UGS: Urogenital sinus
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

ANURIA AND OLIGURIA

Ashley E. Ross, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- Anuria: No urine output.
- Oliguria: Urine output <1 mL/kg/h in infants, <0.5 mL/kg/h in children or adults
- Often the earliest sign of impaired renal function.
- Usually associated with a severe decrease in GFR interfering with kidney's ability to eliminate nitrogenous wastes, maintain fluid, acid–base, and electrolyte balance.

EPIDEMIOLOGY

- Frequency varies greatly depending on clinical setting:
  - Incidence in adults:
    1% at admission
    2–5% during hospitalization
    4–15% after cardiopulmonary bypass
  - Incidence in newborns/children:
    10% of newborn ICU patients
    2–3% of pediatric ICU patients
    Up to 8% of children undergoing cardiac surgery
- Increased in neonatal and older age groups because of comorbid conditions
- Increased in early childhood because of the high incidence of illnesses leading to dehydration.

RISK FACTORS

- Pre-existing renal disease (atherosclerotic, diabetic, intrinsic)
- Nephrotoxic medication use

GENERAL PREVENTION

- Avoid decreased renal perfusion by adequate intravascular volume, adequate cardiac output, and maintaining proper systemic vascular resistance
- Proper dosing of nephrotoxic meds

PATHOPHYSIOLOGY

- Oliguria may result from 3 broad pathophysiologic processes: Prerenal, intrinsic renal, and postrenal mechanisms
- Prerenal:
  - Functional response of structurally normal kidneys to hypoperfusion

– Most common cause of oliguria in both community-acquired and hospital-acquired cases

– Early phase of renal compensation for reduced perfusion: Maintain GFR by afferent arteriolar dilatation (via myogenic responses, tubuloglomerular feedback, and prostaglandins) and efferent arteriolar constriction (mediated by angiotensin II)

– Enhanced tubular reabsorption of salt and water (stimulated by the renin-angiotensin-aldosterone system and sympathetic nervous system)

– Prerenal oliguria/anuria can usually be rapidly reversed following reestablishment of renal perfusion

– Prolonged renal hypoperfusion can result in a deleterious shift from compensation to decompensation.

– Decompensation phase is characterized by excessive stimulation of the sympathetic and renin-angiotensin systems, with resultant profound renal vasoconstriction and ischemic renal injury.

– Iatrogenic interference with renal autoregulation by administration of vasoconstrictors (cyclosporine, tacrolimus), inhibitors of prostaglandin synthesis (NSAIDs), or ACE inhibitors can precipitate oliguric ARF in individuals with reduced renal perfusion.

- Intrinsic renal failure:

– Associated with structural renal damage including acute tubular necrosis (from prolonged ischemia, drugs, or toxins), primary glomerular diseases, or vascular lesions

- Postrenal failure:
  - Mechanical or functional obstruction to the flow of urine
  - Usually responds to release of the obstruction

COMMONLY ASSOCIATED CONDITIONS

- Pre-existing renal disease (vascular, diabetes, etc.)
- Bladder outlet obstruction

DIAGNOSIS

HISTORY

- Age, sex
- Duration of symptoms
- History of pre-existing renal insufficiency
- Diabetes
- Hypertension
- S/P nephrectomy or renal transplant
- Fluid losses:

- Nausea/vomiting/diarrhea
- Trauma, surgery, burns

- History of hypotensive events
- Medications:
  - Can cause or exacerbate
  - Immunosuppressants: Cyclosporine, tacrolimus
  - NSAIDs
  - Antibiotics/antifungals/antivirals: Aminoglycosides, amphotericin B, acyclovir and sulfonamides (acyclovir and sulfonamides can precipitate within the tubular lumen and result in obstruction)
  - Chemotherapeutics: Cisplatin, methotrexate
- Symptoms of urinary tract obstruction:
  - Anuria
  - Alternating periods of polyuria and oligo anuria
  - Poor stream, dribbling
- Symptoms of chronic renal failure

PHYSICAL EXAM

- Signs of intravascular depletion:
  - Tachycardia
  - Orthostatic hypotension
  - Decreased skin turgor
  - Dry mucous membranes
- Signs of myocardial failure:
  - Jugular venous distention
  - Murmurs
  - Crackles on pulmonary exam
- Signs of volume overload:
  - Generalized edema
- Signs of postrenal failure:
  - Palpable bladder
  - Enlarged prostate on rectal exam
  - Meatal stenosis
  - Signs of urethral trauma
  - Patients with indwelling catheters should be irrigated to rule out blockage.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- UA:
  - Prerenal UA has little protein, heme, or red cells and may have a few hyaline and fine granular casts.
  - Intrinsic renal failure may have prominent hematuria and proteinuria, as well as dirty brown granular (type I and II), tubular epithelial, or red or white blood cell casts.
- Urinary indexes:

: Indices of Prerenal and Intrinsic Renal Failure

  - Spot urinary and serum sodium, creatinine, urea nitrogen, and osmolality can help differentiate between prerenal and intrinsic renal conditions.
- Serum electrolytes:
  - BUN-to-serum creatinine ratio >20 suggests prerenal azotemia.

Table 1 Urinary Indices

Prerenal	
Intrinsic Renal	
Urinary sodium concentration	
<20 mEq/L	
>40 mEq/L	
Fractional excretion of sodium, FENA (%)	
<1%	
>2%	
<35%	
>35%	
Urinary-to-plasma creatinine ratio	
>40	
<20	
Urinary-to-plasma osmolarity ratio	
>1.5	
<1.1	

*Helpful when diuretics have been used

Imaging

- Renal/bladder US:
  - Hydronephrosis, bladder dilation
- VCUG for suspected bladder outlet obstruction
- Nuclear renal scans may show blood flow and function of kidneys.
- IVP or contrast generally not indicated, as may exacerbate renal insufficiency

Diagnostic Procedures/Surgery

Catheter placement

DIFFERENTIAL DIAGNOSIS

- Prerenal insufficiency:
  - Absolute decrease in intravascular volume
  - Hemorrhage
  - GI losses (vomiting, diarrhea)
  - Renal losses (diabetes insipidus, diabetes mellitus, diuretics, salt-wasting nephropathy)
  - Cutaneous losses (burns)
  - Relative decrease in intravascular volume (3rd-space losses)
  - Shock (septic, toxic, anaphylactic, spinal)
  - Impaired cardiac output (ischemic heart disease, cardiomyopathy, valvular heart disease, pericardial tamponade
- Intrinsic renal insufficiency (renal/glomerular disease):
  - Tubulointerstitial (ATN, AIN, etc.)
  - Exogenous toxins (aminoglycosides, amphotericin B, contrast)
  - Endogenous toxins (hemoglobin, myoglobin, uric acid)
  - Vascular (renal vein or artery thrombosis)
  - Vasculitis
- Postrenal:
  - Upper urinary tract obstruction:
    External compression ureters
    Retroperitoneal fibrosis
    Nephrolithiasis (bilateral for anuria)
  - Lower urinary tract obstruction:
    Prostatic enlargement
    Poorly functioning bladder (neurogenic, bladder neck contracture)

Urethral stricture

TREATMENT

- Diagnosis of cause for oliguria/anuria to guide treatment
- All patients with oliguria/anuria should have a catheter placed to accurately monitor urinary output and eliminate lower urinary tract obstruction as a cause (if catheter is already present correct position/function should be confirmed).
- If initial treatment is unsuccessful, patient may require HD especially if:
  - Severe hyperkalemia
  - Symptomatic uremia
  - Severe volume overload
  - Refractory metabolic acidosis; uremic pericarditis

MEDICATION

- Prerenal causes:
  - Hydration
- Intrinsic renal causes:

)[A]

SURGERY/OTHER PROCEDURES

Procedures for treatment of postrenal causes of oliguria/anuria:

- Premise is relief of obstruction
- Nephrostomy tube, ureteral stent, Foley catheter depending on level of obstruction and overall condition of patient

ONGOING CARE

PROGNOSIS

In most clinical situations, acute oliguria is reversible and does not result in permanent decreases in GFR. However, identification and timely treatment of reversible causes are crucial because the therapeutic window may be small.

COMPLICATIONS

- Progression to intrinsic renal failure
- Inability to manage electrolytes and fluid balance resulting in a variety of conditions such as:
  - Arrhythmias
  - Congestive heart failure
  - Altered mental status

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Serial renal function testing for resolution

REFERENCES

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See Also (Topic, Algorithm, Electronic Media Element)

- Acute Renal Failure
- Anuria or Oliguria Algorithm

CODES

ICD9

788.5 Oliguria and anuria

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- AIN: Acute intestinal nephritis
- ARF: Acute renal failure
- ATN: Acute tubular nephritis
- GFR: Glomerular filtration rate
- GI: Gastrointestinal
- HD: Hemodialysis
- ICU: Intensive care unit
- IVP: Intravascular pressure
- NSAIDs: Nonsteroidal anti-inflammatory drugs
- UA: Urinalysis
- US: Ultrasound
- VCUG: Voiding cystourethrogram

AUTONOMIC DYSREFLEXIA

Patrick J. Shenot, MD

BASICS

DESCRIPTION

A potentially life-threatening condition that can cause rapid, extreme BP elevation, headache, diaphoresis, bradycardia, sweating, nausea, and piloerection in patients with spinal cord lesions at and above the 6th thoracic level (T6).

EPIDEMIOLOGY

- Incidence is unknown
- ~85% of quadriplegic and high paraplegic individuals are prone to AD in response to noxious stimuli.
- AD is more common in men than in women due to increased bladder outlet resistance

RISK FACTORS

- Male
- High SCI

GENERAL PREVENTION

- Avoid rapid or prolonged bladder and distention
- Maintain regular schedule of bowel emptying

PATHOPHYSIOLOGY

- Stimuli, such as bladder distention, bowel distention, or pain activate sympathetic neurons in the lateral horn of the spinal cord causing unopposed reflex sympathetic activity.
- Vasoconstriction and subsequent HTN develop.
- In response to HTN, vagal nerve triggers bradycardia.
- Vagal nerve is able to vasodilate vessels above injury (flushing in face), but vessels below injury remain vasoconstricted.
- Other symptoms of sympathetic activation noted, including diaphoresis and piloerection

COMMONLY ASSOCIATED CONDITIONS

SCI

DIAGNOSIS

HISTORY

- SCI or transverse myelitis at level of T6 or above
- Screen for urologic causes:
  - Bladder distention
  - Recent instrumentation

  - Indwelling urethral or suprapubic tube
  - Urinary tract infection
  - Renal, ureteral, or bladder calculi
  - Epididymitis or orchitis
  - Ejaculation
- Nonurologic causes:
  - Bowel distention
  - Pressure sores
  - Tight clothing
  - Ingrown toenails
  - Sexual intercourse
  - Pregnancy and labor

PHYSICAL EXAM

- BP often severely elevated
- Flushing above the level of injury
- Evaluate for noxious stimuli below level of SCI
- Skin: Infection, pressure sores
- Nails: Ingrown nails

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urinalysis and urine culture are indicated to determine the presence of infection.

Imaging

CT of abdomen and pelvis to evaluate for urolithiasis if cause not apparent.

Diagnostic Procedures/Surgery

Urodynamic testing to evaluate bladder compliance and rule out persistently elevated bladder pressures.

DIFFERENTIAL DIAGNOSIS

- Paroxysmal HTN
- Pheochromocytoma
- Brain stem tumors
- Preeclampsia

TREATMENT

- Initial treatment is always directed at the removal of the triggering stimulus by bladder drainage or bowel decompression.
- Monitor BP closely during acute episodes.

- Minimize noxious stimuli below level of injury in patients prone to AD.

MEDICATION

- Primary therapy should always be to remove the triggering stimulus.
- Rarely, acute episodes must be managed with IV nitrates or arterial dilators under closely monitored conditions

)[B].

  - Doxazosin 2–8 mg PO qd
  - Terazosin 2–5 mg PO qd–b.i.d.
  - Tamsulosin 0.4 mg PO o.d.
  - Alfuzosin 10 mg PO qd

- Phenoxybenzamine 10 mg PO b.i.d. (nonselective)
- Botulinum toxin injection into the detrusor for patients on intermittent catheterization to decrease bladder pressures
- Botulinum toxin injection into the external sphincter for patients who void reflexively to decrease voiding pressures

SURGERY/OTHER PROCEDURES

)[A]

- Bladder augmentation may be considered in patients with the ability to catheterize who wish to remain continent.

)[B]

ONGOING CARE

PROGNOSIS

AD can generally be managed effectively with little impact on patient.

COMPLICATIONS

Rare complications of acute episodes of AD include intracerebral and subarachnoid hemorrhage.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Frequent (at least 4 times daily) clean, intermittent catheterization and a regular bowel program for every SCI patient
- Assess AD symptoms and BP at every appointment.
- Teach SCI patients the significance of AD: Symptoms should prompt patients to empty their bladder and bowel.

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See Also (Topic, Algorithm, Electronic Media Element)

- Spinal Cord Injury
- Detrusor-Sphincter Dyssynergia

CODES

ICD9

337.3 Autonomic dysreflexia

ABBREVIATIONS

- AD: Autonomic dysreflexia
- BP: Blood pressure
- CT: Computed tomography
- HTN: Hypertension
- IV: Intravenous
- SCI: Spinal cord injury

BACTERIURIA AND PYURIA

Anil A. Thomas, MD

Sandip P. Vasavada, MD

BASICS

DESCRIPTION

- Bacteriuria: Presence of bacteria in the urine:
  - Can be either symptomatic or asymptomatic
  - Significant bacteriuria: Quantitative count >1 × 105 CFU/mL in 2 consecutive specimens
  - Majority of individuals with significant bacteria have significant pyuria
  - Usually 1 organism
  - >1 organism: Either contamination or polymicrobial infection
- Pyuria: Presence of WBC in the urine:
  - Implies an inflammatory response
  - Significant pyuria: >10 WBCs/HPF centrifuged
  - Close association between pyuria and bacteriuria; 96% of patients who are symptomatic and bacteriuric have >10 WBCs/HPF
- Sterile pyuria: Presence of WBCs in the urine in the absence of bacteriuria:
  - Contamination: Vaginal or prepuce secretions
  - Infections: Treated UTI, mycobacterial, TB, chlamydial, gonococcal, fungal (GU or systemic), viral, haemophilus, bilharzia
  - Other infections: Appendicitis, diverticulitis, prostatitis
  - Noninfectious: Nephritis, stones, foreign bodies, transplant rejection, trauma, malignancy, chemotherapy, nephrotoxic substances, drug-induced interstitial nephritis

EPIDEMIOLOGY

- 0.3–0.5 episodes of bacteriuria per person per year among asymptomatic females aged 18–40
- Newborns:
  - Males: 1.5–3.6%; females: 0.4–1.0%
- 1–5 yr:
  - Males: 0.0–0.4%; females: 0.7–2.7%
- School-age:
  - Males: 0.04–0.2%; females 0.7–2.3%
- Adult (middle-age):
  - 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

RISK FACTORS

Age, diabetes mellitus, sexual intercourse, use of diaphragm or spermatocide, delayed postcoital micturition, history of recent infection, immunosuppression, long-term indwelling catheters, pregnancy, neurologic disorders, foreign bodies, stones, obstructive uropathy

Genetics

Certain populations may be more susceptible to bacteriuria and recurrent UTIs due to distinct molecular defects causing impaired host responses.

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 UTIs.
- 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.

PATHOPHYSIOLOGY

- Urinary tract is normally sterile.
- Bacteriuria usually ascends up the urinary tract from colonizing flora of the gut, vagina, or distal urethra.
- Bacteriuria can also invade the urinary tract hematogenously or through direct transfer after instrumentation.
- Bacteria colonize the urinary tract and then multiply, causing an inflammatory response with pyuria.
- Bacterial factors:
  - Certain bacteria are more efficient at adhering to mucosal cells than others due to fimbria.
  - Virulence factors: Hemolysis, adhesions, colicin, metabolic properties, etc.
- Host factors:
  - Cystitis prone: Certain patients are more prone to bacteriuria (transitional cell bacterial receptor sites).
  - Menstrual cycle: Bacteriuria may be influenced by hormones.
  - Postmenopausal: Increasing incidence of bacteriuria
  - Vaginal pH: Normally acidic pH; colonization with uropathogens may occur as vaginal pH rises

– Competitive organisms: Normal vaginal flora discourages uropathogenic colonization

– Buccal and vaginal cells: More receptive to uropathogens' adherence in cystitis-prone patients

– Local production of IgA, IgG may play defense role.

– Production of mucous protective layer as a local bladder defense

– Blood group antigen (secretors) saturate or block bacterial adherence.

COMMONLY ASSOCIATED CONDITIONS

Diabetes mellitus, pregnancy, immunosuppression, structural urinary tract abnormalities, indwelling catheters

DIAGNOSIS

HISTORY

- Dysuria, frequency, urgency, malaise, rarely low-grade fever
- Occasionally hematuria (gross): Especially in the female patient; uncommon in children and men
- Fever and flank pain with upper tract origin: Pyelonephritis
- Asymptomatic or atypical symptoms: Young and old patients
- Young patients: Abdominal discomfort, failure to thrive, fever, vomiting, jaundice
- Older patients: May be asymptomatic or have incontinence, fevers, frequency, and urgency
- Varied symptoms with sterile pyuria associated with varied pathology
- History of childhood fevers: May imply UTIs and associated congenital abnormalities
- Problems with toilet training, urgency, incontinence
- Family history of UTIs: Mothers, daughters, sisters
- History of a risk factor for bacteriuria

PHYSICAL EXAM

- Suprapubic tenderness: Cystitis
- Flank tenderness: Pyelonephritis
- Fever: Usually with upper tract infection
- Children may have abdominal discomfort, tenderness, or distention.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Indications for screening:
  - Symptomatic patients
  - Pregnant women

- Prior to genitourinary procedures

- Urine dipstick: Best for screening:
  - LE test:
    Detects enzyme release by WBCs
    Sensitivity 90%, specificity 95% for UTI
  - Conversion of nitrate to nitrite (Griess test): 70–80% sensitivity for UTI
  - Catalase test: Cannot differentiate infection from inflammation
- Microscopy:
  - Rapid in-office test: 80% accurate; usually fresh unspun
  - Centrifugation: Increases finding 10-fold
  - Difficult to see bacteria if <1 × 105 CFU/mL
  - Vaginal organisms may be misread as uropathogens: Lactobacilli and Corynebacterium
- Gram stain:
  - Increases identification of bacteria with sensitivity and specificity of 96.2% and 93.0%, respectively
- Urine culture:
  - Clean-catch midstream urine: Most commonly used
  - Catheterized urine: May be necessary to assure diagnosis or in special situations (ie, children, patients unable to void, the debilitated, the obese)
  - Segmented urine specimen, initial 10 mL, midstream, post exam: For localization of bacteria or WBCs
  - Quantitative counts in UTI are usually >1 × 105 CFU/mL with a uropathogen
  - Range 1 × 102 to 1 × 106
  - <105 per milliliter in 47% of patients
  - <104 per milliliter in 30% of patients
  - >102 per milliliter: Uropathogen; suspect UTI
- Conditions causing variation: Hydration, bacterial growth rate, urinary pH, pyelonephritis, catheterized specimen:
  - Multiple organisms usually indicate contamination or polymicrobial infection.
- Uncomplicated infections: E. coli, other Enterobacteriaceae, Staphylococcus saprophyticus, enterococci
- Complicated infections: E. coli, other Enterobacteriaceae, Pseudomonas, S. aureus, coagulase negative staph, enterococci
- Contaminants: Lactobacilli, streptococci, diphtheroids, Gardnerella, Mycoplasma, coagulation-negative staph

Imaging

- Bacteriuria:
  - Childhood: US, VCUG, radionuclide cystogram, IV pyelogram
  - Adult: Only indicated if suspicious of pathology or childhood history, obstruction, stone disease, hematuria
  - Imaging in routine UTIs involving normal adult females: Very low yield of pathology
- Pyuria:
  - Associated with infection and bacteriuria: Same indications
  - Sterile pyuria evaluation for other causes
- Isotopic function studies and cystogram
- CT: Localization of nidus or abnormality responsible for bacteriuria/pyuria (i.e., abscess)

Diagnostic Procedures/Surgery

Localization of bacteria: Segmented urine, ureteral catheterization, immunologic antibody studies

DIFFERENTIAL DIAGNOSIS

- Cystitis: Pyuria, positive culture, abrupt onset
- Urethritis: Pyuria, negative urine culture, gradual onset
- Vaginitis: No pyuria, vaginal discharge, pruritus
- Pyelonephritis
- Noninfectious causes
- Interstitial cystitis
- Nonuropathogenic cause, as in sterile pyuria
- Contamination of specimen with vaginal/skin flora

TREATMENT

Obtain urine culture:

- Indwelling catheters should be used as infrequently as possible

MEDICATION

- Asymptomatic bacteriuria is treated as a UTI in childhood, prior to urologic surgery, and in pregnancy.
- Persistent or recurrent bacteriuria may need treatment for more prolonged periods followed by chronic low-dose medication.
- High-risk patients (children with congenital abnormalities and adults with significant risk factors) may need chronic suppressive antimicrobial treatment.
- Postmenopausal: Treated only if symptomatic or associated with complicating factors:

– Diabetes, obstruction, immunosuppression

• Catheter-associated bacteriuria, if asymptomatic, should not be treated (may be due to colonization).

Pregnancy Considerations

• Bacteriuria in pregnancy should be treated, as untreated bacteriuria has been linked with prematurity, IUGR, low birth weight, and neonatal death.

• All pregnant women should be screened for asymptomatic bacteriuria at 16 wks gestation.

Cranberry juice may decrease frequency of bacteriuria and pyuria in select populations.

ONGOING CARE

PROGNOSIS

Variable severity ranging from asymptomatic bacteriuria to severe UTI with urosepsis and secondary organ failure

COMPLICATIONS

20–40% of untreated bacteriuria in pregnancy leads to pyelonephritis.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Repeat exam: 2 wks posttreatment:
  – Microscopic: Urinalysis
  – Culture
• Periodic office visits to verify sterile urine
• 2008 USPSTF guidelines:

)[A]

)[D]

– Although adults with diabetes were included in this recommendation for the general adult population, the USPSTF did not consider evidence for screening specific patient groups at high risk for severe UTIs, including transplant recipients, patients with sickle cell disease, and those with recurrent UTIs.

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See Also (Topic, Algorithm, Electronic Media Element)

- Pyuria Algorithm
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Catheter-Related

CODES

ICD9

- 599.0 Urinary tract infection, unspecified/pyuria
- 791.9 Other nonspecific findings on examination of urine

ABBREVIATIONS

- CFU: Colony-forming units
- CT: Computed tomography
- IUGR: Intrauterine growth restriction
- IV: Intravenous
- LE: Leukocyte esterase
- TB: Tuberculosis

- US: Ultrasound
- USPSTF: US Preventive Services Task Force
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- WBC: White blood cells

BALANITIS AND BALANOPOSTHITIS

Ashley E. Ross, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- Balanitis: Inflammation of the glans penis. Typical presentations include:
  - Erythema and edema of glans
  - Painful glans
  - Urethral discharge, discharge between prepuce and glans
  - Dysuria, difficulty voiding
- Balanoposthitis: Inflammation of the foreskin and glans penis (affects uncircumcised men only)
  - Presents with erythema, edema and pain of the foreskin in addition to findings of balanitis

EPIDEMIOLOGY

- Can occur at any age
- No incidence studies of balanoposthitis have been performed in the US:
  - 1.5% of uncircumcised boys ages 0–15 were affected in a Japanese cohort
- Common; exact prevalence unknown
- Balanitis affects 11% adult men and 3% boys seen in urology clinics

RISK FACTORS

- Presence of a foreskin
- Tight foreskin
- Poor genital hygiene
- Sexual contact (with or without infection)
- Diabetes
- Immunocompromised states:
  - HIV/AIDS
- Coexisting malignancy or chronic illness

GENERAL PREVENTION

- Good genital hygiene
- Safe sexual contact
- Regular retraction of foreskin to help keep glans and prepuce dry
- Optimize management of debilitating or chronic disease:
  - Strict glycemic control in diabetics

- Circumcision

PATHOPHYSIOLOGY

- Both occur by means of the intertrigo syndrome (a condition in which damp, moist areas are particularly predisposed to inflammatory changes):
  - Poor hygiene technique compounded with this degree of dampness predisposes to secondary opportunistic bacterial or fungal infiltration.
  - Candida is most common infectious cause.
- The pathophysiology is usually different in young boys compared with men:
  - Boys:

    Bacterial invasion
  - Men:

    Combination of intertrigo, irritant dermatitis, maceration injury, and bacteria or candidal overgrowth
- BXO is a specific form of balanitis:
  - Loss of elastin occurs and replacement by collagen
  - The penile skin around the urethral meatus becomes white, featureless, and contracted, causing meatal stricturing.
  - The lesion may spread to the prepuce, and the coronal sulcus may be lost.
  - In extreme cases, the entire end of the penis becomes whitened and fibrotic, with complete obliteration of distinction between glans, prepuce, and shaft.

COMMONLY ASSOCIATED CONDITIONS

Diabetes

DIAGNOSIS

HISTORY

- Use of topical allergens/irritants
- Prior episodes and treatment
- Sexual contacts/STDs
- Voiding symptoms (dysuria, hesitancy, and frequency)
- Hygiene techniques
- Systemic diseases (diabetes, malignancy)
- Foreskin retractability

PHYSICAL EXAM

- Genital exam:
  - Inspection (ulcers, lesions, visible pus)
  - Palpation (tenderness, induration, mass effect)

- Lymph nodes:
  - Inspect and palpate the bilateral inguinal nodes (should not be enlarged)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Swab of glans/foreskin for viral, bacterial, and fungal culture
- KOH and Tzanck preparation for men

Diagnostic Procedures/Surgery

Biopsy when indicated:

- Suspected carcinoma or premalignant lesion
- Recurrent cases
- For definitive diagnosis of BXO

Pathological Findings

See above.

DIFFERENTIAL DIAGNOSIS

- Fixed drug eruption (allergy)
- Contact dermatitis
- Squamous cell carcinoma of the penis
- CIS of the penis (erythroplasia of Queyrat)
- Zoon balanitis
- Psoriasis
- Reiter syndrome (associated with circinate balanitis)
- HPV

TREATMENT

- Meticulous personal hygiene, keeping the glans and foreskin clean and dry
- Avoid soaps while inflammation present
- Exposing glans to air as often as possible
- Cleaning with soap and water routinely

MEDICATION

- Treat underlying cause.
- Infectious balanitides:
  - Candidal balanitis:

    Clotrimazole cream 1%

    Miconazole cream 2%

    Apply b.i.d. until symptoms resolve

    Oral fluconazole if symptoms severe

Nystatin cream if allergy to imidazole

Imidazole with hydrocortisone if marked inflammation present

– Anaerobic infection:

Metronidazole 400 mg b.i.d. for 1 wk

Optimum dosage schedule for treatment is unknown

Alternatively, Augmentin PO or clindamycin topically

– Aerobic infection:

Group A streptococci and S. aureus, as well as Gardnerella vaginalis are all reported causes of balanitis.

Treatment based on sensitivities of organism (topical antibiotics/occasionally oral antibiotics)

– BXO:

Topical steroids (clobetasol propionate or Betamethasone valerate)

– Zoon Balanitis:

Topical steroids with or without antibacterial creams

– Circinate balanitis:

Hydrocortisone cream 1% applied b.i.d. for symptomatic relief

Treatment of any underlying infection

– Fixed drug eruptions:

Treatment not essential

Occasionally topical steroids

– Irritant/allergic balanitides:

Avoidance of precipitants, especially soaps

Emollients, aqueous cream: Applied as required and used as a soap substitute

Hydrocortisone 1% applied daily or b.i.d. until resolution of symptoms

SURGERY/OTHER PROCEDURES

- Circumcision is reserved for recurrent cases or phimosis that has failed conservative treatment.
- Occasionally emergent dorsal slit is required
- Care of meatal narrowing or stricture in BXO:
  - Self-dilation
  - Dilation by urologist
  - Incision/formal stricture repair

ONGOING CARE

PROGNOSIS

- Simple balanoposthitis resolves completely with no after-effects
- The condition is often recurrent and relapsing
- Some types require circumcision to enable resolution and prevent recurrence
- 10% recurrence rate
- Tend to be relapsing and recurring

COMPLICATIONS

- Scarring and subsequent phimosis
- Penile shaft cellulitis
- Abscess formation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

After an acute episode and treatment is implemented, the patient should be seen within 4–6 wk, unless problems occur, in which case he should be seen sooner to alter treatment.

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See Also (Topic, Algorithm, Electronic Media Element)

- Balanitis Xerotica Obliterans
- Penis, Lesion
- Zoon Balanitis

CODES

ICD9

607.1 Balanoposthitis

ABBREVIATIONS

- BXO: Balanitis xerotica obliterans
- CIS: Carcinoma in situ
- HIV/AIDS: Human immunodeficiency virus/acquired immunodeficiency syndrome
- HPV: Human papilloma virus
- KOH: Potassium hydroxide
- STD: Sexually transmitted disease

BCG SEPSIS/BCGOSIS

Douglas M. Dahl, MD

Christopher J. Cutie, MD

BASICS

DESCRIPTION

- Potentially life-threatening event secondary to intravasation of BCG into the bloodstream
- Characterized by a hypersensitivity reaction and bacterial sepsis, resulting in cardiovascular collapse and acute respiratory distress:
  - BCGitis: Mild to moderate regional symptoms, in the case of intravesical therapy; cystitis related to localized inflammatory response characterized by irritative voiding symptoms, hematuria, and low-grade fever (<38.5°C) typically lasting up to 48 hr.
- This chapter relates to BGC complications related to intravesical administration

EPIDEMIOLOGY

- 0.4% of patients treated with intravesical BCG will develop BCG sepsis.
- 10 reported deaths proved to be due to BCG sepsis.
- 3% develop transient fever only after intravesical instillation.
- Pneumonitis, granulomatous hepatitis, or arthralgia occur in ~0.7% of patients.

RISK FACTORS

- Recent transurethral instrumentation (ie, biopsy)
- Traumatic catheterization or gross hematuria at the time of intravesical instillation

GENERAL PREVENTION

- Defer instillation of BCG until 6 wk after transurethral instrumentation.
- Abort instillation if immediately preceded by traumatic Foley catheter placement.
- BCGitis: Postpone future instillations until complete resolution of symptoms.

PATHOPHYSIOLOGY

- BCG is attenuated Mycobacterium bovis
- Intravesical instillation proven to prevent recurrence and delay progression of superficial bladder TCC
- Inoculation of BCG through damaged urothelium
- Intravasation of BCG into bloodstream with subsequent urosepsis
- Massive inflammatory cytokine release resulting in septic physiology
- Combination of a hypersensitivity reaction and bacterial sepsis
- BCGitis, in contrast, is a local inflammatory condition involving the bladder epithelium.

COMMONLY ASSOCIATED CONDITIONS

Recent transurethral instrumentation

DIAGNOSIS

HISTORY

- Classically occurs during the induction dose of treatment, but may occur following any instillation.
- Often occurs within 2 hr of instillation
- Instillation of therapy following traumatic catheterization or transurethral manipulation
- Dysuria, fevers, chills, rigors, abdominal pain, urinary frequency/urgency (irritative symptoms)
- Immunocompromised patients receiving BCG
- BCG instillation at the time of active glucocorticoid or antibiotic use
- BCGitis 48 hr of low-grade fever, hematuria, and urinary frequency/urgency

PHYSICAL EXAM

- High fevers (>103.0°F) within 2 hr of treatment, resembling gram-negative sepsis
- Hypotension/shock physiology
- Suprapubic tenderness to palpation
- Hematuria

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC with differential to assess for elevated white count
- Serum electrolytes to assess for renal failure secondary to profound hypotension
- Liver function tests are elevated in TB-induced hepatitis
- Coagulation studies: PT/PTT/fibrinogen; abnormal secondary to DIC
- Urinalysis
- Urine/blood cultures: Routine and mycobacterium (acid-fast staining)

Imaging

CXR to assess for miliary distribution

Diagnostic Procedures/Surgery

See “Lab.”

Pathological Findings

Disseminated infections can include granulomas in nodes and inflammatory hepatitis.

DIFFERENTIAL DIAGNOSIS

- Post-BCG cystitis
- BCGitis (cytokine release without intravasation of BCG into bloodstream)
- Gram-negative sepsis

TREATMENT

- Fluid resuscitation and vasopressors as needed for hypotension/hemodynamic instability
- Invasive monitoring (CVP, Foley catheter, arterial line) for true BCG sepsis

MEDICATION

- Antipyretic medications (acetaminophen, ibuprofen)
- Antituberculin medication (isoniazid 300 mg/d, rifampin 600 mg/d, ethambutol 15.mg/kg/d) for 6 mo
- Broad-spectrum antibiotics for potentially concomitant bacterial infection
- Fluoroquinolone (moderate antituberculin activity)
- Prednisone 40 mg/d (tapered over 2–6 wk)
- BCGitis: Anticholinergics, antispasmodics, analgesics, NSAIDs

SURGERY/OTHER PROCEDURES

Not indicated; supportive care only

ADDITIONAL TREATMENT

Infectious disease consultation recommended

ONGOING CARE

PROGNOSIS

Good, if acute management is accurate and thorough

COMPLICATIONS

Solid organ involvement (prostate, epididymis, lung, liver, kidney, osteomyelitis)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

ICU admission with invasive monitoring equipment (central line, cardiac telemetry, arterial BP monitoring, vasopressor therapy as needed)

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See Also (Topic, Algorithm, Electronic Media Element)

Urosepsis

CODES

ICD9

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

ABBREVIATIONS

- BCG: Bacillus Calmette Guérin
- BP: Blood pressure
- CBC: Complete blood count
- CVP: Central venous pressure
- CXR: Chest x-ray
- DIC: Disseminated intravascular coagulation
- ICU: Intensive care unit
- NSAID: Nonsteroidal anti-inflammatory drug
- PT: Prothrombin time
- PTT: Partial thromboplastin time
- TCC: Transitional cell carcinoma

BLADDER AREFLEXIA (DETRUSOR AREFLEXIA)

Patrick J. Shenot, MD

BASICS

DESCRIPTION

- Bladder areflexia, or detrusor areflexia, implies inability of the detrusor to contract.
- Part of the urodynamic classification scheme of voiding dysfunction
- Described as motor paralytic bladder and complete lower motor neuron lesion in other classification schemes.
- Clinical characteristics may include urinary retention, incomplete bladder emptying, and incontinence.

RISK FACTORS

Neurologic disease and diabetes mellitus

Genetics

Genetic diseases predisposing to bladder dysfunction include:

- Muscular dystrophy
- Neurofibromatosis

GENERAL PREVENTION

Relief of bladder outlet obstruction early in the course of the disease

PATHOPHYSIOLOGY

- May be due to detrusor decompensation secondary to longstanding outlet obstruction
- May be due to neurologic injuries or dysfunctions that produce inhibition of micturition reflexes at the level of brainstem, sacral spinal cord, bladder ganglia, or detrusor smooth muscle
- Patients with poor or absent bladder contractility often attempt to void by abdominal straining.
- Efficiency of bladder emptying depends upon resistance of smooth and striated sphincter mechanisms.
- Males are less likely to be able to void by abdominal straining due to increased outlet resistance.
- Continence depends upon function of sphincteric mechanism.
- Females are more likely to experience incontinence due to lower outlet resistance.

COMMONLY ASSOCIATED CONDITIONS

- Sacral SCI
- Myelodysplasia
- Intervertebral disk disease:

- Cauda equina syndrome
- Diabetes mellitus
- Radical pelvic surgery
- Benign prostatic hyperplasia with longstanding outlet obstruction
- Fowler syndrome:
  - Urinary retention in young women without overt neurologic disease
  - Typically present with distended bladder and little urgency
  - No clinical, laboratory, or imaging studies to suggest neurologic disease
  - Associated with complete repetitive discharges and accelerating bursts on sphincter EMG
  - Often associated with polycystic ovaries

DIAGNOSIS

HISTORY

- Neurologic disease: Onset, duration
- Diabetes
- Congenital disorders:
  - Neural tube defects
- History of radical pelvic surgery
- Medications:
  - Anticholinergic medications may diminish detrusor contractility.
- Voiding symptoms:
  - Irritative or obstructive
  - Incontinence: Urge, stress
  - Nocturnal enuresis
- Method of urinary management:
  - Intermittent self-catheterization
  - Indwelling urethral or suprapubic catheter
  - Credé, Valsalva voiding
- UTI:
  - Severity of infection: Febrile, hospitalization, IV antibiotics required
  - Frequency of recurrence

PHYSICAL EXAM

- Palpable flank mass: Hydronephrosis
- Abdominal mass: Distended bladder, urinary retention
- Incontinence of urine:

- Stress maneuvers: Marshall test
- Prostate:
  - Size: Benign prostatic hyperplasia may coexist with neurogenic bladder dysfunction
- Evaluate for sacral abnormalities:
  - Sacral dimple or tuft of hair
  - Sacral agenesis
- Neurologic:
  - Sacral root
  - Perianal sensation
  - Anal tone, sphincter control
  - Impaired peripheral sensation in diabetics

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood studies:
  - Serum chemistry: Renal function, creatinine, electrolytes
  - CBC: Leukocytosis, secondary anemia due to decreased renal function or chronic infection
- Urinalysis:
  - Proteinuria: Renal dysfunction
  - Pyuria, nitrite, leukocyte esterase: Acute or chronic infection
  - Hematuria: Infection or urolithiasis

Imaging

Renal US to screen for calculus or hydronephrosis.

Diagnostic Procedures/Surgery

- Urodynamics: Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction
- Bladder compliance should be evaluated to predict risk of upper tract complications.

Pathological Findings

Bladder wall thickening and fibrosis is common in patients with chronic outlet obstruction.

DIFFERENTIAL DIAGNOSIS

- Neurologic detrusor areflexia
- Myogenic detrusor areflexia due to outlet obstruction
- Reversible causes of retention:
  - Outlet obstruction

- Medications suppressing bladder contractility
- Fowler syndrome

TREATMENT

- Intermittent catheterization is the preferred method of management, particularly if neurostimulation fails or is not possible.
- Avoid indwelling catheters to decrease risk of infection, stones.

MEDICATION

- Parasympathomimetics have been proposed with little evidence of efficacy
- Bethanechol 10–50 mg t.i.d./q.i.d. is most commonly utilized with variable results

SURGERY/OTHER PROCEDURES

- Sacral neuromodulation:

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- Bladder augmentation may be needed in some patients with poor bladder compliance.

ONGOING CARE

PROGNOSIS

Urinary retention is often permanent, but with proper urologic management, secondary complications can be minimized.

COMPLICATIONS

- Recurrent UTI
- Urinary retention
- Hydroureteronephrosis
- Neoplastic transformation: Associated with chronic catheter
- Urethral erosion with chronic catheters

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patients with poor bladder compliance require periodic urodynamic studies and upper tract imaging to minimize risk of complications.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Neurogenic Bladder, General
- Sacral Neuromodulation
- Urodynamics, Indications and Normal Values

CODES

ICD9

- 596.53 Paralysis of bladder
- 596.54 Neurogenic bladder

ABBREVIATIONS

- CBC: Complete blood count
- EMG: Electromyography
- IV: Intravenous
- SCI: Spinal cord injury
- US: Ultrasound
- UTI: Urinary tract infection

BLADDER CALCULI (VESICAL CALCULI)

David M. Albala, MD

Daniel A. Bazewicz, BS

BASICS

DESCRIPTION

- Presence of calculus material in the bladder that does not pass with normal micturition
- Usually associated with urinary stasis, but can form in healthy individuals without evidence of anatomic defects, strictures, infections, or foreign bodies.
- The presence of upper urinary tract calculi is not necessarily a predisposition to the formation of bladder stones.

EPIDEMIOLOGY

- In US and Western Europe, bladder calculi have been steadily declining since the 19th century because of improved diet, nutrition, and infection control. In these countries, bladder calculi affect adults, with a lesser frequency in children.
- In the Western hemisphere, bladder calculi primarily affect men, usually >50 years, and have associated bladder outlet obstruction (BPH).
- Bladder calculi are more common in Pacific rim countries (Thailand, Myanmar [formerly Burma] Indonesia), the Middle East, North Africa, and, in less-developed countries. Here it is often a disease of children and is far more common in boys than in girls.
- The incidence of bladder stones in children is slowly declining due to improved nutrition, better pre- and postnatal care, and improved awareness of the problem in endemic areas.
- No definitive worldwide data accurately reflect the prevalence of bladder calculi.
- In patients with new spinal cord injuries and neurogenic bladders, up to 36% developed bladder calculi over 8 yr. Because of better care, this rate has dropped to <10%.
- Bladder inflammation secondary to external beam radiation or schistosomiasis can also predispose patients to bladder calculi.

RISK FACTORS

- Bladder outlet obstruction with stasis
- Infection
- Poor diet (see “Pathophysiology”)
- Foreign bodies in the bladder that act as a nidus for stone formation. These are subclassified into iatrogenic and noniatrogenic bodies:
  - Iatrogenic: Ureteral and prostatic stents, staples, metal from endourologic instruments, suture material, retained sponges, shattered latex balloons, chronic Foley catheter, etc.

– Noniatrogenic: Objects placed into the bladder by the patient

• Metabolic abnormalities are not usually a significant cause of stone formation in patients with urinary diversions. In this group of patients, the stones are primarily composed of calcium and struvite.

• Women who have undergone anti-incontinence surgeries and those with genital prolapse

GENERAL PREVENTION

Treatment of the underlying cause of the stone is essential:

• Stone analysis is performed. Directed medical therapy is initiated as necessary.

• Encourage hydration; utilize intermittent catheterization to avoid an indwelling catheter.

• Treat bladder outlet obstruction.

• Remove foreign bodies (ie, retained nonabsorbable sutures)

Geriatric Considerations

Men >50 are at increased risk of bladder outlet obstruction and increased risk of bladder stone formation.

Pediatric Considerations

In undeveloped countries, calculi occur in children, more commonly in boys <10. These stones are generally related to poor nutrition, low social status, specifically a low-protein diet.

PATHOPHYSIOLOGY

• Bladder stones may form primarily within the bladder or in the kidney and pass into the bladder, where they can grow. A combination of an increased post-void residual and an elevated bladder neck results in the formation of stones in static urine, which cannot overcome gravity to get over the intravesical prostate and out through the urethra.

• Ammonium acid urate is a common type of bladder stone and may be pure or admixed with other mineral components. In endemic regions, low phosphorus intake leads to increased ammonium uric acid. Further high-oxylate vegetable diet and low urinary citrate due to low intake of animal proteins contribute to stone formation.

• Bladder stones can be uric acid, calcium oxalate, and calcium phosphate as well.

• Usually, if the stone is small enough to pass through the ureter, it will pass through the urethra. However, once remaining in the bladder, the stone may continue to grow.

• There may be single or multiple stones. Some may be very hard and laminated. Shapes vary from elliptical to jack stones. Some will have a faceted surface. Stones may be free floating or fixed to the bladder wall.

COMMONLY ASSOCIATED CONDITIONS

• BPH

- Urethral stricture
- Spinal cord injury
- History of schistosomiasis or bladder radiation
- History of renal calculi
- Bladder diverticuli with stasis

DIAGNOSIS

HISTORY

- Bladder stones may be completely asymptomatic.
- Symptoms of suprapubic pain, dysuria, stranguria, hesitancy, frequency, urgency, intermittent stream, hematuria, bladder outlet obstructive symptoms, pain radiating to the tip of the penis, or infection. Urinary stream may abruptly stop.
- Previous surgery (bladder, prostate, urethral)

PHYSICAL EXAM

Abdominal exam:

- Percuss the top of the bladder to look for distension.
- Palpate for abdominal or suprapubic or costovertebral angle tenderness.
- Examine for previous surgical scars

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis with microscopy. Look for hematuria, pyuria, and crystalluria.
- Urine culture and sensitivity help document and direct treatment of associated infections.
- Urine cytology if cancer suspected
- Creatinine

Imaging

- A plain radiograph (kidneys, ureters, bladder) will often demonstrate radiopaque bladder stones; however, uric acid and ammonium acid urate stones are radiolucent
- A voiding cystourethrogram or excretory urogram reveals a filling defect in the bladder, which moves when the patient is repositioned.
- Pelvic US readily diagnoses the presence of a bladder stone.
- CT (unenhanced) is highly sensitive and specific for calculi anywhere within the urinary tract. Radiolucent uric acid calculi may be seen on CT.
- MRI is typically not used for calculi but may show a black hole of low water content in the bladder

Diagnostic Procedures/Surgery

Cystoscopy is ideal for visualizing stones, to assess their number, size, and position; often used in the removal of bladder calculi.

Pathological Findings

- Evidence of acute or chronic inflammation.
- Chronic inflammation due to the stone or recurrent infection may cause premalignant or malignant changes in the bladder.

DIFFERENTIAL DIAGNOSIS

- Interstitial cystitis
- Bacterial cystitis
- Urethral stricture, bladder neck contracture
- Ureterocele
- Fungal bezoar
- Squamous cell carcinoma
- Transitional cell carcinoma/carcinoma in situ
- Prostatitis
- Neurogenic bladder
- Urethritis

TREATMENT

- Bladder stones should be removed surgically, and if bladder outlet obstruction is a causative factor, the patient should be counseled to have definitive treatment for the obstruction.
- In general, men with prostate volumes >100 g should be considered for an open simple suprapubic prostatectomy.
- Others may benefit from TUIP or TURP at the time of endoscopic stone removal to treat the underlying pathology.
- If a calculus is found adherent to a transitional cell carcinoma, and if a suspicious area does not clear after successful removal of the calculus and treatment of any associated infection, biopsy is performed to rule out malignancy.

MEDICATION

- Surgery is the mainstay of therapy. Dissolution of bladder stones is possible if the stones are composed of pure uric acid.
- Alkalization therapy to raise the urine pH to ~6.5 may dissolve uric acid stones; however, over-alkalization can lead to a deposit of calcium phosphate on the surface of the stone. Use potassium citrate (Polycitra K, Urocit K) 60 mEq/d PO.

SURGERY/OTHER PROCEDURES

• Most bladder calculi procedures are performed cystoscopically. If stone is too large or hard or when the patient's urethra is too small (eg, in children), the open or percutaneous suprapubic surgical approach is preferable.

• 3 approaches to the bladder can be used to treat bladder stones:

– Retrograde urethroscopic (Cystolitholapaxy): Cystoscopy is used to visualize the stone, an energy source is used to fragment the stone, and the fragments are irrigated through the cystoscope. Energy sources include:

Mechanical: The lithotrite, a hand-activated device like pliers, crushes the stone in its jaws. The lithoclast, a device that uses a pneumatic piston, breaks the stone through direct contact.

EHL: An electrical shock wave near the stone creates a plasma energy that fragments the stone.

Relative contraindications to EHL: Small-capacity bladder, possible pregnancy, and the presence of cardiac-pacing or defibrillation devices.

Laser: Pulsed-dye and holmium-YAG lasers are used to break bladder stones.

– Open: An open cystotomy is done to remove the stone (or stones) intact. If the stone is due to a grossly enlarged prostate (>100 g), a suprapubic prostatectomy can be done simultaneously.

– Percutaneous: Percutaneous suprapubic access is obtained in a fashion similar to that for percutaneous renal access. A rigid nephroscope, graspers, and ultrasonic lithotripsy with suction are used to rapidly evacuate the stone.

Contraindications to percutaneous lithotripsy include prior lower abdominal surgery, prior pelvic surgery, and small-capacity noncompliant bladders.

• ESWL has little efficacy for bladder calculi.

ADDITIONAL TREATMENT

In patients with multiple small calculi or a history of urolithiasis, consider metabolic stone evaluation

ONGOING CARE

PROGNOSIS

Excellent when the entire bladder stone is removed and the bladder outlet obstruction treated.

COMPLICATIONS

• The presence of longstanding untreated bladder calculi is associated with dysplasia and squamous cell carcinoma of the bladder.

• Stones may cause recurrent infection.

• Transurethral litholapaxy is the most common modality used to treat bladder calculi and has been associated with relatively few and minor complications such as UTI (11%), fever (9%), bladder perforation (2%), hyponatremia (2%), and hemorrhage (1%). Gross hematuria is common and usually self-limiting.

• Hyponatremia can be a consequence of cystolitholapaxy in combination with TURP.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Urinalysis

• Periodic assessment of uroflow and post void residual urine

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Bladder Filling Defect

• Urolithiasis, Adult

• Urolithiasis, Pediatric

CODES

ICD9

– 594.0 Calculus in diverticulum of bladder

– 594.1 Other calculus in bladder

ABBREVIATIONS

• BPH: Benign prostatic hypertrophy

• CT: Computed tomography

• EHL: Electrohydraulic lithotripsy

- ESWL: Extracorporeal shock wave lithotripsy
- TUIP: Transurethral incision of the prostate
- TURP: Transurethral resection of the prostate
- US: Ultrasound
- UTI: Urinary tract infection

BLADDER CANCER, ADENOCARCINOMA

Edmund Chiong, MBBS

H. Barton Grossman, MD

BASICS

DESCRIPTION

- An uncommon and often aggressive nonurothelial malignancy of the bladder
- It carries a poor prognosis, as it is frequently advanced at initial presentation (muscle invasive or metastatic).

EPIDEMIOLOGY

- 0.5–2.0% of all primary bladder cancers.
- Can arise from the urachus or the nonurachal epithelium; is also the most common tumor arising in exstrophy of the bladder.
- A majority of nonurachal-, nonexstrophy-associated adenocarcinomas occur in men, frequently with an associated history of long-term inflammation or infection (it occurs more frequently in areas where schistosomia is endemic).
- Urachal cancers: <1% of primary bladder cancers; ~1/3 of vesical adenocarcinomas.
- Prevalence is unknown

RISK FACTORS

- Chronic irritation, inflammation, or infection
- Bladder exstrophy
- Schistosomiasis

GENERAL PREVENTION

Avoidance of chronic bladder inflammation

PATHOPHYSIOLOGY

- Classification: 3 groups are related to the site of tumor origin:
  - Primary vesical adenocarcinoma
  - Urachal adenocarcinoma
  - Extravesical adenocarcinoma (metastasis)
- Primary vesical adenocarcinoma:
  - Most are poorly differentiated and invasive at the time of diagnosis
  - Most common type of cancer in bladder exstrophy
  - Poor response to radiotherapy and cytotoxic chemotherapy
- Urachal carcinoma (rare):
  - Tumor arises from urachal remnant; sited at the bladder dome. Adenocarcinomas at bladder dome are usually considered urachal in origin until proven otherwise.

):

Presence of an urachal remnant

Intact or ulcerated urothelium without metaplastic changes

Predominant invasion of the muscularis propria or deeper structures of the bladder or extension to the space of Retzius, anterior abdominal wall, or umbilicus.

– Urachal cancers are usually adenocarcinomas.

– It may produce mucoid drainage from the umbilicus.

– Tumors tend to have more extensive bladder wall infiltration than expected and are relatively chemotherapy- and radiation-resistant.

- Metastatic lesions (rare, only 0.26% of cases):

– Adenocarcinomas from the rectum/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.

COMMONLY ASSOCIATED CONDITIONS

- Bladder exstrophy
- Schistosomiasis

DIAGNOSIS

HISTORY

- Hematuria (gross or microscopic):
  - Usually painless
  - Cancer is found in up to 10% of patients with microscopic hematuria.
  - Amount of blood does not predict the probability of cancer.
- Irritative voiding symptoms (frequency, urgency, dysuria):
  - Seen in ~1/3 of patients with bladder cancer and more commonly in patients with carcinoma in situ and invasive cancer
- Mucinuria: Uncommon
- Foreign travel: 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

- Bimanual/rectal exam: Pelvic mass

- Bloody or mucoid umbilical discharge or umbilical mass
- Lower extremity edema: Suggests retroperitoneal lymphadenopathy
- Digital rectal exam: Presence of blood in stools or rectal tumor/infiltration.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine studies: Urinalysis, urine culture and sensitivity, urine cytology
- Serum electrolytes: BUN/creatinine, liver function tests

Imaging

- ExU can provide anatomic detail of the upper urinary tract and show filling defects in the bladder; however, it is not helpful in staging.
- Urachal cancers may show stippled calcifications on plain radiograph films.
- CT: Imaging method of choice for staging of bladder tumors and for detecting presence of pelvic lymphadenopathy and extravesical tumor extension:
  - Sensitivity: 64–94%; specificity: 62–100%; accuracy: 80%.
- Other investigations: CXR (staging), bone scan (staging, if bone pain present), GI endoscopy, and breast exam (exclude primary tumor) if clinically indicated

Diagnostic Procedures/Surgery

Diagnostic cystoscopy and biopsy for definitive diagnosis

Pathological Findings

- All histologic variants of enteric carcinoma may occur in the bladder.
- Adenocarcinoma can have glandular, colloid or signet-ring patterns. Most produce mucin.
- Primary adenocarcinoma of the bladder is associated with cystitis glandularis and is thought to arise from glandular metaplasia of the urothelium. They can be papillary or solid.
- Signet ring tumors (rare) produce linitis plastica of the bladder. They are aggressive, and radical surgical excision should be considered.
- Most are poorly differentiated, present at advanced stage, and are invasive.

DIFFERENTIAL DIAGNOSIS

Other nonurothelial or urothelial tumors

TREATMENT

)[C]

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MEDICATION

)[C]

- Some respond to standard regimens such as combination methotrexate, vinblastine, Adriamycin, cisplatinum (MVAC)

)[C]

SURGERY/OTHER PROCEDURES

- Site of origin, tumor extent, and tumor behavior are factors important in determining treatment.
- TURBT alone is usually inadequate, as most tumors are invasive.
- Partial cystectomy (with bladder mucosal sampling) with en bloc removal of urachal ligament and umbilicus is an option for low-volume, low-stage urachal carcinoma.

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ADDITIONAL TREATMENT

Poor efficacy

ONGOING CARE

PROGNOSIS

- As many as 1/2 of patients with signet cell variant will succumb to their disease within 1 yr.

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COMPLICATIONS

- Ureteral obstruction from local spread of tumor
- Metastasis to pelvic lymph nodes, liver, lung, mediastinum, and bone
- Surgical complications: Bleeding, infection, rectal injury, urinary leakage, etc.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Abdominal imaging (CT)
- Metastasis workup if suspected

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, General
- Bladder Mass, Differential Diagnosis
- Urachal Carcinoma

CODES

ICD9

- 188.0 Malignant neoplasm of trigone of urinary bladder
- 188.1 Malignant neoplasm of dome of urinary bladder
- 188.2 Malignant neoplasm of lateral wall of urinary bladder

ABBREVIATIONS

- CT: Computed tomography
- CXR: Chest x-ray
- ExU: Excretory urography
- TURBT: Transurethral resection of bladder tumor

BLADDER CANCER, GENERAL

Robert L. Grubb, III, MD

BASICS

DESCRIPTION

- Bladder cancer includes multiple histologic types of malignant tumors that can arise in the urinary bladder. Broadly categorized as muscle-invasive or non–muscle invasive (superficial):
  - Urothelial (transitional) cell carcinoma is the most common type.
  - Others: Adenocarcinoma, squamous cell carcinoma, and small-cell carcinoma
- TNM staging:
  - Staging can be clinical (bladder biopsy and staging
  - T staging: Primary tumor:

    Ta: Papillary, epithelium confined

    Tis: CIS; noninvasive flat carcinoma

    T1: Lamina propria invasion

    T2a: Tumor has grown into the inner half of the muscle layer

    T2b: Tumor has grown into the outer half of the muscle layer

    T3a: Microscopic perivesical fat extension

    T3b: Macroscopic perivesical fat extension

    T4a: Tumor invades pelvic viscera (prostatic stroma, rectum, uterus, and/or vagina)

    T4b: Tumor extends to the pelvic sidewall, abdominal wall or bony pelvis
  - Regional lymph node (N) staging: Regional lymph nodes (the true pelvis); all others are considered distant lymph nodes:

    NX: Nodes cannot be assessed

    N0: No regional lymph node spread

    N1: Spread in a single lymph node, 2 cm

    N2: Spread in a single lymph node, >2 cm, <5 cm, or multiple lymph nodes <5 cm

    N3: Spread in a lymph node >5 cm
  - Distant metastasis (M) staging:

    MX: Distant metastasis cannot be determined

    M0: No distant metastasis

    M1: Distant metastasis
- Stage grouping:
  - Stage 0is, Tis, N0, M0

- Stage I: Ta-T1, N0, M0
- Stage II: T2, N0, M0
- Stage III: T3a-T4a, N0, M0
- Stage IV: T4b, N0, M0 or any T, N 1,2,3, M0, or any T, any N, M1

EPIDEMIOLOGY

- Estimated 68,810 new cases/yr, 2008:
  - 4th most common cancer among males
  - Estimated 14,100 deaths/yr, 2008
- Male > Female (3:1)
- Incidence increases with age:
  - Median age of diagnosis is 70 yr
- Because of the high rate of recurrence of non–muscle invasive bladder cancer, it is the 2nd most prevalent cancer in men.

RISK FACTORS

- Tobacco smoking confers a 2–4 times risk vs. never smoked:
  - Risk reduction after quitting takes up to 20 yr
- Occupational exposures:
  - Painters, leather workers, metal workers, dry cleaners, truck drivers, hairdressers, petroleum workers, chemical workers
  - Aromatic amines such as aniline dyes, benzidine and others and combustion gases, and soot from coal
- Chronic inflammation:
  - Risk for squamous cell carcinoma:
    Indwelling catheters, calculi
    Schistosomiasis (Schistosoma hematobium)
- Cyclophosphamide treatment:
  - Caused by toxic metabolite, acrolein

Genetics

- No clear hereditary causes identified
- Tumor suppressor P53 is the most commonly altered gene in bladder cancer (associated with DNA repair and cell-cycle progression)
- Other common genetic abnormalities include altered expression of EGF receptor (ErbB2)

GENERAL PREVENTION

- Several studies have suggested that screening for bladder cancer by home chemical reagent strip testing for hematuria is effective.

- Dietary:
  - Vitamins:

Multiple animal and epidemiologic studies of vitamin A and B compounds do not show conclusive benefit for primary prevention.

Patients receiving Oncovite (high-dose vitamin A, B6, C, E, and zinc) after TUR and induction cycle of BCG had a significant reduction in recurrence rate vs. those receiving recommended daily dose of vitamins (secondary prevention).

  - High-fat diet has been associated with increased risk of bladder cancer.
  - Genistein (soy isoflavone) is being studied in as a possible chemopreventive agent.
- Role of NSAIDs and Cox-2 inhibitors unclear

PATHOPHYSIOLOGY

- Natural history
- 70% of tumors present as non–muscle invasive tumors:
  - 70% 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:
  - Ta low-grade: 5–10%
  - Ta high-grade: 15–40%
  - T1 high-grade: 30–50%
  - CIS >50%

COMMONLY ASSOCIATED CONDITIONS

Other smoking-related illnesses:

- COPD

DIAGNOSIS

HISTORY

- Hematuria (present in 85%): When did you 1st experience blood in the urine? Could you see it (gross)? Was it apparent only on lab tests (microscopic)? Was there associated pain?
  - Gross, painless hematuria is the most common presentation.

- Irritative voiding symptoms (present in 20%): Dysuria, frequency, urgency:
  - Occasionally associated with tumors, especially CIS
- Smoking history (quantify in pack years and if and when patient quit)
- Occupational exposures:
  - Naphthylamine, benzidine, aniline dyes, and 4-aminobiphenyl (rubber, dye, printing, or petroleum industries)

PHYSICAL EXAM

- Rarely abnormal for non–muscle invasive cancer
- General:
  - Weight loss, abdominal/pelvic masses, lymphadenopathy, flank tenderness
- DRE (men)
- Bimanual pelvic exam (women) may reveal palpable mass in bladder

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis including microscopy looking for RBCs
- Urine cytology:
  - High specificity, more sensitive for high-grade tumors or CIS:
    Sensitivity 50%, specificity 96%
- Other urinary markers:
  - FISH:
    Sensitivity 77%, specificity 98%
  - NMP-22:
    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:
  - Can detect lymphadenopathy and other intra-abdominal disease
  - Bladder way thickening suggests tumor.
  - CT urography has replaced IVP as standard for evaluating upper tracts at many centers.
- MRI may be useful for local staging
- IVP:

– To exclude concurrent upper-tract UCC in patients with bladder cancer (2%)

Diagnostic Procedures/Surgery

- Cystoscopy is most accurate diagnostic procedure:
  – Can be done in office with local anesthesia
- Bladder biopsy:
  – Establishes pathologic diagnosis
  – May be definitive treatment if tumor can be completely removed
- Retrograde pyelography:
  – May be used to evaluate upper tracts in setting of renal impairment or contrast allergy
  – Can be used to further evaluate equivocal findings on CT or IVP

Pathological Findings

- PUNLMP
- Stage better predictor of survival than grade
- Histologic types:
  – Transitional cell carcinoma (urothelial carcinoma), 90%
  – Squamous cell carcinoma, 3–7%
  – Adenocarcinoma, <2%
  – Small cell, sarcomas (leiomyosarcoma, rhabdomyosarcoma) uncommon

DIFFERENTIAL DIAGNOSIS

- Other causes of hematuria:
  – UTI (especially in women) is a common cause of delay in evaluation
  – Radiation cystitis
- Rare: Metastatic lesions to the bladder

TREATMENT

MEDICATION

- Intravesical therapy for higher risk non–muscle invasive disease
- Adjuvant therapy to surgery with goal of reducing recurrence
- BCG:
  – Should be given only after bladder is healed (usually 4 wk); 40% reduction in recurrence

)[A]

- Mitomycin C:
  – Alternative when BCG cannot be used. Also, reduces tumor recurrence given as a single dose within 24 hr of TURBT (40 mg in 40 mL of saline or sterile water); contraindicated with bladder perforation

- Platinum-based drug regimens:
  - Metastatic disease (Stage IV)

)[A]

  - MVAC (mitomycin, vinblastine, Adriamycin, cisplatin):
    Common side effects: Mucositis, renal toxicity, myelosuppression, sepsis
    Overall response rate 40–50%
  - Gemcitabine and cisplatin:
    Common toxicity; myelosuppression
    Overall response rate 40–50%, similar to MVAC

SURGERY/OTHER PROCEDURES

- Primary treatment for bladder cancer is surgical.
- Transurethral resection of bladder tumor:
  - Bladder biopsy
  - Can be both diagnostic and therapeutic (for non–muscle invasive tumors)
- Radical cystectomy:
  - Initial therapy for invasive tumors
  - Occasionally needed for recurrent T1 high-grade tumors or CIS that has failed to respond to intravesical therapy

ADDITIONAL TREATMENT

Bladder preservation approaches (trimodality therapy):

- TURBT: Tumor must be completely resected
- Chemotherapy: Platinum-based regimens
- Radiation therapy
- Optimal patients have solitary T2 tumors, no hydronephrosis, no associated CIS
- Usually biopsy mid cycle with cystectomy if no response

)[B]

ONGOING CARE

PROGNOSIS

5-yr survival by stage:

- I: 85–96%
- II: 55–65%
- III: 38–59%
- IV: 15–27%

COMPLICATIONS

- Urinary retention from gross hematuria or tumor infiltrating or blocking bladder outlet

- Ureteral obstruction (renal insufficiency)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Non–muscle invasive disease:
  - Cystoscopy every 3 mo for 2 yr, then every 6 mo for 2 yr, then annually
  - Upper tract surveillance every 1–2 yr
- Muscle-invasive disease:
  - Liver function test, creatinine, electrolytes, CXR every 6–12 mo
  - Collecting system imaging at baseline and every 2 yr
  - Imaging of abdomen, pelvis and upper tracts at every 3–6 mo for 2 yr, then as clinically indicated.
  - Cytology every 6–12 mo ± urethral wash cytology (cutaneous diversion)

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, Sarcoma
- Bladder Cancer, Small Cell (Oat Cell, Signet Ring)
- Bladder Cancer, Squamous Cell Carcinoma
- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Urothelial, Metastatic (N+, M+)
- Bladder Cancer, Urothelial, Superficial (CIS,Ta,T1)
- Bladder Tumor Algorithm
- Bladder Tumors, Benign and Malignant, General

CODES

ICD9

- 188.0 Malignant neoplasm of trigone of urinary bladder
- 188.1 Malignant neoplasm of dome of urinary bladder
- 188.2 Malignant neoplasm of lateral wall of urinary bladder

ABBREVIATIONS

- BCG: Bacillus Calmette-Guérin
- CIS: Carcinoma-in-situ
- COPD: Chronic obstructive pulmonary disease
- CT: Computed tomography
- CXR: Chest x-ray

- IVP: Intravascular pressure
- MVAC: Methotrexate, vinblastine, Adriamycin, cisplatin
- PUNLMP: Papillary urothelial neoplasm of low malignant potential
- TUR: Transurethral recession
- TURBT: Transurethral resection of bladder tumor
- UTI: Urinary tract infection

BLADDER CANCER, SQUAMOUS CELL CARCINOMA

Nicholas T. Karanikolas, MD

BASICS

DESCRIPTION

- SCC of the bladder is a nonurothelial variant of bladder cancer; the cells are of epithelial origin.
- SCC occurs in bladders infected with and free of bilharziasis. The incidence, epidemiology, and natural history of the 2 subpopulations are different.
- Nonbilharzial SCC is the 2nd most common form of bladder cancer in North America and Europe.
- Bilharzial SCC is the most common form of bladder cancer in East Africa and the Middle East and is related to infection with Schistosoma hematobium.

EPIDEMIOLOGY

- Nonbilharzial SCC:
  - 2–5% of all neoplastic bladder tumors in North America and Europe
  - Increased injury in spinal cord injured patients (2.5–10% develop SCC)
  - Patients usually are diagnosed in the 7th decade of life
  - Black Americans are twice as likely to develop SCC as white Americans. Annual incidence in blacks of 1.2/100,000 person years as compared to 0.6/100,000 person years in whites.
  - Male = Female
- Bilharzial SCC:
  - In endemic regions with S. hematobium infection (East Africa and Middle East): ~75–80% of bladder cancers are SCC.
  - Patients usually present at 40–50 yr.
  - Male > Female (5:1)

RISK FACTORS

- Urothelial irritants: Chronic cystitis, bladder stones, chronic indwelling catheters.
- Cyclophosphamide especially with associated hemorrhagic cystitis
- Intravesical BCG
- Smoking
- Pelvic XRT
- HPV infection
- Squamous metaplasia
- S. hematobium infection; the eggs cause a foreign-body reaction in the bladder wall.

– Bilharzial granulomas form that coalesce forming nodules.

– Foreign-body reaction results in squamous metaplasia and eventual fibrosis/necrosis and calcifications.

Genetics

- Mutations in chromosomes 3,8,10,13, and 17
- Variations in uroplakin II expression
- Mutations of tumor suppressor gene CDKN2
- Psoriasin
- SCC antigen
- Tumor suppressor genes p53 and bcl-2

GENERAL PREVENTION

- Nonbilharzial SCC:
  – Early screening of patients at risk; SCI patients with cytology and surveillance cystoscopy.
  – Some advocate yearly bladder biopsies in those with indwelling catheters for >10 yr.
- Bilharzial SCC:
  – Primary prevention by controlling the snail population and treating patients in endemic areas with oral anti-bilharzial medicine such as praziquantel.
  – Secondary prevention with urine cytology and selective screening.

PATHOPHYSIOLOGY

- Tissue metaplasia develops in response to chronic infection and inflammation, which can lead to the development of either squamous epithelium and leukoplakia or mucinous and glandular epithelium:
  – The factors that lead to neoplastic transformation are not known.
- Histologic characteristics of pure SCC: Squamous pearls, intercellular bridges, and keratotic cellular debris.

COMMONLY ASSOCIATED CONDITIONS

- Neurogenic bladder with chronic catheterization
- Bladder calculi
- Bladder diverticulum
- Conditions treated with cyclophosphamide (Hodgkin lymphoma, myeloma, breast and lung cancer, bone marrow transplants, rheumatologic diseases)

DIAGNOSIS

HISTORY

- SCI, duration of catheterization
- Hematuria: 60–70%
- Irritative voiding complaints: 35–50%
- Chronic UTI
- Upper tract obstruction: 10–20%
- Back/pelvic pain
- Acute retention
- Weight loss
- Country of origin in patients with suspected schistosomal infection

PHYSICAL EXAM

- Abdominal and pelvic exam with rectal exam for clinical staging
- Inguinal exam to assess for palpable lymphadenopathy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis
- Metabolic panel
- Alkaline phosphatase
- CBC

Imaging

- CT to detect extent of disease; lymph node involvement, metastatic spread, hydronephrosis, and assess extravesical spread
- Bone scan to assess for metastatic spread when associated with bone pain or elevated alkaline phosphatase
- CXR to rule out metastatic spread to the lungs

Diagnostic Procedures/Surgery

- Cystoscopy with diagnostic biopsy
- Urine cytology

Pathological Findings

- Pure SCC must be distinguished from urothelial carcinoma with squamous differentiation.
- Superficial tumors are rarely seen; most present with advanced disease.
- Tumors appear sessile with ulcerations and often with area of adjacent squamous metaplasia.
- Tumors extend into the ureters and urethra and involve bladder diverticula.

DIFFERENTIAL DIAGNOSIS

- Urothelial carcinoma with squamous differentiation
- Inflammatory conditions: Chronic cystitis, squamous metaplasia, leukoplakia, hemorrhagic cystitis
- Cervical cancer

TREATMENT

- Understaging is common in up to 35% of patients.
- Tumor grade and stage influence survival.
- Low rate of metastatic disease (8–10%). Most patients die from local regional disease progression.

MEDICATION

- Primary management is surgical. No reliable chemotherapy regimen has been identified.
- MVAC and standard urothelial carcinoma regimens are ineffective.

SURGERY/OTHER PROCEDURES

- Nonbilharzial SCC:
  - Radical cystectomy remains the mainstay of treatment:
    5-yr survival rates of 34–48% have been reported
- Bilharzial SCC:
  - Radical cystectomy provides an overall survival rate of 50.3%.
  - Tumor stage, grade, and lymph node involvement influence survival.

ADDITIONAL TREATMENT

Radiotherapy

- Nonbilharzial SCC:
  - Poor survival data results for patients treated with radiation alone
  - No improvement in survival characteristics when radiation is used in the adjuvant or neoadjuvant setting
  - No level I evidence to support use of radiation therapy in the setting of SCC
- Bilharzial SCC:
  - Poor survival data results from patients treated radiation alone
  - No improvement in survival characteristics when radiation therapy is utilized in the adjuvant or neoadjuvant setting
  - No level I evidence to support the use of radiation therapy in the setting of SCC

Additional Therapies

- Chemotherapy is generally not recommended since responsiveness to MVAC chemotherapy.

- Neoadjuvant chemotherapy has been tried without any objective response.

ONGOING CARE

PROGNOSIS

Generally poor prognosis with average survival of 1–3 yr from time of diagnosis

COMPLICATIONS

Perioperative mortality rates as high as 13.7% have been reported.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- CT, lab testing to include LFTs
- Physical exam

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, Sarcoma
- Bladder Cancer, Small Cell (Oat Cell, Signet Ring)
- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Urothelial, Metastatic (N+, M+)
- Bladder Cancer, Urothelial, Superficial (CIS,Ta,T1)
- Bladder Tumor Algorithm
- Bladder Tumors, Benign and Malignant, General
- Schistosomiasis, Urologic Considerations

CODES

ICD9

- 188.0 Malignant neoplasm of trigone of urinary bladder
- 188.1 Malignant neoplasm of dome of urinary bladder
- 188.2 Malignant neoplasm of lateral wall of urinary bladder

ABBREVIATIONS

- BCG: Bacille Calmette-Guérin
- CT: Computed tomography
- CXR: Chest x-ray

- HPV: Human papilloma virus
- LFT: Liver function test
- MVAC: Methotrexate, vinblastine, Adriamycin, cisplatin
- SCI: Spinal cord injury
- SCC: Squamous cell carcinoma
- UTI: Urinary tract infection
- XRT: External bean radiation therapy

BLADDER CANCER, UROTHELIAL SUPERFICIAL (CIS, TA, T1)

Edmund Chiong, MBBS
H. Barton Grossman, MD

BASICS

DESCRIPTION

- Malignant neoplasm originating from the surface lining (uroepithelium) of the bladder.
- The most common histologic form is TCC or (preferred term) urothelial carcinoma.
- 60–75% of bladder cancers are “superficial” (cancer is confined to the mucosa and/or submucosa).

EPIDEMIOLOGY

- In the US, estimated 68,810 new cases diagnosed in 2008; 14,100 cancer-related deaths annually.
- 4th most common cancer in men
- Male > Female (~3:1)
- Highest incidence: Men >60 and women >70
- Ethnic predominance: White > Black > Latino
- Due to high recurrence rates, 2nd most prevalent cancer in middle-aged and elderly men (after prostate cancer)

RISK FACTORS

- Tobacco smoking, especially cigarettes:
  - Up to 4 times higher incidence of bladder cancer.
  - Dose relationship exists between number of pack-years and bladder cancer risk.
  - Latency often >20 yr from time of exposure
  - Quitting smoking decreases risk (over 20 yr) but never returns to level of nonsmoker
- Occupational exposure:
  - Organic chemicals, especially aromatic (aryl)-amines such as naphthalenes, benzidine, aniline dyes, and 4-aminobiphenyl
  - High-risk occupations: Petroleum chemical/rubber/textile workers, hairdressers, workers, truck drivers, aluminum electroplaters
- Medications:
  - Phenacetin-containing analgesics
  - Cyclophosphamide (Cytoxan)

- Pelvic irradiation: Up to 4 times increased risk in women treated for cervical cancer.
- Chronic cystitis:
  – Indwelling catheters or calculi for many years and cystitis due to Schistosoma haematobium may predispose to squamous cell carcinoma of the bladder.

Genetics

- Chromosome 9 deletions most common
- Mutation of FGFR3 is associated with good prognosis.
- No familial clustering described.
- Rare hereditary form: Muir-Torre syndrome (a familial multicancer syndrome characterized by sebaceous tumors and visceral malignancy)

GENERAL PREVENTION

- Increased fluid intake
- Smoking cessation reduces bladder cancer risk, and may decrease recurrence rate of superficial (non–muscle invasive) TCC.

PATHOPHYSIOLOGY

- Natural history: Superficial TCC comprises ~70% of bladder tumors.
  – 5-yr recurrence rate: ~60%:
    Most recurrences occur within 1st 6 mo after resection.
    Recurrences can occur after many years.
    Recurrent TCC can appear in the upper tracts or the prostatic urethra.
    High frequency of recurrence with both low- and high-grade disease.
    High frequency of recurrence with carcinoma in situ (Tis, CIS), mucosal disease (Ta), and invasion of the lamina propria (T1).
  – Progression influenced by stage and grade:
    Stage Ta, Gr 1: 2–5%; Gr 2: 10–15%
    Stage T1, Gr 2: 20–30%; Gr 3: 30–50%
    CIS: 50–80% (worse when associated with visible tumor [secondary CIS])
  – Fatality rate from superficial TCC: Estimated 20% at 20 yr from onset
- Other risk factors for progression:
  – Architecture: Nodular/sessile/broad based > papillary
  – Multifocality > solitary; size >5 cm
  – Lymphatic and/or vascular invasion; high blood vessel density (angiogenesis)
- Molecular tumor markers associated with higher risk of progression:
  – p53-positive staining/retinoblastoma (RB)-negative staining/epidermal growth factor receptor positivity/E-cadherin loss

– Insufficient evidence to use tumor markers for clinical decision making.

COMMONLY ASSOCIATED CONDITIONS

See “Risk Factors.”

DIAGNOSIS

HISTORY

- Age and sex: Most common in men >50; Males > Females
- 1st occurrence: 85% present with either gross or microscopic hematuria. Painless gross hematuria is the hallmark of bladder cancer, even if intermittent.
- Irritative bladder symptoms (eg, dysuria, urgency, frequency): Occasionally associated with bladder cancer (20%), especially CIS, and usually accompanied by at least microscopic hematuria.
- Smoking history:
  - Record age of onset, total years, packs per day, and years since quitting.
  - Cigarette smoking is the leading cause of bladder cancer, with risks proportional to duration and amount. A long latency (>20 yr) is common.
- Occupational risk factors: Naphthylamine, benzenes, aniline dyes, and 4-aminobiphenyl (rubber, dye, petroleum industries)

PHYSICAL EXAM

Usually unremarkable for superficial bladder cancer.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis, including standard dipstick and microscopic evaluation for RBCs
- Urine cytology: High specificity but low overall sensitivity. Positive readings are usually reliable, but negative or atypical results do not exclude TCC. Best at detecting high-grade TCC and CIS.
- Other urinary tests (eg, BTA-Stat, NMP22, and UroVysion) have higher sensitivity but lower specificity than cytology; alternate to cytology.

Imaging

- ExU/IVP: Excludes concomitant upper-tract TCC in patients with bladder cancer (~2% incidence)
- Abdominal/pelvic US: Detects hydronephrosis and occasionally bladder tumors. Especially useful in low-risk patients (eg, younger women) with unexplained hematuria when combined with cystoscopy.
- CT abdomen and pelvis with contrast: Study of choice for initial evaluation of gross painless hematuria in high-risk patients or prior to tumor resection in high-volume, aggressive-appearing bladder tumors suspected of being invasive. CT urogram is now increasingly

used to replace ExU for evaluation of hematuria.

Diagnostic Procedures/Surgery

- Cystoscopy: Standard of care for evaluating bladder lesions:
  - In office, under local anesthesia, at time of initial presentation. It may be combined with biopsy.
  - TURBT under general or spinal anesthesia room is definitive (bladder tumor strongly suspected, positive radiologic image and positive cytology).
- Retrograde pyelography is used for equivocal ExU or CT or in cases of contrast allergy to exclude concomitant upper-tract lesions.

Pathological Findings

- Urothelial dysplasia: Epithelial and nuclear changes < CIS. Significance is uncertain.
- CIS: Severe dysplasia that may appear as erythema or be invisible endoscopically. Considered to be high-grade TCC confined to the urothelium and a precursor to invasive cancer. Urine cytology is positive in 80–90% of CIS. When diagnosed, superficial TCC is associated with higher risk of tumor recurrence and progression.
- TCC: Comprises >90% of bladder cancers. Superficial TCC are usually papillary lesions, confined to either mucosal (stage Ta) or invasion of lamina propria (stage T1):
  - New WHO/ISUP grading system: Papillary urothelial tumor of low malignant potential, low-grade urothelial carcinoma, high-grade urothelial carcinoma.
  - High-grade T1 tumors have greater propensity (30%) to recur; may progress to invasive TCC.

DIFFERENTIAL DIAGNOSIS

Nonurothelial cancers (squamous cell carcinoma, adenocarcinoma, etc.)

TREATMENT

Resection with selective use of intravesical therapy is the mainstay.

MEDICATION

- Intravesical therapy: Adjuvant to surgery to reduce tumor recurrence, or as a definitive treatment to eliminate small-volume residual disease and/or inaccessible disease such as CIS. Usually administered as an induction course of 6 weekly sequential treatments via Foley catheter and retained for 2 hr.
  - Intravesical chemotherapy:

Drugs: (US, elsewhere) thiotepa, doxorubicin (Adriamycin), mitomycin, valrubicin; (outside US) epirubicin, ethoglucid

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)[A]

– Intravesical immunotherapy:

Drugs: BCG: Live suspension of the attenuated Mycobacterium bovis vaccine strain.

)[A]

BCG is single most effective intravesical agent, with complete response rates of ~55–75% for residual disease and CIS, respectively. It is 3 times more effective than chemotherapy for prophylaxis. 2/3 of responses persist for 5 yr.

BCG has a low (<5%) but serious risk of systemic BCG infection (BCGosis), especially if administered in a setting of recent surgery or traumatic catheterization.

)[B]

SURGERY/OTHER PROCEDURES

- TURBT: 1st-line treatment for all visible tumors; both diagnostic and therapeutic.
- Bladder biopsies (random): Helpful in cases of positive cytology with no obvious lesion. In men, biopsy of the prostatic urethra should be performed.
- Laser or electrofulguration: Useful for recurrent, small-volume, low-grade papillary tumors; can be performed under local anesthesia.
- Radical cystectomy: Indicated for refractory superficial cancer (eg, T1, high-grade disease or multifocal CIS that has failed to respond to 1 or 2 courses of BCG therapy). Rarely, it may be necessary for extensive unresectable superficial disease.

ADDITIONAL TREATMENT

Radiotherapy

No role in superficial disease

Additional Therapies

Repeat TURBT recommended for T1 tumors.

)[B]

ONGOING CARE

PROGNOSIS

See “Pathophysiology.”

COMPLICATIONS

- TURBT: Bleeding, irritative symptoms, bladder perforations (mainly extraperitoneal); usually can be managed conservatively with catheter drainage and anticholinergics.
- BCG therapy: Bladder irritative symptoms most common (90%). BCGosis (<5%) and BCG sepsis (0.4%) can be treated with triple-drug antituberculin therapy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Cystoscopic and cytologic monitoring every 3 mo for 2 yr, every 6 mo for 2 yr, then annually. Schedule resets with each recurrence. Low-risk tumors can be monitored less intensively.
- TURBT as necessary, depending on cytology results and cystoscopic appearance.
- Upper-tract surveillance studies (eg, ExU or CT urogram) are suggested every 2–3 yr for high-grade bladder tumors and CIS.

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ADDITIONAL READING

- AUA Guideline for the Management of Nonmuscle Invasive Bladder Cancer: (stages Ta, T1, and Tis). Accessed 11/2008 at http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=bc.
- National Comprehensive Cancer Network. Accessed 11/2008 at http://www.nccn.org/professionals/physician_gls/PDF/bladder.pdf.

See Also (Topic, Algorithm, Electronic Media Element)

- BCG Sepsis/BCGosis
- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Urothelial, Metastatic (N+, M+)
- Bladder Tumor Algorithm
- Bladder Tumors, Benign and Malignant, General

CODES

ICD9

- 188.9 Malignant neoplasm of bladder, part unspecified
- 233.7 Carcinoma in situ of bladder

ABBREVIATIONS

- BCG: Bacillus Calmette-Guérin
- CIS: Carcinoma in situ
- CT: Computed tomography
- ExU: Excretory urography
- IFN-: Interferon-
- IVP: Intravenous pyelogram
- TCC: Transitional cell carcinoma
- TURBT: Transurethral resection of bladder tumor

BLADDER CANCER, UROTHELIAL, INVASIVE (T2/3/4)

Gary W. Bong, MD
Timothy R. Yoost, MD

BASICS

DESCRIPTION

- Urothelial carcinoma accounts for >90% of BC; other etiologies include SCC (5%), adenocarcinoma (2%), and urachal carcinoma (<1%)
- Invasive urothelial cancer refers to invasion into or through the muscularis propria of the bladder wall

EPIDEMIOLOGY

- Incidence: 67,000/yr (2007); incidence increasing, but mortality decreasing
- Male > Female (3:1)
- Median age at diagnosis: 69 (men) and 71 (women)
- ~550,000 in US

RISK FACTORS

- Cigarette smoking accounts for >50% of cases
- Occupational exposure (dye, textile, rubber and leather factory workers)

Genetics

- Hereditary patterns: Autosomal dominant and multifactorial polygenic
- Cytogenetic abnormalities: Loss of heterozygosity in chromosome 9 (>50% all grades and stages BC); loss of chromosomes 17q, 5q, 3p (invasive BC); inactivating mutation in p53, p21, or Rb (invasive BC); TP53 and/or P16 abnormalities (high grade BC)

GENERAL PREVENTION

- Avoid exposure to cigarette smoke and reduce industrial risk factors.
- Adequate workup for microscopic hematuria

PATHOPHYSIOLOGY

- TCC growth patterns: Papillary (70%), nodular (10%), and sessile or mixed (20%)
- Invasive tumors (T2–T4) are present in 25% at initial presentation.
- Recurrent superficial BC will become invasive in 10–15%
- High-grade T1 lesions, especially if associated with LVI and/or CIS, have high progression rate, requiring aggressive management.
- Grading (WHO and ISUP, 1998):
  - Papillary urothelial neoplasia of low malignant potential (well-differentiated, former grade 1)
  - Low-grade (moderately differentiated, former grade 2)

- High-grade (poorly differentiated, former grade 3)

- Metastases occurs via hematogenous and/or lymphatic spread:
  - Location (most to least common): Lymph nodes (obturator, external iliac, common iliac), liver, lung, bone, adrenal gland
  - Most patients with metastasis die within 2 yr

COMMONLY ASSOCIATED CONDITIONS

Lung disease secondary to smoking

DIAGNOSIS

HISTORY

- History of smoking or other risk factors
- Prior bladder tumors or hematuria
- Family history of bladder cancer
- Signs and symptoms:
  - Painless hematuria (80%)
  - Irritative voiding symptoms (frequency, urgency, dysuria, 35%)
  - Locally invasive/metastatic disease (pelvic pain/fullness, fixed bladder or palpable mass, inguinal lymphadenopathy, flank pain, weight loss, bone pain)

PHYSICAL EXAM

- General: Weight loss, abdominal/pelvic masses; lymphadenopathy
- DRE/bimanual pelvic exam (can be performed under anesthesia before TURBT)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood: CBC, electrolytes, LFT (elevated alkaline phosphatase suggests liver or bone involvement)
- Urine (urinalysis, cytology):
  - Cytology: 95% specific for high grade or CIS
  - Other markers: FISH, survivin, NP22, etc. being studied

Imaging

- CT urogram (precontrast, corticomedullary and delayed phases) current standard of care
- IVU and renal US also acceptable, although does not stage nodes
- MRI or retrograde pyelogram to evaluate upper tracts if elevated creatinine
- CXR

Diagnostic Procedures/Surgery

TURBT establishes diagnosis

Pathological Findings

Tumor invasion into detrusor muscle (T2), perivesical fat (T3), or adjacent structures (T4): prostate, uterus, vagina, pelvic/abdominal wall

DIFFERENTIAL DIAGNOSIS

Gynecologic and other pelvic tumors; adenocarcinomas more likely to be metastatic in origin

TREATMENT

- Preoperative evaluation, as most patients also have significant cardiopulmonary disease
- Discuss treatment options and urinary diversion options.
- If ileal conduit, meet with stoma therapy nurse preop (for marking) and postop for care/teaching.
- For continent diversion, do preop teaching
- If bladder preservation chosen, get radiation oncology and medical oncology consults.
- Discuss high depression rates following RC (up to 45%) to prepare patient for possible treatment.

MEDICATION

- Chemotherapy:
  - Used only in metastatic disease, neoadjuvant therapy for surgery, or as combination with XRT or TURBT for bladder preservation protocols
  - MVAC is the old standard.
  - Gemcitabine plus cisplatin has equivalent efficacy with much less toxicity and is treatment of choice.
  - May use gemcitabine plus carboplatin if renal insufficient.
  - Taxanes also promising as both single and combination agent
- Intravesical therapy not indicated for T2 disease

SURGERY/OTHER PROCEDURES

- Radical cystectomy with pelvic lymphadenectomy considered gold standard therapy for invasive disease
- Radical cystectomy:
  - Indications: High risk T1 and T2 stage diseases with clinically localized disease
  - Wide excision and PLND provide best chances for local control
  - Ureteral frozen sections to ensure negative margins before urinary tract reconstruction is standard practice
  - Patients with T3 disease may be offered neoadjuvant chemotherapy.

– Palliative radical cystectomy in patients with metastases for intractable hematuria or pelvic pain

- Lymphadenectomy:
  - Positive nodes in ~25%
  - Patients with limited nodal burden have higher than expected survival rates
  - Extended PLND (to include presacral, para-aortic and paracaval nodes) may improve survival
  - May identify patients most suited for future adjuvant therapies
- Partial cystectomy:
  - Very select patients: Solitary lesion <2 cm with T2 stage
  - Recurrence usually within 1st 2 yr
- TURBT:
  - Usually palliative in patients who will not tolerate RC (such as elderly with significant comorbidities)
- Urethrectomy:
  - Simultaneous 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.
- Urinary diversion:
  - Options include continent catheterizable pouches, orthotopic neobladder, or ileal conduit; each with advantages and disadvantages:
  - Ileal conduit used most commonly; neobladders typically reserved for younger, motivated patients

ADDITIONAL TREATMENT

Radiotherapy

- Radiation alone appears inferior to RC, but no RCTs
- Used most commonly in combination with chemotherapy for bladder preservation protocols:
  - Best outcomes in patients with complete visual resection on repeat TURBT
  - With hydronephrosis, bladder preservation relative contraindication
- 5-yr overall survival 40% (37–43%)

Additional Therapies

- Chemotherapy: See “Medication”
- Neoadjuvant platinum-based chemotherapy may benefit some patients before radical cystectomy

Bladder preservation protocols: See “Medication,” “Surgery and Radiotherapy” sections

ONGOING CARE

PROGNOSIS

- Prognostic factors:
  - Tumor type, tumor grade and stage
  - Disease-free survival correlates best with pathologic vs. clinical stage
  - Node burden (>8 positive) and node density (>20%) has worse prognosis
- Survival rates:
  - Disease-free survival (5-yr) without positive nodes: 72% (62–84%) for pT2; 40% (19–57%) for pT3; 24% (0–36%) for pT4
  - Disease-free survival with positive nodes: 30% (15–48%)

COMPLICATIONS

- Generally due to local invasion and advancement of disease:
  - Urinary obstruction, hydronephrosis
  - Hematuria, clot retention
  - Malnutrition, infection, etc.
- Surgical (see “Treatment”): Overall 25%; mortality for radical cystectomy 1–2%
  - Bowel obstruction (4–10%), ureteral anastomotic stricture (3%), PE (2%)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up remains controversial and dependent on disease severity. Example:
  - 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 with semiannual CT scan
  - If disease free at 5 yr, surveillance can be lessened per patient and practitioner comfort level
  - Patients with intact urethra should have urethral washing every 6–12 mo

ADDITIONAL READING

- Advanced Bladder Cancer Meta-analysis Collaboration. Neoadjuvant chemotherapy for invasive bladder cancer. Cochrane Database Syst Rev 2004;1:CD005246.
- America Urological Association Clinical Guidelines, Bladder Cancer, 2007. At: www.auanet.org
- Bellmunt J, Albiol SA, Kataja V. Invasive bladder cancer: ESMO Clinical follow-up. Ann Oncol 2008;19(Suppl 2): Ii47–ii48.
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• Huang GJ, Stein JP. Open radical cystectomy with lymphadenectomy remains the treatment of choice for invasive bladder cancer. Curr Opin Urol 2007;17(5):369–375.

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, General
- Bladder Cancer, Urothelial, Metastatic
- Bladder Cancer, Urothelial, Superficial
- Bladder Mass, Differential Diagnosis
- Bladder Tumor Algorithm
- TNM Classification

CODES

ICD9

- 188.0 Malignant neoplasm of trigone of urinary bladder
- 188.1 Malignant neoplasm of dome of urinary bladder
- 188.2 Malignant neoplasm of lateral wall of urinary bladder

ABBREVIATIONS

- BC: Bladder cancer
- CIS: Carcinoma in situ
- CT: Computed tomography
- CXR: Chest x-ray
- DRE: Digital rectal exam
- FISH: Fluorescence in situ hybridization
- WHO: World Health Organization
- ISUP: International Society of Urological Pathology
- IVU: Intravenous urography/urogram
- LVI: Lymphovascular invasion
- PLND: Pelvic lymph node dissection
- RC: Radical cystectomy
- RCT: Randomized controlled trial
- SCC: Squamous cell carcinoma
- TCC: Transitional cell carcinoma
- TURBT: Transurethral resection of bladder tumor
- XRT: External beam radiotherapy

BLADDER CANCER, UROTHELIAL, METASTATIC (N+, M+)

Daniel P. Petrylak, MD

BASICS

DESCRIPTION

- The most common presentation of urothelial bladder cancer is early-stage disease confined to the bladder, but 20–40% of patients present with or develop muscle-invasive disease.
- 5-yr recurrence-free survival for non–organ- confined node-negative tumors is ~58%.
- Both the depth of invasion (stage) and the presence of nodal metastases are predictors for relapse after cystectomy.
- Patients with lymph node involvement had a recurrence-free survival at 5 yr of 35%.
- Although radical cystectomy for muscle-invasive bladder cancer can be curative, 50% of those with invasive tumors subsequently develop distant metastases within 2 yr:
  - Most deaths from bladder cancer result from metastatic disease; however, local recurrences can also cause significant morbidity and mortality

EPIDEMIOLOGY

- Estimated >68,810 new cases of bladder cancer will be diagnosed in 2008
- Carcinoma of the bladder is the 5th most commonly diagnosed noncutaneous solid malignancy, and the 2nd most commonly diagnosed genitourinary malignancy among people in the US.
- >14,000 patients will die of bladder cancer in 2008.

RISK FACTORS

- Smoking
- Chemical exposure to dyes, paint products
- Chronic bladder inflammation

Genetics

Molecular changes identified in patients with advanced bladder cancer include H-ras, erbB-2, EGFR, MDM2, C-MYC, p53, Rb, p21, p27/KIP1, p16, and PTEN.

GENERAL PREVENTION

- Smoking cessation
- Limit chemical exposure

PATHOPHYSIOLOGY

The multifocality of bladder cancer can be attributed to a field defect, which may be related to carcinogen exposure. Recurrences can be due to either an increased risk of malig-

nant transformation due to this defect or to the implantation of an established tumor.

COMMONLY ASSOCIATED CONDITIONS

Some forms of bladder cancer are associated with chronic inflammation.

DIAGNOSIS

HISTORY

The most common presentation of bladder cancer is hematuria.

PHYSICAL EXAM

Findings consistent with metastatic disease include hepatomegaly, abdominal masses, and lymphadenopathy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

CBC, serum creatinine, liver function tests, urine cytology. There are no specific bladder tumor markers.

Imaging

Staging workup includes CT of the abdomen and pelvis, as well as a CXR.

Diagnostic Procedures/Surgery

- For patients with localized disease, a transurethral resection of the bladder can confirm the diagnosis.
- Metastatic lesions can be removed and evaluated pathologically through surgical procedures or CT-guided biopsies.

Pathological Findings

The most common histology is transitional cell carcinoma, accounting for >90% of cases. Other histologies include squamous cell carcinoma, adenocarcinoma, and small cell carcinoma.

DIFFERENTIAL DIAGNOSIS

- For patients with radiographically localized disease, the differential diagnosis includes kidney or bladder stones, trauma, cystitis, prostatitis, and UTIs.
- For patients with metastatic disease presenting >2 yr after initial diagnosis, rebiopsy of the lesion is recommended.

TREATMENT

Local control with TURBT and fulguration of bleeding essential to maintain quality of life

MEDICATION

- The most active agents include cisplatin, taxanes (docetaxel, paclitaxel), and gemcitabine.
- Complete responses are rare with single agents. When chemotherapeutic agents are combined, however, complete responses are observed.

• Randomized trials established MVAC as the standard of care; this multidrug treatment has been found to be superior to single-agent cisplatin, the combination of docetaxel and cisplatin, and to the multidrug regimen CISCA:

– The median survival of patients treated with MVAC for metastatic disease is 14.2–16.1 mo.

• A randomized trial comparing gemcitabine combined with cisplatin to MVAC found similar survivals. Gemcitabine/cisplatin-treated patients had with significantly less neutropenia and fewer hospitalization days due to infection. Thus, the gemcitabine/cisplatin is considered an alternative standard of care to MVAC.

• Neoadjuvant chemotherapy with MVAC should be considered in all patients with muscle-invasive (T2–4a) disease. A randomized trial comparing median survival among patients assigned to cystectomy alone was 46 mo, compared with 77 mo among patients assigned to 3 cycles of MVAC combined with cystectomy.

• Similar findings have been demonstrated using CMV chemotherapy.

• Patients with T3–4a, or N+ disease are at high risk for relapse post cystectomy. Adjuvant MVAC or gemcitabine/cisplatin can be considered, although no trials demonstrate a survival advantage for adjuvant therapy. Clinical trial enrollment should be encouraged.

• For patients who fail either gemcitabine cisplatin or MVAC, there is no standard of care.

• Unfortunately, the median time to progression is ~3 mo, and the median survival range is 6–9 mo. Single-agent therapy is used over combination treatment, since this has fewer toxicities.

• Survival of patients treated with single-agent chemotherapeutic agents include docetaxel (9 mo), paclitaxel (7.2 mo), pemetrexed (9.6 mo), and gemcitabine (8.7 mo).

• Patients who relapse within 2 yr of adjuvant or neoadjuvant therapy should be considered for salvage therapy rather than retreated with primary chemotherapeutic regimen.

SURGERY/OTHER PROCEDURES

• Radical cystectomy is considered standard of care for patients with localized (T2–4) bladder cancer, but is rarely used in metastatic disease.

• Some publications suggest that surgical resection of metastatic lesions that have responded to chemotherapy can result in durable responses.

ADDITIONAL TREATMENT

• Radiation therapy can be used to treat painful bony metastases. It also can palliate pelvic recurrences.

– For patients who are elderly, and who are ineligible for cystectomy, multimodality therapy of radiation therapy combined with chemotherapy can be effective, with 5-yr survivals

approaching 40%.

- Bisphosphonate therapy can be used to treat patients with bone metastases.

ONGOING CARE

PROGNOSIS

- For patients with localized disease, pathologic complete response (Po) after chemotherapy results in a relapse-free survival at 5 yr of 85%.
- For patients who do not have a complete response to therapy, patients treated with MVAC chemotherapy prior to cystectomy have similar survivals to cystectomy alone.
- 6-yr survival in metastatic patients treated with MVAC or gemcitabine and cisplatin is 6–9% and 7%, respectively.

COMPLICATIONS

- Patients who receive chemotherapy should be monitored for fevers. Neutropenia generally occurs 7–14 days after chemotherapy is administered.
- Colony stimulating factors such as G or G MCSF can be used to improve blood counts.
- Complications specifically associated with cisplatin include renal insufficiency, hearing loss, peripheral neuropathy, fatigue.
- Side effects associated with gemcitabine include neutropenia, rash, renal insufficiency.
- Adriamycin can cause cardiac dysfunction.
- Taxane treatment is associated with peripheral neuropathy as well as fluid retention.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- For patients receiving neoadjuvant chemotherapy, CT of abdomen and pelvis should be performed prior to start of chemotherapy, then after 3 cycles of treatment with MVAC. CXR should be performed every 3 mo.
- For patients receiving adjuvant chemotherapy, CT of the abdomen and pelvis and CXR should be performed prior to and at the completion of chemotherapy, and should be repeated every 3 mo for 2 yr. These imaging studies should then be repeated every 6 mo afterwards.
- Metastatic patients should be imaged with a CT of abdomen and pelvis and CXR every 2–3 mo while on treatment, and then every 3 mo for 2 yr after treatment. If a patient remains without evaluable disease at 2 yr, he should then be imaged every 6 mo.
- CBC, creatinine, and liver function tests every 3 mo for 2 yr post chemotherapy

ADDITIONAL READING

- Grossman HB, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med 2003;349:1880.
- National Comprehensive Cancer Center (NCCN) Guidelines for bladder cancer. Accessed 12/2008 at http://www.nccn.org/patients/patient_gls/_english/_bladder/contents.asp.

• Roberts JT. Long term survival results of a randomized trial comparing gemcitabine/cisplatin and methotrexate/vinblastine/doxorubicin/cisplatin in patients with locally advanced and metastatic bladder cancer. J Clin Oncol 2005;23:4602.

• Sternberg CN. Chemotherapy for bladder cancer: Treatment guidelines for neoadjuvant chemotherapy, bladder preservation, adjuvant chemotherapy, and metastatic cancer. Urology 2007:69(1Suppl):62.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, Sarcoma
- Bladder Cancer, Small Cell (Oat Cell, Signet Ring)
- Bladder Cancer, Squamous Cell Carcinoma
- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Urothelial, Superficial (CIS,Ta,T1)
- Bladder Tumors, Benign and Malignant, General
- Lymphonectopathy, Pelvic and Retroperitoneal

CODES

ICD9

- 188.9 Malignant neoplasm of bladder, part unspecified
- 198.1 Secondary malignant neoplasm of other urinary organs

ABBREVIATIONS

- CBC: Complete blood count
- CISCA: Cisplatin, Cytoxan, Adriamycin
- CMV: Cisplatin, methotrexate, vinblastine
- CT: Computed tomography
- CXR: Chest x-ray
- MVAC: Methotrexate, vinblastine, Adriamycin, cisplatin
- TURBT: Transurethral resection of bladder tumor
- UTI: Urinary tract infection

BLADDER INJURY, INTRAOPERATIVE

Richard H. Jadick, DO

James A. Brown, MD

BASICS

DESCRIPTION

- Bladder injury during surgery
- Intra- or extraperitoneal
- Laparoscopic or open surgery
- May be blunt/sharp dissection, trocar or electrocautery injury
- Needle or trocar passage during transvaginal tape or pubovaginal sling procedures are particularly high-risk procedures.
- Cystoscopy with overdistension and transurethral bladder tumor resections are also high risk for bladder perforation injury.

EPIDEMIOLOGY

Intraoperative bladder injuries account for:

- Laparoscopic injuries (0.2–8.3%)
- Intraperitoneal (38–40%)
- Extraperitoneal (54–56%) of injuries
- Laparoscopic injuries diagnosed: 53.2% intraoperatively

RISK FACTORS

- Inexperienced surgeon
- Complex surgical anatomy (prior surgery or radiation therapy)
- Poor laparoscopic visualization
- Full bladder

GENERAL PREVENTION

- Decompress bladder with a catheter placed before initial incision.
- Know bladder anatomy:
  - Pediatric bladder is intraperitoneal.
  - Adult bladder is retropubic extraperitoneal.
  - Peritoneum is cephalad to bladder.
  - Bladder is attached laterally and at bladder neck.
  - Bladder wall consists of 3 layers: Mucosa, submucosa, muscularis
  - Ureters attached posteriolateral in trigone.

PATHOPHYSIOLOGY

- Consistent with complete tear through mucosa, submucosa, and muscularis

- Leakage of urine into the extra- or intraperitoneal space

COMMONLY ASSOCIATED CONDITIONS

- Pelvic anomalies
- Prior pelvic surgery
- Pelvic trauma
- Tissue fibrosis or inflammation (ie radiation, chronic catheter)

DIAGNOSIS

HISTORY

Bladder injury can be found intraoperatively or postoperatively, and will be intra- or extraperitoneal.

PHYSICAL EXAM

- Postoperative:
  - Distended abdomen
  - Peritonitis
  - Decreased urine production
  - Abdominopelvic ascites
  - Urinoma
  - Urine leakage from wound
- Intraoperative:
  - Findings may be subtle. Need high degree of suspicion
  - Blood or gas in Foley, especially during transperitoneal laparoscopic procedure
  - Urine in wound

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Drain fluid sent for creatinine:

- Urine vs. serum
- Elevated creatinine over serum level observed with urine leak

Imaging

- Extraperitoneal injury: Contrast contained in the extraperitoneal space
- Intraperitoneal injury: Contrast extravasates between loops of small bowel and the anterior pararenal fascia
- Cystogram can be done using standard or CT imaging with post-contrast evacuation
  - 300 cc/3-view cystogram
  - CT cystogram
  - All cystograms must include a postcontrast evacuation study to evaluate for residual contrast outside of the bladder.

- US can identify urinoma.
- CT for pelvic ascites or urinoma
- Intraoperative:
  - Normal saline with indigo carmine into Foley and observe for extravasation (blue staining)

Pathological Findings

Rupture through mucosa, submucosa, and muscularis of detrusor usually causes urine leak

DIFFERENTIAL DIAGNOSIS

- Ureteral injury
- Prostatic or urethral injury
- Small or large bowel injury
- Vascular injury

TREATMENT

Prompt recognition improves opportunity for improved outcome.

MEDICATION

- Antibiotics: Gentamicin or fluoroquinolone for 24 hr
- Anticholinergic: Ditropan or B+O Supp

SURGERY/OTHER PROCEDURES

- Laparoscopic injury:
  - 1-layer laparoscopic repair
- Intraoperative intraperitoneal injury:
  - Open bladder/2-layer repair
  - Suprapubic tube or Foley
- Intraoperative extraperitoneal injury:
  - Foley or 2-layer repair
- Postoperative intraperitoneal injury:
  - Ex-lap with repair
- Postoperative extraperitoneal injury:
  - Foley catheter for 10–14 days

ONGOING CARE

PROGNOSIS

- Extraperitoneal: Usually heals with Foley catheter drainage and without further intervention
- Intraperitoneal: Good prognosis if identified intraoperatively and repaired:

- Prognosis worse if injury not recognized or identified late

COMPLICATIONS

- Peritonitis
- Ileus
- Return to OR

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Foley catheter or suprapubic tube to monitor urine output
- No need for outpatient antibiotics

ADDITIONAL READING

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- Gomez et al. Consensus statement on bladder injuries. BJU Int 2004;94(1):27–32.
- Ostrzenski, et al. Bladder injury during laparoscopic surgery. Obstet Gynecol Surv 1998;53(3):175–180.
- Diagnosis and management of bladder injuries. Urol Clin North Am 2006;33:67–71.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Trauma
- Bladder Trauma Algorithm
- Ureter Intraoperative Injury

CODES

ICD9

- 867.0 Injury to bladder and urethra without open wound into cavity
- 867.1 Injury to bladder and urethra with open wound into cavity
- 998.2 Accidental puncture or laceration during a procedure, not elsewhere classified

ABBREVIATIONS

- CT: Computed tomography
- OR: Operating room
- US: Ultrasound

BLADDER OUTLET OBSTRUCTION (BOO)

Arnold D. Bullock, MD

BASICS

DESCRIPTION

- BOO is a pathologic obstruction to urinary flow as documented by pressure-flow studies.
- Defined as a reduction in urinary flow to <12–15 cc/sec during a sustained detrusor contraction of over 40–50 cm H2O.

EPIDEMIOLOGY

- Bladder outlet obstruction can have many different causes.
- In males, the most common cause is an obstructive prostate (BPH).
- In females, the most common cause is iatrogenic, secondary to urethropexy or sling procedures.
- Other common causes include:
  - Urethral strictures from prior urologic procedures or infections.
  - Bladder calculi (stones occluding the bladder neck)
  - Pelvic tumors (prostate, cervix, uterus, rectal)
- Other less common causes of BOO include:
  - Posterior urethral valves
  - Cystocele
  - Foreign bodies
  - Urethral diverticula

RISK FACTORS

- Increasing age: Microscopic BPH starts as early as the 30s but clinical BPH usually presents after the age of 50.
- Strictures can be secondary to infection, urethral trauma, or prior urologic procedures
- Adrenergic medication used for cold and sinus problems can exacerbate other BOO conditions.

GENERAL PREVENTION

It is essential to prevent upper-tract damage from chronic high-pressure voiding.

PATHOPHYSIOLOGY

Bladder outlet obstruction can be due to both static and dynamic factors:

- The dynamic component is the result of stimulation of the smooth muscle along the proximal urethra or bladder neck (and prostate in men) resulting in an increased resistance along the urethra.

- The static obstruction is due to a constriction by enlarged prostatic tissue, bladder neck contracture, or urethral stricture.
- Outlet obstruction leads to detrusor hypertrophy and the symptoms of BOO.

COMMONLY ASSOCIATED CONDITIONS

- BPH
- Urethral stricture disease
- Detrusor sphincter dyssynergia

DIAGNOSIS

- The symptoms of BOO may vary but typically include:
  - Slow urinary stream
  - Urinary hesitancy
  - Intermittent urinary stream
  - Straining to void
  - Sense of incomplete bladder emptying
  - Urinary retention
- Less frequent symptoms could include:
  - Abdominal pain
  - Dysuria (pain or burning on urination)
- Difficult to predict the presence of BOO in females based on symptoms alone

HISTORY

- Detailed description of obstructive voiding symptoms consistent with BOO
- History of irritative symptoms suggestive of detrusor instability
- Medical history of gynecologic, neurologic, and GI illness
- Past surgical history for pelvic and spinal procedures
- Medication review for anticholinergics, -agonists, psychotropic agents
- Voiding diary

PHYSICAL EXAM

- Abdominal exam:
  - Palpate for bladder distention (>150 cc retained urine needed to be palpable in an adult)
  - Inguinal hernia can be associated with severe BPH and retention.
- Digital rectal exam:
  - Examine for an enlarged prostate (>30 cc)
  - Note any findings suspicious for cancer: Nodules, firmness, and asymmetry
  - Assess anal sphincter tone

- Pelvic exam (women) for cystoceles and diverticula
- Neurologic exam for gross defects

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PSA:
  - Standard range of normal is 0–4.0 ng/dL
  - If elevated, consider prostate cancer
  - Can be used to predict prostate volume:
    PSA <1.4 correlates with a gland <30 cc
    1.4–3.2 suggests moderate enlargement
    >3.2 is consistent with a gland over 50 cc in volume
- Urinalysis by dipstick microscopic analysis:
  - If hematuria or urinary infection is present, further evaluation is necessary (see "Hematuria" section)
- Creatinine: Not necessary unless patient is in urinary retention

Imaging

- Renal US is appropriate to evaluate for hydronephrosis if there is renal insufficiency. Also allows determination of noninvasive residual urine
- Upper-tract imaging with CT urogram or IVP to evaluate hematuria (or UTI in men)

Diagnostic Procedures/Surgery

- PVR to assess for incomplete emptying with urethral catheter or bladder scanning machine.
  - Volume >100 cc is consistent with BOO.
- Uroflowmetry: Measures peak flow, demonstrate voiding pattern, and voided volume. Peak flow <15 cc/sec (for voided volume >125 cc) is consistent with obstruction.
- Cystoscopy: Endoscopic evaluation of urethra and bladder. Used to evaluate prostatic length, median lobe component of prostatic obstruction, and bladder mucosa.
  - Cystoscopy can reveal other etiology for the BOO, such as strictures, stones, diverticula, urethral masses and bladder tumors.
- Urodynamics: Pressure-flow study to determine if a low flow rate is due to obstruction or reduced bladder contractility:
  - The Abrams-Griffiths nomogram is the most widely used measurement of BOO; plots maximal flow against detrusor pressure at the time of flow.
- EMG: Evaluates for neurogenic etiology of BOO.

Pathological Findings

Depends on etiology of BOO

DIFFERENTIAL DIAGNOSIS

- Inadequate bladder contractility. This is the most common etiology of urinary retention in women.
- Prostatic obstruction (BPH) is by far the most common etiology of urinary retention in men.
- Infection: Prostatitis, intraurethral condyloma (men and woman)
- Neurologic: Detrusor sphincter dyssynergia, diabetes mellitus with atonic bladder
- Medications that affect bladder contractility (anesthetics, narcotic, psychotropics)
- Urethral carancle, diverticulum (primarily women)
- Urethral cancer
- Penile cancer (usually advanced)

TREATMENT

- Management of BOO depends on etiology and severity.
- A urethral catheter is used for temporary management of severe obstruction.
- A suprapubic tube is used if a urethral catheter cannot be placed (severe stricture or BPH) or urethral catheter is contraindicated (prostatitis).
- Long-term treatment of most causes of BOO is surgical.

MEDICATION

BOO due to BPH (without complications) is managed with either:

– -Blockers: Rapidly relax the smooth muscles of the bladder neck and prostate without impairing bladder body contractility:

Alfuzosin (Uroxatral)
Doxazosin (Cardura, Cardura XL)
Tamsulosin (Flomax)
Terazosin (Hytrin)
Silodosin (Rapaflo)

– 5--reductase inhibitors: Effective in larger glands (>40 cc) to reduce prostate size, improve symptoms, and reduce complication risk:

Dutasteride (Avodart)
Finasteride (Proscar)

SURGERY/OTHER PROCEDURES

- Strictures are managed with urethral dilation, endoscopic incision, or open excision (with direct anastomosis, grafts, or flaps).
- Urethrolysis is the primary surgical approach to urethral obstruction following anti-incontinence surgery.

- Sphincterotomy can be used in highly selective patients with failed detrusor sphincter dyssynergia.
- BPH can be managed surgically with TURP, laser ablation, transurethral technologies (microwave or water induced hyperthermia), or simple open resection.

ADDITIONAL TREATMENT

- Long-term catheter drainage for patients with severe comorbidities
- Intermittent catheterization
- Prostatic stents
- Urinary diversion

Management of possible concurrent bladder dysfunction

ONGOING CARE

PROGNOSIS

Excellent with definitive management

COMPLICATIONS

- Increased resistance along the bladder neck and prostatic urethra leads to detrusor decompensation with larger residual urine volumes and complications:
  - Urinary retention
  - Gross hematuria
  - Renal insufficiency/failure
  - Bladder stones
  - UTIs
  - Bladder diverticula and flaccid bladder
- Postobstructive diuresis:
  - Usually with severe BOO and bilateral ureteral obstruction due to urinary retention
  - Usually self-limited and corrected by the patient drinking water
  - If the patient cannot keep up with the urine output, then IV replacement with 1/2 normal saline at a rate of 1/2 of the urine output
  - Serum electrolytes must be monitored closely.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Periodic follow-up visits to assess symptom progression
- Yearly urinalysis and PSA measurement:
  - Can include serial measurement of uroflow and PVR urine
- IPSS periodically
- Patients should be counseled on the possibility of progression of symptoms and complications. Men should be encouraged to discuss voiding problems and assured of effective

treatment options. Management of BPH does not eliminate their risk of developing prostate cancer.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate, Benign Hyperplasia (BPH)
- Lower Urinary Tract Symptoms (LUTS)
- Lower Urinary Tract Symptoms (LUTs), Male Algorithm

CODES

ICD9

596.0 Bladder neck obstruction

ABBREVIATIONS

- BOO: Bladder outlet obstruction
- BPH: Benign hyperplasia
- EMG: Electromyography
- GI: Gastrointestinal
- IPSS: International Prostate Symptom Score
- IVP: Intravenous pyelogram
- PSA: Prostate-specific antigen
- PVR: Postvoid residual
- TURP: Transurethral resection of prostate
- UTI: Urinary tract infection

BLADDER TRAUMA

Jack H. Mydlo, MD

John M. Mai, MD

BASICS

DESCRIPTION

- Typically secondary to traumatic (blunt or penetrating) or iatrogenic injury
- It is important to define intraperitoneal vs. extraperitoneal injury because this influences management.

EPIDEMIOLOGY

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RISK FACTORS

- Pelvic fracture
- Penetrating injuries
- Deceleration injury
- Motor vehicle accident
- Blow to lower abdomen with distended bladder
- Iatrogenic/intraoperative injury (laparoscopy, hysterectomy, etc.)
- Prior bladder surgery
- Alcohol abuse can account for up to 3% of cases of bladder trauma
- Rarely, prolonged labor can cause ischemic necrosis of a portion of bladder.

GENERAL PREVENTION

- Iatrogenic injuries can be minimized by placing a Foley catheter during procedures such as laparoscopy to minimize bladder injury.
- Avoid an overdistended bladder.

PATHOPHYSIOLOGY

- In the adult, the bladder is located in the extraperitoneal space of Retzius and generally protected from blunt trauma unless significantly distended.
- A full bladder can raise to the level of the umbilicus in an adult.
- In children, the majority of trauma is intraperitoneal, as the bladder in children is primarily in an intraperitoneal position.
- Bladder contusion:
  - Results from damage to mucosal wall or muscularis
  - Not a full-thickness injury

- Intraperitoneal bladder injury:
  - The sudden onset of increased intravesical pressure leads to rupture.
  - Occurs most commonly at the bladder dome in blunt trauma. The urachus is a weak point at the dome.
  - Distended bladder at time of trauma is a primary cause.
- Extraperitoneal bladder injury:
  - Seen most commonly with pelvic fractures and penetrating injuries (eg, knife, gun-shot wounds)
  - Can also be seen in blunt trauma
  - More common than intraperitoneal rupture

COMMONLY ASSOCIATED CONDITIONS

Traumatic abdominal solid organ injuries

DIAGNOSIS

HISTORY

- Blunt or penetrating trauma to pelvis
- Does not usually occur as isolated event
- Lower abdominal pain
- Unable to urinate
- Gross hematuria

PHYSICAL EXAM

- Distended abdomen
- Blood at urethral meatus, high riding or floating prostate on rectal exam, perineal hematoma or scrotal swelling or hematoma
- Suprapubic tenderness
- Lower abdominal bruising, especially along seat belt/lap belt region

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DIAGNOSTIC TESTS & INTERPRETATION

Lab

- UA: Blood usually present
- BUN/Cr: Can be elevated with intraperitoneal rupture due to intraperitoneal resorption of urine
- Hyperkalemia, hypernatremia, uremia, acidosis can also be seen with urinary extravasation into the peritoneum
- CBC for infection or to monitor blood loss

Imaging

- Indications for performing cystography:
  - Gross hematuria following blunt trauma with/without pelvic fracture
  - Microhematuria with associated pelvic fracture
  - Penetrating injury to buttock, pelvis, or lower abdomen with any degree of hematuria
- CT cystogram:

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  - Fill bladder with 300–400 cc diluted contrast (6:1 with saline) to limit contrast interference.
  - Postdrainage film not required
- Retrograde cystogram:
  - Fill bladder with 300–400 cc of iodinated contrast instilled by gravity via Foley catheter.
  - In children, estimate filling for the cystogram based on the following formula:
    Bladder capacity = 60 cc + (30 cc × age in yr)
  - Obtain AP, oblique, and post drainage film to exclude posterior injury.
  - False negatives can be seen, more commonly with penetrating injury.
  - Extraperitoneal rupture: Contrast limited to the space of Retzius; may occasionally leak out through urogenital diaphragm and into scrotum
  - Intraperitoneal rupture: Contrast is seen between loops of small bowel and along the paracolic gutters

ALERT

If blood is present at meatus, a high riding prostate or extensive perineal and/or scrotal swelling and bruising, perform RUG prior to attempting Foley placement.

Diagnostic Procedures/Surgery

- If no blood is present at meatus and suspicion of urethral injury is low, then insert Foley catheter to assess urine.
- Little to no role for emergency cystoscopy

DIFFERENTIAL DIAGNOSIS

- Abdominal solid organ injury
- Renal or ureteral trauma with gross hematuria
- Urethral trauma

TREATMENT

- Stabilize patient if major trauma present
- Associated injuries must be addressed

MEDICATION

If a Foley catheter is inserted, then antibiotics are recommended for the duration of the indwelling period until 3 days post catheter removal:

- Ciprofloxacin 250–500 mg PO b.i.d.
- Levofloxacin 250–500 mg/d q.d.

SURGERY/OTHER PROCEDURES

- Often other injuries are more immediately life-threatening than the emergent repair of the bladder injury.
- Bladder trauma may be associated with significant bowel or vascular trauma.
- Intraperitoneal injury:
  - Requires urgent/emergent operative repair
  - Catheter drainage alone only if minor iatrogenic identified during time of surgery.
  - Postop Foley catheter for 10–14 days following bladder repair with cystogram prior to removal.
- Extraperitoneal injury:
  - Insert 20–24 Fr Foley catheter for 10–14 days.
  - Obtain cystogram prior to catheter removal.
  - Antibiotics recommended while catheter is indwelling
  - Require operative repair if already undergoing exploratory laparotomy or pelvic fracture fixation

ADDITIONAL TREATMENT

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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 (but not limited to) fistula, sepsis, ileus, incontinence, and stricture.
- The mechanism causing bladder trauma can be associated with a relatively high mortality rate of 22–44%.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Require admission for minimum of 24-hr observation to rule out associated injuries and monitor signs/symptoms.

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Injury, Intraoperative
- Bladder Trauma Algorithm
- Hematuria, Traumatic Algorithm
- Ureter, Trauma
- Urethra, Trauma

CODES

ICD9

- 867.0 Injury to bladder and urethra without mention of open wound into cavity
- 867.1 Injury to bladder and urethra with open wound into cavity

ABBREVIATIONS

- BUN/Cr: Blood urea nitrogen/creatinine
- RUG: Retrograde urethrography
- UA: Urinalysis

BLADDER TUMORS, BENIGN AND MALIGNANT, GENERAL

Michelle J. Kim, MD
Ihor S. Sawczuk, MD

BASICS

DESCRIPTION

Bladder tumors encompass benign lesions, indolent low-grade, and aggressive high-grade malignancies.

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- 4th most common cancer in men, 12th most common cancer in women
- Male > Female (3:1)
- 2× more common in White than Black men
- 1.5× more common in White than Black women

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- Median age: 69 in men, 71 in women
- 9× the incidence
- 2nd most prevalent malignancy in middle aged and elderly men

RISK FACTORS

- Malignant bladder tumors
- Smoking:
  - Dose-related, with a 15–20-yr latency
  - 4× increased incidence of bladder tumors
  - 2nd-hand smoke is a risk factor
- Chronic cystitis is a risk for SCC:
  - Indwelling catheters
  - Chronic UTIs
  - Schistosoma hematobium infection
  - Chronic bladder stones
- Chemical exposure:
  - Especially aniline dyes and aromatic amines
  - High-risk industries include textiles, aluminum, dye, leather, paint, petroleum, tire and rubber, hairdressers, dry cleaning, plumbers, and metal workers
- Analgesic abuse: 5–15 g of phenacetin over 10 yr
- Pelvic irradiation: For cervical, ovarian, anal, and prostate cancers

- Chemotherapy:
  - Cyclophosphamide has a 4–9× increased risk for bladder cancer
  - Acrolein is the responsible metabolite.
- Blackfoot disease: Arsenic-related development of bladder tumors
- Aristolochia fangchi: Chinese herb in weight-loss drugs

Genetics

- Heredity plays a minor role.
- p53 gene on chromosome 17:
  - Overexpression leads to higher rates of progression and lower rates of response to chemotherapy
- Loss of Rb gene on chromosome 9:
  - Development of superficial tumors
- Slow acetylators:
  - Higher susceptibility to carcinogens (ie, in smokers)

GENERAL PREVENTION

- Smoking cessation reduces the risk of bladder tumors after 20 yr.
- Avoid occupational exposures.
- Drink more fluids.
- Take vitamin A and multivitamins (RDA doses).

PATHOPHYSIOLOGY

Patterns of spread:

- Lymphatic spread
- Vascular spread: To liver, lung, bone, adrenal, intestines
- Implantation

DIAGNOSIS

HISTORY

- Painless hematuria
- Irritative voiding symptoms: Dysuria, frequency, urgency
- Weight loss or cachexia
- Mucosuria: With adenocarcinoma
- History of spinal cord injury, chronic indwelling catheter
- Egyptian or Middle-Eastern heritage are risks for SCC
- History of bladder exstrophy: Risk for adenocarcinoma
- Pain:
  - Flank: From ureteral obstruction or retroperitoneal disease

- Bone pain from metastasis
- Pelvic mass

PHYSICAL EXAM

- Rarely abnormal
- Bimanual exam under anesthesia before and after transurethral resection
- Digital rectal exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and culture
- Cytology: 95% specific:
  - Better for CIS and high-grade tumors
  - Not cost-effective for screening in the general population
- Flow cytometry:
  - Measures DNA content of cells to quantitate aneuploid cell populations
- Other urine markers such as BTA Stat, NMP 22 Bladderchek, and FISH have better sensitivities but worse specifities than cytology.

Imaging

- Upper tract evaluation:
  - CT urogram
  - IVP
  - Retrograde pyelogram
- CXR
- Bone scan: Rarely positive

Diagnostic Procedures/Surgery

- Cystoscopy with bladder resection or biopsy:
  - Fluorescence cystoscopy may increase detection of non–muscle invasive disease
- Exam under anesthesia

Pathological Findings

- Benign lesions:
  - Nephrogenic adenoma: Metaplastic response to trauma, inflammation, or radiation. Classic hobnail epithelial cells on microscopy.
  - Von Brunn nests: Benign urothelial cells within the lamina propria
  - Squamous metaplasia: Common and normal in women
  - Cystitis cystica: Von Brunn nests that have undergone central cystic degeneration
  - Cystitis follicularis: Inflammatory lesions

  - Pseudosarcoma: Spindle cell tumor that develops after prior surgery
  - Malacoplakia: Chronic reaction, Michaelis-Gutmann bodies: Bulls-eyed histiocytes that are needed for diagnosis
  - Papilloma: Benign papillary lesion usually seen as small, solitary lesions
- Premalignant lesions:
  - Leukoplakia: Squamous metaplasia with keratin, 20% risk for SCC
  - Cystitis glandularis: Glandular metaplasia, risk for adenocarcinoma
  - Inverted papilloma: Associated with urothelial carcinomas elsewhere in the bladder
- Urothelial carcinomas (90–95%):
  - PUNLMP
  - CIS: High-grade tumor confined to the urothelium that often looks red and velvety.
    40–83% progress to muscle invasive disease.
    80–90% have positive urine cytologies.
  - TCC:
    75% present as superficial tumors; 70% papillary; 10% nodular; 20% mixed.
    Strong correlation between grading and stage
  - SCC (5%): Seen in SCI, chronic infections, foreign bodies, or with Schistosoma hematobium infections
  - Adenocarcinoma (0.5–2%): Seen in exstrophic bladders, urachal tumors, and tumors in ureterosigmoidostomies. Must rule out metastatic adenocarcinomas
- Nonurothelial cancers:
  - SCC: Aggressive neuroendocrine tumor
  - Sarcomatoid carcinosarcoma: Epithelial elements that appear sarcoma-like
  - Carcinosarcoma: Mixed epithelial and mesenchymal elements
  - Leiomyosarcoma: Most common sarcoma
- Metastatic cancer: Melanoma, colon, prostate, lung, breast, ovary, endometrium, stomach

Pediatric Considerations

- Rhabdomyosarcoma: Common in children, often located at trigone; can produce polypoid lesions called sarcoma botryoides
- Eosinophilic cystitis: Seen more in children

DIFFERENTIAL DIAGNOSIS

- UTI
- Urinary calculi
- Interstitial cystitis or prostatitis

TREATMENT

Based on stage and pathology

MEDICATION

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– Attenuated strain of Mycobacterium bovis that stimulates an immune reaction in the bladder

– Decreases recurrence and progression for high-risk patients (multiple tumors, high-grade tumors, CIS)

– Maintenance schedule may improve response, but ideal schedule is unknown

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– Alkylating antibiotic that inhibits DNA synthesis: Low systemic absorption

– Decreases recurrence

– Can be used as prophylactic postoperative instillation after TURBT

- Interferon -2B:
  - As monotherapy or in combination with BCG
- Thiotepa:
  - Alkylating agent that inhibits DNA synthesis
  - Can be absorbed systemically and lead to myelosuppression
  - FDA-approved for papillary bladder cancers
- Doxorubicin:
  - Anthracycline antibiotic that inhibits topoisomerase II
  - Prevents recurrence but not progression
- Valrubicin:
  - For BCG refractory CIS
- Gemcitabine:
  - Activity in non–muscle invasive bladder cancer

SURGERY/OTHER PROCEDURES

- TURBT:
  - Diagnostic: Consider repeat resections if T1 disease and no muscle on specimen
  - Therapeutic: For superficial disease
- Partial cystectomy: For selective patients with localized tumors, without diffuse disease or CIS, or urachal tumors
- Radical cystectomy:
  - For muscle invasive, nonmetastatic tumors
  - Consider for aggressive tumors such as SCC, carcinosarcoma, and sarcomatoid carcinomas.

ADDITIONAL TREATMENT

Radiotherapy

- Can be used in bladder-sparing therapy
- Controls locally invasive tumor in 30–50% of patients

Additional Therapies

- Cisplatin-based chemotherapy is 1st-line for small cell carcinoma
- Chemotherapy for metastatic disease:
  - Methotrexate, vinblastine, doxorubicin, and cisplatin
  - Gemcitabine and cisplatin
- Phototherapy: No long-term data
- Laser therapy

ONGOING CARE

PROGNOSIS

- Pathology: SCC, carcinosarcoma, sarcomatoid carcinoma are aggressive tumors
- Progression and recurrence depend upon grade, stage, size, the presence of CIS, multifocality, and frequency of prior recurrences.

COMPLICATIONS

- Hematuria
- Urinary retention
- Bladder perforation from TURBT
- Progression of disease and development of metastasis
- Infections
- Ureteral obstruction

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Cystoscopy every 3 mo for 2 yr, then every 6 mo for 2 yr, then once a year.

REFERENCES

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, Adenocarcinoma,
- Bladder Cancer, Choriocarcinoma
- Bladder Cancer, General
- Bladder Cancer, Sarcoma
- Bladder Cancer, Small Cell
- Bladder Cancer, Squamous Cell Carcinoma
- Bladder Cancer, Urothelial, Superficial
- Bladder Mass, Differential Diagnosis
- Carcinosarcoma, Bladder

CODES

ICD9

- 188.9 Malignant neoplasm of bladder, part unspecified
- 223.3 Benign neoplasm of bladder
- 236.7 Neoplasm of uncertain behavior of bladder

ABBREVIATIONS

- BCG: Bacillus Calmette-Guérin
- CIS: Carcinoma in situ
- CXR: Chest x-ray
- IVP: Intravenous pyelogram
- PUNLMP: Papillary urothelial tumor of unknown malignant potential
- SCC: Squamous cell carcinoma
- SCI: Spinal cord injury
- TURBT: Transurethral resection of bladder tumor
- UTI: Urinary tract infection

BOWEN DISEASE AND ERYTHROPLASIA OF QUEYRAT

Joseph C. Klink, MD
Judd W. Moul, MD

BASICS

DESCRIPTION

- EQ is a squamous cell CIS of the mucosal surfaces of the glans penis and inner aspect of the foreskin. Almost exclusively limited to uncircumcised men.
- BD is squamous cell CIS of the keratinized skin of the penile shaft and scrotum instead of the glans penis.

EPIDEMIOLOGY

- Carcinoma of the penis occurs in <1% of all malignancies in the American male, with EQ comprising only a fraction of these cases.
- Most common in Caucasian males
- Most patients >50 yr of age, but described in men from 20–80
- >90% of cases in uncircumcised males

RISK FACTORS

- Almost exclusively in uncircumcised men:
  - Phimosis present in 75% of cases
  - Smegma thought to be carcinogenic
- Infection with HPV is a common association:
  - HPV type 16 DNA has been isolated from biopsies of BD. Its presence in EQ has not yet been established, but it may play a role in disease progression.
  - HPV+ lesions do not have increased cell proliferation compared to HPV lesions.
- Men whose sexual partners have cervical neoplasia are more likely to develop penile neoplasia:
  - This is possibly due to HPV as a common pathogen.
- Sexual promiscuity and poor genital hygiene
- Immunosuppression including HIV/AIDS
- Irradiation: Solar, photochemotherapy, radiotherapy
- Carcinogens: Arsenic, smoking

GENERAL PREVENTION

- Daily cleansing of the glans penis
- Circumcision protects against EQ:
  - Prophylactic circumcision controversial due to high cost-to-benefit ratio

PATHOPHYSIOLOGY

- Carcinogenic insults from:
  - Chronic injury or dermatoses from smegma, urine, or poor hygiene
  - Irradiation
  - Chemical carcinogens
  - Viral infection
- Decreased immune surveillance secondary to immunosuppression

COMMONLY ASSOCIATED CONDITIONS

- SCC of the penis
- Lichen planus, balanitis xerotica sclerosis

DIAGNOSIS

HISTORY

- Age:
  - Median age >50 (younger for Bowenoid papulosis)
- Sexual history:
  - Having multiple sexual partners increases the likelihood of HPV-16 infection
- History of phimosis:
  - Increases likelihood of EQ
- History of chronic sun exposure of genitals or of arsenic poisoning:
  - Associated with BD, not EQ
- History of nonhealing lesion on glans after treatment with topical antifungals

PHYSICAL EXAM

- Appearance and location of lesion(s):
  - EQ: Solitary or multiple red plaques on glans, nontender, velvety, smooth, or scaly
  - BD: Solitary thick, gray-white, scaly plaque on shaft or scrotum
  - Bowenoid papulosis: Multiple reddish-brown, papular lesions on penis
- Presence of ulceration:
  - Increased likelihood of invasive carcinoma rather than CIS
- Examine the inguinal nodes

DIAGNOSTIC TESTS & INTERPRETATION

Lab

DNA testing for HPV-16 of biopsy specimen

Imaging

- MRI or CT of pelvis only if invasive carcinoma present
- Routine cross-sectional imaging not indicated for BD or EQ as neither are associated with internal malignancy

Diagnostic Procedures/Surgery

Definitive diagnosis only made by biopsy and histopathologic exam

Pathological Findings

- Microscopically, each looks like squamous cell CIS
- Lesion confined to the epithelium, exhibiting cytologic changes of malignancy:
  - Cellular atypia and pleomorphism, mostly in keratinocytes
  - Nuclear hyperchromicity and mitotic figures
- Thin granular layer, elongation of rete ridges
- Parakeratosis, hyperkeratosis, papillomatosis, acanthosis
- Chronic inflammatory infiltrate in the dermis

DIFFERENTIAL DIAGNOSIS

- Invasive SCI:
  - Ruled out by deep biopsy
- BD of the penis:
  - Squamous cell CIS of penile shaft and scrotum instead of glans penis
  - Gray-white, solitary plaque
  - Age >35
  - Historically thought to be associated with visceral malignancies (not seen with EQ)
  - Recent studies found no association between BD of the penis and internal malignancies.
  - Histologically identical to EQ
- Bowenoid papulosis:
  - Histologically similar to squamous cell CIS of penis, but with benign course
  - Appear as multiple rather than solitary, reddish to brown pigmented lesions
  - Younger patients affected, typically 20–35 yr
  - Strong association with HPV
  - Considered to be a transitional lesion between a genital wart and BD
- Balanitis circinata:
  - Dry and scaling lesions on glans and corona of circumcised or uncircumcised males
  - Associated with Reiter syndrome
  - Can be moist and erythematous in uncircumcised males
- Candidal balanitis:
  - Reddened and edematous lesion found in uncircumcised diabetics
  - Patients unresponsive to antifungal therapy should undergo biopsy to rule out CIS

- Zoon balanitis (balanitis plasmacellularis circumscripta):
  - Red, raised lesion occurring in elderly, uncircumcised men
  - Stippled with tiny red specks—cayenne pepper
  - Biopsy generally required to distinguish from CIS
  - Band-like infiltrate of plasma cells on histology
- Penile psoriasis:
  - Well-demarcated, red to whitish lesion that tends to scale
  - Usually accompanied by lesions at other sites
- Fixed drug eruptions (dermatitis medicamentosa):
  - Can appear as recurring erythema or bulla on the penis
- Others include lichen planus, herpes simplex, genital warts, and secondary syphilis

TREATMENT

- Circumcision is recommended to decrease the likelihood of recurrence.
- Management of CIS of the penis is related to the surface area and the size of the lesion:
  - Efficacy of invasive treatment should be weighed against the degree of disfigurement caused by that modality
- Regardless of treatment modality, biopsy of the lesion and deeper tissue is absolutely required for accurate diagnosis.

MEDICATION

- 5% 5-fluorouracil cream b.i.d. daily for 4–5 wk:
  - Effective on large lesions not amenable to surgery or laser
  - Rubber condom to occlude cream, prolong contact time
  - Increased efficacy also possible by using dinitrochlorobenzene as a vehicle, pretreatment with a laser, or iontophoresis
  - Concurrent topical anesthetic reduces irritation symptoms
- Used in recurrent lesions
- 5% imiquimod cream daily for 16 wk can be used as 2nd-line therapy

SURGERY/OTHER PROCEDURES

- Consider circumcision.
- Small lesions: Complete surgical excision:
  - Complete surgical excision most effective modality of treatment
  - Obtain 5-mm margins.
  - Obtain deep subcutaneous tissue to rule out invasive disease.
- Laser excision for larger lesions not amenable to complete surgical excision without disfigurement:

  - Neodymium: YAG preferred over CO2 laser due to depth of penetration
- Mohs micrographic surgical excision for larger lesions not amenable to laser due to risk of disfigurement

ADDITIONAL TREATMENT

Radiotherapy

- Treatment of large lesions not amenable to complete surgical excision or laser due to risk of disfigurement
- Treatment of recurrent lesions

Additional Therapies

Cryotherapy, curettage, and photodynamic therapy also described

None proven effective

ONGOING CARE

PROGNOSIS

Variable:

- Cure in up to 80% of case
- Recurrence
- Malignant transformation to invasive carcinoma carries significant risk of death

COMPLICATIONS

Malignant transformation in 5–10% BD, 10–33% of EQ

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- No clear guidelines for follow-up have been established.
- Recurrence rates 20–30%, so patients must be re-examined on a regular basis.
- Consider rebiopsy of recurrent lesions to rule out transformation to invasive carcinoma.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bowenoid Papulosis
- Genital Ulcer Algorithm

- Penis Cancer, General
- Penis, Lesion
- Penis, Squamous Cell Carcinoma
- Penis, Squamous Cell Carcinom Algorithm

CODES

ICD9

233.5 Carcinoma in situ of penis

ABBREVIATIONS

- BD: Bowen disease
- CIS: Carcinoma in situ
- CT: Computed tomography
- EQ: Erythroplasia of Queyrat
- HIV/AIDS: Human immunodeficiency virus/acquired immunodeficiency syndrome
- HPV: Human papilloma virus
- MRI: Magnetic resonance imaging
- SCI: Spinal cord injury

BURNS, EXTERNAL GENITALIA AND PERINEUM

Matthew A. Collins, MD

James A. Brown, MD

BASICS

DESCRIPTION

- Damage to skin, tissue, and surrounding organs 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 1 point to another through the body
- Chemical: Corrosive and alkali substances found in household and industrial chemicals

EPIDEMIOLOGY

- 5–13% of burns involve the genitalia and perineum (rare as an isolated incident).
- 3–10% of pediatric burns are nonaccidental.
- Increasing amount of male spousal abuse is being seen

RISK FACTORS

- Age: Very young (scald burns common in abused children) and very old
- Employment: Exposure to flames or caustic substances (eg, refrigerator technician, firefighter)
- Gender: Women are less likely to experience genital or perineal burns due to proximity to rest of the body.

GENERAL PREVENTION

- Follow occupational specific safety precautions.
- Handle caustic chemicals with care.

PATHOPHYSIOLOGY

Classification:

- 1st-degree (superficial): Involvement of the epidermis
- 2nd-degree (partial thickness): Involves the dermis and can be classified as superficial (involving the superficial, papillary dermis) and deep (involving the reticular dermis)
- 3rd-degree: Involves epidermis, dermis, and underlying tissue including nerves
- 4th-degree: Extends into bone and muscle; can cause compartment syndrome and often fatal
- Systemic changes: Multiple cardiovascular, respiratory, and metabolic changes are seen including:

Increased capillary permeability

Peripheral and splanchnic vasoconstriction

Decreased myocardial contractility and subsequent hypotension/end organ hypoperfusion

Bronchoconstriction

Increased metabolic rate

- Electrical: Death can occur by halting of cardiac and brain activity leading to cardiac arrest

COMMONLY ASSOCIATED CONDITIONS

- Child and spousal abuse
- Sexual abuse
- Myoglobinuria (electrical burns)

DIAGNOSIS

HISTORY

- Type of burn (thermal, chemical, or electrical)
- Causative agent or heat source (eg, flame vs water, noxious substance)
- Location and areas involved (Rule of 9s)
- Possibility of other injuries (eg, fractures from motor vehicle accidents, shrapnel)

Pediatric Considerations

Evaluate for scald and immersion injuries

PHYSICAL EXAM

- Complete assessment including ABCs of ATLS. Often associated with concomitant injuries or further burns.
- Rule of 9s: 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 phallus, meatus, glans, and scrotum
- Classification:
  - 1st-degree: Characterized by erythema, white plaques, and mild pain
  - 2nd-degree: Characterized by erythema, pain, superficial blisters
  - 3rd/4th-degree: Characterized by eschars, 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

Imaging

Any indicated by physical findings

Pathological Findings

Jackson described 3 zones of burns in 1947:

- Zone of coagulation: Occurs at point of maximum damage. In this zone, there is irreversible tissue loss due to coagulation of the constituent proteins.
- 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 edema—can convert this zone into an area of complete tissue loss.
- Zone of hyperemia: In this outermost zone, tissue perfusion is increased. The tissue here will invariably recover unless there is severe sepsis or prolonged hypoperfusion.

DIFFERENTIAL DIAGNOSIS

Diagnosis is usually evident.

TREATMENT

ALERT

- Treat any-life threatening conditions (ABCDs)
- IVF: Resuscitation is critical if patient has severe burns:
  - With any burn >20% TBSA, shock may occur so should replace per the modified Brooke formula:

    2 mL/kg/TBSA
  - Chemical burns should be copiously flushed with water and, if chemical agent is known, neutralizing agent should be used.

MEDICATION

- Silver sulfadiazine 1%: Apply to affected area but does not penetrate eschar
- Mafenide acetate (Sulfamylon) 11.1% suspension: Able to penetrate eschar
- Pain control with narcotics and anti-inflammatories
- Fluid resuscitation; replace electrolytes as needed
- Tetanus prophylaxis
- There is no indication for prophylactic antibiotic therapy.
- Treat specific infections as they arise.

SURGERY/OTHER PROCEDURES

• Most burns, particularly in children, should be managed with conservative treatment and require no surgical intervention.

• Mainstay of surgical treatment, if needed, is safe debridement.

• Affected areas may require split- or full-thickness skin grafts:

– Penile and perineal scarring and contracture in children have been reported and may require intervention.

– Catheter placement is not usually necessary unless needed during the resuscitation period.

ADDITIONAL TREATMENT

Many burns will require release of contractures, skin grafts, or Z-plasty.

ONGOING CARE

PROGNOSIS

• Based on degree of burn and GU structures affected

• Most burns have matured by 6–12 mo and decisions regarding reconstruction can be made at that time.

COMPLICATIONS

Urethral strictures or scars and erectile dysfunction have all been associated with burns involving the perineum and genitalia.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow-up as indicated

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Penis, Trauma

• Urethra, Trauma

CODES

ICD9

• 942.05 Burn of unspecified degree of genitalia

- 942.15 Erythema due to burn (first degree) of genitalia
- 942.25 Blisters with epidermal loss due to burn (second degree) of genitalia

ABBREVIATIONS

- ABCDs: Airway, breathing, circulation, and disability
- ATLS: Advanced trauma life support
- IVF: Intravenous fluid
- TBSA: Total body surface area

CALYCEAL DIVERTICULUM

Margaret S. Pearle, MD, PhD

BASICS

DESCRIPTION

Eventration of the collecting system that is lined with transitional epithelium and connected via a narrow infundibulum

EPIDEMIOLOGY

- Radiographic incidence: 0.2–0.5%
- No side or sex predilection
- Bilateral in 3% of affected individuals

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.

COMMONLY ASSOCIATED CONDITIONS

- Calculi occur in 10–50% of cases
- Infection
- Hematuria
- Flank pain

DIAGNOSIS

HISTORY

- May be asymptomatic and diagnosed incidentally on imaging studies
- Flank pain commonly associated with stones in calyceal diverticula
- Recurrent UTIs
- Gross or microscopic hematuria

PHYSICAL EXAM

- May be completely unremarkable
- Flank or abdominal tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Creatinine and electrolytes typically normal or unaffected
- CBC may show leukocytosis if associated with pyelonephritis
- Urinalysis may be normal or show microhematuria, pyuria

Imaging

- Plain abdominal radiograph (kidney, ureter, bladder) may show a radiopaque density consistent with a calculus:

– Small stones clustered in a round configuration
– Radiodense fluid level consistent with milk of calcium in diverticulum

- Renal US may show a cystic structure with thin overlying parenchyma with or without a contained echogenic focus
- IVU shows delayed opacification of the diverticulum adjacent to a calyx and may or may not reveal the infundibulum
- CT shows a cystic structure at the periphery of the kidney with little overlying parenchyma:

– With contrast, CT may or may not show delayed filling of the diverticulum or layering of contrast within the diverticulum.

- Retrograde pyelogram typically fills the diverticulum if the infundibulum is patent.

Diagnostic Procedures/Surgery

Cystoscopy and retrograde pyelogram may be necessary to adequately opacify the diverticulum.

Pathological Findings

- Calculus within diverticulum
- Rare transitional cell carcinoma within diverticulum

DIFFERENTIAL DIAGNOSIS

- Collecting system stone
- Uncomplicated pyelonephritis
- Simple or complex renal cyst
- Renal abscess

TREATMENT

Observation can be considered if patient is asymptomatic.

MEDICATION

Antibiotics only to treat associated infection

SURGERY/OTHER PROCEDURES

- SWL:

)[B]

– In unselected cases, stone-free rates are low although symptom-free rates are surprisingly better

- Ureteroscopy:

)[B]

– Identify ostium of diverticular neck, then incise/dilate neck to access diverticular cavity.

– Treat stone with laser lithotripsy.

- PCNL:
  – Highest likelihood of successful treatment of stones and ablation of diverticulum
  – Access the diverticulum directly in most cases, or indirectly if safe access into diverticulum cannot be achieved.
  – Remove stones.

)[B]

– Optional: Identify diverticular neck and dilate/incise, then place a nephrostomy tube across neck into collecting system.

)[B]:

– Reserved for large and/or anterior diverticula
– Transperitoneal or retroperitoneal approach
– Diverticulum unroofed and cavity/diverticular neck ablated

ONGOING CARE

PROGNOSIS

- Surgical interventions have a high rate of symptom resolution.
- PCNL with ablation of diverticulum has a very high rate of stone, diverticulum, and symptom resolution.
- Low likelihood of recurrence of diverticulum if diverticular wall is ablated.

COMPLICATIONS

- Spontaneous rupture or infection
- SWL:
  – Bleeding, subcapsular or perinephric hematoma
  – Infection
- Ureteroscopy:
  – Bleeding
  – Rupture of diverticulum and extravasation of stones/fragments
  – Infection
  – Perforation of the ureter
  – Late ureteral stricture formation
- PCNL:
  – Bleeding
  – Extravasation of stones/fragments
  – Hydropneumothorax
  – Persistent urine leak

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- After definitive treatment, follow-up should include a contrast study (IVU or CT urogram) to demonstrate complete stone removal and resolution of diverticulum.

)[B]

- If observation, rather than surgical intervention is pursued, patients with stone-bearing diverticula should be periodically imaged to identify stone growth (ie, every 6–12 mo).

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See Also (Topic, Algorithm, Electronic Media Element)

- Calcifications, Renal
- Flank Pain
- Urolithiasis, Adult, General

CODES

ICD9

- 594.0 Calculus in diverticulum of bladder
- 596.3 Diverticulum of bladder
- 753.8 Other specified congenital anomalies of bladder and urethra

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- IVU: Intravenous urogram
- PCNL: Percutaneous nephrostolithotomy
- SWL: Shock wave lithotripsy
- US: Ultrasound
- UTI: Urinary tract infection

CATHETERIZABLE STOMA PROBLEMS

Paul L. Crispen, MD

Michal L. Blute, MD

BASICS

DESCRIPTION

- CSs are utilized in all age groups and provide a means of emptying the native bladder or neobladder.
- Most common indications for CS vary with age groups:
  - Pediatrics: Incontinence related to neurologic conditions
  - Adults: Urinary diversion following extirpative surgery for malignancy
- Location of CS can vary, but is most often located in the umbilicus or right lower quadrant.
- Catheterizable channels are commonly constructed from a segment of small bowel or the appendix.
- Mechanism of CS continence depends on the type of urinary reservoir.
- Patients with CS often have routine catheterization schedules.
- CS problems can be related to the stoma, catheterizable channel, or urinary reservoir.

Pediatric Considerations

In addition to having a CS to a urinary reservoir, children with neurologic deficits may have a 2nd CS with access to the large bowel to assist with fecal continence.

EPIDEMIOLOGY

Complications are reported in 10–50% of patients with CS:

- Stomal stenosis has been reported in up to 40% of CS

)[C]

- Incontinence is reported 1–20% of cases and is associated with the mechanism of continence.
- Parastomal hernias have been noted in 0–5% of patients.

RISK FACTORS

- Infrequent use of CS
- Surgical technique
- Obesity
- Wound infections
- Multiple prior abdominal procedures
- Improper stomal positioning

GENERAL PREVENTION

- Maintenance of a regular catheterization regimen
- Several complications can be prevented at the time of surgery when creating the catheterizable channel:
  - Maintenance of vascular supply to catheterizable channel
  - Minimized redundancy catheterizable channel with fixation and stabilization of the continence mechanism
  - Adequate construction of continence mechanism
  - Tension-free mucocutaneous anastomosis
  - Use of V-flap of skin to prevent stomal stenosis

PATHOPHYSIOLOGY

- Stomal stenosis can be attributed to infrequent catheterization, scar formation, ischemia secondary to compromised vascular supply to catheterizable channel, or a non-tension free mucocutaneous anastomosis.
- Difficulty catheterizing the catheterizable channel can be attributed to angulation of a mobile and/or redundant channel.
- Improper creation of continence mechanism
- Incomplete detubulization or augmentation of the urinary reservoir can lead to incontinence secondary to low compliance and small reservoir capacity.
- Pouchitis is rare. Can cause temporary failure of the continence mechanism because of the hypercontractility of the bowel segment; can be caused by inflammation of the mucosa, sometimes due to infection

COMMONLY ASSOCIATED CONDITIONS

- Urologic, gynecologic, and colorectal malignancies
- Spinal dysraphisms
- Traumatic spinal cord injuries

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
- Normal cath 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.)
- Status of the bladder neck in patients with native bladder intact:
  - Urethral catheterization can be attempted in patients whose native urethra is intact and who have an open bladder neck.
- Review of systems should focus on abdominal symptomatology.

Pediatric Considerations

Patients may have 2 CS; be sure to ask patient or the patient's caretaker to identify which CS has the complication.

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:
  - Stenosis
  - 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
  - Instill 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.
  - 1 of 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: Hyperchloremic 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

Diagnostic Procedures/Surgery

Urodynamics in patients with incontinence may reveal uninhibited contractions or a poorly compliant high pressure reservoir.

DIFFERENTIAL DIAGNOSIS

- Perforation of CS channel or urinary reservoir
- Stomal stenosis
- Incontinence
- False passage
- Parastomal hernia
- Fistula
- Inability to catheterize due to redundancy of catheterizable channel

TREATMENT

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.
- Perforation of CS conduit or urinary reservoir mandates emergent exploratory laparotomy, drainage of urinary extravasation, and repair of urinary reservoir.

MEDICATION

- Incontinence related to uninhibited pouch contractions:

)[C]

- Pouchitis may sometimes be due to infection and can be treated with antibiotics.

SURGERY/OTHER PROCEDURES

- Stomal stenosis:

)[C]

- Incontinence:
  - Elective surgical revision of continence mechanism
  - Injection of bulking agent into CS

)[C]

- Parastomal hernia:
  - Elective hernia repair with or without repositioning stoma site on abdominal wall
  - Surveillance in asymptomatic patients
- Fistula:
  - Elective revision
- Inability to catheterize secondary to false passage or redundancy of CS channel:
  - Elective revision

ADDITIONAL TREATMENT

- Stomal stenosis:
  - Routine catheterization schedule
  - Dilatation of stenosis
- Inability to catheterize secondary to false passage or redundancy of CS channel:
  - Change type of catheter
  - Change method of catheterization

ONGOING CARE

PROGNOSIS

)[C]

COMPLICATIONS

Recurrence of prior complication

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Maintenance of routine catheterization schedule
- Additional follow-up with enterostomal therapist

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Squamous Cell Carcinoma
- Parastomal Hernia
- Pouchitis
- Urostomy Problems

CODES

ICD9

- 598.2 Postoperative urethral stricture
- 788.30 Urinary incontinence, unspecified
- V53.6 Fitting and adjustment of urinary devices

ABBREVIATIONS

- CBC: Complete blood count
- CS: Catheterizable stoma
- MRI: Magnetic resonance imaging

CHORDEE

Harry P. Koo, MD

BASICS

DESCRIPTION

Chordee is penile curvature that usually accompanies hypospadias (ventral) but also can occur independent of hypospadias:

- Epispadias is associated with dorsal chordee.
- Lateral chordee may occur with or without hypospadias.

EPIDEMIOLOGY

- Specific incidence of chordee is not available.
- Hypospadias occurs in ~1 in 250 live male births (chordee is present in about 1/3 of children with hypospadias).
- It is found in 44% of fetuses through the 2nd trimester, suggesting that chordee is a normal part of penile development.
- 35% of hypospadias have associated chordee.
- Isolated chordee without hypospadias represents ~4–10% of cases of congenital chordee.

RISK FACTORS

- Congenital; especially associated with hypospadias
- Induced by prior penile surgery

Genetics

- May be found in syndromes associated with hypospadias:
  - Chromosomal abnormalities (22%) present in individuals with severe hypospadias and cryptorchidism
- 14% incidence of hypospadias in male siblings and 8% incidence in offsprings

PATHOPHYSIOLOGY

- Chordee could be considered as an arrest of normal embryologic development, analogous to the failure of testicular descent.
- 3 major theories are proposed:
  - Abnormal development of urethral plate
  - Abnormal, fibrotic mesenchymal tissue at the urethral meatus
  - Corporeal disproportion
- Different etiologies for chordee without hypospadias:
  - 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

COMMONLY ASSOCIATED CONDITIONS

- Hypospadias
- Epispadias
- Cryptorchidism
- Intersex

DIAGNOSIS

HISTORY

- Presence of hypospadias in infant or family
- Visualization of penile bend during erection
- History of circumcision or other penile surgery

PHYSICAL EXAM

- Observe the patient's erection, if possible, to determine extent and direction of penile curvature
- Presence of hypospadias or epispadias
- Presence of incomplete foreskin
- Penoscrotal web
- Hypoplastic ventral penile skin
- Evaluation for undescended testis(es) or inguinal hernia

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Chromosomal and biochemical evaluation for the neonate with a suspicion for intersex state

Imaging

- No imaging required for isolated chordee or hypospadias
- In children with hypospadias (or chordee) in association with other organ system anomalies such as congenital cardiac condition, imperforate anus, limb malformation, obtain renal and bladder imaging with US

Diagnostic Procedures/Surgery

Intraoperative artificial erection test:

- To be performed only under general anesthesia in infant or child at the time of definitive surgery
- Infusion of isotonic saline into the corpora with a tourniquet at the base of the penis

- Injection of saline with a butterfly needle passed through the glans eliminates the possibility of hematoma formation beneath Buck fascia

DIFFERENTIAL DIAGNOSIS

- Hypospadias
- Epispadias
- Intersex
- Penile torsion
- Normal penile variant

TREATMENT

SURGERY/OTHER PROCEDURES

- Surgery is the standard approach to correct chordee.
- Specific treatment depends on the causes of chordee and the degree of bending.
- Surgical correction after infant reaches 6 mo of age
- General points for orthoplasty (chordee correction):
  - Following penile skin release, induce artificial erection
  - Chordee secondary to skin tethering, dartos, or Buck abnormality requires skin release and dissection of abnormal tissue anterior to the urethra.
  - Chordee secondary to fibrous or absent spongiosum tissue requires deeper dissection with urethral mobilization and/or transaction (if foreshortened urethra). Curvature >30 degrees has traditionally led to transaction of the urethral plate. In select cases, careful mobilization of the urethral plate with dorsal plication has led to the preservation of the urethral plate.
  - Chordee secondary to corporeal disproportion involves incising the tunica albuginea on the ventral surface of the penis, in transverse direction over the point of maximal curvature; cover the defect with either a free dermal or tunica vaginalis graft
  - An alternative to the latter surgical techniques is to plicate the tunica albuginea dorsally or laterally as needed to reverse the chordee.
  - It is critical to identify and preserve the neurovascular bundles during the tunica albuginea plication (TAP) procedure.

ONGOING CARE

PROGNOSIS

- Several observations support the idea of chordee progression during pubertal penile development.
- Recommend long-term follow-up of children with successful chordee repairs, particularly at puberty

COMPLICATIONS

Recurrence of chordee

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Surgery for chordee is an outpatient procedure.
- For chordee correction without hypospadias, children have a routine penile surgery follow-up within several weeks of surgery.
- For children getting chordee correction, along with hypospadias correction, urethral catheter may need to be in place for several days.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Disorders of Sexual Development (Intersex Disorders)
- Epispadias
- Hypospadias

CODES

ICD9

- 607.89 Other specified disorders of penis
- 752.61 Hypospadias
- 752.63 Congenital chordee

ABBREVIATIONS

TAP: Tunica albuginea plication

US: Ultrasound

CHYLURIA

Paul Crow, MD

Francis X. Keeley, MD

BASICS

DESCRIPTION

- The presence of chyle (a combination of lymphatic fluid and triglycerides) in urine
- Presents as milky white urine
- Often self-limiting
- If chronic or recurrent can lead to malnutrition and vitamin deficiency

EPIDEMIOLOGY

- ~2% of patients infected with filariasis can manifest chyluria.
- 90 million people suffer from filariasis worldwide. Chyluria is a manifestation of chronic infection with Wuchereria bancrofti.
- Rare in developed countries; most common in areas of endemic parasitic filariasis.

RISK FACTORS

- Parasitic chyluria:
  - Residence in tropics predisposing to filariasis
  - In addition to W. bancrofti, less common parasitic infections have been reported to cause chyluria (echinococcus, bilharzias, ascariasis)
- Nonparasitic chyluria:
  - Retroperitoneal tumors
  - Trauma
  - TB
  - Congenital fistula or lymphangioma

GENERAL PREVENTION

- Control of mosquito vector that transmits W. bancrofti.
- Insect repellant and mosquito net
- Diethylcarbamazine can be used to treat asymptomatic filariasis via its action on microfilaria.

PATHOPHYSIOLOGY

- Obstruction of suprarenal lymphatics
- Results in rupture of lymphatic vessel into calyceal fornix, forming intrarenal lymphatic-urinary fistula.
- Adult filaria cause lymphangitis.
- Lymphatic HTN, and valvular incompetence:

– With obstruction between intestinal lacteals and thoracic duct, the resulting cavernous malformation opens into the urinary system creating a fistula.

– The common fistula sites are: Renal fornix, pelvicaliceal system, trigone

- Prostatic urethra:
  - Most commonly due to filariasis due to infection with W. bancrofti
  - Less commonly can be caused by trauma, tumor, or TB
- Congenital fistulous connections between urinary tract and lymphatic system also described

COMMONLY ASSOCIATED CONDITIONS

Filariasis resulting from nematode infection with W. bancrofti or more rarely Brugia malayi or B. timori. Mosquitoes serve as vectors.

DIAGNOSIS

HISTORY

- Patient complains of milky or cloudy urine
- Country of origin of patient:
  - Endemic areas include Africa and Indian subcontinent
- Travel to any tropical regions
- History of TB exposure/infection
- History of trauma
- Significant weight loss, anemia, and proteinuria
- Heavy chyluria can cause clot colic or rarely urinary retention.

PHYSICAL EXAM

- Lymphadenitis/lymphangitis, genital edema, hydrocele.
- Palpable abdominal or flank mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis typically positive for albuminuria
- Postprandial urinary triglycerides
- Fat globules in urine identified by Sudan stain
- Peripheral blood eosinophilia; may be indication of parasitic infection. May also indicate presence of parasites
- Evaluate for TB if clinically indicated (tuberculin test, urine stain, and culture for acid-fast bacillus)

Imaging

- Abdominal/pelvic CT:

  - Exclude a retroperitoneal mass.
- Pedal lymphangiography:
  - Demonstrates abnormal lymphatics and entrance of contrast material into renal collecting system.
- Retrograde pyelography:
  - Rarely warranted as diagnostic study; may show diffuse pyelolymphatic backflow.

Diagnostic Procedures/Surgery

- Serodiagnostic tests for W. bancrofti are available from the CDC.
- Exam of peripheral blood for microfilaria, using Giemsa stain.

Pathological Findings

Lipid contents of chyluria are mainly chylomicrons, 90% of which is in the form of triglycerides.

DIFFERENTIAL DIAGNOSIS

- Appearance of urine is usually diagnostic; urinary chemistries are confirmatory.
- Phosphaturia, most common cause of cloudy urine
- Pyuria
- Enterovesical fistula

TREATMENT

- Up to 50% of cases resolve spontaneously
- Bed rest and/or use of an abdominal binder to increase intra-abdominal pressure may allow spontaneous closure.
- Medium-chain fatty-acid diet:
  - Transported from gut by portal system, not by chylomicrons entering the thoracic duct.

MEDICATION

- Dietary modifications to reduce chylomicrons in diet
- Diethylcarbamazine or other antifilarial agent for parasitic cause

SURGERY/OTHER PROCEDURES

- Procedures of choice involve the principles of chylolymphatic disconnection
- Nephrolysis:
  - Stripping and ligation of all lymphatic vessels to the kidney and upper ureter; open or laparoscopic technique.
  - Laparoscopic transabdominal and retroperitoneoscopic approaches described
  - Success rates of 88–98% reported.
- Endoscopic coagulation of fistula

- Lymphangiovenous anastomosis with ligation of renal lymphatics
- Renal autotransplantation
- Nephrectomy was the treatment of choice before the advent of more minimally invasive therapies.

ADDITIONAL TREATMENT

- Sclerotherapy with various agents instilled into collecting system
- Povidone iodine and 50% dextrose renal pelvic instillation sclerotherapy with 87% success reported
- Silver nitrate (1–3%) instillation into the affected collecting system causes sclerosis of lymphatic fistulas:
  - Success rate of 48% reported

ONGOING CARE

PROGNOSIS

Rarely fatal, with good success rates reported for surgical intervention.

COMPLICATIONS

- Hypoalbuminemia and anasarca from massive protein loss
- Underlying filariasis may cause epididymitis, hydrocele, and elephantiasis of the penis/scrotum.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Treatment failures are readily apparent.
- Re-evaluate if chyluria recurs following treatment; consider the contralateral kidney as the source.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Filariasis, Urologic Considerations
- Urine, Abnormal-Colored

CODES

ICD9

- 125.0 Bancroftian filariasis
- 125.9 Unspecified filariasis
- 791.1 Chyluria

ABBREVIATIONS

- CDC: Centers for Disease Control and Prevention
- CT: Computed tomography
- HTN: Hypertension
- TB: Tuberculosis

CONDYLOMA ACUMINATA (VENEREAL WARTS)

Perry R. Weiner, DO

Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Anogenital lesions caused by the transmission of HPV
- Also called genital warts, venereal warts
- Most common sites: Penis, vulva, vagina, cervix, perineum, and perianal area.
- Less commonly, the oropharynx, larynx, and trachea

EPIDEMIOLOGY

- Most common STD
- ~1% of sexually active adults in the US
- Highest prevalence: 18–28-yr-olds and exceeds 50%
- HPV DNA can be detected in 10–15% of the US population

Pediatric Considerations

Consider sexual abuse if lesions are documented.

Pregnancy Considerations

Maternal to neonatal transmission may cause respiratory or laryngeal papillomatosis.

RISK FACTORS

- Increased risk with number of sex partners, frequency of sexual activity, early coitus, and presence of condyloma on partners
- Immunocompromised status
- Cigarette smoking and oral contraceptives may be associated with an increased risk.

GENERAL PREVENTION

- Sexual abstinence
- Condoms

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 most often associated with potential for malignancy.
- >80 different subtypes can potentially associated with condylomata.
- Transmission is by direct sexual contact.
- Less common mode is autoinoculation from nongenital lesions.
- Basal layer of epidermis is invaded by the virus.
- Latent phase can last months to years.

COMMONLY ASSOCIATED CONDITIONS

Carefully search for coexistent STDs

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 of exposure
- Practice of anal intercourse
- Immunocompromised state

PHYSICAL EXAM

- Lesions are pinkish to red-grayish white cauliflowerlike lesions found on moist surfaces, often coalescing.
- Lesions appear pearly white and granular.
- Lesions may be typically verrucous or flat in configuration.
- With magnification, a central venule can be seen within each projection.
- Male: Penis, scrotum, perineum, suprapubic, and perianal regions. Examine meatus.
- Female: Vagina, introitus, perineum, cervix, and perianal region
- Examine for evidence of coexisting STD (ulcers, discharge, adenopathy).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- HPV cannot be readily grown in culture.
- Cytologic testing with Pap smear: Exfoliated genital cells are stained and examined for koilocytosis and neoplasia.
- Serologic assays not useful in screening for HPV infection, but may provide prognostic information for patients with abnormal Pap smears.
- Histologic analysis from biopsy specimens
- Rapid commercial screening tests available and are fairly accurate: ViraPap, ThinPrep Pap, Hybrid capture II
- If necessary, molecular characterization for diagnosis and serotyping (eg Southern and or slot blot hybridization, PCR)
- Consider screening for other associated STDs: HIV, GC, chlamydia, syphilis

Diagnostic Procedures/Surgery

- Magnification with colposcope or 10× hand-held magnifying lens of the suspected region after application of 3–5% acetic acid-soaked gauze pad for 5 min allows visualization of nonvisible lesions, but has low specificity.

- Subclinical lesions may appear shiny white.
- Urethroscopy for any patients with suspected urethral warts, with care to occlude proximal urethra to prevent flushing of virus toward bladder
- Proctoscopy for patients at risk for anal condyloma

Pathological 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
- Buschke-Lowenstein tumor
- Condyloma latum (syphilis)
- Extramammary Paget disease
- Fibroepitheliomas
- Herpes simplex virus
- Malignant melanoma
- Molluscum contagiosum
- Nevi
- Pearly penile papules
- Seborrheic keratosis
- Squamous cell carcinoma/basal cell carcinoma

TREATMENT

- Diagnosis usually based on observation of characteristic lesions
- Current therapies have an equally low effectiveness in preventing wart recurrence and may not reduce disease transmission.
- Vaccine: HPV quadrivalent recombinant (types 6, 11, 16, 18): Gardasil (Merck) is currently available for administration to females ages 9–26 for prevention of condyloma acuminata and associated diseases.

MEDICATION

- Podophyllin (Podoben 25%, Podocon, Podofin): Applied to lesion (concentration 10–25%) by healthcare worker once weekly for up to 6 wk
- Podofilox (Condylox): Self-application of a 0.5% solution to warts twice daily for 3 days, followed by 4 days without treatment; can be repeated 4–6 times.

• 5-FU (Efudex, Fluoroplex): Topical treatment with 5% cream 1–3 times per week for several weeks, as needed

• Trichloroacetic acid (Tri-Chlor): An 80–90% solution of trichloroacetic acid; apply directly to lesions; repeat weekly

• Imiquimod (Aldara): Potent inducer of interferon-, 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

• Interferon- IM or intralesional 3 million units 3 times a week for 3 wk

SURGERY/OTHER PROCEDURES

• Electrosurgery (electrodesiccation/loop electrosurgical excisional procedure): To destroy lesions; local anesthesia is usually sufficient

• CO2 laser therapy: Useful for lesions that have not responded to other therapies and for extensive disease. Magnification necessary to maximize efficacy; may produce less scarring

• Surgical excision: Often reserved for extensive disease; also effective for isolated warts

• Cryotherapy: Application of liquid nitrogen on patients without extensive disease. This procedure can be repeated at 1- or 2-wk intervals.

ONGOING CARE

PROGNOSIS

• Subclinical infections are probably not curative.

• Women should undergo routine Pap smears.

• Cervical cancer is associated with HPV infection. HPV infection is not solely responsible for the malignant transformation of genital cells, but it may be a cofactor in development of malignancy. HPV-6 and -11 are low-risk subtypes, and are seldom associated with malignancy.

• Homosexuals are at 25–50 times greater risk for anal cancer.

• Long-term, increased risk of malignancy secondary to HPV infection (HPV types 16, 18, 31, 33, and 51 highest risk of anogenital malignancy).

COMPLICATIONS

Malignant transformation

FOLLOW-UP RECOMMENDATIONS

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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bowen Disease and Erythroplasia of Queyrat
- Bowenoid Papulosis
- Buschke-Lowenstein Tumor
- Condyloma Latum (Syphilis)
- Fibroepitheliomas
- Herpes Simplex Virus
- Malignant Melanoma
- Molluscum Contagiosum
- Pearly Penile Papules
- Penis, Cancer General
- Penis, Lesion
- Seborrheic Keratosis
- Urethra, Condyloma (Warts)

CODES

ICD9

078.11 Condyloma acuminatum

ABBREVIATIONS

- CO2: Carbon dioxide
- DNA: Deoxyribonucleic acid
- GC: Gonococcal infection
- HIV: Human immunodeficiency virus
- HPV: Human papilloma virus
- PCR: Polymerase chain reaction

- STD: Sexually transmitted disease

CONTRAST ALLERGY AND REACTIONS

Matthew D. Katz, MD

Gerald L. Andriole, MD

BASICS

DESCRIPTION

- An immune system–based response to IV administration of RCM used for IV studies such as excretory urography and CT.
- May be divided into 3 groups: Idiosyncratic anaphylactoid reactions, nonidiosyncratic reactions, and delayed reactions
- Reactions to MRI contrast media are discussed in the section “Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy (NSF/NFD)”

EPIDEMIOLOGY

)[B]

- It is estimated that up to 12% of patients may experience a contrast-related reaction.

RISK FACTORS

)[B]

- Other significant risks include: Cardiac disease, dehydration, sickle cell disease, polycythemia, multiple myeloma, pheochromocytoma, renal disease, anxiety, and the use of ionic vs. nonionic contrast material
- Possible risk factors: -blockers, IL-2, aspirin, NSAIDs

GENERAL PREVENTION

- Use of nonionic LOCM
- Antihistamines (diphenhydramine 50 mg 1 hr prior to study). An H2 blocker can be used in conjunction with H1, but never without H1 blockers
- Preprocedure hydration

)[B]

- Patients with pre-existing renal impairment should stop metformin 24 hrs prior to procedure to avoid RCM-related biguanide lactic acidosis.
- To limit risk for contrast-induced nephropathy, special arrangements should be made with the radiology department for any patient with a GFR <60 mL/min1.73 m2.
- Prevention in patient with known allergy:
  - Review radiology department procedures at site where testing scheduled.
  - Give patient Rx for Medrol 32 mg PO 12 and 2 hrs prior to scheduled test and 50 mg Benadryl
  - Patients with allergies to other substances (food, medicines), with history of asthma, who are allergic to iodinated contrast, who are receiving gadolinium (or those with al-

lergy to gadolinium who are to receive IV contrast) DO NOT need steroid prep.

PATHOPHYSIOLOGY

- Idiosyncratic anaphylactoid:
  - Not dose dependent
  - Most serious and potentially fatal type of reaction
  - Occurs without warning, previous exposure not a prerequisite, not preventable
  - Not considered anaphylactic due to lack of IgE antibody formation
  - Usually begins with or immediately after injection of RCM (<30 min)
- Nonidiosyncratic:
  - Dose dependent
  - Related to osmolality, chemical composition, volume, and concentration of contrast medium used
  - Idiosyncratic and nonidiosyncratic reactions may be classified as minor, moderate, or severe
  - Minor: Urticaria, nausea and vomiting, sense of warmth, pruritus, diaphoresis
  - Moderate: Faintness, severe vomiting, facial edema, laryngeal edema, mild bronchospasm
  - Severe: Hypotensive shock, pulmonary edema, respiratory arrest, seizures, cardiovascular collapse
- Delayed:
  - Occurs 1 hr to 7 days from injection of RCM
  - Usually mild to moderate, transient, and self-limiting
  - Commonly includes rash, urticaria, pruritus, and erythema

COMMONLY ASSOCIATED CONDITIONS

- Asthma
- Cardiac disease
- Dehydration
- History of allergy or atopy
- Previous ADR
- Renal disease
- Sickle cell disease

DIAGNOSIS

HISTORY

- Previous ADR
- Cardiac or renal disease

- Metformin with CRD
- Allergies

PHYSICAL EXAM

- ABCs of resuscitation
- Vital signs (BP, heart rate, respirations)
- Observe for urticaria, wheezing, shortness of breath

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- In acute setting, no labs are usually needed
- Blood gas may be useful

DIFFERENTIAL DIAGNOSIS

Complex of symptoms after contrast administration supports diagnosis

TREATMENT

Use of alternative imaging in patients with history of previous ADR

MEDICATION

- Benadryl 50 mg IV for skin reactions
- Epinephrine 0.3–0.4 mL 1:1,000 solution SQ for moderate reaction without hypotension
- Epinephrine 1 mL 1:10,000 solution slow IV injection over 5 min repeated every 5–10 min as needed for severe reaction
- For life-threatening reactions: ABCs of resuscitation, IV fluids, vasopressors for BP support if IV fluids not adequate
- IV hydrocortisone 300–500 mg
- Prevention medications in cases of known allergy see above

ONGOING CARE

PROGNOSIS

- Depends on severity of ADR
- Risk of death 1 in 170,000 for both ionic HOCM and nonionic LOCM

COMPLICATIONS

- Renal failure occurs in up to 5%
- Generally supportive measures only with renal function returning to normal in a few weeks

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Appropriate supportive measures until recovery depending on severity of ADR

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Contrast-Induced Nephropathy (CIN)
- Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy (NSF/NFD)

CODES

ICD9

- 995.27 Other drug allergy
- V15.08 Allergy to radiographic dye

ABBREVIATIONS

- ADR: Adverse reactions
- BP: Blood pressure
- CRD: Chronic renal disease
- CT: Computed tomography
- HOCM: High-osmolar contrast material (nonionic)
- IV: Intravenous
- LOCM: Low-osmolar contrast material
- MRI: Magnetic resonance imaging
- RCM: Radiocontrast material
- SQ: Subcutaneously

CUSHING DISEASE AND SYNDROME

Douglas M. Dahl, MD

Christopher J. Cutie, MD

BASICS

DESCRIPTION

- Cushing disease: Hypercortisolism due to an ACTH-secreting adenoma
- Cushing syndrome: Characterized by an excess exposure to glucocorticoids
- Pituitary adenomas account for 70% of patients with endogenously elevated cortisol (15% primary adrenal tumor, 15% ectopic ACTH production)
- Iatrogenic supplementation of glucocorticoids is the most common cause of hypercortisolism.

EPIDEMIOLOGY

- Cushing syndrome: 13/1,000,000
- Cushing syndrome is 5–10× more common in women than men
- In patients with difficult-to-manage diabetes, prevalence is 2–5%

RISK FACTORS

- Iatrogenic exposure to glucocorticoids, including steroid creams
- Hypersecretion of pituitary ACTH by pituitary tumor
- Primary cortisol production by an adrenal adenoma or carcinoma
- Ectopic ACTH production: Nonendocrine tumors (small cell lung cancer, thymomas, ovarian tumors)

Genetics

- Associated with MEN type 1
- Carney complex
- Mutation of GNAS1 gene causing McCune-Albright syndrome

GENERAL PREVENTION

Diligent management of iatrogenic administration of glucocorticoids; avoid excess

Pediatric Considerations

Very rare in infancy and childhood

Pregnancy Considerations

Pregnancy can worsen course of the disease

PATHOPHYSIOLOGY

- Elevated serum levels of cortisol, either from exogenous intake or endogenous production
- Cushing disease: Unopposed adrenal stimulation from excess circulating ACTH:

– ACTH, produced in the anterior pituitary, stimulates cortisol production in the zona fasciculate of the adrenal cortex.

– ACTH release is governed by CRH, produced in the hypothalamus.

– Cortisol, through feedback inhibition, regulates CRH and ACTH production

COMMONLY ASSOCIATED CONDITIONS

- Pituitary tumor
- Concomitant steroid consumption (ie, transplant antirejection regimen, autoimmune disorder therapy)
- Adrenal adenoma/carcinoma

DIAGNOSIS

HISTORY

- Progressive weight gain
- Fatigue
- Proximal limb weakness
- Skin abnormalities
- Abnormal menses/decreased libido
- Impotence
- New-onset hypertension/diabetes mellitus
- Frequent infections
- Osteopenia/osteoporosis

PHYSICAL EXAM

- Obesity/weight gain (80%)
- Thin skin with striae (abdominal) (70%)
- Moon facies (75%)
- Buffalo hump (50%)
- Hypertension (75%)
- Truncal obesity (50%)
- Amenorrhea (60%)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC, serum glucose, electrolytes, lipids
  – Hyperglycemia, hypokalemia, neutrophilia, lymphopenia, hyperlipidemia
- Initial screen: Late-night salivary cortisol or 24-hr urinary free cortisol. Does not distinguish etiology of hypercortisolism
- Elevated late-night salivary cortisol sensitivity: 93%; specificity 93% (contact lab for processing instructions) levels <1.3 ng/mL (RIA) or 1.5 ng/mL (competitive binding assay) ex-

clude Cushing syndrome.

- 24-hr urinary free cortisol with 24-hr creatine clearance: Obtain at least 3 samples to rule out intermittent hypercortisolemia; sensitivity 90–97%; specificity 85–96%.
- Late-night serum cortisol on 3 consecutive evenings or midnight plasma cortisol sensitivity 90%; specificity 96%:
  - Persistently elevated serum cortisol implies Cushing syndrome; nadir of serum cortisol is maintained in obese patients, but not in those with Cushing.
- Plasma ACTH concentration: Elevated in Cushing disease, decreased in adrenal adenoma or carcinoma, nodular adrenal hyperplasia, steroid use
- Dexamethasone suppression test: Sensitivity 95%, specificity 70%:
  - Low-dose dexamethasone suppression test is not currently used for 1st-line test. High-dose dexamethasone suppression test distinguishes Cushing disease and syndrome.
  - Low-dose dexamethasone suppression testing: 1.0 mg of dexamethasone is given between 11 PM and 12 AM; 8 AM serum cortisol and salivary cortisol are obtained. Patients without Cushing syndrome have suppression of AM cortisol
  - High-dose dexamethasone suppression test: 0.5 mg Dexamethasone is given q6h for 8 doses, with serum cortisol measured at 2 and 6 hrs after last dose.

Imaging

- Brain MRI for pituitary lesion
- Abdominopelvic CT: Adrenal protocol

Diagnostic Procedures/Surgery

Inferior petrosal vein sampling following CRH stimulation

Pathological Findings

- Pituitary adenoma
- Adrenal adenoma or carcinoma
- Micronodular or macronodular adrenal hyperplasia
- Nephrosclerosis

DIFFERENTIAL DIAGNOSIS

- Alcoholism (pseudo-Cushing)
- Anorexia nervosa
- Bulimia
- Depression
- Hypertension
- Obesity
- Polycystic ovarian syndrome

TREATMENT

- Steroid replacement for the 1st 12 mo following surgical resection: A majority of patients will experience adrenal insufficiency in the early postoperative period
- Potassium supplementation and high-protein diet

MEDICATION

- Mitotane: Suppresses cortisol secretion by inhibiting 11-hydroxylase
- Ketoconazole: Inhibits p450 enzymes, resulting in cortisol consumption
- Metyrapone: Inhibits 11-hydroxylase activity

SURGERY/OTHER PROCEDURES

- Transsphenoidal resection of pituitary adenoma: 5% recurrence
- Bilateral adrenalectomy: Reserved for those who fail pituitary surgery
- Adrenalectomy for primary adrenal tumors

ADDITIONAL TREATMENT

Pituitary irradiation is effective in 15% of refractory cases; not considered primary therapy.

ONGOING CARE

PROGNOSIS

- Excellent with recognition and appropriate treatment
- 20% recurrence after surgery

COMPLICATIONS

- Adrenal insufficiency requiring temporary or life-long glucocorticoid replacement
- Osteoporosis
- Increased infection risk
- Nelson syndrome (pituitary tumor) after bilateral adrenalectomy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Invasive monitoring may be required in those patients developing acute postoperative adrenal insufficiency.
- Periodic laboratory follow-up
- Re-evaluation of previously treated patients with any new-onset symptoms

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Cushing Syndrome Algorithm
- Dexamethasone Suppression Test
- Urine Studies

CODES

ICD9

255.0 Cushing’s syndrome

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- CBC: Complete blood count
- CRH: Corticotropin releasing factor
- CT: Computed tomography
- MEN: Multiple endocrine neoplasia
- MRI: Magnetic resonance imaging

CYSTITIS, GENERAL

Deborah T. Glassman, MD
Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Inflammatory process of the bladder
- 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, IC or due to other irritants (drugs), or a complication of another illness

Geriatric Considerations

Bacterial cystitis increases with advancing age.

Pediatric Considerations

- Cystitis in children is rare. Bacterial cystitis in an infant necessitates a urologic workup.
- Eosinophilic cystitis most common in this age group.

Pregnancy Considerations

- Bacterial cystitis in pregnancy requires appropriate antibiotic coverage to prevent complications to the mother or fetus.
- Screening and treatment of asymptomatic bacteruria in pregnant women is encouraged to prevent the development of cystitis or more severe UTI and fetal harm.

EPIDEMIOLOGY

- 33% of women experience an episode of bacterial cystitis by age 24. 50% of women will have an episode in their lifetime.
- Annual incidence of 0.5–0.7 infections per patient-year in this group
- Bacterial cystitis in healthy men is rare:
  - Annual incidence <0.01% in men aged 21–50 yrs.
- Hemorrhagic cystitis occurs in ~15% of patients who underwent bone marrow transplantation:
  - Adenovirus in the urine preceding transplantation is greatest associated factor.
- Reported rates of IC from 52/100,000 to 67/100,000

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

GENERAL PREVENTION

- Infectious: Minimize bacterial exposure, avoid indwelling Foley catheter if possible; intermittent catheterization
- Hemorrhagic: Avoid radiation or cyclophosphamide/Iphosphamide exposure

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.
- Increases in tumor necrosis factor in bladder mucosa
- Increased mast cell degranulation and histamine release
- Changes in purinergic signalling

COMMONLY ASSOCIATED CONDITIONS

See “Differential Diagnosis.”

DIAGNOSIS

HISTORY

- Characterization of symptoms: Frequency, urgency, dysuria, suprapubic pain, perineal or scrotal pain, dyspareunia
- Exposure to radiation:
  - Obliterative endarteritis causing ischemia
  - May occur several years after exposure.
- Exposure to cyclophosphamide/Iphosphamide:
  - Common cause of hemorrhagic cystitis thought to be due to acrolein metabolite dwelling in bladder
- History of UTI; previous treatments
- If patient immunosuppressed:
  - Suspect viral or fungal infection
- Travel history to areas with parasites
- Use of personal hygiene products that can cause local irritation (douches, vaginal preparations)
- Indwelling catheters
- History of hematuria
- History of fevers, chills
- Symptoms of vaginitis or discharge present

PHYSICAL EXAM

- Vital signs: Fever, tachycardia (from anemia or sepsis), pallor (anemia due to hemorrhagic cystitis)
- Abdomen: Suprapubic tenderness, costovertebral angle tenderness
- GYN: Bladder or vaginal tenderness, vaginal discharge
- GU, male: Tender and/or boggy prostate, testicular tenderness, penile discharge

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis with microscopy
- Urine culture:
  - Anaerobic, aerobic
  - Fungal and viral, if high suspicion
- CBC: Anemia in hemorrhagic cystitis, leukocytosis in infectious cystitis
- Creatinine
- Urine cytology: If patient with symptoms of cystitis, risk factors for TCC and negative workup for UTI or overactive bladder
- Urine culture for Mycobacterium in presence of sterile pyuria and suspicion for TB
- Vaginal discharge evaluation if present

Imaging

- CT urogram or US:
  - To rule out associated upper-tract pathology
  - May show thickened bladder wall or filling defect such as blood clots or tumor
- Cystogram:
  - 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
- Bladder biopsy: To rule out carcinoma in situ or for tissue culture

Pathological Findings

- Evidence of acute or chronic inflammation
- Michaelis-Gutmann bodies in malakoplakia

DIFFERENTIAL DIAGNOSIS

- Anxiety
- Balanitis
- Bladder cancer or other malignancy

- Chronic pelvic pain syndromes
- Cystitis cystica, cystitis glandularis
- Diabetes insipidus, excess fluid intake
- Diabetes mellitus
- Diuretics, excessive caffeine, alcohol
- Eosinophilic cystitis
- Epididymitis
- Extrinsic bladder compression (eg, pelvic tumor, radiation-induced fibrosis)
- Genital herpes
- Hemorrhagic cystitis
- Infectious cystitis: Bacterial, viral, parasitic, fungal
- IC (painful bladder syndrome)
- Neurogenic bladder, chronic urinary retention
- Overactive bladder
- Prostatitis
- Prostatodynia
- Pyelonephritis
- Urethral syndrome
- Urethritis (eg, gonorrhea, chlamydia)
- Urinary calculi
- Vulvovaginitis and/or pelvic inflammatory disease

TREATMENT

- Encourage adequate hydration.
- Proper toilet hygiene for females to limit urethral exposure to pathogens
- Encourage voiding immediately before and after sexual activity in females.

MEDICATION

- Antimicrobials for bacterial cystitis
- TMP-SMZ for 3 days is a standard therapy for simple uncomplicated bacterial cystitis in females.
- Other combinations may include cephalexin, 250–500 mg q6h for 1–3 days; ciprofloxacin, 250–500 mg q12h for 1–3 days; nitrofurantoin (macrocrystals), 100 mg q12h for 7 days; ofloxacin, 200 mg q12h for 1–3 days
- Phenazopyridine (Pyridium) for relief of dysuria:
  - Pregnancy category B
  - Contraindicated in glomerulonephritis, renal insufficiency or failure, severe hepatitis, G6PD deficiency

– Side effects: Orange urine, renal failure, rash, nausea, headache, vertigo, hemolytic anemia, methemoglobinemia

– Dose:

Adults: 200 mg PO t.i.d.

Pediatric: 4 mg/kg PO t.i.d.

SURGERY/OTHER PROCEDURES

- Cystoscopy with biopsy to diagnose cystitis cystica or glandularis
- Cystoscopy with hydrodistention to diagnose IC; look for characteristic glomerulations.
- Cystoscopy with clot evacuation and electro- or laser fulguration for hemorrhagic cystitis
- Cystectomy for refractory hemorrhagic cystitis

ADDITIONAL TREATMENT

RADIOTHERAPY

May induce radiation cystitis

Additional Therapies

- Intravesical installations of alum, silver nitrate for hemorrhagic cystitis
- Hyperbaric oxygen for hemorrhagic cystitis.

Cranberry tablets for prevention of recurrent bacterial cystitis

ONGOING CARE

PROGNOSIS

Simple bacterial cystitis prognosis is excellent.

COMPLICATIONS

- Depends on etiology of cystitis
- Untreated simple bacterial cystitis can cause pyelonephritis.
- Hemorrhagic cystitis may recur and/or be refractory to therapy, resulting in multiple transfusions or requiring cystectomy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Urinalysis
- History and physical
- Females with >3 episodes of cystitis per year should be considered candidates for prophylaxis:

– Prior to institution of therapy, exclude anatomic abnormality (eg, stones, reflux, fistula).

– Single dosing at bedtime or at time of intercourse is recommended.

– Common oral agents are TMP-SMZ (40 mg/200 mg), nitrofurantoin (100 mg), and cephalexin (250 mg).

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bacteruria and Pyuria
- Cystitis, Hemorrhagic
- Cystitis, Radiation
- Interstitial Cystitis
- Prostatitis, General
- Pyuria Algorithm
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

- 595.0 Acute cystitis
- 595.2 Other chronic cystitis
- 595.9 Cystitis, unspecified

ABBREVIATIONS

- CT: Computed tomography
- GU: Genitourinary
- GYN: Gynecology
- IC: Interstitial cystitis
- TB: Tuberculosis

- TCC: Transitional cell carcinoma
- US: Ultrasound
- UTI: Urinary tract infection

CYSTITIS, HEMORRHAGIC (INFECTIOUS, NONINFECTIOUS, RADIATION)

Gaurav Bandi, MD

BASICS

DESCRIPTION

HC is an acute or insidious inflammation of the bladder leading to diffuse bleeding from the luminal surface.

EPIDEMIOLOGY

- Cyclophosphamide-induced HC: 5–7%
- Radiation-induced HC: 10–15% in patients with history of pelvic radiation

RISK FACTORS

- No age, sex, or race predilection
- Previous treatment with oxazaphosphorine alkylating agents (for lymphoproliferative disorders, solid tumors, collagen diseases, bone marrow transplant recipients) such as cyclophosphamide, isophosphamide
- History of prior pelvic radiation (prostate and cervical cancers)
- History of bone marrow transplant

GENERAL PREVENTION

- Patients treated with cyclophosphamide once had a very high incidence of HC (~70%), with high mortality rates (as high as 75%) if it became severe:

)[A]

  – Mercaptoethane (Mesna) and N-acetylcysteine (Mucomyst) bind to acrolein, creating nontoxic compounds.

)[A], sodium pentosan polysulfate (Elmiron), and amifostine (Ethyol) have been investigated in prevention of radiation-induced cystitis.

PATHOPHYSIOLOGY

- Direct contact by toxin (acrolein) to the bladder wall is believed to be the most common cause of cyclophosphamide-induced HC. Platelet-activating factor, nitric oxide, tumor necrosis factor-, and IL-1 are key mediators.
- Radiation-induced cystitis results from a progressive obliterative endarteritis leading to mucosal ischemia, ulceration, and neovascularity.
- Penicillin toxicity is immune-mediated, whereas danazol toxicity is likely from damaging vascular changes.

COMMONLY ASSOCIATED CONDITIONS

See “Differential Diagnosis.”

DIAGNOSIS

HISTORY

- Gross hematuria (with or without pain):
  - Mild: Easily controlled, no acute hematocrit change
  - Moderate: Drops hematocrit, requiring <6 U PRBCs and local therapy
  - Severe: Refractory to simple therapies, requires >6 U PRBCs
- Frequency, urgency, dysuria
- Urinary retention from clots
- Occasional mucosal sloughing
- Suprapubic pain
- Fevers with chills
- Previous history of cyclophosphamide therapy, pelvic radiation, bone marrow transplant

PHYSICAL EXAM

- Suprapubic pain/mass: Distended bladder, infected and/or clot-filled bladder
- Signs and symptoms of hypovolemia, hemorrhagic shock, or anemia if severe
- Ocular infections: Common with adenovirus infection
- Large hypertrophied tongue: Amyloidosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine for analysis, cytology, and cultures (including fungal and viral cultures, if indicated)
- Coagulation factors (especially platelets, which can be depleted)
- Serial hematocrits
- Serum creatinine
- 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 thickened irregular bladder wall, and/or small capacity.

Diagnostic Procedures/Surgery

Cystoscopy ± biopsy, ± clot evacuation:

- Consider electro- or laser fulguration if focal bleeding visualized.

Pathological Findings

- Urothelial damage: Edema, necrosis, ulceration, hemorrhage, leukocyte infiltration, and neovascularization
- May reveal amyloid deposits; eosinophilic inflammatory response of schistosomiasis; IgG, IgM, and C3 depositions; penicillin toxicity; whitish pseudomembranes or plaques of fungal infections; inclusion bodies of viral infections

DIFFERENTIAL DIAGNOSIS

- Oxazaphosphorine agents (cyclophosphamide and isophosphamide):
  - Most common cause of severe HC
  - Acrolein, a liver metabolite of the agents, is the toxin believed to be directly implicated.
  - Higher dosages, IV route of administration (vs. oral), and increased contact time between the bladder wall and the acrolein (because of dehydration and/or infrequent emptying) all worsen HC.
- Pelvic radiation:
  - Usually initiated by bladder distension, minor trauma, infection, instrumentation
  - Acute episodes wane within 12–18 mo
  - Can occur as late as 15–20 yr after exposure
- Viral infection:
  - Adenovirus 11 and 35, influenza A, CMV, BK and JC viruses
  - 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, Staphylococcus saprophyticus, Proteus, Klebsiella, Mycobacterium tuberculosis
  - Fungal: Candida, Aspergillus, Cryptococcus, Torulopsis
  - Parasitic: Schistosoma haematobium, Echinococcus granulosus
- Systemic hematologic disease: Rare; often refractory to fulguration and irrigation
- Systemic amyloidosis associated with rheumatoid arthritis or Crohn disease
- Chemical toxins:
  - Anilines, toluidines and chlordimeform are common industrial exposures (dyes, pesticides).
  - Overdoses of methenamine mandelate; accidental urethral instillation of gentian violet douche or nonoxynol-9 contraceptive suppositories

- Thiotepa and acetic acid intravesical instillations
- Medications:
  - Penicillin, piperacillin, methicillin, carbenicillin
  - Danazol, bleomycin, allopurinol, busulfan
- Prolonged high-altitude travel (Boon disease)
- Carcinomas of the urinary tract
- Acute UTIs
- Benign prostatic hypertrophy
- Trauma to the urinary system
- Arteriovenous malformation, vascular fistulae

TREATMENT

- Catheterization; initially bladder irrigation with normal saline to clear bleeding and evacuate clots
- Remove the offending toxin.
- Treat the infectious agent.
- Hydration and diuresis
- Blood products transfusion, when necessary

MEDICATION

- Alum irrigation often considered 1st-line:
  - Astringent, forms precipitates over bleeding surface
  - 1–4% solution at 300 to 1,000 mL/h
  - No need for anesthesia
  - Adverse effects: Spasms, precipitation and clogged catheters, rare encephalopathy from aluminum toxicity
- -Aminocaproic acid (Amicar):
  - Inhibits clot lysis by urinary urokinase
  - Can be given orally or parenterally
  - Contraindicated in upper-tract bleeding, as dense clots can lead to ureteral obstruction
- Silver nitrate instillation:
  - 0.5–1.0% solution in bladder for 10–20 min, followed by saline flush
  - Causes a chemical cauterization
  - Painful, requires anesthesia
  - Adverse effect: Crusty build-up can clog catheters
  - Duration of response is often short

- Prostaglandin instillation:
  - Carboprost tromethamine (synthetic PGF2) 0.1–0.8 mg/dL solution. Dwell for 1–4 hr, 4 times a day for 5–7 days
  - Stabilizes membranes, decreasing edema; causes vasoconstriction and platelet aggregation
  - Low morbidity: No anesthesia required, no precipitate forms, so no clogging of catheters
  - Adverse effects: Cost, requires intensive nursing care, moderate bladder spasms
- Phenol instillation:
  - 30 mL of 100% phenol in 30 mL of glycine for 1 min, followed by ethanol and saline washes
  - Destroys urothelium, not muscularis; less bladder fibrosis than with formalin
  - Painful, requires anesthesia
  - Duration of response is often short
- Formalin instillation:
  - 1–4% solution of 50 mL for 5–30 min, with patient in reverse Trendelenburg to minimize vesicoureteral reflux
  - Check cystogram before instillation to rule out reflux; may need to occlude ureter with balloon to prevent potentially fatal renal absorption
  - Hydrolyzes proteins, coagulating mucosa and submucosa; 80% effective
  - Excruciatingly painful, requires anesthesia
  - Adverse effects: Reflux could cause ureteral fibrosis and obstruction or papillary necrosis; extravasation could cause peritonitis and/or fistulas

SURGERY/OTHER PROCEDURES

- Should be considered only after all conservative modalities have failed, and if the patient is unstable
- Bilateral percutaneous nephrostomy tubes with occlusive balloons decrease the exposure of nascent clots to urokinase, allowing bladder to self-tamponade.
- Supravesical urinary diversion, cutaneous ureterostomy, ureterosigmoidostomy, cystectomy

ADDITIONAL TREATMENT

Contraindicated and is a recognized cause of HC

Additional Therapies

- Hyperbaric oxygen:
  - Promotes granulation tissue and neovascularization, causes vasoconstriction

  - Better for radiation-induced cystitis
  - Requires a hyperbaric chamber, which may not always be readily available

)[B]; helps acutely in most cases, but bleeding often recurs after treatment

- Selective hypogastric artery embolization:
  - Can be done under local anesthesia on risky patients
  - Complications range from gluteal claudication to bladder necrosis, lower limb paralysis, or impotence
  - Low success rate, as most bleeding is venous

ONGOING CARE

PROGNOSIS

- Related to the successful treatment of etiology of HC
- Long term increases risk of secondary urothelial malignancy

COMPLICATIONS

- Secondary UTIs from prolonged catheterization
- Bladder perforation
- Bladder fibrosis with small, noncompliant bladder that may need further surgical reconstruction
- Vesicoureteral reflux resulting from bladder fibrosis
- Anemia, renal failure
- Increased risk for transitional cell carcinoma from cyclophosphamide and similar agents; may be years later

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Repeated hematocrit, renal function, urine culture, and sensitivities
- Maintain sterile urine.
- Continue hydration for many days after bleeding ceases as rebleeding is common.
- Evaluate long-term sequelae after acute episode.

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Chemotherapy Toxicity, Urologic Toxicity
- Cystitis, Radiation
- Cystitis, Viral
- Cytoxan Toxicity
- Polyoma Virus (BK, JC), Urologic Consideration

CODES

ICD9

595.82 Irradiation cystitis

ABBREVIATIONS

- BMT: Bone marrow transplantation
- HC: Hemorrhagic cystitis
- IV: Intravenous
- PRBCs: Packed red blood cells
- UTI: Urinary tract infection

CYSTOCELE

Steven P. Petrou, MD

Alexandra E. Rogers, MD

BASICS

DESCRIPTION

Prolapse of the bladder into the vagina

EPIDEMIOLOGY

- Reported in the context of surgical treatment
- 11% lifetime risk of surgery for prolapse or incontinence
- ~50% of mature women have some degree of anterior prolapse.
- Few reports due to inconsistent symptoms and requirement of a vaginal exam

RISK FACTORS

- Vaginal delivery (nerve, muscle, and tissue damage from trauma)
- Parity (tissue softening from progesterone)
- Aging
- Pelvic surgery (hysterectomy)
- Neurogenic (multiple sclerosis, spinal dysraphism)
- Conditions causing increased intra-abdominal pressure (COPD, BOO, ascites, obesity, constipation)
  - Congenital (Ehlers-Danlos syndrome)

Genetics

Connective tissue disorders, bladder exstrophy, Hispanic descent

PATHOPHYSIOLOGY

- Weakening of supporting and suspending structures: Cardinal ligaments, uterosacral ligaments, pubourethral ligaments, urethropelvic ligaments, levator ani muscles, vesicopelvic fascia
- Defect location:
  - Central: Attenuation of the perivesical or pubocervical fascia in the midline under the bladder base
  - Lateral: Disruption of lateral attachments of the vesicopelvic fascia

COMMONLY ASSOCIATED CONDITIONS

Stress and urge incontinence, pelvic pain, multicompartment prolapse, BOO, urinary retention

DIAGNOSIS

HISTORY

- Symptoms and signs: Pelvic pressure, vaginal bulging sensation, stress/urge/overflow incontinence, obstructive voiding symptoms, recurrent cystitis
- Previous pelvic/vaginal surgical procedures
- Hormonal status
- Obstetric history
- Comorbidities (COPD)

PHYSICAL EXAM

- Baden and Walker grading system based on degree of bladder descent with respect to the hymenal ring:
  - Grade 0: Bladder at the vaginal fornix
  - Grade 1: Leading edge of the prolapse stays within the upper half of the vagina
  - Grade 2: Descent of the bladder to the hymen
  - Grade 3: Descent of the bladder 1 cm beyond the hymen
  - Grade 4: The bladder extends outside of the hymen at rest
- POP-Q staging objectively quantifies POP accounting for patient positioning and assessing 9 areas during a sustained Valsalva maneuver:
  - Areas Aa (bladder neck) and Ba (upper anterior vaginal wall) correspond to cystocele stage
  - Stage 0: Vaginal fornix
  - Stage 1: Hymenal ring to 1 cm from hymenal ring
  - Stage 2: Hymenal ring to +1 cm from hymenal ring
  - Stage 3: Half of vaginal length (+1–+3 cm)
  - Stage 4: Total vaginal length (+3–+6 cm)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis
- Urine culture as indicated

Imaging

- Cystogram
- Voiding cystourethrogram
- Pelvic US: Operator dependent; poor soft tissue visualization
- Dynamic MRI: Examines other pelvic floor pathology including hypermobility and ureteral obstruction without radiation exposure

Diagnostic Procedures/Surgery

- Pelvic exam

- PVR assessment (catheterization/US)
- Video urodynamics

DIFFERENTIAL DIAGNOSIS

- Cystocele vs. enterocele vs. rectocele
- Urethral diverticulum
- Vulva cystic masses: Sebaceous cysts, apocrine sweat gland cyst, Bartholin duct cyst, Gartner duct cyst
- Vulva solid tumors: Leiomyoma, fibroma, lipoma

TREATMENT

- Kegel exercises
- Pessary

MEDICATION

- Hormonal replacement

SURGERY/OTHER PROCEDURES

- Preoperative preparation:
  - Hormonal replacement
  - Bowel preparation optional
  - DVT prophylaxis
- Perioperative 24 hr:
  - Antibiotic prophylaxis
  - Vaginal packing impregnated with estrogen cream
  - Keep urethral catheter overnight
  - If indwelling urethral catheter required >24 hr consider suprapubic tube or intermittent catheterization
- Transabdominal vs. vaginal repairs
- Efficacy between approaches debatable due to limited controlled trials
- Advantage of vaginal approach: Fewer wound complications, less postoperative pain, potential lower cost and shorter hospital stay
- Transabdominal repair:
  - Apposition of vaginal wall and fascia to the lateral pelvic wall by Burch colposuspension (to Cooper's ligament) or Richardson paravaginal repair (to obturator fascia)
  - Only repair lateral defects
- Transvaginal repair:
  - Central defect repair: Reduced by approximating the perivesical fascia in the midline with horizontal mattress sutures

– Lateral defect repair: Reattachment of the fascia to the arcus tendineus fascia pelvis with sutures (transvaginal paravaginal)

- Grade 4 cystocele: Perform a simultaneous repair of all defects
- Consider a concomitant anti-incontinence operation in patients with urethral or bladder neck malposition, hypermobility, and/or history of urinary incontinence

ADDITIONAL TREATMENT

Closure or removal of the vagina (colpocleisis or colpectomy):

- Efficacious option in geriatric women but disadvantage of terminating coital function and risk of developing stress incontinence
- Pessary:
  – Used in poor surgical candidate but risk of vaginal discharge, inflammation, vesicovaginal fistula formation, erosion, ulceration, or uterine/cervical incarceration

ONGOING CARE

PROGNOSIS

- Traditional anterior colporrhaphy and paravaginal repair of cystocele are associated with recurrence rates as high as 30–70%
- Mixed data with regards to long-term benefit and safety of synthetic mesh and biologic graft utilization

COMPLICATIONS

- Vaginal mucosa venous congestion leading to edema, serous seepage, ulceration, or bleeding
- Postoperative early: Pain, bladder dysfunction, infection, fistula formation, and ureteral obstruction
- Postoperative late: Vaginal shortening/narrowing, dyspareunia, recurrent pelvic organ pro-lapse, and erosion of suture material
- Voiding dysfunction
- Recurrent UTI

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Evaluation for recurrent incontinence, retention, prolapse, or recurrent UTI
- Consider serial PVR on serial exam

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Pelvic Organ Prolapse Quantification System (POPQ)
- Pelvic Prolapse (Cystocele and Enterocoele)
- Vaginal Pessaries, Urologic Considerations
- Vaginal Wall Prolapse

CODES

ICD9

- 618.01 Cystocele, midline
- 618.02 Cystocele, lateral

ABBREVIATIONS

- BOO: Bladder outlet obstruction
- COPD: Chronic obstructive pulmonary disease
- DVT: Deep vein thrombosis
- MRI: Magnetic resonance imaging
- POP-Q: Pelvic organ prolapse quantification
- PVR: Post void residual
- US: Ultrasound
- UTI: Urinary tract infection

DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM, UROLOGIC CONSIDERATIONS

Neil E. Fleshner, MD, MPH
Leonard G. Gomella, MD

BASICS

DESCRIPTION

- DVT: Aggregation of platelets and fibrin within a deep pelvic or lower extremity vein that may lead to venous obstruction
- PE: Migration of a thrombus within the pulmonary artery or its branches that has arrived to its location by blood flow. Often arises from a DVT. Can be an acute life-threatening illness.

EPIDEMIOLOGY

- DVT:
  - 2.5 million per year in US, 0.5–2.7% in urologic procedures
- PE:
  - 100,000 deaths per year and contribution to another 100,000

RISK FACTORS

- Acute medical illness
- Central venous catheterization
- Estrogen-containing oral contraception or hormone replacement therapy
- Heart or respiratory failure
- Immobility (paresis, long plane flights)
- Increasing age
- Inflammatory bowel disease
- Inherited or acquired thrombophilia
- Malignancy and related therapy (hormonal, chemotherapy, radiotherapy)
- Myeloproliferative disorders
- Nephrotic syndrome
- Obesity
- Paroxysmal nocturnal hemoglobinuria
- Pregnancy and the postpartum period
- History of venous thromboembolism
- Selective estrogen receptor modulators
- Smoking

- Surgery (especially deep pelvic, hip and lower extremity)
- Trauma (major or lower extremity)
- Varicose veins

Genetics

- Inherited deficiency/disorder
- Proteins C, S deficiency
- Antithrombin III deficiency: Can be decreased after surgery, congenitally, or through trauma
- Plasminogen deficiency: Abnormal structure

GENERAL PREVENTION

DVT prophylaxis:

- Mechanical (nonpharmacologic) therapies: Early postoperative ambulation, graduated compression stockings, and intermittent pneumatic compression
- Pharmacologic: Low-dose unfractionated heparin and low-molecular-weight heparin as appropriate (see “Deep Venous Thrombosis AUA Guidelines”)

PATHOPHYSIOLOGY

- Most PEs arise from DVT
- DVT:
  - Initiating factors of Virchow triad: Stasis, intimal injury, and hypercoagulability
  - Stasis: Stagnant hypoxemia causes endothelial injury
  - Injury: Platelet accumulation and fibrin deposition
  - Hypercoagulability: Regional activation of coagulation cascade: Obstruction, edema, pain
- Should differentiate from superficial thrombophlebitis/thrombosis that does not usually lead to DVT or PE

DIAGNOSIS

HISTORY

- Recent high-risk surgery or risk factors for venous thrombosis
- DVT:
  - History of prolonged immobilization, postoperative statis, especially in patient with risk factors
  - Complaint of calf pain/swelling especially with ambulation
- PE:
  - Must have high clinical suspicion with above history
  - Acute onset of dyspnea, tachycardia, arrhythmia

PHYSICAL EXAM

- DVT: Determined by level of obstruction
  - Inspection: Unilateral edema, discoloration below level of (occlusion), dilated superficial veins
  - Palpation: Tender cord or knot; Homans sign (limitation of passive dorsiflexion of foot, 55% unreliable)
- PE:
  - Inspection: Cyanotic, dyspneic, prominent jugular veins, hemoptysis, tachypnea
  - Auscultation: Pleural rub, rales, S3–S4 heart sounds

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- DVT:
  - D-dimers: Sensitivity approaches 95% for ELISA method
- PE:
  - ABG: Increased P(A-a)O2
  - PaO2 <80 mm Hg

)[A]

Imaging

- DVT:
  - Contrast venography (gold standard): Invasive, expensive, not always available, contrast risks
  - Doppler US: 90% accurate above knee, versatile, noninvasive, painless
  - Venous duplex scanning: More accurate than Doppler and plethysmography
  - I-125 fibrinogen scan:

    No longer available secondary to hepatitis risks with human fibrinogen
- PE:
  - CXR:

    Generally unremarkable; small unilateral effusion

    Westermark sign (asymmetric vascular markings with segmental or lobar ischemia)
  - Ventilation/perfusion scan:

    A perfusion defect in 1 pulmonary segment and all unmatched with ventilation defects supports a high probability of PE.

)[A]

- CT:

– Most common current test

)[A]

Diagnostic Procedures/Surgery

Pulmonary angiogram is the gold standard but rarely done.

Pathological Findings

Thrombi are woven congealed mass of fibrin and platelets.

DIFFERENTIAL DIAGNOSIS

- DVT: Cellulitis, thrombophlebitis, muscle sprain/strain, claudication, lymphedema
- PE: Pneumonitis/pneumonia, pneumothorax, CHF, esophageal perforation, myocardial infarction

TREATMENT

ALERT

DVT and especially 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.

- DVT: Extremity elevation, bed rest, pain relief
- PE: Oxygen therapy, fluid resuscitation; maintain cardiac output with pressors as needed

MEDICATION

- DVT:
  - Proximal to knee: Anticoagulation with IV heparin for therapeutic PT for 5 days. Start Coumadin on day 1 and continue for 3–6 mo, depending on risk.
  - Distal to knee: Carries low risk of embolization but should be monitored noninvasively over next 2 wk
- PE:
  - Systemic anticoagulation as for DVT
  - Therapy with streptokinase (rare)

SURGERY/OTHER PROCEDURES

- DVT:
  - Thrombectomy: Rarely needed
  - IVC filter: Used as prophylaxis in high-risk or multiple-trauma patient; useful if anticoagulation contraindicated
- PE:
  - Pulmonary embolectomy; considered rarely for patient who remains in shock despite medical therapy (rare)

ADDITIONAL TREATMENT

Anticoagulation therapy will last 3–6 mo at least.

ONGOING CARE

PROGNOSIS

Good with prompt recognition and therapy

COMPLICATIONS

- DVT:
  - Pulmonary embolus; recurrent venous thrombosis
  - Postphlebitic syndrome: Caused by destruction of valves and chronic pain, edema, and skin changes
- PE:
  - Death; pulmonary infarction; pain; arrhythmia, shortness of breath
- PE and DVT:
  - Both require anticoagulation with its associated risk factors (ie, increased bleeding risk from minor trauma), increased healthcare costs, and prolonged or rehospitalization

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Measurement of INR will be required for patients while on warfarin therapy.

REFERENCES

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See Also (Topic, Algorithm, Electronic Media Element)

Deep Venous Thrombosis, Prophylaxis, AUA Guidelines

CODES

ICD9

- 453.40 Venous embolism and thrombosis of unspecified deep vessels of lower extremity
- 453.41 Venous embolism and thrombosis of deep vessels of proximal lower extremity
- 453.42 Venous embolism and thrombosis of deep vessels of distal lower extremity

ABBREVIATIONS

- CHF: Congestive heart failure
- CT: Computed tomography
- CXR: Chest x-ray
- DVT: Deep venous thrombosis
- LDUH: Low-dose unfractionated heparin
- LMWH: Low-molecular-weight heparin
- PE: Pulmonary embolus
- US: Ultrasound

DETRUSOR OVERACTIVITY

Melissa R. Kaufman, MD
Douglas F. Milam, MD

BASICS

DESCRIPTION

- OAB syndrome presents with symptoms of urinary urgency, usually combined with frequency and nocturia:
  - Either associated with urinary incontinence (OAB wet) or without urinary incontinence (OAB dry)
  - Key symptom is urinary urgency.
  - Urgency is defined as a sudden compelling desire to void that is difficult to defer.
- DO is a urodynamic observation characterized by involuntary detrusor (bladder muscle) contractions during bladder filling:
  - DO is classified as neurogenic when associated with a relevant neurologic condition and idiopathic when there is no defined cause.

EPIDEMIOLOGY

Current population-based estimates from Europe and the US suggest 11–17% of adults display OAB symptoms.

Geriatric Considerations

- Prevalence of OAB increases with age, with over 1/3 of the population over 75 yr of age affected. Dementia causing loss of central bladder reflex inhibition is a common cause of OAB.
- Urinary incontinence has been found independently associated with falls and fractures in elderly women.
- Can be a cause of incontinence and hygienic concern

RISK FACTORS

Several comorbid medical conditions are associated with OAB including diabetes:

- Bladder, prostate, and anti-incontinence surgeries are risk factors for the development of de novo symptomatic OAB.

GENERAL PREVENTION

- Dramatic influence on patient QOL:
  - OAB syndrome significantly impacts overall QOL measures, depression-related symptoms, sleep disturbance, sexual dysfunction. Urinary urgency, frequency, and incontinence can also result in social isolation.
- UTIs

- Skin breakdown

PATHOPHYSIOLOGY

2 prevailing theories: Neurogenic and myogenic:

- Neurogenic theory implicates hyperreflexic detrusor in patients with known or occult neurologic lesion.
- Myogenic theory entails smooth muscle dysfunction in the detrusor that bypasses normal neural regulation.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- UTI
- Multiple sclerosis
- Parkinson disease
- Dementia
- Stroke
- Spinal cord injury
- Spinal disc disease
- Myelodysplasia
- Transverse myelitis
- Bladder cancer and carcinoma in situ
- Obstructive prostatism

DIAGNOSIS

HISTORY

- Gather details of voiding habits including frequency, incontinence episodes, and associated symptoms such as dysuria, hematuria, pain, stress urinary incontinence:
  - Primary aim is to rule out any severe pathologic conditions that may present with urinary urgency symptoms, such as urinary infections or bladder cancer.
- Past medical history:
  - Neurologic disorders
  - Trauma
- Past surgical history:
  - Pelvic surgeries including gynecologic procedures
  - Spinal surgeries
  - Bladder surgeries
  - Prostate surgeries
  - Anti-incontinence surgeries or procedures

- Medications:
  - Diuretic use
  - Psychoactive drugs
- Social history:
  - Smoking history (risk for urologic cancer)
  - Occupational history (toxin exposures)
  - Alcohol use (promotes polyuria)
  - Caffeine use (promotes diuresis)
- Family history:
  - Particularly important for cancer assessment

PHYSICAL EXAM

- Palpate the abdomen to reveal bladder distention that may reflect overactivity related to obstruction and overflow incontinence.
- Pelvic exam:
  - Female: Evaluate for pelvic organ prolapse or urethral diverticula that could contribute to obstructive voiding and OAB.
  - Male: Digital rectal exam to assess prostate size and presence of nodules or asymmetry
- Neurologic exam:
  - Focused to perineum to assess bulbocavernosus reflex, anal sphincter tone, perineal and perianal sensation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Determine presence of infection, hematuria, glycosuria
- Urine cytology:
  - Rule out malignancy

Imaging

- Bladder US:
  - To determine post-void residual (PVR). May alternatively perform in and out catheterization
- Renal US:
  - Of particular importance in the neurogenic bladder with poor compliance (decreased bladder elasticity) to determine presence of hydronephrosis resulting from vesicoureteral reflux

Diagnostic Procedures/Surgery

- Cystoscopy:
  - For patients with prior surgeries, who are refractory to medical management, or who display suspicious findings on urinalysis or cytology
- Pressure-flow UDS:
  - To determine the presence of possible bladder outlet obstruction from the prostate or bladder neck
  - For OAB, UDS is performed with simultaneous fluoroscopy in patients with high PVR; failed conservative, medical, or surgical therapies; and complicated cases with possible mixed incontinence or any neurologic condition.

DIFFERENTIAL DIAGNOSIS

- Congenital:
  - Spina bifida or other neurologic abnormalities
- Traumatic:
  - SCI
  - Pelvic trauma
  - Iatrogenic trauma
  - Foreign body (bladder stone, stent, etc.)
- Inflammatory:
  - UTI
  - Radiation cystitis
  - Urethritis
  - Interstitial cystitis
  - Endometriosis
- Bladder outlet obstruction from benign
- prostatic hyperplasia
- Neoplastic:
  - Bladder cancer or carcinoma in situ
  - Urethral tumors
  - Nonurologic cancers via local extension

TREATMENT

Behavioral therapies:

- Timed voiding regimen
- Voiding diary
- Pelvic floor exercises with biofeedback

MEDICATION

1st-line antimuscarinic agents:

- Mainstay of pharmacotherapy for OAB; they assist in reduction of incontinence episodes and improve storage parameters for neurogenic bladder patients with DO.
- Antimuscarinics exert effect by blocking M3 receptor activity in the bladder reducing involuntary contractions.
- Multiple compounds and formulations are currently available including oxybutynin, tolterodine, solifenacin, trospium chloride, and darifenacin. No agent has significantly better efficacy, but adverse side effects may be mitigated by receptor-selective agents.
- Doses are often titrated for maximum clinical benefit and minimal side effect profile.
- Side effects most commonly encountered include dry mouth, constipation, and blurred vision.

Geriatric Considerations

- Caution with anticholinergic use in the elderly with regards to potential for cognitive impairment:
  - 2nd-line therapy such as tricyclic antidepressants such as imipramine
  - -blockers
  - To decrease outflow obstruction in men with BPH
  - 5-reductase inhibitors
- Reduces outflow obstruction by 20–25%; prostatic size reduction. Note: Reduces PSA value 50%

SURGERY/OTHER PROCEDURES

- Neuromodulation:
  - Sacral nerve neuromodulation for patients refractory to medical therapies.
  - Indicated for treatment of urge incontinence, urgency-frequency as well as urinary retention.
- Botulinum toxin bladder wall injection:
  - Approved for detrusor overactivity of neurologic origin
  - Can be performed in the office with local anesthesia
- Pelvic organ prolapse surgery
- Bladder outlet obstruction surgery
- Bladder augmentation or urinary diversion:
  - Consider in the neurogenic bladder patient with impaired compliance and incontinence

ONGOING CARE

PROGNOSIS

Generally responds to therapy when properly diagnosed

COMPLICATIONS

Hygienic and social

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Periodic review of behavioral and/or medication compliance.
- Also periodic adjustments of pharmaceutic regimens to optimize efficacy while minimizing side effects

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Incontinence, Urinary, Adult Female
- Incontinence, Urinary, Adult Male
- Incontinence, Urinary, Pediatric
- Overactive Bladder (OAB)
- Sacral Neuromodulation
- Urgency, Urinary (Frequency and Urgency)

CODES

ICD9

- 596.51 Hypertonicity of bladder
- 788.30 Urinary incontinence, unspecified
- 788.31 Urge incontinence

ABBREVIATIONS

- BPH: Benign prostatic hyperplasia
- DO: Detrusor overactivity
- OAB: Overactive bladder
- PSA: Prostate-specific antigen
- QOL: Quality of life
- SCI: Spinal cord injury
- UDS: Urodynamic study
- US: Ultrasound
- UTI: Urinary tract infection

DETRUSOR-SPHINCTER DYSSYNERGIA (DSD)

Patrick J. Shenot, MD

BASICS

DESCRIPTION

Contraction of the sphincter mechanism occurring simultaneously with uninhibited involuntary contraction of the bladder detrusor muscle (neurogenic detrusor overactivity, NDO) in cases of neurogenic lower urinary tract dysfunction

EPIDEMIOLOGY

- Incidence is unknown.
- Depends on incidence of underlying neurologic condition
- Prevalent among those with spinal cord lesions; more prevalent at higher levels (especially cervical) than lower (sacral) injury or disease.
- May affect those with MS, spinal cord tumor, traumatic SCI, arteriovenous malformation
- Uninhibited, involuntary detrusor contraction (ie, NDO) must be present for DSD to occur

RISK FACTORS

- Neurologic processes affecting the CNS below the level of the pons
- Associated with autonomic hyperreflexia

PATHOPHYSIOLOGY

- DSD causes a functional bladder outflow obstruction, resulting in dramatic elevation of intravesical pressure, which damages the urinary tract directly with pressure and upper tract drainage and secondarily with infection and urolithiasis.
- DSD is always associated with detrusor overactivity although NDO may occur with synergic sphincter function (without DSD).
- Pontine mesencephalic reticular formation is responsible for coordinating sphincter relaxation with detrusor contraction:
  - Spinal cord lesions impair the 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% of patients have internal (bladder neck) sphincter dyssynergia coexistent with external sphincter dyssynergia.

COMMONLY ASSOCIATED CONDITIONS

- SCI

- MS
- Transverse myelitis

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 or suprapubic catheter
- UTI:
  - Severity of infection:
    Response to antibiotics
    Need for parenteral antibiotics
  - Frequency of recurrence of infection
  - Urolithiasis:
    Episodes of lithiasis
    Surgical intervention
    Calculus composition

PHYSICAL EXAM

- Fever
- Parenchymal UTI:
  - Men: Prostate, testes/epididymis/renal
  - Female: Renal
- Hypertension:
  - During manipulation of the GI/GU systems, autonomic hyperreflexia may result
- Generalized edema:
  - Severe renal insufficiency
- Palpable flank mass:
  - Secondary hydronephrosis
- Flank tenderness:
  - Ureteral obstruction
  - Pyelonephritis
- Abdominal mass:
  - Distended bladder; urinary retention

- Incontinence of urine:
  - Spontaneously
  - With stress maneuvers
  - During abdominal/pelvic palpation
- Testicular mass:
  - Epididymo-orchitis/epididymitis
  - Secondary abscess formation
  - Hydrocele from recurrent infection
- Prostate mass/nodule:
  - Focal prostatitis
  - Prostate abscess

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood studies:
  - Serum chemistry to evaluate renal function, electrolyte levels
  - CBC to rule out secondary anemia due to decreased renal function or chronic infection
- Urine studies:
  - Urine analysis
  - Proteinuria: Renal dysfunction
  - Pyuria, nitrite, leukocyte esterase: Acute or chronic infection
  - Hematuria: Infection or lithiasis

Imaging

- Renal US:
  - Effective in screening for upper urinary tracts
  - Calculus
  - Hydronephrosis
  - Masses
- ExU:
  - Contraindicated in those with decreased renal function (serum creatinine <2.0)
  - Delayed excretion of contrast with high urinary storage pressures
  - Hydroureteronephrosis:
    Marked elevation of intravesical pressure
    May be due to urinary calculi
- Bladder:

- Wall thickening
- Trabeculation
- Diverticulum formation
- Incomplete emptying

- Voiding cystourethrogram:
  - Bladder:
    Wall thickening
    Trabeculation
    Diverticulum formation
    Incomplete emptying
  - Ureter:
    Vesicoureteral reflux
    Hydroureter
    Hydroureteronephrosis
  - Urethra:
    Prostatic urethra dilated
    Membranous urethra persistently narrow, stenotic, nonrelaxing
    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

- Urodynamic evaluation is essential to diagnose detrusor overactivity with detrusor-sphincter.
- Cystoscopy:
  - Normal penile urethra
  - Spastic, nonrelaxing, stenotic membranous urethra
  - Dilated prostatic urethra
  - Bladder trabeculation/diverticula
  - Rule out calculus or bladder tumor

DIFFERENTIAL DIAGNOSIS

- In patients with detrusor overactivity, bladder outflow obstruction from other etiologies:
  - Benign prostatic hyperplasia
  - Adenocarcinoma of the prostate

– Urethral stricture disease
– Urethral tumor

• In patients with urinary retention/incomplete emptying and coexistent neurologic disease, consider impaired detrusor contractility/detrusor areflexia.

TREATMENT

• Intermittent catheterization should be considered.
• Decrease intravesical pressure:
– Decrease bladder contractility to allow low-pressure urinary storage
– Defeat sphincter function to establish low-pressure urinary drainage per urethra:

This is an option only for males as there is no effective external urinary collection device for females.

MEDICATION

First Line

• Anticholinergic therapy is effective in improving urinary storage under low pressure:
– Oxybutynin 5 mg PO t.i.d.–q.i.d.
– Oxybutynin extended release 5–30 mg/d PO
– Hyoscyamine 0.375 mg PO b.i.d.-t.i.d.
– Tolterodine 2–4 mg PO b.i.d.
• -Adrenergic blockade may decrease internal sphincter function but is largely ineffective for external sphincter dyssynergia:
– Doxazosin 2–8 mg/d PO
– Terazosin 2–5 mg PO daily–b.i.d.
– Tamsulosin 0.4 mg PO o.d.
– Alfuzosin 10 mg/d PO
– Phenoxybenzamine 10 mg PO b.i.d. (nonselective)

Second Line

)[B]

SURGERY/OTHER PROCEDURES

• Endoscopic sphincter ablation: Only in males as it requires condom catheter urinary collection:
– Electrosurgical or laser sphincterotomy: Incise external sphincter from bulbous urethra to mid-prostatic urethra
– Further incision through the prostate and bladder neck may be required if internal sphincter dyssynergia is present.

)[A]:

– Maintains caliber of membranous urethra at 42 French
– Suprapubic tube cystostomy may be required in perioperative period.

• Augmentation cystoplasty: Bladder is incised in clamshell fashion to disrupt detrusor contraction; GI segment used to enlarge bladder, increasing urinary storage with decreased pressure;

– May use large intestine, ileum, or gastric segment
– Requires intermittent catheterization for urinary drainage
– Limited dexterity may mandate creation of continent catheterizable stoma for the urinary reservoir, especially in females

• Ileal conduit cutaneous vesicostomy: Conduit of ileum connecting dome of bladder to anterior abdominal wall:

– Continuous low-pressure drainage through incontinent ileal conduit urostomy requires stomal appliance urinary collection.
– Useful for those who cannot perform self-catheterization, especially in quadriplegia.

ADDITIONAL TREATMENT

Sacral deafferentation with sacral nerve root stimulation:

• Deafferentation with dorsal rhizotomy abolishes spontaneous detrusor contraction, improving urinary storage.
• Nerve root stimulation allows control over detrusor contraction.
• Obstruction by sphincter may require adjunctive sphincteric ablation.

ONGOING CARE

PROGNOSIS

• Excellent prognosis if effectively treated
• Untreated, ~50% of men will develop significant complication.

COMPLICATIONS

• Vesicoureteral reflux
• Renal insufficiency
• Urolithiasis
• Urosepsis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Annual evaluation:

• Urodynamic testing to assure low intravesical pressure
• Upper-tract imaging (US, ExU) to rule out upper-tract changes (calculi, hydronephrosis)

- Serum chemistry to confirm normal renal function and electrolyte balance

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See Also (Topic, Algorithm, Electronic Media Element)

- Guillain-Barré Syndrome (Transverse Myelitis), Urologic Considerations
- Multiple Sclerosis, Urologic Considerations
- Spinal Cord Injury, Urologic Considerations

CODES

ICD9

596.55 Detrusor sphincter dyssynergia

ABBREVIATIONS

- CBC: Complete blood count
- DESD: Detrusor-external sphincter dyssynergia
- DSD: Detrusor-sphincter dyssynergia
- ExU: Excretory urography
- GFR: Glomerular filtration rate
- GI: Gastrointestinal
- GU: Genitourinary
- MS: Multiple sclerosis
- NDO: Neurogenic detrusor overactivity
- SCI: Spinal cord injury
- US: Ultrasound

- UTI: Urinary tract infection

DIABETES MELLITUS, UROLOGIC CONSIDERATIONS

Vanessa L. Elliott, MD

J. C. Trussell, MD

BASICS

DESCRIPTION

- Hyperglycemia with secondary metabolic abnormalities
- 2 subtypes including insulin deficiency (DM1) and insulin resistance (DM2)

EPIDEMIOLOGY

- 1–6% of the population
- 30% with DM1 and 10–40% of those with DM2 will develop kidney failure.
- 59% of diabetics have urologic complications/symptoms

RISK FACTORS

- UTIs
- ED
- VD
- DN
- Infertility
- Polyuria

Genetics

- Type I: Chromosome 6p
- Type II: Complex polygenic risk factors

GENERAL PREVENTION

- Glycemic control
- Weight control
- Smoking cessation

PATHOPHYSIOLOGY

)[A]:

  - 80% associated with upper-tract infections
  - Association with glucosuria and DC

)[B]:

  - Neurogenic: Peripheral neuropathy and CNS involvement
  - Vascular: Endothelial cell dysfunction, atherosclerosis
  - Endocrine: Deficient androgen secretion
  - Psychologic: Secondary to depression

)[B]:

  - DC secondary to peripheral/autonomic neuropathy (AN)
- Polyuria: Secondary to osmotic diuresis
- Infertility:
  - ED/ejaculatory failure: Secondary to AN
  - Abnormal semen analysis secondary to deficient androgen secretion

COMMONLY ASSOCIATED CONDITIONS

Obesity

DIAGNOSIS

HISTORY

- General:
  - Polyuria, polydipsia, polyphagia
  - Weight loss, malaise
  - Family history
  - ED in young men
- UTI:
  - Recurrent UTI (may be asymptomatic)
  - Fever, nausea, vomiting, flank pain
  - Dysuria, hematuria
- VD:
  - Urgency, frequency, urinary retention

PHYSICAL EXAM

- Flank: CVA tenderness
- Abdomen: Bladder distention, suprapubic tenderness
- Genitals: Testicular atrophy, phimosis, balanitis, dermatitis (yeast), vaginitis
- Rectal: Tone, BCR
- Prostate: Symmetry/nodules

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- General:
  - Fasting glucose >126 mg/dL
  - Oral glucose tolerance test, 2 hr value >200 mg/dL
  - Microalbuminuria predicts renal disease
  - 0–30 mg/d is normal; 30–300 mg is microalbuminuria and is predictive for development of diabetic nephropathy.
- UTI:

- UA, C&S
- BUN/creatinine

- ED:
  - Testosterone: If low, FSH and LH
  - BUN/creatinine
- VD:
  - UA (including urine glucose), C&S
  - Urine specific gravity: Dilute if <1.007
- Infertility:
  - Testosterone, FSH, LH, and prolactin
  - Semen analysis

Imaging

- UTI:
  - CT (noncontrast and contrast films if possible): Emphysematous pyelonephritis, urolithiasis
- ED:
  - Cavernosal Doppler's (used infrequently)
- VD:
  - RUS, bladder US

Diagnostic Procedures/Surgery

- VD:

)[B]

- PVR: Acceptable if < 150cc
- Voiding diary: Quantify fluid intake and voided volumes
- Uroflow: Flow rate 20–25 cc/sec (males) >25–30 cc/sec (female). Probable obstruction <10 cc/sec

DIFFERENTIAL DIAGNOSIS

- UTI: Pyelonephritis, emphysematous pyelonephritis, XGM, urolithiasis, papillary necrosis, perinephric abscess, hematogenous infection
- VD: Bladder outlet obstruction, neurologic disease, pelvic surgery
- Polyuria: Voluntary excess fluid intake, psychogenic polydipsia, diabetes insipidus, renal failure
- Infertility: Ejaculatory obstruction, retrograde ejaculation, testicular causes

TREATMENT

- Educate patients in urologic issues relating to diabetes.

- Optimal blood glucose control:
  - Diet
  - Exercise

MEDICATION

- UTI:
  - Antibiotics
  - Fluid resuscitation
  - If urinary retention, intermittent catheter drainage

)[B]:

  - Oral phosphodiesterase inhibitors
  - Intracavernosal therapy
  - Intraurethral therapy, MUSE
  - Vacuum erection device
  - Hormonal replacement with low testosterone
- VD:
  - -Blockers
  - Anticholinergics
  - Timed voiding
  - CIC
- Ejaculatory failure:
  - -Agonist (Sudafed)

SURGERY/OTHER PROCEDURES

- UTI:
  - Urolithiasis: Ureteral stent vs. nephrostomy tube
  - XGP or EP: Possible nephrectomy
- ED:
  - Penile prosthesis
- VD:
  - Neuromodulation (ie, InterStim)
  - Bladder outlet obstruction: TURP, TUNA, TUIP, Laser TURP, etc.
  - Urinary diversion
- Infertility:
  - Assisted reproduction

ADDITIONAL TREATMENT

With significant microalbuminuria, ACE inhibitors may be prescribed to protect against nephropathy.

ONGOING CARE

PROGNOSIS

Good with tight control of glucose levels

COMPLICATIONS

- UTI:
  - Upper-tract infection
  - Staghorn calculus
  - Renal failure
- ED:
  - Peyronie disease
- VD:
  - UTI
  - Urolithiasis
  - Upper-tract deterioration
  - Renal failure
  - Incontinence
  - Atonic bladder

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- UTI:
  - UA: Follow asymptomatic infection
  - RUS, bladder US
- ED:
  - Testosterone replacement; testosterone. PSA, hematocrit followed serially
- VD:
  - RUS, bladder US
  - BUN/creatinine
  - PVR
  - UA
  - Repeat CMG if changes in symptomatology

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Erectile Dysfunction/Impotence (ED)
- Infertility, Urologic Considerations
- Neurogenic Bladder, General
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

– 250.40 Diabetes mellitus with renal manifestations, type ii or unspecified type, not stated as uncontrolled

– 250.41 Diabetes mellitus with renal manifestations, type I (juvenile type) not stated as uncontrolled

– 586 Renal failure, unspecified

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- AN: Autonomic neuropathy
- BUN: Blood urea nitrogen
- BCR: Bulbocavernosus reflex
- CIC: Clean intermittent catheterization
- CT: Computed tomography
- CVA: Costovertebral angle
- C&S: Culture/Sensitivities
- CMG: Cystometrogram
- DI: Detrusor instability
- DM1: Diabetes mellitus type 1
- DM2: Diabetes mellitus type 2

- DC: Diabetic cystopathy
- DN: Diabetic nephropathy
- EP: Emphysematous pyelonephritis
- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- LH: Luteinizing hormone
- PVR: Postvoid residual
- PSA: Prostate-specific antigen
- RUS: Renal ultrasound
- TUIP: Transurethral incision of the prostate
- TUNA: Transurethral needle ablation of the prostate
- TURP: Transurethral resection of the prostate
- US: Ultrasound
- UA: Urinalysis
- UTI: Urinary tract infection
- VD: Voiding dysfunction
- XGP: Xanthogranulomatous pyelonephritis

DISORDERS OF SEXUAL DEVELOPMENT (DSD)

Jordan Gitlin, MD
Jared Cox, MD
C. D. Anthony Herndon, MD

BASICS

DESCRIPTION

- Congenital condition in which chromosomal sex is inconsistent with phenotypic sex. Unable to easily classify child as male or female
- Ambiguous genitalia and intersex disorders are no longer considered correct terms for this condition but are still used.
- Gonadal classification:
  - FP: Ovary
  - MP: Testes
  - TH: Ovotestis
  - MGD: 1 streak gonad
  - PGD: 2 streak gonads

EPIDEMIOLOGY

- 0.018–1.7% of live births depending on definition of DSD
- CAH 60–70% of neonatal DSD
- 90% of CAH due to 21-OH deficiency
- True hermaphrodite: 10% of neonatal DSD
- 5-Reductase deficiency: Up to 1:90 in Dominican Republic
- Complete androgen insensitivity 1/13,000
- Congenital adrenal hyperplasia: 1/13,000
- Gonadal dysgenesis: 1/150,000
- Ovotestis–hermaphrodite: 1/83,000
- Partial androgen insensitivity: 1/130,000

ALERT

CAH Type II and III (salt wasting) may present with neonatal shock due to profound hypovolemia, hyperkalemia and hyponatremia.

RISK FACTORS

- Inherited disorders/genetic abnormalities—CAH, CAIS, PAIS, 5-reductase deficiency, gonadal dysgenesis
- In utero exposure to androgens: Maternal-adrenal tumor, ingestion (birth control, infertility medication, phytoestrogens), environmental

Genetics

- 5-Reductase deficiency: 46XY (autosomal recessive, defect on chromosome 19)
- CAH: Mostly defect of 21 OHase gene (CYP21) on chromosome 6p.21.3 (Type III CAH)
- CAIS: 46XY
- FP:46XX
- Lipoid CAH: (StAR) chromosome 8p11.2 (Type I CAH)
- MP: 46XY
- MGD: 46XY or 45XO/46XY
- Mutations of MIS receptor chromosome 12q13
- Mutations of MIS gene chromosome 19p3.3
- PAIS: 46XY
- Persistent Müllerian duct syndrome: 46XY
- PGD/Turner: 45XO, 46 XX or 46XY
- True hermaphrodite: Usually mosaic 46XX/46XY, or 47XXX/46XY
- XX Male sex reversal: 46XX with positive SRY

GENERAL PREVENTION

- CAH: If positive family history, can pretreat at 8 wk of pregnancy with dexamethasone to prevent virilization of females
- CVS sampling: To check karyotype at 10–12 wk and continue treatment if XX
- Amniocentesis at 10–15 wk to check for elevated 17-hydroxyprogesterone
- Treatment improves clitoral hypertrophy, but vagina may still be concealed and need treatment.

PATHOPHYSIOLOGY

- Genetic sex determined at conception.
- Father contributes X or Y, mother only X
- Y contains SRY (sex determining region on Y chromosome) that causes testicle to develop
- Until 8 wk, gonad is indifferent
- Testis makes T and MIS
- T and eventual conversion to DHT lead to development of penis, scrotum, and internal male structures
- MIS: Causes regression of female structures of uterus, fallopian tube, upper 2/3 of vagina
- Females (XY and ovary) do not make T or MIS; female structures by default

- CAH: Deficient 21-OHase (Type III): Cholesterol pathway is shifted toward increased androgens, and does not produce aldosterone and cortisol. Salt wasting, hyperkalemia, dehydration, adrenal crisis
- CAH: 3 -hydroxysteroid dehydrogenase (type II) severe salt loss and death; virilization variable.
- CAIS: Intra-abdominal testes, produces T and MIS, but defective T receptors. No female internal structures (because of MIS), no male external genitalia (because no T receptors)
- PAIS: Wide range of phenotypes
- TH: Gonads contain both testicular and ovarian tissue; mixed phenotypes
- 5-Reductase deficiency: Unable to convert T to DHT (virilizing agent for external genitalia); usually appear as female or severe penoscrotal hypospadias; virilize at puberty
- Mixed gonadal dysgenesis: Testis on 1 side, streak gonad on the other side, usually with severe hypospadias

COMMONLY ASSOCIATED CONDITIONS

- Klinefelter syndrome, Turner syndrome, Reifenstein syndrome, Kennedy disease
- Gonadoblastoma: Develops in dysgenetic gonad; benign, but 50% malignant transformation
- Dysgerminoma: Similar to malignant seminoma in behavior.
- Need to remove any gonads that are dysgenetic or contain a Y component
- Inguinal hernia in a presumed girl: May be CAIS female with testicle found in the sac
- Amenorrhea: May be CAIS female who lacks internal female structures due to MIS from intra-abdominal testicles
- Virilization in a presumed female: May be 5-reductase deficiency in which, at puberty, T alone increases to virilize the patient.

DIAGNOSIS

HISTORY

- Family history: Genital abnormalities, sterility, amenorrhea, hirsutism, ambiguous genitalia
- Maternal exposure to androgens
- Early infant deaths, from possible adrenal insufficiency from CAH
- Pregnancy history

PHYSICAL EXAM

- Phallus will not help in diagnosis; will range from Prader 1–5 (normal phallus to perineal hypospadias)

- Most important finding is location of gonads; ovaries typically do not descend
- BP, signs of dehydration
- Abdomen: Masses, distended uterus
- Skin: Hyperpigmentation from ACTH
- Penis: Size, length (stretch), location of meatus
- Scrotum: Developed or hypoplastic; 1 or both testicles
- Clitoris: Size, length
- Vagina: Present, patency, length
- Labia: Normal or labia-scrotal folds. Feel for masses (ovotestis in labia)
- Rectal exam: May be able to feel uterus (engorged from maternal hormones in newborn)
- Turner: Web neck, short stature, shield chest

DIAGNOSTIC TESTS & INTERPRETATION

ALERT

SMA-7 mandatory if CAH II or III is in question in newborn with hypospadias and bilateral nonpalpable testis: Hyponatremia, hyperkalemia, metabolic acidosis

Lab

- Biochemical markers (elevated in CAH):17-OH progesterone, 17-OH pregnenolone, urinary 17-ketosteroids, 11-deoxycortisol to identify adrenal enzyme defect
- Sex hormones:
  - LH, FSH: Elevated in CAIS
  - T: Elevated in CAIS, CAH
  - T/DHT ratio increased in 5-reductase deficiency
  - MIS detected in serum only if presence of testicular tissue; made from Sertoli cells
- Karyotype:
  - Check genetic sex of child and for mosaicism
  - May need FISH analysis to check for possible Y fragment in dysgenetic gonad
  - Buccal smear for Barr body may confirm female genotype, but unreliable
  - Gene probe for specific mutations and deletions

Imaging

- Pelvic US: Uterus is seen in CAH
- Genitogram: Visualize urogenital sinus, vagina
- MRI: Define internal anatomy
- CXR: Rib notching in Turner syndrome

Diagnostic Procedures/Surgery

- Laparoscopy to visualize internal anatomy
- Gonadal biopsy: Ovarian or testicular tissue
- Cysto/vaginoscopy helpful to confirm gender and measure level of confluence of UG sinus

Pathological Findings

Entity-specific

DIFFERENTIAL DIAGNOSIS

- CAH: Virilized female, uterus on US, XX karyotype, elevated 17-OH progesterone
- CAIS: Appears female, with short vagina. No female structures on US. XY karyotype, elevated T and LH levels
- PAIS: Wide range of phenotypes, usually ambiguous. Labs inconclusive; may need gene probe studies of androgen receptor
- True hermaphrodite:
  - Ambiguous genitalia usually more male with hypospadias
  - Gonads with both testicular and ovarian tissue
  - Endocrine studies to check for functioning testicular tissue
  - Need biopsy of gonad
- 5-Reductase deficiency:
  - Appear female at birth, with enlarged clitoris.
  - May look like severe hypospadias, with perineal opening.
  - Testes usually in groin
  - Elevated T/DHT ratio, ± LH elevation. XY karyotype.
  - No uterus on US.

TREATMENT

- Ambiguous genitalia in newborn: FP, MP, MGD, and cloacal anomalies
- Nonambiguous genitalia: CAIS, CAH (17-OH), XX sex reversal, Klinefelter, Turner, PGD
- Consider gender assignment; multidisciplinary approach mandatory. Cannot assign gender based on karyotype, gonad, or phenotype in isolation.
- Phallic length may play role in decision
- Long-term consequences of assignment must be taken into consideration
- Brain imprinting with T may play a role in gender identity.
- Timing of surgery is debated:
  - Early surgery: Earlier identification with gender
  - Late surgery: Patient involvement in decisions of gender

- Alternative view: Do not assign gender. Gender-neutral assignment. After puberty, patient declares own gender.

MEDICATION

CAH 21-OHase deficiency:

- Solu-Cortef 10 mg/m2/d and fludrocortisone 0.1 mg/d
- Ensure adequate sodium chloride supplementation.

SURGERY/OTHER PROCEDURES

- CAH: Adrenalectomy for severe salt wasters. Vaginoplasty with labioplasty to move vagina out to skin. Clitoroplasty with nerve preservation for enlarged clitoris
- CAIS: Removal of intra-abdominal testicles; timing is debatable. Vaginoplasty if vagina is short
- TH: Laparoscopy and gonadal biopsy
- 5-Reductase deficiency: If raised female, need gonadectomy; if raised male, hypospadias repair
- MGD: Usually need hypospadias repair, removal of streak gonad, given Y component
- Vaginoplasty: Dilating with sounds; pull through/flap; bowel replacement
- MGD, TH, PGD, Turner: Must have orchiectomy because of risk of neoplasm (gonadoblastoma, dysgerminoma, seminoma)

ONGOING CARE

PROGNOSIS

- Many can remain fertile: All CAH, some MGD, 5-reductase deficiency
- All CAIS are infertile.

COMPLICATIONS

- Adrenal insufficiency: CAH not on appropriate meds
- Clitoroplasty: Diminished clitoral sensation; newer techniques preserve all nerves
- Vaginoplasty: Vaginal stenosis; re-evaluate all at puberty to assess vaginal patency
- Urethroplasty: Incontinence, urethral stricture
- Urogenital sinus mobilization: Rectal injury, vaginal devascularization, urinary incontinence
- Hypospadias: Meatal stenosis, fistula

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- All intersex conditions in an XY patient should be monitored for development of gonadoblastoma, seminoma, or dysgerminoma.
- Follow labs in CAH

- Follow sexual function (menstruation) sexual activity, psychological issues

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- 5-Alpha Reductase Deficiency
- Adrenal Hyperplasia
- Ambiguous Genitalia (Disorders of Sexual Development Algorithm)
- Androgen Insensitivity Syndrome (Androgen Resistance Syndrome)
- Gonadal Dysgenesis, (Mixed and Pure)
- Klinefelter Syndrome
- Pseudohermaphroditism, Male and Female
- Turner Syndrome

CODES

ICD9

- 752.7 Indeterminate sex and pseudohermaphroditism
- 758.6 Gonadal dysgenesis
- 758.7 Klinefelter’s syndrome

ABBREVIATIONS

- CAH: Congenital adrenal hyperplasia
- CAIS: Complete androgen insensitivity syndrome
- CVS: Chorionic villus sample
- CXR: Chest x-ray
- DHT: Dihydrotestosterone

- DSD: Disorders of sexual development
- FP: Female pseudohermaphrodite
- FSH: Follicle-stimulating hormone
- LH: Luteinizing hormone
- MGD: Mixed gonadal dysgenesis
- MIS: Müllerian inhibiting substance
- MP: Male pseudohermaphrodite
- MRI: Magnetic resonance imaging
- PAIS: Partial androgen insensitivity syndrome
- PGD: Pure gonadal dysgenesis
- StAR: Steroidogenic acute regulatory protein
- T: Testosterone
- TH: True hermaphrodite
- US: Ultrasound

DYSPAREUNIA

Debra L. Fromer, MD

Daniel I. Brison, MD

BASICS

DESCRIPTION

Pain during or resulting from sexual intercourse:

- May be primary or secondary
- May be anatomic, psychological, or mixed

EPIDEMIOLOGY

- Depends on the definition used and the sampled population
- 45–60% depending on the definition utilized:
  - Many do not seek medical attention; prevalence may be higher than reported

RISK FACTORS

- Traumatic deliveries
- Vaginal infections
- Menopause
- Psychiatric history/trauma

PATHOPHYSIOLOGY

The anatomic site of pain during intercourse may be subdivided into 3 areas:

- Entrance dyspareunia; pain concentrated at the vaginal opening
- Vaginal dyspareunia; pain along the entire length of the vagina
- Deep-thrust dyspareunia; pelvic pain during partner's penile thrust

COMMONLY ASSOCIATED CONDITIONS

- Vaginal agenesis
- Vaginal atrophy
- PID

DIAGNOSIS

HISTORY

- Location of pain; association with deep thrusts:
  - Localization
- Pain always or sometimes present with sexual intercourse:
  - Primary vs. secondary
- Describe the pain:
  - Aching, dull, sharp, burning, itching
  - Pain related to a certain position

- Prior pelvic and/or vaginal surgery or radiation:
  - Cause of vaginal stenosis or pelvic adhesions
- STDs or UTIs:
  - Cause of inflammatory changes/infections
- Childbirth or other trauma:
  - Vaginal/rectal tears, episiotomy
- Postmenopausal:
  - Decreased lubrication/atrophy if not on HRT
- Pain related to your menstrual cycle:
  - Endometriosis
- Recent use of feminine hygiene products/latex material/soaps/deodorants:
  - Allergic reaction
  - History of sexual abuse or any other psychological insults
  - Psychological causes
  - History of chronic diseases
- Bowel or bladder symptoms:
  - IBS, urethritis, diverticula

PHYSICAL EXAM

- 3 parts:
  - Visual inspection
  - Vaginal exam:
    Manual
    Speculum
  - Other (Pap smear, colposcopy)
- Erythema of vulva:
  - Allergic reaction or infection
- Ulcers and lesions surrounding vulva and introitus:
  - Infectious causes, STDs, clear cell carcinoma of vagina
- Decreased lubrication with thinning of the vaginal mucosa:
  - Atrophy
- Tenderness at vestibule and hymenal area:
  - Vulvovaginitis or vulvovestibulitis
- Pain with vaginal palpation of the pelvic floor muscles:
  - Pelvic floor muscle spasm
- Palpable mass on anterior vaginal wall that may exude discharge per urethra when compressed:

- Urethral diverticulum
- Tenderness with palpation of the cul-de-sac, if uterus is not retroverted:
  - May be endometriosis or pelvic adhesions
- Tenderness with gentle manipulation of the cervix:
  - Suggestive of PID/cervicitis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urine culture:

- Evaluate for infections

Imaging

Endovaginal US:

- May identify ovarian, uterine, or other pelvic masses

Diagnostic Procedures/Surgery

- Pap smear:
  - Rule out malignancy
- KOH test of cervical secretions:
  - Differentiate between Gardnerella and Trichomonas
- Endocervical cultures:
  - Rule out infections with Chlamydia and/or Gonorrhea
- Colposcopy of vulva and cervix:
  - Identify HPV and/or malignant changes
- Vaginal mucosa biopsy:
  - Identify dystrophies
- Diagnostic laparoscopy:
  - Differentiate endometriosis from adhesions and identify pelvic masses
- VCUG (double-balloon urethrogram):
  - Identify urethral diverticula

DIFFERENTIAL DIAGNOSIS

- Congenital: Rigid hymen, hymenal tags, imperforate hymen, vaginal deviations, vaginal agenesis, uterine retroversion
- Vaginal:
  - Masses: Cystocele, rectocele, uterine prolapse, neoplasm
  - Stenosis: Introitus or vaginal canal due to surgery or radiation
  - Atrophy: Loss of lubrication due to hormonal influences
  - Trauma: Childbirth, assault

  - Infections: HPV, HSV, STDs, fungal (Candida), PID
  - Allergic reactions: Contraceptives, douching material, latex, semen
  - Vulvar: Dystrophies (hyperplasia, lichen sclerosis)
  - Urethra: Caruncle, diverticulum, urethritis, neoplasm
  - Pelvis: Endometriosis, fibroids, ectopic pregnancy, adnexal cysts, adnexal prolapse, pelvic adhesions, neoplasm, pelvic floor muscle spasm
  - Rectal: Constipation, proctitis, hemorrhoids
- Psychological:
  - Lack of arousal
  - Guilt, shame, tension: Due to unusual sexual situations
  - Fear, anxiety: Due to history of sexual abuse

TREATMENT

- Vulvovaginitis and allergic reactions:
  - Avoid vaginal deodorants, douches, latex, or constant use of panty liners.
- Vaginal stenosis:
  - Passive dilation with vaginal dilators used daily
  - Endometriosis
  - GnRH analogues (eg, Lupron)
- Retroverted uterus:
  - Pessary to antevert uterus out of cul-de-sac

MEDICATION

- Estrogen replacement (oral, transdermal, intramuscular) for vaginal atrophy
- Topical corticosteroids b.i.d./t.i.d. for vulvar hyperplastic dystrophy
- Testosterone propionate 2% ointment b.i.d./t.i.d. for 3–6 mo for lichen sclerosis
- Antibiotics/antifungal for infections
- Oral contraceptives as an alternative to latex contraceptives for possible allergic reactions
- OTC water-based lubricant such as K-Y jelly, Replens, or Astroglide for vaginal dryness/atrophy

SURGERY/OTHER PROCEDURES

- Laparoscopic laser/fulguration or excision for endometriosis
- Sacrocolpopexy for retroverted uterus
- Laparoscopic lysis for pelvic adhesions

ADDITIONAL TREATMENT

Psychotherapy:

- Psychological counseling
- Couples therapy

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Electrical nerve stimulation (TENS), muscle stimulators, ultrasound, biofeedback, relaxation and breathing exercises
- Injection of anesthetics into trigger points
- Relaxation

ONGOING CARE

PROGNOSIS

Treatment may take months to years and results vary.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Close follow-up is recommended when behavior or medical therapy is instituted. When patient satisfaction is increased, time to follow-up is gradually lengthened to a routine annual check-up.

ADDITIONAL READING

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- Meana M, et al. Dyspareunia: Sexual dysfunction or pain syndrome? J Nerv Ment Dis 1997;185:561.
- Sarazin SK, et al. Causes and treatment options for women with dyspareunia. Nurse Pract 1991;16:30.
- Steege JF, et al. Dyspareunia: A special type of chronic pelvic pain. Obstet Gynelcol Clin N Am 1993;20:779.

See Also (Topic, Algorithm, Electronic Media Element)

- Dyspareunia Algorithm
- Vaginal Atrophy, Urologic Considerations
- Vaginal Discharge, Urologic Considerations
- Vaginitis/Vulvovaginitis

CODES

ICD9

- 302.76 Dyspareunia, psychogenic
- 625.0 Dyspareunia

ABBREVIATIONS

- HPV: Human papilloma virus
- HRT: Hormone replacement therapy
- HSV: Herpes simplex virus
- IBS: Irritable bowel syndrome
- OTC: Over-the-counter
- PID: Pelvic inflammatory disease
- STD: Sexually transmitted disease
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

DYSURIA

H. Henry Lai, MD

BASICS

DESCRIPTION

- Sensation of pain or burning on urination
- May feel at the start, middle, end of urination
- In men, usually felt in the distal urethra
- Frequently accompanied by other symptoms
- Workup guided by associated symptoms/signs
- UTI is the most common cause of dysuria

ALERT

Unexplained persistent dysuria should NEVER be ignored; must rule out occult malignancy, such as carcinoma in situ of the bladder.

EPIDEMIOLOGY

- Acute dysuria: 7 million office visits/yr in US
- Gonococcal urethritis: 700,000 new cases/yr
- Nongonococcal urethritis: 3 million cases/yr
- Urethritis: Estimated at 4 million Americans

RISK FACTORS

Female sex, recent urinary tract instrumentation, recent catheterization, trauma, indiscreet sexual activity, history of STD, history of UTI, history of pelvic radiation

GENERAL PREVENTION

For gonococcal and nongonococcal urethritis, practice protected intercourse and treat partners

PATHOPHYSIOLOGY

- Irritation to the afferent urethral nerve endings may be due to primary urethral pathology (eg, urethritis, urethral diverticulum)
- The discomfort may initiate from the bladder or prostate (eg, cystitis) and radiate to the urethral meatus in women or distal urethra in men.

COMMONLY ASSOCIATED CONDITIONS

- Cystitis
- Urethritis (specific, nonspecific)
- Prostatitis
- Vaginitis
- Urethral diverticulum (female)

DIAGNOSIS

HISTORY

- Workup guided by associated symptoms/signs
- Ask about associated symptoms
- Sex and age:
  - Cystitis more common in younger women
  - Likelihood of malignancy increase with age
  - Infectious urethritis common in age 20–24
- Timing of pain or burning:
  - Pain at the onset of urination indicates urethral inflammation (eg, urethritis)
  - Pain in the middle of urination may indicate obstruction (eg, urethral stricture)
  - Pain at the end of urination (strangury) is usually bladder or trigonal in origin (eg, cystitis, bladder stone, distal ureteral stone)
- Location of pain or burning (adult women):
  - External dysuria (pain as urine passes over the inflamed vaginal labia) suggests vaginal infection or inflammation.
  - Internal dysuria (pain felt inside the body) suggests cystitis or urethritis.
- Frequency, urgency, acute suprapubic pain:
  - Indicates cystitis
- Fever, chills, acute flank pain:
  - Indicates acute pyelonephritis
- Scrotal pain, discomfort, or heaviness:
  - Consider epididymitis, orchitis
- Absence of other urinary tract symptoms:
  - Suggests urethra as source of symptoms
- Hematuria or bloody urethral discharge:
  - Must rule out urothelial and GU malignancy
  - Persistent hematuria after treatment of UTI must have formal hematuria workup
- Urethral discharge:
  - Indicates infectious urethritis, STD
  - Gonococcal: Thick, discolored (yellow, gray)
  - Nongonococcal: Watery, scant, or mucoid
- Vaginal symptoms (vaginal discharge, irritation, itching, dyspareunia):
  - Vulvovaginitis, candidal or trichomonas vaginitis (recent antibiotic exposure, peri-menstrual exacerbation of symptoms), postmenopausal atrophic vaginitis, STD (herpes)

- Dyspareunia + dribbling + dysuria (3 Ds):
  - Look for urethral diverticulum on exam
- Associated polyarthritis and anterior uveitis:
  - Reiter syndrome (most common in white men 16–42, HLA-B27 associated)
- Chronic pelvic pain, perineal or vaginal pain, or suprapubic pain (worse when bladder is full):
  - Interstitial cystitis or chronic prostatitis
- Sexual history, sexual intercourse:
  - Postcoital cystitis (within a few days of intercourse), honeymoon cystitis, gonococcal and nongonococcal urethritis (1–2 wk after intercourse), STD
  - Sexual practice: Contraceptive use, number of partners, sexual preference, STD history, spermicide use, sexual trauma
  - Young men with dysuria, frequency, and urethral discharge following recent sexual intercourse most likely have urethritis.
- Recent trauma, instrumentation, foreign body:
  - Indicates inflammation or infection
  - Dysuria occurs in 2–20% of patients practicing intermittent catheterization; more likely to occur with latex than silicone catheters
- Recent midurethral sling surgery:
  - Suspect sling erosion into the urinary tract if new onset of dysuria, UTI, or hematuria after mid-urethral synthetic sling placement.
- History of smoking or tobacco use:
  - Rule out transitional cell carcinoma
- History of pelvic radiation:
  - Consider radiation cystitis (with hematuria)
- History of TB or schistosomiasis:
  - Consider tuberculous or parasitic cystitis
- History of urinary stones:
  - Consider distal ureteral stone (with strangury)

PHYSICAL EXAM

- Abdominal exam:
  - Flank tenderness: Pyelonephritis, stone
  - Suprapubic tenderness: Cystitis
  - Palpable bladder: BPH, urethral stricture
  - Abdominal mass

- Male genital exam:
  - Look for urethral discharge, meatal stenosis:
    Inspect underwear for evidence of discharge
    Strip the urethra by milking from base to glans to express urethral discharge.
  - Look for other STDs: Herpes, condyloma, or syphilis. Retract foreskin if not circumcised.
  - Scrotal exam: Rule out epididymitis, orchitis
  - Digital rectal exam:
    Acute prostatitis: Boggy, tender, inflamed
    Chronic prostatitis: Perform 4-glass test (VB1, VB2, EPS, VB3) or 2-glass test (pre- and postprostatic message)
    Prostate cancer: Asymmetry, nodule
    Benign prostatic hyperplasia
- Female pelvic exam:
  - Look for urethral discharge (above), meatal stenosis, urethral caruncle, other STD
  - Palpate underneath the urethra: Rule out urethritis, urethral diverticulum, mass, stone
  - Palpate underneath bladder neck: Trigonitis
  - Vaginal epithelium: Atrophy and dryness, inflammation, vaginal discharge
  - Bimanual exam for bladder or adnexal mass
  - Tender adnexa associated with urethritis suggests pelvic inflammatory disease

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine dipstick:
  - Positive nitrite test: Suggests the presence of bacteria. This test is accurate only 50–60% of the time when used alone. False negative: If bacteria do not contain nitrate reductase (eg, Enterococcus), or urine is present in the bladder for <4 hr
  - Positive leukocyte esterase test: Identifies WBC. When used with nitrite, the 2 tests are indicative of UTI or bladder colonization
  - pH >7: Presence of urea-splitting bacteria
- Microscopic analysis:
  - >3 RBCs/HPF indicates hematuria
  - >5 WBCs/HPF indicates pyuria
  - WBC casts indicate pyelonephritis
  - Sterile pyuria: Suspect TB, perform serial urine acid-fast bacilli stain

  - Crystals: Stones, with characteristic shapes
  - Bacteria, yeast under microscope
- Urine culture: If clinically indicated
- Voided urine cytology: If suspect malignancy. More accurate for high-grade TCC than low-grade
- Urethral or vaginal secretion smear:
  - Since current recommendation suggests patients with infectious urethritis receive treatment for both gonorrhea and chlamydia, distinguishing between the 2 with Gram staining (gram-negative intracellular diplococcus in gonorrhea) or urethral swap culture for chlamydia may not be necessary.

Imaging

Further imaging workup based on associated symptoms and likely diagnosis. For example:

- MRI of urethra: Evaluate urethral diverticulum
- Retrograde urethrogram: Urethral stricture
- CT stone protocol: Evaluate ureteral stone
- CT urogram, IVU: Urothelial cancer

Diagnostic Procedures/Surgery

Cystoscopy:

- Use only for specific indications (eg, to evaluate urethral stricture, fistula, urethritis, urethral diverticulum, mid-urethral sling erosion, trigonitis, interstitial cystitis, bladder stone, bladder tumor, foreign body)

Pathological Findings

Based on specific cause

DIFFERENTIAL DIAGNOSIS

Inflammatory or infection:

- Bladder: Cystitis (bacterial, viral, schistosomiasis, TB), interstitial cystitis, radiation cystitis, chemical cystitis
- Urethra: Infectious urethritis (gonococcal, nongonococcal), post-instrumentation, post-catheterization, traumatic urethritis, urethral diverticulum, caruncle, stricture, fistula, or local irritation by douches, spermicides, lubricants, toilet papers, perfumed soaps
- Prostate: Prostatitis (bacterial, nonbacterial)
- Scrotum: Epididymitis, orchitis
- Upper tract: Pyelonephritis, distal ureteral stone
- Adjacent organs: Vaginitis (candidal, trichomonas), STD (herpes), cervicitis

- Systemic: Reiter syndrome

TREATMENT

Treat the underlying diagnosis.

MEDICATION

Symptomatic relief with Pyridium (phenazopyridine hydrochloride, 200 mg PO t.i.d.):

- An azo dye with local anesthetic and analgesic effects on the urethra
- Stains urine or undergarments orange
- Contraindicated in renal insufficiency and children <12 yr of age
- Side effects: Renal and hepatic toxicity, methemoglobinemia, hemolytic anemia

SURGERY/OTHER PROCEDURES

Only for specific diagnosis (eg, excision of urethral diverticulum, removal of tumor, stone)

ONGOING CARE

PROGNOSIS

- Dysuria alone is usually not indicative of serious disorder. Most diagnoses are self-limiting or not progressive, and may be managed conservatively.
- Prognosis of malignancy depends on stage

COMPLICATIONS

Based on the primary diagnosis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

ALERT

- 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 UTI must have formal hematuria workup.

ADDITIONAL READING

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- Roberts RG, Hartlaub PP. Evaluation of dysuria in men. Am Fam Physician 1999;60:865–872.

See Also (Topic, Algorithm, Electronic Media Element)

- Bacteruria and Pyuria

- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

  - 098.0 Gonococcal infection (acute) of lower genitourinary tract
  - 597.80 Urethritis, unspecified
  - 788.1 Dysuria

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- CT: Computed tomography
- GU: Genitourinary
- HPF: High-power field
- MRI: Magnetic resonance imaging
- RBC: Red blood cell
- STD: Sexually transmitted disease
- TB: Tuberculosis
- UTI: Urinary tract infection
- WBC: White blood cell

EDEMA, EXTERNAL GENITALIA (PENO–SCROTAL EDEMA)

Jeffrey D. Branch, MD

BASICS

DESCRIPTION

Pitting or nonpitting edema of 1 or both sides of the penile shaft and scrotal skin due to the accumulation of transudative fluid in the dartos (scrotal) or subcutaneous layer of the penile skin

EPIDEMIOLOGY

- The incidence is not reported.
- Prevalent condition in nursing home and hospitalized patients

RISK FACTORS

- Congestive heart failure
- Epididymo-orchitis
- Genital trauma or penile fracture
- Hypervolemia
- Indwelling Foley catheter
- Lymphoma
- Medications know to cause lymphedema
- Paraphimosis
- Pelvic or inguinal surgery
- Peritoneal dialysis
- Radiation to the pelvic or inguinal region
- Retroperitoneal surgery
- Squamous carcinoma of the penis

GENERAL PREVENTION

- Maintenance of euvolemia
- Foley catheter care

PATHOPHYSIOLOGY

- Accumulation of transudate within the subcutaneous tissue of the penile shaft and scrotal skin:
  - May be localized to the genital region or part of more extensive lower extremity edema or massive body edema (anasarca)
  - Transient lymphedema can be seen after pelvic surgery, such as radical prostatectomy or radical cystectomy.

  - Often is localized to the peno-scrotal region.
- Rarely, STDs such as lymphogranuloma venereum or donovanosis may cause lymphangitis and lymphatic genital obstruction resulting in chronic fibrosis (elephantiasis).

COMMONLY ASSOCIATED CONDITIONS

- Advanced prostate cancer
- Anasarca
- Ascites/hepatic failure
- Congestive heart failure
- Fournier gangrene
- Lymphatic obstruction (lymphangitis, filariasis)
- Lymphoma
- Pelvic or inguinal surgery
- Renal insufficiency/peritoneal dialysis
- Retroperitoneal lymphadenectomy
- Testicular torsion

Geriatric Considerations

Common finding in patients confined to bed or wheelchairs

Pediatric Considerations

- Acute scrotal edema in a child may indicate testicular torsion, a urologic emergency.
- Acute idiopathic scrotal edema is seen in pediatric patients.

DIAGNOSIS

ALERT

- Edema of the penis and scrotum in an uncircumcised male may indicate paraphimosis, which requires immediate foreskin reduction or urology consultation to avoid glans penis vascular compromise.
- Edema of the scrotum associated with areas of necrosis or devitalized skin may indicate Fournier gangrene and requires emergent urologic consultation.

HISTORY

- Chronic vs. acute condition
- Acute scrotal pain in a child may indicate torsion.
- Peritoneal dialysis: Dialysate can leak through inguinal hernias into the scrotum
- Indwelling Foley catheter:
  - BPH or indwelling Foley catheter patients can develop epididymo-orchitis.
- Circumcision: Beware that severe paraphimosis can compromise the glans penis.
- Trauma

- History of lower extremity lymphedema
- Medication history:
  - Pantoprazole, sirolimus, mycophenolate can cause lymphedema.
  - ACE inhibitors: Angioedema of the genitals reported

PHYSICAL EXAM

- Foul odor of Fournier gangrene
- Examine for anasarca.
- Evaluate for lower extremity edema.
- Pitting or nonpitting edema of the penile shaft and/or scrotal skin
- Inspection for skin integrity
- Bruising or induration with crepitation seen in Fournier gangrene
- Reduce foreskin in uncircumcised males
- Exam of the testis and epididymis for signs of epidimo-orchitis
- Transilluminate the scrotum for hydrocele.
- Examine external inguinal ring for herniation.
- Cremasteric reflex test for testicular viability

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No specific laboratory tests
- Urinalysis may suggest epididymo-orchitis.
- Fractional sodium excretion may suggest fluid overload.

Imaging

- US confirms thickened subcutaneous tissue and may suggest etiology.
- CT may suggest retroperitoneal etiology.

Diagnostic Procedures/Surgery

Physical exam significant for pitting edema of the genital skin

Pathological Findings

Edematous subcutaneous tissue of the scrotum and penile shaft with possible areas of devitalized skin or necrosis

DIFFERENTIAL DIAGNOSIS

- Acute idiopathic scrotal edema
- Angioedema of the genital skin
- Cellulitis
- Chemical or allergic dermatitis
- Elephantiasis

- Epididymo-orchitis
- Fournier gangrene
- Hydrocele
- Idiopathic scrotal edema (usually children)
- Inguinal hernia
- Paraphimosis
- Squamous carcinoma of the penis

TREATMENT

- Scrotal elevation
- Genital or scrotal compression NOT recommended
- Meticulous care of cuts and skin breakdown
- Dialysis if due to severe volume overload
- Immediate postoperative edema usually resolves spontaneously.

MEDICATION

- Limited utility
- Diuretics may be of some utility
- Chemotherapy for lymphoma

SURGERY/OTHER PROCEDURES

- Indicated to address the etiologic process: Testicular torsion, inguinal hernia, penile fracture, or Fournier gangrene
- Rarely, radical excision with gracilis flap may be required for severe refractory cases.

ADDITIONAL TREATMENT

Radiotherapy

While this can be a cause of genital lymphedema, it may have a role in primary or palliative treatment of prostate and retroperitoneal malignancies causing scrotal edema.

Additional Therapies

Supportive undergarments/briefs for patient comfort

ONGOING CARE

PROGNOSIS

Depends on etiology

COMPLICATIONS

- Skin breakdown/ulceration
- Genital and scrotal compression is NOT recommended

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Physical exam for resolution

ADDITIONAL READING

- A diagnostic algorithm for male genital oedema. J Eur Acad Dermatol Venereol 2007;21(2):156–162.
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See Also (Topic, Algorithm, Electronic Media Element)

- Edema, Lower Extremity, Urologic Considerations
- Fournier Gangrene

CODES

ICD9

- 605 Redundant prepuce and phimosis
- 607.83 Edema of penis
- 608.86 Edema of male genital organs

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- CT: Computed tomography
- STD: Sexually transmitted disease
- US: Ultrasound

EJACULATION, PREMATURE

Benjamin L. Dehner, MD
James F. Donovan, Jr., MD

BASICS

DESCRIPTION

- PE is an evolving definition consisting of 3 categories:
  - Short ejaculatory latency:
    DSM-IV-R defines <15 sec
    IVELT <2 min has greater association with PE than >2 min
  - Perceived lack of control over ejaculation
  - Distress and sexual dissatisfaction
- May also be classified as primary (longstanding PE or secondary (PE developing after no previous history of PE)

EPIDEMIOLOGY

- Most common sexual dysfunction in men <40
- In 1 study, 66% of respondents age 40–49 yr reported PE.

RISK FACTORS

Increased levels of arousal due to new partner or situation, low frequency of sexual activity

GENERAL PREVENTION

Techniques and therapeutic approaches are described below

PATHOPHYSIOLOGY

Possible causes supported by evidence-based studies:

- Serotonin receptor stimulation:
  - Serotonin T2c receptors inhibit ejaculation, T1a receptors facilitate
  - Hyposensitivity of T2C or hypersensitivity of T1a may cause PE
- Penile hypersensitivity:
  - Dorsal nerve distribution of the penis is greater in men with PE.

COMMONLY ASSOCIATED CONDITIONS

- Erectile dysfunction
- General anxiety
- Situation anxiety
- Depression
- Substance abuse
- Relationship distress

- Prostatitis

DIAGNOSIS

HISTORY

- Discuss with patient ejaculatory latency, perceived lack of control, and resultant sexual dissatisfaction.
- Any indiction of ED
- Issues in the partner, such as dyspareunia or other medical problem
- Rule out symptoms consistent with cystitis or prostatitis.
- PE must be exclusive of PE due to substance abuse or medication:
  - Withdrawal from narcotics or trifluoperazine (Stelazine)
- Global to all sexual encounters, or with specific situations and/or partners:
  - Religious upbringing, early sexual experiences, sexual relationships, past and present, conflicts or concerns within current relationship may provide insight into the nature of the PE

PHYSICAL EXAM

- Complete physical exam with focus to rule out biologic causes including recent pelvic surgery or infectious source.
- Rectal exam to assess for prostatitis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

If indicated by history or physical exam, then check appropriate labs or imaging.

DIFFERENTIAL DIAGNOSIS

- Erectile dysfunction
- General anxiety
- Substance abuse

TREATMENT

- Behavioral treatment:
  - Stop-squeeze method (Masters and Johnson) involves removal of penis at point of ejaculation with squeezing of glans.
  - Stop-pause method (Kaplan) replaces above glans squeezing with pause in inter-course.
  - High initial success rates are reported, but poor long-term rates are present due to the time-consuming nature of treatment.
- Establish understanding between sexual stimulation patterns of men vs. women. Often females require more stimulation than the male partner; this may contribute to the PE.

- Psychotherapy may be beneficial in selected cases.

MEDICATION

- None is specifically approved for PE.
- SSRIs:
  - Daily treatment with PO paroxetine 20–40 mg (greatest evidence), clomipramine 10–50 mg, sertraline 50–100 mg, fluoxetine 20–40 mg
  - On-demand treatment with clomipramine 50 mg PO 5 hr prior to intercourse
- Lidocaine 2.5% or prilocaine 2.5% cream applied 1 hr prior to intercourse may improve ejaculatory control.

ONGOING CARE

PROGNOSIS

Varies by treatment modality. May have 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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Dyspareunia
- Ejaculation, Premature Algorithm
- Ejaculatory Disturbances

CODES

ICD9

302.75 Premature ejaculation

ABBREVIATIONS

- IVELT: Intravaginal ejaculatory latency time
- PE: Premature ejaculation
- SSRI: Selective serotonin reuptake inhibitor

EJACULATORY DISTURBANCES (DELAYED, ABSENT, REDUCED)

Christian J. Nelson, PhD
Serkan Deveci, MD
John P. Mulhall, MD

BASICS

DESCRIPTION

- 2 major types of ejaculatory disturbance: Failure of emission and failure of ejaculation (anejaculation), which is due to either retarded orgasm (or complete anorgasmia) or retrograde ejaculation.
- Ejaculatory dysfunction should be suspected in any male with no ejaculate or a volume of ejaculate <1 mL.
- Anejaculation is defined as absence of antegrade semen production despite achievement of orgasm.
- Retrograde ejaculation is defined as the presence of spermatozoa in the urine retrieved after orgasm in the absence of ejaculation or with diminished ejaculate volume.
- Retarded orgasm is a condition characterized by difficulty achieving orgasm and ejaculation. Some men may be able to reach orgasm during masturbation, but have difficulty during sexual intercourse.
- Anorgasmia is the complete inability to achieve an orgasm.

EPIDEMIOLOGY

- Retrograde ejaculation occurs in the majority of men after prostate resection due to failure of bladder neck closure, but its incidence in the general population is unknown.
- Historically, incidence rates of retarded orgasm are generally low, with rates of 1–4%.
- Due to the side effects of SSRIs, which have the potential to extend ejaculatory latency time in men, rates of retarded orgasm range from 16–37% for men on these mediations.
- Anorgasmia is rare, and incidents rates have been reported between 0.14% and 0.4% of the general population.

RISK FACTORS

- Retarded orgasm:
  - SSRI medications, alcohol
  - Penile hyposensitivity
  - Penile hyperstimulation
  - Psychogenic

  - Hypogonadism
- Retrograde ejaculation:
  - -blockers
  - Risperidone
  - Bladder neck surgery (TURP, TUIP), microwave hyperthermia
  - Bladder neck incompetence
  - Retroperitoneal surgery
- Failure of emission:
  - Retroperitoneal surgery
  - -blockers such as tamsulosin
  - Autonomic neuropathy
  - SCI

PATHOPHYSIOLOGY

- Ejaculation is controlled by the sympathetic nervous system. Combined autonomic and somatic innervation originating at the sacral and lumbar spinal cord levels mediates ejaculation.
- The passage of the semen distally through urethra is a result of closure of the bladder neck (sympathetic reflex), relaxation of the external sphincter (parasympathetic reflex), and contraction of the bulbocavernous muscle (somatic innervation).
- The sympathetic nerves responsible for emission and bladder neck closure are the roots from T12–L3 spinal nerves.
- The innervations, anatomy, and function of ejaculatory ducts, bladder neck, external sphincter, and bulbocavernous muscle are essential for normal ejaculation.
- With aging, a natural decline occurs in the volume of ejaculate (decreases by ~0.03 mL/yr of life).
- Finasteride and dutasteride can cause reduced ejaculate.

COMMONLY ASSOCIATED CONDITIONS

- Prostate surgery, including radical prostatectomy, TURP, TUIP
- SCI
- BPH
- Prostatitis
- Depression
- Psychosis
- Hypertension

DIAGNOSIS

HISTORY

- Duration of the symptoms, amount of ejaculation, pain at ejaculation should be noted.
- Surgical procedures (prostate, bladder neck, pelvic) or retroperitoneal interventions should be sought. Neurologic abnormalities such as SCI, transverse myelitis, multiple sclerosis, familial history of cystic fibrosis should be noted.
- Defining a source of personal stress or interpersonal conflict or penile sensation loss may be useful in diagnosing retarded orgasm.
- Medications: Finasteride, dutasteride, MAOI antidepressants, SSRI antidepressants (fluoxetine), antipsychotics setoperone acetate, clonidine, methyldopa, -blockers (tamsulosin, others)

PHYSICAL EXAM

- Testicles, epididymis, and vas deferentia should be examined carefully whether present or absent on each side.
- Digital rectal exam should be done to palpate enlarged seminal vesicle or tenderness.
- Urethral meatus should be examined for the presence of hypospadias or epispadias.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- To establish whether there is anejaculation or retrograde ejaculation, postorgasmic urine analysis should be conducted after centrifugation.
- The presence of >10–15 sperm/HPF spermatozoa and/or seminal fluid in the urine indicates retrograde ejaculation.

Imaging

Rarely TRUS or MRI may be necessary to identify structural anomalies

Diagnostic Procedures/Surgery

- In cases where penile sensory changes are suspected, performing biothesiometry (penile vibration sensation threshold testing) may be of benefit. When abnormal, somatosensory evoked potentials of the dorsal nerves of the penis may be indicated.
- Psychological assessment may be indicated for men in whom a psychogenic cause is suspected.

TREATMENT

- Attempt to identify medications or other correctible causes.
- PVS can be applied using a commercially available vibrator (Pressure Point Massager, Brookstone) in retarded orgasm patients. Patients apply the vibrator to the frenular area of the penis for three 1-min periods separated by 1-min rest periods.
- Useful in up to 75% of men with SCI

• PVS may be a viable option to integrate into cognitive-behavioral therapy techniques, similar to a combined medical and psychotherapy model for treating ED.

MEDICATION

• Retrograde ejaculation can be treated with -adrenergic agents such as pseudoephedrine.

• The suggested dosage of pseudoephedrine ranges between 60 mg/d for 2–14 days. Ephedrine (25–50 mg/d) and imipramine (25–50 mg q.h.s.) are other agents that can be used.

• No oral agents have ever been shown to be consistently effective in the treatment of retarded orgasm.

• Spermatozoa can be retrieved from postorgasmic urine after retrograde ejaculation for artificial insemination.

SURGERY/OTHER PROCEDURES

• For men with anejaculation (whether psychogenic or due to failure of emission), electroejaculation can be performed to acquire spermatozoa to be used in artificial insemination/in vitro fertilization.

• TESE can be used in recalcitrant cases.

ADDITIONAL TREATMENT

• Cognitive-behavioral sex therapy

• Changing idiosyncratic masturbation style if present

• Rectal probe electroejaculation in SCI patients

ONGOING CARE

PROGNOSIS

Depends on the etiology, duration, and severity

COMPLICATIONS

• Can be accompanied with relationship stress and difficulty

• There is often concern about achieving pregnancy in young patients.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Anorgasmia/Dysorgasmia
- Ejaculation, Painful
- Ejaculation, Premature
- Ejaculatory Anhedonia
- Hematospermia
- Retrograde Ejaculation

CODES

ICD9

- 302.74 Male orgasmic disorder
- 608.87 Retrograde ejaculation

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- ED: Erectile dysfunction
- HPF: High-power field
- MAOI: Monoamine oxidase inhibitor
- MRI: Magnetic resonance imaging
- PVS: Penile vibratory stimulation
- SCI: Spinal cord injury
- SSRI: Selective serotonin reuptake inhibitor
- TESE: Testicular sperm extraction
- TUIP: Transurethral incision of prostate
- TURP: Transurethral resection of prostate

ENURESIS, ADULT

Gaurav Bandi, MD

BASICS

DESCRIPTION

- Enuresis is involuntary loss of urine.
- Nocturnal enuresis is nighttime involuntary incontinence.
- Adult NE occurs as 2 separate entities:
  - Persistent primary NE:
    NE in childhood that continues into adulthood
  - Adult onset or secondary NE:
    New-onset NE in adulthood
    Common particularly in patients with advanced age, altered mental status, and impaired mobility.
    The majority of adults with secondary NE have organic disease.
    Chronic urinary retention secondary to bladder outflow obstruction is the most common cause.
    Usually associated with diurnal symptoms, voiding dysfunction, and UTI.
    UDS needed to assess for lower urinary tract dysfunction (anatomic or neurologic).
    See chapters on Urinary Incontinence—Adult Female and Urinary Incontinence—Adult Male) for details.

EPIDEMIOLOGY

1–3% of adult population

RISK FACTORS

Family history of NE

Genetics

- Hereditary background is present.
- 40% of offspring will be enuretic if 1 parent has the condition; 70% both are affected.
- Genetic linkage to specific chromosomes, 13q and 12q have been identified.

PATHOPHYSIOLOGY

- As in children, the exact cause is unknown.
- Several theories:
  - Nocturnal alteration in vasopressin secretion or reduction in renal sensitivity to the antidiuretic action of AVP leading to nocturnal polyuria
  - Decreased functional bladder capacity, which sends a signal to the brain, which initiates involuntary voiding reflex

- Detrusor overactivity or instability (spontaneous detrusor muscle contractions) during filling
- Subtle neurologic maturational arrest
- Disturbance in sensory function, cortical arousal, or sphincter function
- Obstructive sleep apnea

DIAGNOSIS

HISTORY

- Never achieved total nocturnal urinary continence or achieved nighttime dryness for <1 yr
- No daytime symptoms, or subtle diurnal symptoms: Mild urgency, frequency, and urge incontinence
- No clearly identifiable medical or neurologic conditions
- Voiding diaries can be helpful to determine the frequency, volume, and pattern of voiding/enuresis as well as for providing clues to the underlying causes and contributing factors like drinking patterns.

Pediatric Considerations

Incidence of organic disease in adults with NE similar to that in children with NE.

PHYSICAL EXAM

- Complete urologic exam (including DRE in males and pelvic exam):
  - Usually normal
- Neurologic exam:
  - Abnormalities may be subtle

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture:
  - Rule out UTI.
  - Rule out proteinuria, glycosuria, and poor concentrating ability.
  - Rule out hematuria and pyuria.
- BUN and creatinine:
  - Rule out renal insufficiency.
- Urine cytology if carcinoma/CIS suspected

Imaging

- IVP, renal US, CT urogram or retrograde pyelogram:
  - Rule out anatomic abnormalities like ureteral duplication with ectopia.
- Spine x-rays:

– Rule out spina bifida occulta.

- PVR urine measurement:
  – Rule out chronic urinary retention.

Diagnostic Procedures/Surgery

Video-urodynamics are recommended in adults, particularly with diurnal symptoms:

- Identify anatomic abnormalities like urethral strictures or diverticula.
- Rule out neurogenic vesical dysfunction.

)[B]

- Bladder instability and reduced capacity are most common findings.

Pediatric Considerations

Incidence of UDS findings in patients with adult primary NE is higher than those in children.

DIFFERENTIAL DIAGNOSIS

- Emotional disturbances/psychological diseases
- Spina bifida occulta
- Obstructive sleep apnea
- Idiopathic detrusor instability
- Previously unrecognized myelopathy or neuropathy (multiple sclerosis, tethered cord, epilepsy)
- Secondary NE

TREATMENT

- If no anatomic or neurologic abnormalities are found, treatment is the same as in children (see chapter “Enuresis, Pediatric”)
- Dietary modification:
  – Varying success rates
  – Involves educating patients about bladder function and appropriate fluid intake, with the avoidance of caffeine and alcohol.
  – The timing of fluid intake should be stressed, explaining the importance of reducing urine output at night by restricting fluid intake in the evening.

MEDICATION

)[B]:

- Synthetic analogue of vasopressin
- Acts by reducing urine production for 5–6 hr.
- Reduction in the nocturnal urine volume prevents the individual reaching their bladder capacity.

• More effective at reducing the number of wet nights per week than curing bedwetting; it cures <1/3 of patients and its effect is temporary.

• Available as a nasal spray and oral tablet

• Side-effects: Nasal irritation, mood changes, dry mouth, sleep disturbances, rarely water intoxication leading to hyponatremic seizures and congestive heart failure

Geriatric Considerations

• DDAVP should be used judiciously or avoided in elderly patients at risk for electrolyte changes or fluid retention (congestive heart failure, renal insufficiency, and cystic fibrosis).

)[B]:

– Includes oxybutynin, tolterodine, solifenacin, darifenacin, and trospium

– Increases functional volume and reduces detrusor instability by inhibiting muscarinic receptors

– Effective for treating enuretics with detrusor instability

– Success in 5–40% of cases

– Side-effects: Dry mouth, dizziness, blurred vision

)[B]:

– Tricyclic antidepressant that has pharmacologic actions on both the peripheral and central nervous systems.

– Reduces the time spent in REM sleep and has both a mild anticholinergic and an -adrenergic action, thus tightening the internal sphincter while relaxing the bladder.

– Has a cure rate of 50% in adolescents, but a large percentage relapse once the drug is stopped.

– Side-effects: Sleep disturbance, loss of appetite and GI symptoms, as well as personality changes

SURGERY/OTHER PROCEDURES

Should only be considered in patients with severe detrusor instability not responding to both conservative and pharmacologic methods:

• Botulinum toxin injection

• Sacral neuromodulation

)(B)

• Detrusor myectomy

ADDITIONAL TREATMENT

• Conditioning therapy using enuresis alarms:

– Involves using a device that awakens an individual from sleep as soon as the accident begins

– Multiple variations of the alarm exist, ranging from vibrating to sounding alarms and wet-detection devices that can be attached to the underwear or a pad on which the individual sleeps

– Once awoken, the individual is able to stop the flow of urine, finish voiding in the bathroom, and return to bed.

– Success can be achieved in up to 70% of individuals, if they are motivated.

– Most commercially available alarms are easy to use, free of risk, inexpensive, and relatively comfortable.

– Disadvantage: Time commitment, with an average of 17 wks' use necessary before they can be discontinued.

- Bladder volume training:

– Involves combination of patient education, scheduled voiding, and pelvic muscle exercises

– Retention-control training involves progressively increasing voiding interval to counteract the reduced functional bladder capacity that characterizes many enuretics.

– When combined with conditioning therapy such as urinary alarms, results can be highly successful.

ONGOING CARE

PROGNOSIS

It has been suggested, although never confirmed, that all NE patients become dry eventually.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Long-term follow-up until NE resolves
- Worsening of symptoms: Re-evaluation

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ADDITIONAL READING

www.nafc.org/bladder-bowel-health/bedwetting-2/adult-bedwetting

See Also (Topic, Algorithm, Electronic Media Element)

- Enuresis, Pediatric
- Incontinence, Adult Male
- Urge Incontinence

CODES

ICD9

788.36 Nocturnal enuresis

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CIS: Carcinoma in situ
- CT: Computed tomography
- DDAVP: Desmopressin acetate
- DRE: Digital rectal exam
- GI: Gastrointestinal
- IVP: Intravenous pyelography
- NE: Nocturnal enuresis
- PVR: Postvoid residual
- REM: Rapid eye movement
- UDS: Urodynamics
- US: Ultrasound
- UTI: Urinary tract infection

ENURESIS, PEDIATRIC

Harry P. Koo, MD

Aaron B. Stike, MD

BASICS

DESCRIPTION

- Enuresis is the involuntary loss of urine.
- Nocturnal enuresis is wetting during the night.
- Diurnal enuresis is wetting during the day.
- A condition is primary if there has been no dry period longer than 6 consecutive mo; secondary if a dry period has lasted 6 mo.
- Monosymptomatic nocturnal enuresis refers to bedwetting exclusively.
- Polysymptomatic nocturnal enuresis may co-exist with daytime wetting, urgency, or frequency.

EPIDEMIOLOGY

- 15% of normal children have nocturnal enuresis at age 5.
- Of all children with enuresis, ~15% have daytime issues, 70% are bedwetters, 15% have both day and night enuresis.
- 5–7 million with nocturnal enuresis in the US

RISK FACTORS

- Nocturnal enuresis probably has a multifactorial etiology.
- See “Pathophysiology.”

Genetics

- Primary nocturnal enuresis tends to be familial:
  - When both parents had a history of nocturnal enuresis, there was 77% incidence in their children.
  - If 1 parent had a history of nocturnal enuresis, the incidence was 44% in children.
  - Several chromosomes have been found to have a genetic linkage to nocturnal enuresis, including chromosome regions 12q, 13q, 22q; a specific gene has yet to be identified.

GENERAL PREVENTION

Maintenance of regular voiding and bowel patterns may help reduce risks of developing functional enuresis.

PATHOPHYSIOLOGY

- Both functional and organic causes
- Functional enuresis comprises a heterogeneous group of disorders including urge syndrome, dysfunctional voiding.

- Organic urologic causes (1–4% of enuresis):
  - UTI, occult spina bifida, ectopic ureter, posterior urethral valves
- Organic nonurologic causes:
  - Epilepsy, sleep apnea, diabetes insipidus, diabetes mellitus
- Among monosymptomatic enuretics, there may be an absence of the normal diurnal variation in the secretion of arginine vasopressin by the anterior pituitary.
- CNS maturational delay is implicated as a cause:
  - Higher rate of low Apgar scores, intrauterine growth restriction, implicating possible perinatal neurologic insult
  - Higher incidence of poorer visual motor and spatial perception skills
  - Intelligence tests have shown no difference between enuretics and other children.
- Association between nocturnal enuresis and obstructive sleep apnea; apneic episodes result in increased secretion of atrial natriuretic factor.
- Conflicting data regarding psychological factors in the etiology of nocturnal enuresis:
  - Possible relationship between ADHD and nocturnal enuresis: Children with ADHD are 2.7 times more likely than other children to have enuresis.

COMMONLY ASSOCIATED CONDITIONS

- Higher incidence of nocturnal enuresis seen in children with cystic fibrosis and sickle cell disease.
- Daytime enuresis is associated with:
  - Bowel dysfunction including constipation and encopresis, UTI, vesicoureteral reflux

DIAGNOSIS

HISTORY

- A detailed medical history helps delineate the pattern of enuresis and may identify organic causes.
- Child's voiding habits including frequency, urgency, dysuria, straining, posturing
- Pattern of fluid intake including intake of caffeinated beverages
- History of UTI
- Impaired upper or lower extremity motor skills warrant neurologic evaluation
- Obstetrical history including fetal distress, anoxia, birth trauma, oligohydramnios, hydronephrosis
- Association with encopresis
- Family history of nocturnal enuresis
- Social history that includes how wetting affects the child is essential to assess the child's level of motivation (especially in planning for behaviorally oriented treatment programs).

PHYSICAL EXAM

- General exam should include the child's general level of developmental maturity; inspection of the abdomen, genitalia; and a directed neurologic exam.
- Abdominal exam for distended bladder and bowel
- Lower back inspection for stigmata of occult spinal dysraphism such as sacral dimple, hair tuft, hemangioma, or lipoma
- Genital exam for congenital anomalies including labial adhesions (girls); urethral abnormalities (boys)
- Abnormal rectal tone or absent perineal sensation can point toward neurogenic etiology for wetting
- Determination of any gait abnormalities

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: Including specific gravity to evaluate for diabetes insipidus
- Urine culture: If urinalysis or history is suggestive of UTI

Imaging

- Children with monosymptomatic nocturnal enuresis do not need any further evaluation (other than UA)
  - US: May be considered in older enuretic patients who have failed initial therapy; as an additional level of reassurance for the older child and family that no anatomic problem is present
- Children with history of UTI or polysymptomatic or daytime enuresis should undergo more detailed evaluation:
  - US: To evaluate kidneys and bladder; provides information about bladder wall thickening, PVR urine
  - VCUG gives information about whether vesicoureteral reflux is present. The VCUG may also reveal changes compatible with dysfunctional voiding in girls or findings diagnostic of posterior urethral valves in boys.
  - Scout abdominal x-ray: May provide information about any spinal abnormality and also assesses for degree of stool retention
  - MRI of the spine for children suspected of having a possible neurogenic bladder as the etiology for enuresis

Diagnostic Procedures/Surgery

- Voiding diary: Helpful in evaluating children with daytime or polysymptomatic enuresis:
  - Record of at least two 24-hr periods, the timing and amount of each void, as well as the number of incontinence episodes

- Uroflowmetry to assess any degree of bladder outlet obstruction or hypocontractility; staccato voiding pattern
- Urodynamics: Especially helpful in evaluating bladder compliance and function in children with severe dysfunctional voiding or enuresis due to neurogenic bladder or posterior urethral valves
- Cystoscopy: Routine use should be avoided. However, it may be helpful in the assessment of select patients with potential anatomic causes for enuresis.

Pathological Findings

Related to specific organic causes of enuresis

DIFFERENTIAL DIAGNOSIS

- Ectopic ureter (girls)
- Posterior urethral valves (boys)
- Occult spina bifida
- Giggle incontinence (enuresis risoria)
- Vaginal voiding

TREATMENT

- Before embarking on any therapy, the interest and ability of the child and the family to comply should be determined. In addition, patience and compliance should be emphasized because many months may be required to achieve improvement and resolution.
- Motivational therapy should be encouraged in almost every case; it is useful in conjunction with other treatments.

MEDICATION

First Line

DDAVP (desmopressin) for nocturnal enuresis:

- 0.2–0.6 mg PO
- Success rate about 20–50%
- Caution in patients with cystic fibrosis (hyponatremia)

Second Line

Imipramine for nocturnal enuresis:

- Tricyclic antidepressant with anticholinergic effects
- Success rates of 25–40%, but relapse rates can be high
- 25–50 mg, with a maximum dose of 0.9–1.5 mg/kg/d

ALERT

Imipramine overdose can result in seizure, hypotension, coma, and fatal arrhythmias.

- Oxybutynin for polysymptomatic or daytime enuresis:

– 2.5–5 mg b.i.d.–q.i.d. (0.2 mg/kg/dose)
– Also available in the long-acting form (5–15 mg/d)
– More success when the medication is used in conjunction with a well-organized treatment program

- Tolterodine for polysymptomatic or daytime enuresis:
  – 1–2 mg b.i.d.
  – Also available in the long-acting form (2–4 mg/d)
  – More success when the medication is used in conjunction with a well-organized treatment program
- Hyoscyamine for polysymptomatic or daytime enuresis:
  – 0.375–0.75 mg b.i.d.
  – More success when the medication is used in conjunction with a well-organized treatment program
- Doxazosin for polysymptomatic or daytime enuresis:
  – 0.5–1 mg/d
  – -blocker; may help relax the internal sphincter
  – More success when the medication is used in conjunction with a well-organized treatment program
- Low-dose prophylactic antibiotics for polysymptomatic or daytime enuresis:
  – Helpful for children where recurrent UTI or bacteriuria are involved in the problem of dysfunctional voiding.
  – Trimethoprim and sulfamethoxazole or nitrofurantoin is recommended (see chapter on “Vesicoureteral Reflux, Pediatric”)

SURGERY/OTHER PROCEDURES

Surgery only in cases of congenital anomalies (eg, ectopic ureter, posterior urethral valves)

ADDITIONAL TREATMENT

- Children with dysfunctional voiding may benefit from elimination retraining program and selective use of anticholinergic medications.
- Enuresis alarm for monosymptomatic nocturnal enuresis works well in the older child with a motivated family:
  – Treatment can take up to 2–3 mo
  – Mechanism of action of the behavioral conditioning remains unclear
  – Initial cure rate is as high as 70%; relapse can be high, but 50% achieve long-term cure

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Pediatric biofeedback can be effective for dysfunctional voiding cause of enuresis:

- Most helpful as an adjunct to elimination retraining program
- The child must have sufficient cognitive ability to understand what he is being taught.

ONGOING CARE

PROGNOSIS

- After age 5, spontaneous resolution rate of 15%/yr for bedwetters
- After age 15, <1% have nocturnal enuresis.
- Over 6.5 yr of follow-up, 91% no longer wet during the day, 84% no longer wet at night; and among those with history of UTI, 82% no longer have infections.

COMPLICATIONS

- Recurrent UTI
- Persistence of incontinence or urge symptoms

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Children with history of UTI or organic causes of enuresis should be followed for the specific condition.
- Children should be monitored closely while on medication to treat the enuresis.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Enuresis, Adult
- Enuresis, Pediatric Algorithm
- Urinary Tract Infection, Pediatric
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

- 307.6 Enuresis
- 788.36 Nocturnal enuresis

ABBREVIATIONS

- ADHD: Attention-deficit hyperactivity disorder
- CNS: Central nervous system
- DDAVP: Desmopressin acetate
- PVR: Postvoid residual
- UA: Urinalysis
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

EPIDIDYMIS, MASS (EPIDIDYMAL TUMORS AND CYSTS)

Charles D. Scales, Jr., MD

Judd W. Moul, MD

BASICS

DESCRIPTION

- Small solid paratesticular mass located in any portion of the epididymis
- Frequently asymptomatic; usually discovered on routine urologic physical exam
- Occasionally, pain is presenting complaint.
- Enlarging masses are concerning for possible tumor.

EPIDEMIOLOGY

- Not well defined
- Benign cysts more common with aging

RISK FACTORS

- Von Hippel-Lindau associated with cystadenoma
- DES exposure in utero: Epididymal cysts

PATHOPHYSIOLOGY

- Most solid lesions benign
- Malignant lesions uncommon
- Metastasis rare but reported

COMMONLY ASSOCIATED CONDITIONS

Von Hippel-Lindau

DIAGNOSIS

HISTORY

- Age: Cystic lesion are more common >40 yr of age.
- Painful masses are more likely inflammatory.
- Growth rate: Enlarging mass is concerning for malignancy.
- Frequency, urgency, dysuria, fever, chills may suggest infection.
- History of cancer: Consider metastatic disease
- Travel history: Consider TB
- History of vasectomy

PHYSICAL EXAM

- Scrotal exam: Determine location of mass
- Physical signs of infection: Tender prostate, tender epididymis
- Compare with contralateral scrotum/testis.
- Evaluate for inguinal lymphadenopathy.

- Evaluate for hernia.
- Lesion fixed or mobile

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis to evaluate for infection
- Blood count: Leukocytosis may suggest infection.
- Tumor markers: AFP, -HCG, LDH
- PPD testing if TB suspected

Imaging

- Scrotal US:
  - Solid vs. cystic
  - Testicular or paratesticular location
  - Cannot differentiate between benign and malignant lesions
  - Doppler can indicate flow pattern
- CXR if TB suspected

Diagnostic Procedures/Surgery

Open biopsy or excisional biopsy by inguinal approach

Pathological Findings

- Adenomatoid tumor: Benign behavior; no metastasis
- Adenocarcinoma: Primary is extremely rare
- Rhabdosarcoma
- Leiomyosarcoma
- Fibrosarcoma

DIFFERENTIAL DIAGNOSIS

- Epididymal cyst: Most common
- Epididymitis:
  - Consider sexually transmitted etiology in young men
- Benign solid tumors:
  - Adenomatoid tumors most common
  - Cystadenoma: 1/3 of cases bilateral:
    Associated with VHL
- Leiomyoma
- Primary malignant tumor [C]:
  - Rhabdomyosarcoma most frequent
  - Leiomyosarcomas, fibrosarcomas also reported

  - Adenocarcinoma exceedingly rare as primary tumor
- Metastatic tumor:
  - Adenocarcinoma: Mandates evaluation for primary site, if unknown
  - Lymphoma

Pediatric Considerations

- Rhabdomyosarcoma predominantly occur in children and adolescents.

TREATMENT

Observation for asymptomatic cystic masses

MEDICATION

- Levofloxacin 500 mg/d for 10 days for epididymitis likely from enteric organisms
- If gonorrhea or chlamydia suspected:
  - Ceftriaxone 250 mg in 1 single dose PLUS
  - Doxycycline 100 mg PO b.i.d. for 10 days

SURGERY/OTHER PROCEDURES

- Excision via inguinal approach for solid masses, especially if enlarging [C]
- Orchiectomy if frozen section demonstrates malignant tumor
- Consider RPLND for rhabdomyosarcoma

ADDITIONAL TREATMENT

Radiotherapy

Consider for rhabdomyosarcoma [C]

Additional Therapies

- Consider infectious disease consult for persistent infection in setting of suspected gonorrhea or chlamydia.
- Consider chemotherapy for rhabdomyosarcoma [C]:
  - Vincristine, cyclophosphamide, and dactinomycin

ONGOING CARE

PROGNOSIS

- Adenomatoid tumors behave in benign fashion.
- Rhabdomyosarcoma has poor prognosis.
- Multimodal therapy for rhabdomyosarcoma in pediatric cases has better survival.

COMPLICATIONS

Lymphatic spread of malignant tumors

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Monitor for metastasis in malignant disease.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Adenomatoid Tumors, Paratesticular
- Epididymis, Cystadenoma
- Epididymis, Metastasis to
- Epididymis, Obstruction
- Epididymitis
- Scrotum and Testicle, Mass
- Scrotum and Testicle Mass Algorithm
- Sexually Transmitted Diseases, General
- Spermatocele
- Von Hippel-Lindau Disease/Syndrome

CODES

ICD9

- 222.3 Benign neoplasm of epididymis
- 239.5 Neoplasm of unspecified nature of other genitourinary organs
- 608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- AFP: Alpha feto-protein
- CXR: Chest x-ray
- DES: Diethylstilbestrol
- LDH: Lactate dehydrogenase
- PPD: Purified protein derivative
- RPLND: Retroperitoneal lymph node dissection
- TB: Tuberculosis
- US: Ultrasound

EPIDIDYMITIS

Benjamin M. Brucker, MD
S. Bruce Malkowicz, MD

BASICS

DESCRIPTION

- An inflammatory condition of the epididymis
- The entity of epididymo-orchitis implies there is also inflammation of the testicle (ie, orchitis):
  - Acute
    Infectious (bacterial, viral, fungal, parasitic)
    Noninfectious (inflammatory, systemic disease, medication, obstructive, idiopathic)
  - Chronic:
    Lasting >3 mo

EPIDEMIOLOGY

- Estimated at <1 in 1,000 in the US
- 42% of cases are in men 20–39 yrs old
- 5th most common urologic diagnosis in men 18–50
- Mean age at presentation:
  - Acute: 41 yrs
  - Chronic: 49 yrs
- Reported from infancy to age 90
- Diagnosed in 1% of Canadian men presenting to outpatient urologist
- 80% of epididymitis is chronic:
  - Average patient with chronic epididymitis has had symptoms for 2.5–5 yrs at the time of diagnosis

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- Epididymitis caused by an STD has the following risk factors:
  - High-risk sexual behavior (multiple sexual partners, sex with a partner with an STD, having sex without a condom
  - A personal history of STD
- Non-STD infectious epididymitis has the same risk factors as male UTI:
  - History of prostate and UTI
  - Being uncircumcised or having anatomic abnormality of the GU tract
  - Recent catheterization or manipulation of the GU tract (ie, cystoscopy, clean intermittent catheterization)

– Urinary tract obstruction- BPH/urethral stricture/prostate cancer:

56% of men >60 with epididymitis had lower urinary tract obstruction

• African American race is a risk factor for sarcoidosis, a noninfectious, noncaseating chronic granulomatous disease. This can lead to granulomas of the epididymis.

GENERAL PREVENTION

• Abstinence
• Condom use
• Avoiding unnecessary instrumentation while urine is actively infected
• Avoidance of inciting medication (amiodarone)

PATHOPHYSIOLOGY

• Retrograde inoculation of epididymitis from infected urine:

– Remains a plausible theory, supported by increased risk of epididymitis following instrumentation (especially if urine is infected). Animal models also support this theory.

Chlamydia trachomatis: <35 yr

Coliform bacteria (ie, E. coli): >35 yr

Other: Ureaplasma urealyticum, Mycoplasma, Corynebacterium, Mima polymorph, Brucella

Filarial infection/invasion of lymphatic system: Most common Wucheria bancrofti

• Reflux of sterile urine is a proposed mechanism of noninfectious epididymitis:

– High pressure from bladder contraction against a closed outlet causes retrograde flow of sterile urine into the vas deferens. This then causes a chemical irritation of the epididymis, resulting in inflammation and swelling.

• Amiodarone: This cardiac antiarrhythmic concentrates 300 times serum level in the epididymis. Antiamiodarone antibodies develop and cause inflammation on the lining of the epididymis.

• The most common cause of chronic infectious epididymitis is TB:

– Thought to be secondary to hematogenous spread.
– Consider this diagnosis with known exposure or history of TB.
– Also can be related to BCG used in the treatment of superficial bladder cancer.

• Systemic diseases:

– Behçet disease: Idiopathic vasculitic disease that can cause a noninfectious epididymitis

– Sarcoidosis: Noncaseating granulomas form in the epididymis, causing pain and swelling

Pediatric Considerations

- Often attributed to viral infection
- Classically, mumps had been a frequent cause; however, this is virtually eradicated since widespread use of the mumps vaccine.
- M Pneumoniae, enteroviruses, and adenoviruses have been implicated as a cause of epididymitis in children.
- Usually not bacterial in children
- Henoch-Schönlein purpura: A small-vessel vasculitis can cause a painful swollen scrotum. This usually prompts imaging that reveals epididymitis.

COMMONLY ASSOCIATED CONDITIONS

- Orchitis or inflammation of the testicle. This entity rarely exists without epididymitis.
- Hydrocele: A reactive process

DIAGNOSIS

HISTORY

- Testicular pain:
  - Usually gradually worsening from mild to more intense

    In torsion, the onset of pain is rapid and intense
- Urethritis and or urethral discharge may be noted in cases with STD-related epididymitis.
- Review of systems is helpful to elucidate for systemic disease (ie, sarcoid, TB, Behçet, brucellosis)

PHYSICAL EXAM

- Erythema of scrotal skin
- Swelling and tenderness to palpation
- Fever
- Involvement of the adjacent testicle
- Hydrocele: This is reactive and may resolve more slowly than the acute infection.
- Genital exam to look for lesions:
  - Coinfection from high-risk sexual behavior
  - Ulcerations from Behçet disease
- Prostate exam: Especially when dealing with chronic noninfectious epididymitis to evaluate for prostatitis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Gram stain of urethral exudates for WBC and/or bacteria (ie, presence of WBC containing intracellular gram-negative diplococci is very sensitive and specific for diagnosing gonorrhea)

- Urine analysis: May be leukocyte esterase positive
- CBC: May demonstrate a leukocytosis
- Midstream clean catch urine culture and sensitivities
- When STD is suspected, the clinician should test for gonorrhea, chlamydia, and other STDs (such as HIV):
  - Culture and nucleic acid hybridization tests require urethral swab specimens.
  - Nucleic acid amplification tests can be performed on urine specimens:
    Amplification tests are preferred for the detection of C. trachomatis

Imaging

- US:
  - Most useful to rule out testicular torsion
  - Color duplex Doppler US can identify hyperemia and swelling in the epididymis
  - For diagnosing acute epididymitis:
    Sensitivity of 70%; specificity of 88%
    Thus, a negative US in the clinical setting of epididymitis should not necessarily alter management.
  - May identify abscess formation
- Scrotal radionuclide scintigraphy has a high sensitivity and specificity in differentiating torsion from epididymitis:
  - Rarely used secondary to advances in US
  - Late torsion can look like epididymitis.

Pediatric Considerations

- Some have suggested a radiologic workup for pediatric patients with epididymitis:
- Acute epididymitis with a urine culture or recurrent epididymitis:
  - Renal bladder US and voiding cysto-urethrogram
- Acute epididymitis culture negative:
  - Renal bladder US only

Diagnostic Procedures/Surgery

Testicular exploration may show hyperemia and inflammation of epididymis:

- Usually if the clinical suspicion is high for torsion and not used as a 1st-line diagnostic procedure

Pathological Findings

Inflammation, infection, possible fibrosis

DIFFERENTIAL DIAGNOSIS

- Testicular or epididymal tumor

- Varicocele
- Prostatitis/chronic pelvic pain syndrome/interstitial cystitis
- Referred pain (hernia, prior hernia repair, renal colic, aneurysm, back pain)

TREATMENT

- NSAIDS (ibuprofen, etc.) for pain and inflammation

)[C]

- Scrotal support
- Ice/heat based on response

MEDICATION

Tailored to age and history (ie, instrumentation):

First Line

- <35 with sexual risk factors: Doxycycline 100 mg PO b.i.d. for 10 days + ceftriaxone 250 mg IM for 1 day
- >35 and no STD suspected: Levofloxacin 500 mg/d or ofloxacin 300 mg b.i.d. for 10 days
- TB: 6 mo of isoniazid, rifampin, pyrazinamide (plus ethambutol pending sensitivity if in high resistance area)

Second Line

<35 with allergies to 1st-line: Levofloxacin or ofloxacin vs. desensitization (increasing resistance of gonorrhea to fluoroquinolones)

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- Drainage if abscess forms
- Epididymectomy for unremitting/severe acute or chronic epididymitis
- Orchiectomy for severe epididymal orchitis unresponsive to conservative treatment
- Testicular denervation for chronic pain: Not widely used

ADDITIONAL TREATMENT

- Acute: Bed rest, scrotal elevation, NSAIDs, analgesia
- Chronic: Heat therapy, nerve blocks, anticonvulsants/tricyclic antidepressants:
  - Gabapentin
  - Amitriptyline

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Acupuncture for chronic pain; no clinical studies support this.
- Patients with STDs should avoid sex with partners until treated.
- Patients should advise their sexual partners to be evaluated and treated as well.

ONGOING CARE

)[C]

- Most acute cases show clinical improvement after 48–72 hrs of appropriate antibiotics.
- Swelling and edema may persist for days to weeks.
- Testicular atrophy can occur.
- Sperm motility, and morphology can spontaneously improve.
- Chronic cases can be difficult to treat; counseling is important:
  - Those with a structural abnormalities had excellent outcomes with surgery.
  - Normal exam and US had at best a 55% chance of improvement with epididymectomy.

COMPLICATIONS

- Epididymal and/or testicular abscess
- Pyocele
- Sepsis
- Progression of epididymitis to epididymal orchitis
- Chronic epididymitis/chronic pain
- Testicular atrophy
- Infertility: More likely from bilateral cases

ALERT

Failure to make accurate diagnosis:

- Acute scrotal pain that is caused by testicular torsion can be misdiagnosed as epididymitis. This can have serious medical and legal implications.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Many men in large studies have no identifiable organism.
- No specific guidelines exist for long-term follow-up.
- Any test for concurrent STDs need appropriate follow-up.

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See Also (Topic, Algorithm, Electronic Media Element)

- Epididymis, Mass (Epididymal Tumor and Cysts)
- Scrotum and Testicle, Mass
- Testis, Pain (Orchalgia)
- Urinary Tract Infection (UTI), Adult Male

CODES

ICD9

- 604.0 Orchitis, epididymitis, and epididymo-orchitis, with abscess
- 604.90 Orchitis and epididymitis, unspecified

ABBREVIATIONS

- BCG: Bacille Calmette-Guérin
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- GU: Genitourinary
- HIV: Human immunodeficiency virus
- NSAID: Nonsteroidal anti-inflammatory drug
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound
- WBC: White blood cell

EPISPADIAS

Erica J. Traxel, MD

Paul H. Noh, MD

BASICS

DESCRIPTION

- Congenital anomaly characterized by a dorsal deficiency of the urethra, resulting in dorsal displacement of the urethral meatus in relation to the phallus.
- Usually occurs in conjunction with exstrophy, but can be an isolated phenomenon.

EPIDEMIOLOGY

)[A]

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RISK FACTORS

Genetics

Likely a sporadic defect without a single gene or environmental factor being responsible

PATHOPHYSIOLOGY

- On the same spectrum of embryologic maldevelopment as 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.

COMMONLY ASSOCIATED CONDITIONS

- Most commonly occurs in the setting of exstrophy
- Deformities of the external genitalia
- Urinary incontinence

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DIAGNOSIS

HISTORY

- More severe forms recognized at birth and referred early on to urologist
- 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

- Atypical disease spectrum, as more severe forms are more common than less severe forms.
- Males:
  - Displaced meatus, ranging from glans to penile shaft to penopubic region to subsymphyseal location
  - Open urethral plate visible on dorsum of phallus
  - Divergent penopubic attachments due to pubic diastasis, resulting in splaying of corpora cavernosa and a short, pendular penis with dorsal chordee, similar to that seen in exstrophy.
  - Ventral hood of foreskin
  - Should assess position of testes.
- Females:

)[A]:

I: Urethral orifice appears patulous.

II: Urethra split dorsally along most of urethra.

III: Urethra open dorsally along its entire length into the bladder neck, rendering patient incontinent. Most common female type.

  - Bifid clitoris
  - Mons pubis depressed and covered in glabrous skin
  - Labia minora poorly developed and terminated anteriorly at clitoris
  - Vagina and internal genitalia usually normal
- Other:
  - Should asses for any degree of bladder prolapse or exstrophy.
  - Low-set umbilicus
  - Pubic diastasis due to outward rotation of innominate bones, usually not as wide as in exstrophy-epispadias complex
  - Should assess possible inguinal hernias.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

CBC, renal profile.

Imaging

- Plain x-ray to assess orientation of pelvic bones
- 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.

• Voiding cystourethrogram to assess bladder capacity, bladder outlet, presence/absence of VUR.

Diagnostic Procedures/Surgery

Cystourethroscopy to assess length of urethra, presence/competency of sphincter, bladder capacity/quality, location/quality of ureteral orifices.

DIFFERENTIAL DIAGNOSIS

- Varying degree of epispadias
- Classic bladder exstrophy

TREATMENT

- Usually managed along with bladder exstrophy, which is commonly present
- Complete continence may not be achieved for months to years after initial surgery.
- In males, continence may not occur until puberty with maturation of prostate.

MEDICATION

- Surgery is 1st-line therapy, but medications can serve as an adjunct.
- Anticholinergic therapy may help with bladder development and modeling to promote increased capacity with good compliance once surgery has increased outlet resistance.

SURGERY/OTHER PROCEDURES

- Goals:
  - Protection of upper tracts, including correction of VUR and maintenance of a low-pressure system
  - Attainment of urinary continence
  - Reconstruction of external genitalia for optimal functional and cosmetic results
- 1st stage:
  - Address external genitalia and urethra 1st, as the resultant increase in bladder outlet resistance will increase capacity in the majority of patients.
  - Males:

    Administer testosterone stimulation preoperatively.

    At 6–12 mo of age, perform modified Cantwell-Ransley epispadias repair (± Mitchell modification), involving tubularization of intact urethral plate with reverse meatal advancement and transposition of urethra ventral to corpora cavernosa.

    Also must correct dorsal chordee by division of suspensory ligaments, freeing attachments from undersurface of inferior pubic ramus, and medially rotating the corpora cavernosa, and occasionally performing cavernostomy
  - Females:

    At 12–18 mo of age, perform genitoplasty and urethroplasty.

Edges of urethra approximated for tubularization

Clitoris and labia minora reapproximated

Mons may be reconfigured

- 2nd stage:
  - Typically performed at 3–5 yr
  - Waiting between 1st and 2nd stages usually allows for increase in bladder capacity.
  - When child is older, he/she is interested in playing active role in toilet-training and achieving continence
  - Most commonly, Young-Dees-Leadbetter bladder neck reconstruction affords best chance at continence.
  - Often, ureters must be reimplanted at same time due to proximity to bladder neck or VUR. Cohen technique usually preferred.

ADDITIONAL TREATMENT

Further surgery may be necessary to correct complications of initial surgery or to achieve improved cosmesis or complete continence.

Some prefer a single-stage operation, involving simultaneous genitoplasty, urethroplasty, and bladder neck reconstruction.

ONGOING CARE

PROGNOSIS

)[B]

)[B]

- 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 seem to indicate the majority of patients can have intercourse and many males have even fathered children.

COMPLICATIONS

)[B]

- Other less common complications are stricture, meatal stenosis, wound infection, diverticulum, and ureteral obstruction.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- After epispadias repair:
  - Remove urethral catheter 1–2 wks after surgery.
  - Regular cystoscopy to assess urethra and bladder capacity

– Regular upper-tract monitoring with renal/bladder US to ensure healthy upper tracts.

- After bladder neck repair:
  - Initiate suprapubic tube capping trials a few weeks after surgery.
  - Can remove SP tube once PVRs are minimal.
  - Continuation of prophylactic antibiotics until resolution of VUR confirmed and child voiding well.
  - Regular upper-tract monitoring with US.
  - Urodynamics may be necessary with cystometrogram and urethral pressure profilometry in cases of persistent incontinence or infection.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Exstrophy, Bladder (Classic Exstrophy)
- Exstrophy, Cloacal
- Exstrophy-Epispadias Complex

CODES

ICD9

- 752.62 Epispadias
- 753.5 Exstrophy of urinary bladder

ABBREVIATIONS

- CBC: Complete blood cell count
- PVR: Postvoid residual
- US: Ultrasound
- UTI: Urinary tract infection
- VUR: Vesicoureteral reflux

ERECTILE DYSFUNCTION FOLLOWING PELVIC SURGERY OR RADIATION

Patrick E. Teloken, MD
John P. Mulhall, MD

BASICS

DESCRIPTION

- Inability to achieve a penile erection sufficient for sexual intercourse is common after major pelvic surgery (eg, RP, radical cystectomy, colonic surgery) and pelvic radiation therapy.
- After surgery, erectile function declines suddenly; it usually improves slowly over the ensuing 24 mo.
- Conversely, RT causes insidious-onset ED, usually after 1 yr of treatment, with progressive worsening over a 3–5-yr period.
- Sexual function is the factor most strongly associated with outcome satisfaction in patients treated for prostate cancer.

EPIDEMIOLOGY

- ED is more common immediately after RP than immediately after RT, but rates level off upon long-term follow-up. After 2 years of treatment for prostate cancer ED rates range as follows:
  - Surgery: 20–80%
  - Radiation: 30–70%
- The wide discrepancy in ED rates is related to variability in 3 factors:
  - Definition of adequate erectile function
  - Populations studied
  - Means of data acquisition

RISK FACTORS

- Pretreatment of erectile function
- Patient age at time of treatment
- Vascular comorbidity status
- Nonnerve sparing surgery
- Surgeon
- Surgeon volume
- Radiation dose and treatment plan
- ADT combined with radiation

- Time after radiation

GENERAL PREVENTION

- Surgery-related: Factors likely to translate into better long-term erectile function after radical prostatectomy include:
  - Cavernous nerve sparing, accessory pudendal artery sparing, and possibly pharmacologic penile rehabilitation and neuromodulatory agents.

Penile rehabilitation is widely practiced despite lack of definitive evidence. Studies with immunophilin ligand neuromodulators (tacrolimus and GPI-1485) have been completed. Data are awaited.

- Radiation-related: Attempts to limit prostate cancer radiation dose to corpora cavernosa and internal pudendal artery have been achieved with IMRT compared to brachytherapy and 3D conformal therapy. Whether such a reduction in exposure translates into better long-term erectile function outcomes is as of yet unanswered.

PATHOPHYSIOLOGY

- Surgery:
  - Cavernous nerve injury is main mechanism. Denervation leads to structural alterations in corporal smooth muscle (erectile tissue apoptosis and collagenization).
  - Arterial trauma may also be involved in some cases. Structural changes may be augmented by the absence of cavernosal oxygenation.
  - Structural changes lead to venous leak, a poor prognostic indicator for recovery of natural erectile function and response to phosphodiesterase type-5 (PDE5) inhibitors.
- Radiation therapy:
  - Primarily arteriogenic
  - Veno-occlusive dysfunction plays a role in men in whom erectile tissue is exposed to radiation.
  - With 3D-conformal therapy, 40% of the total radiation is delivered to the most proximal 1 inch of the corporal bodies. It is likely that some mild cavernous neuropathy occurs after radiation, although most patients respond to PDE5 inhibitor for the 1st 24 mo after radiation completion.

DIAGNOSIS

HISTORY

- Medical history: Look for ED risk factors.
- Surgical history: Type and date of procedure; nerve-sparing status is critical to outcome.
- Radiation history: Dose and template of radiation. The concomitant use of ADT has been shown to lead to poorer outcomes. The threshold period of ADT exposure for the worst

outcomes appears to be 4–6 mo.

- Characterization of ED: Onset, severity, consistency, prior therapy use and response

PHYSICAL EXAM

- Penis: Penile compliance (stretch of the penis), Peyronie disease plaques
- Testicular volumes to screen for hypogonadism

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Early-morning serum total testosterone level

Diagnostic Procedures/Surgery

Vascular studies:

- Duplex Doppler penile US: Peak systolic velocity <30 cm/s indicates arterial insufficiency; end diastolic velocities >5 cm/s indicate venous leak

DIFFERENTIAL DIAGNOSIS

- Hyperprolactinemia
- Medications (commonly implicated):
  - Antihypertensives especially thiazide diuretics, -blockers and methyldopa
  - Antidepressants especially the SSRIs, anticholinergics
  - Addictive medications: Alcohol, narcotics, antipsychotics, antiandrogens
  - Histamine H2-blockers, finasteride, dutasteride, LHRH analogues, spironolactone, others
- Neurologic (spinal cord injury, radical prostatectomy, rectal surgery, aortic bypass)
- Pelvic radiation
- Peyronie disease
- Priapism history
- Psychogenic
- Testicular failure/hypogonadism
- Vascular

TREATMENT

)[C].

- Cardiovascular risk assessment (done before proceeding with any therapy)

MEDICATION

First Line

)[A]:

- Sildenafil 50–100 mg or vardenafil 10–20 mg or tadalapil 10–20 mg
- These agents are likely to be ineffective in the 1st few months after surgery.

• The time to best PDE5 inhibitor response is ~2 yr after surgery, the point in time of maximum cavernous nerve regeneration.

• These agents are used in a variety of rehabilitation (daily, regular dosing) regimens.

• After radiation, most men are good PDE5 inhibitor responders in the 1st yr, but a steady decrease in response occurs over years 2 and 3.

Second Line

• Intracavernosal injection therapy:

– Single-agent (prostaglandin E1), Bimix (phentolamine and papaverine), Trimix (phentolamine, papaverine, and prostaglandin E1) are used.

– High efficacy in range of 70–90% is reported.

– Risks are predominantly pain with PGE compounds and priapism overall, although with good education, training, and monitoring the priapism rate is <1%.

• Vacuum device: Poor compliance over time due to the fact the erection is nonphysiologic (does not appear or feel normal).

• Transurethral PGE suppository (MUSE): At doses in excess of 250 mcg, is associated with significant burning penile pain within the 1st 6 mo of RP. May be useful as a rehabilitation strategy.

OTHER

Penile prosthesis implantation: Reserved for patients who fail or refuse other treatments.

ADDITIONAL TREATMENT

Post-RP penile rehabilitation:

• Strategy to preserve erectile tissue health while nerves recuperate and therefore maximize the chances of recovery of erectile function

• Consists of inducing increase in blood flow to the penis during period of nerve recuperation to prevent irreversible structural damage to cavernous smooth muscle.

• Various techniques described, including PDE5 inhibitors, PGE administration. and vacuum devices

ALERT

Herbal and dietary supplements used to treat ED are not FDA-approved; those listed here are for reference only

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Therapies reported to possibly improve ED in general are ginkgo biloba, red ginseng, yohimbine. None adequately studied for effectiveness or safety in the posttherapy group.

ONGOING CARE

PROGNOSIS

- Erectile function improves with time after surgery. Mean time to maximal recovery of erectile function after RP is 18–24 mo. Significant improvement in erectile function is unlikely after 2 yr.
- Erectile function progressively worsens after RT with nadir at 3–5 yr after completion of treatment

COMPLICATIONS

- Significant impairment of quality of life
- Depression

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Depends on patient response to treatment
- Every 3 mo if on penile rehabilitation

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See Also (Topic, Algorithm, Electronic Media Element)

- Erectile Dysfunction/Impotence, General
- Penile Rehabilitation

CODES

ICD9

607.84 Impotence of organic origin

ABBREVIATIONS

- ADT: Androgen deprivation therapy
- ED: Erectile dysfunction
- PGE: Prostaglandin E1
- RP: Radical prostatectomy
- RT: Radiation therapy

ERECTILE DYSFUNCTION/IMPOTENCE (ED)

Anthony John Schaeffer, MD
Trinity J. Bivalacqua, MD, PhD

BASICS

DESCRIPTION

- Consistent or recurrent inability to attain and/or maintain an erection sufficient for satisfactory sexual activity
- Synonym(s): Impotence

EPIDEMIOLOGY

Incidence

)[C]:

- 12 cases per 1,000 men-yrs 40–49 yr
- 30 cases per 1,000 men-yrs 50–59 yr
- 46 cases per 1,000 men-yrs 60–69 yr

Increases universally with age and medical comorbidities (DM, cardiovascular disease):

- Up to 40% of men at age 40 have some degree of ED.
- Up to 75% of men >70 have some degree of ED.

RISK FACTORS

)[C].

- DM:
  - 35–75% of all men w/diabetes have some degree of erectile dysfunction.
- Cardiovascular disease (hyperlipidemia, hypertension, peripheral vascular disease)
- Chronic renal failure, chronic liver disease
- Endocrine (hypogonadism, Cushing disease)
- Prior abdominal/pelvic/penile surgery, radiation, or trauma
- Priapism, Peyronie disease
- Long-distance cycling
- Depression, other CNS pathology
- Medications:
  - Antihypertensives (thiazide diuretics, -adrenergic blockers, and 2-adrenergic agonists):

    ACE inhibitors and 1-adrenergic blockers cause less ED.
  - Psychotropics (SSRIs, lithium, MAOIs)
  - Antiandrogens, others (ketoconazole, spironolactone, cimetidine, digoxin, marijuana)

- Smoking

GENERAL PREVENTION

- Avoid smoking.
- Split bicycle seat for long distance riding

PATHOPHYSIOLOGY

)[C]:

– Relaxation of cavernosal artery smooth muscle (smooth muscle is contracted in flaccid state, limiting penile blood flow):

Mediated by release of NO from pelvic nerves, causing

Increase in cyclic GMP (cGMP), causing decrease in smooth muscle intracellular calcium, causing smooth muscle relaxation, increased penile blood flow, and tumescence.

cGMP is degraded primarily by phosphodiesterase type 5 (PDE5).

– Restriction of venous outflow from penis

- Organic ED:
  – Vasculogenic (arteriogenic via atherosclerotic changes, traumatic injury to arteries; failure of corporal vasoocclusion)
  – Neurogenic (Alzheimer disease, Parkinson disease, injury to CNS, spinal cord, or peripheral nerves)
  – Anatomic
  – Endocrinologic (hyperprolactinemia decreased testosterone, hyper- or hypo-thyroidism, adrenal disorders/Cushing syndrome):

5–10% of organic ED

- Psychogenic ED:
  – Only 10% of men
  – More common in men <35
  – May result from lack of interest in partner, performance-related anxiety, negative mood, major life stress

COMMONLY ASSOCIATED CONDITIONS

- Atherosclerosis
- Depression
- Diabetes
- Hypertension
- Multiple sclerosis
- Obesity
- Parkinson disease

- Peyronie disease
- Priapism
- Stroke

DIAGNOSIS

HISTORY

- Medical history
- Surgical history
- Psychosexual history (status of current relationship, level of libido, duration of ED, onset of ED (gradual or sudden), presence of nocturnal/early morning erections, presence of penile curvature, quality of erection):
  - International Index of Erectile Function Questionnaire-5:

    5 questions each ranging from 0–5 (total 25 points); higher scores with better function

    Classifies ED into severe (5–7), moderate (8–11), mild to moderate (12–16), mild (17–21), and no ED (22–25)
- Medication history
- Social history: Alcohol, smoking, recreational drugs, cycling history

PHYSICAL EXAM

- Neurologic: Stroke, CNS disease, visual field defects, peripheral neuropathy, perineal sensation
- Endocrinologic: Loss of secondary sexual characteristics, atrophic testes, gynecomastia
- Abdomen: AAA, cirrhosis
- Cardiovascular: BP, femoral and pedal pulses, evidence of lower extremity ischemia
- Penile: Peyronie disease plaques
- Rectal exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC
- Random glucose level, hemoglobin A1C,
- Lipid profile
- Early-morning serum testosterone
- PSA
- Urinalysis
- TSH

- LH

)[C]

Diagnostic Procedures/Surgery

)[C].

- Specialized testing indicated:
  - In young men <40
  - In men with no risk factors
  - In men with previous perineal/pelvic trauma
  - When it will direct therapy
- CIS with duplex US:
  - CIS: Intracavernous injection of vasodilator and genital/audiovisual sexual stimulation with measurement of erection
  - With US, allows objective evaluation of vascular status of penis
- Nocturnal penile tumescence (RigiScan):
  - Automated, portable measurement of nocturnal erection
  - Presence of full erection proves intact neurovascular axis; diagnoses psychogenic ED
- Tests no longer used: PBI, Penile plethysmography

Pathological Findings

Based on primary disease process

TREATMENT

)[C]

- Cardiovascular risk assessment (done before proceeding with any therapy):
  - Low risk: Asymptomatic, <3 risk factors; may proceed with treatment
  - Intermediate risk: Asymptomatic, 3 risk factors, stable angina, mild heart failure; full cardiovascular assessment to re-classify as low or high risk
  - High risk: Unstable angina, recent MI, uncontrolled HTN, advanced heart failure or valvular disease; defer until cardiac condition stabilized
- Due to the availability of PDE5 inhibitors, often empiric therapy is used.

MEDICATION

First Line

)[C]:

- Mechanism: Inhibit breakdown of corporal cGMP, thus promote smooth muscle relaxation
- Drugs:

Sildenafil (Viagra): Onset 15–60 min duration of action 4 hr

Vardenafil (Levitra): Onset 15–60 min, duration of action 2–8 hr

Tadalafil (Cialis): Onset 15–120 min, duration of action 24–36 hr

– Contraindications to PDE5 inhibitor:

Absolute: Use of nitrates, use of -adrenergic antagonist (vardenafil and tadalafil only), priapism risk (relative)

Sildenafil: Should be postponed for 4 hr after taking -adrenergic antagonist

Vardenafil: Should not be taken with type 1A or type 3 antiarrhythmics or in patients with long QT syndrome

– Side effects:

– All: Headache, dyspepsia, facial flushing

– Tadalafil: Backache, myalgia

– Sildenafil: Blurred/Blue vision

• Efficacy: Well over 50% of patients with organic ED respond; effective even in diabetic and postprostatectomy patients

Second Line

• Intracavernous injection therapy:

– Mechanism: Self-injection of vasoactive agent into corpora cavernosa; produces rapid erection

– Drugs: Alprostadil (PGE1, Caverject), papaverine, phentolamine, or Trimix (all 3 drugs)

– Contraindications: Concomitant monoamine oxidase medications, decreased dexterity

– Side effects: Fibrosis, priapism, painful erection, hematoma

)[C]

• Intraurethral injection therapy:

– MUSE (Medicated Urethral System for Erection)

Insertion of alprostadil (PGE1)-containing pellet in distal urethra; absorption into corpora cavernosa, erection in 30 min

– Contraindications: Priapism risk

– Side effects: Penile pain, dysuria, vaginal pain

)[C]

• Vacuum constriction device:

– Good 2nd line nonpharmacologic alternative or adjunct to pharmacotherapy

– Should be pursued prior to IPP

- Device used to produce negative penile pressure, thus engorging penis
- Constricting ring at base of penis maintains tumescence
- Side effects: Penile ischemia (>30 min of use), pain

SURGERY/OTHER PROCEDURES

- IPP:
  - Indications: Failed 1st- and 2nd-line pharmacotherapy or 2nd-line vacuum erection device
  - Definitive treatment of ED, with placement of inflatable cylinders into corpora cavernosa
  - Complications: Infection (1–3%), erosion (<5%), mechanical malfunction (5–10%)
- Penile revascularization:
  - Indications: Reserved for select young patients with clearly documented arterial occlusion

ADDITIONAL TREATMENT

- Psychosexual therapy:
  - Patients with psychogenic ED should be referred for sex therapy
  - Cognitive-behavioral intervention used to identify sexual stressor and refocus maladaptive thought process
- Yohimbine:
  - 2-adrenergic agonist; centrally acting
  - No evidence that drug augments erections in organic ED
  - May have role in psychogenic ED

ALERT

Herbal and dietary supplements used to treat ED are not FDA-approved; those listed here are for reference only

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Therapies reported to possibly improve ED are ginkgo biloba, red ginseng, yohimbine

ONGOING CARE

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patients should be re-evaluated on frequent basis, with following considerations:

- Response to initial therapy
- Need for dose titration
- Need for patient education (taking PDE5 inhibitor on empty stomach at appropriate time point, proper administration/use of local therapy)

- Progression to 2nd-line therapy or surgery based on response to dose titration, therapeutic effectiveness, patient satisfaction
- Consider using serial, validated questionnaires to evaluate effectiveness

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

Erectile Dysfunction, Following Pelvic Surgery or Radiation

CODES

ICD9

- 302.72 Psychosexual dysfunction with inhibited sexual excitement
- 607.84 Impotence of organic origin

ABBREVIATIONS

- AAA: Abdominal aortic aneurysm
- ACE: Angiotensin-converting enzyme
- BP: Blood pressure
- CBC: Complete blood count
- CIS: Combined intracavernous injection and stimulation
- CNS: Central nervous system
- ED: Erectile dysfunction
- IPP: Inflatable penile prosthesis
- LH: Leuteinizing hormone
- MAOI: Monoamine oxidase inhibitor
- NO: Nitric oxide
- PBI: Penile brachial index
- PDE5: Phosphodiesterase type 5
- PSA: Prostate-stimulating antigen
- SSRI: Selective serotonin reuptake inhibitor
- TSH: Thyroid-stimulating hormone
- US: Ultrasound

EXSTROPHY, BLADDER (CLASSIC EXTROPHY)

Peter D. Metcalfe, MD

BASICS

DESCRIPTION

- Classic bladder exstrophy is major genitourinary anomaly characterized by the bladder being open on the abdominal wall, as a flat plate instead of a closed sphere within the pelvis. The defect extends from the umbilicus to the distal end of the phallus, resulting in coexistent epispadias.
- Classic exstrophy is considered midway in severity between cloacal exstrophy and epispadias, as part of exstrophy–epispadias complex.

EPIDEMIOLOGY

- 1 in 10,000–50,000
- Male > Female (2.3:1)

RISK FACTORS

Genetics

- Multifactorial etiology without definite genetic link
- Risk in sibling is 1 in 100; risk in offspring is 1 in 70.

PATHOPHYSIOLOGY

- Incompletely understood, 2 predominant theories
- 1 theory postulates that an incomplete ingrowth of mesoderm is unable to reinforce cloacal membrane, which results in premature rupture.
- Results in a failure to develop ectoderm and mesoderm
- Timing of rupture determines cloacal (earlier) vs. classic exstrophy vs. epispadias (later)
- 2nd theory describes an overgrowth of cloacal membrane preventing medial migration of mesenchymal tissue.

COMMONLY ASSOCIATED CONDITIONS

- Usually healthy without any other major organ system defects.
- In contrast, cloacal exstrophy has much more extensive anomalies.

DIAGNOSIS

HISTORY

- Any family history of exstrophy
- Any prenatal abnormalities
- Prenatal diagnosis made by absence of bladder and foreshortened anal–pubic distance.

PHYSICAL EXAM

- Bladder exposed on abdominal wall
- Bladder plates
- Lateral ureteric orifices
- Open bladder neck and prostate
- Short and broad phallus is bifid
- Male urethra is bivalved dorsally from bladder to tip of glans with dorsal chordee.
- Females have bifid vagina and clitoris lateral to urethra.
- Low-set umbilicus with foreshortened distance to anus
- Pubic diastasis with external rotation of pelvis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC, electrolytes, creatinine
- Blood type and cross-match in preparation for surgery

Imaging

- Renal US
- Pelvic x-ray to document pubic diastasis

Pathological Findings

- Exstrophic bladders may have more type III collagen and fewer myelinated nerve fibers.
- If left untreated and exposed, the urothelium undergoes squamous metaplasia as a response to acute and chronic inflammation.

DIFFERENTIAL DIAGNOSIS

- Cloacal exstrophy
- Epispadias

TREATMENT

Immediate postnatal care:

- 2-0 silk suture on umbilical cord as close to abdominal wall as possible
- Cover bladder with nonadherent plastic (eg, Saran Wrap) to prevent excoriation.
- Irrigate with normal saline and apply new dressing with each diaper change.

MEDICATION

No medical treatment is available to close the bladder wall.

SURGERY/OTHER PROCEDURES

- Ideally closed within 1st wk:
  - Requires adequate bladder plate.

- If unable to easily approximate pubis, will need pelvic osteotomy.

- 2 popular contemporary closures
- Classic repair involves 3 stages:
  - Immediate bladder closure
  - Epispadias repair at 6 mo
  - Previous 2 combined at birth in selected patients
  - Bladder neck repair at 5 yr:

    Requires >100 cc bladder capacity and motivation for continence
- Complete primary repair:
  - Epispadias closed with bladder as neonate with penile disassembly

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Delayed closure in the case of a late presentation
- All need osteotomy with option of external fixation
- Inadequate bladder plate:
  - Delay closure and close, 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.
  - Immobilize pelvis in traction (Buck vs. Bryant).
  - Monitor for infection.
  - Avoid abdominal distension from overfeeding.
  - Remove stents 1 at a time; suprapubic only removed after ensuring appropriate bladder emptying.

ONGOING CARE

PROGNOSIS

- Life expectancy normal
- Urinary continence in 50–90%
- Usually requires multiple surgeries

COMPLICATIONS

- Failure of primary closure
- Urinary incontinence
- Upper tract damage
- Male: Infertility, urethrocutaneous fistula, inadequate phallus
- Female: Inadequate vagina, uterine prolapse:

- Normal fertility possible
- Increased risk of adenocarcinoma of bladder

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

After discharge:

- Urinary prophylaxis for vesicoureteral reflux
- Regular US to assess for hydronephrosis and bladder volume
- Epispadias repair if required
- May need hypospadias repair after complete primary repair
- Bladder neck repair at 5 yr if bladder capacity adequate and prepared to attempt continence

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See Also (Topic, Algorithm, Electronic Media Element)

- Epispadias
- Exstrophy, Cloacal
- Exstrophy–Epispadias Complex

CODES

ICD9

753.5 Exstrophy of urinary bladder

ABBREVIATIONS

- CBC: Complete blood count
- US: Ultrasound

EXSTROPHY, CLOACAL

Julian Wan, MD
David A. Bloom, MD
John M. Park, MD

BASICS

DESCRIPTION

- Cloacal exstrophy is a congenital abnormality of the anterior abdominal wall. It is manifest with defects in the urogenital system and conditions of the neurospinal axis, intestinal tract, and skeletal systems.
- When neurospinal defects and omphalocele occur with cloacal exstrophy, it is termed OEIS complex (omphalocele, exstrophy, imperforate anus, spinal defects).

EPIDEMIOLOGY

- 1 of the rarest urologic anomalies.
- The incidence is about 1:200,000 to 1:400,000.
- Male Female (1:1–2:1)
- Rare condition but with survival improving due to better cardiovascular and myelodysplasia care.

RISK FACTORS

Genetics

- Most cases are sporadic, but isolated cases of unbalanced translocations have been reported.
- Multifactorial etiology may also occur.
- More common in whites

PATHOPHYSIOLOGY

Anterior abdominal wall defect due to complex mesodermal migration failure:

- Urorectal septum does not form.
- Mesodermal proliferation that will comprise infraumbilical abdominal wall and genital tubercle fails to occur.

COMMONLY ASSOCIATED CONDITIONS

- Other urinary anomalies: ~50% have upper-tract anomalies
- Most common: Pelvic kidney and renal agenesis (up to 33%)
- Hydronephrosis and hydroureter common
- Multicystic kidneys and fusion anomalies are rarer.
- Lower limb malformations
- Intestinal anomalies:

- Omphalocele
- Malrotation
- Short gut
- Short-gut syndrome
- Anatomically short gut

• Serious cardiovascular and pulmonary anomalies are uncommon with cloacal exstrophy

DIAGNOSIS

ALERT

Cloacal exstrophy is a major congenital anomaly. Prompt referral and coordination with a variety of specialists including pediatric urology, pediatric general surgery, pediatric orthopedics, neonatology, pediatric gastroenterology, pediatric neurosurgery, endocrinology, genetics, and psychological counseling is needed.

HISTORY

• Usually suspicions raised on prenatal US
• Major diagnostic criteria at 15–32 wk gestational age:
  - Large midline infraumbilical anterior abdominal wall defect or cystic anterior wall structure
  - Lumbar myelomeningocele
  - Failure to visualize the urinary bladder
  - Other criteria: Abnormal genitalia, increased bony pelvis diameter, limb anomalies, trunk sign of prolapsed intestine

PHYSICAL EXAM

• Immediately recognizable as a major anomaly at delivery
• The classic collection of findings include:
  - Exstrophy of the bladder
  - Complete phallic separation
  - Wide pubic diastasis
  - Exstrophy of the terminal ileum between 2 halves of the bladder
  - Rudimentary hindgut; no well-formed colon or rectum
  - Imperforate anus
  - Omphalocele
• Thorough assessment from head to toe, front and back, paying particular attention to the following:
  - Many will also have spinal defects and lower extremity malformations

- 85–100% will have anomalies of the spinal cord or vertebral column:
  - Usually lumbar myelodysplasia: 80%
  - Thoracic defects in 10%
  - Sacral defects in 10%
- Clubfoot deformities are common.
- Other findings include: Absence of feet and severe tibia or fibula abnormalities

- Associated intestinal abnormalities:
  - Omphaloceles
  - Malrotation
  - Intestinal duplication
  - Anatomically short gut:
    - Short-gut syndrome
    - Absorptive dysfunction
- Genitourinary anomalies:
  - Müllerian anomalies with uterine duplication seen in 95% of female patients
  - Bicornate uterus
  - Vaginal duplication and/or agenesis
  - Males have separate phallic and scrotal halves.
  - Testes can be palpated but may be undescended.
  - In females, the clitoris is divided into 2 widely divergent halves.
  - The 2 exstrophied hemibladders are on either side of the extrophied intestinal segment. Each half usually drains the ipsilateral ureter.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Basic metabolic panel:

- Need to monitor losses and changes in electrolytes
- Karyotype

Imaging

- MRI of the spinal cord:
  - Due to the very high percentage of myelomeningocele
- Spinal US is an alternative if the baby is not stable enough to transport to the MRI scanner.
- US of urinary tract
- CT or MRI of abdomen and pelvis
- Skeletal and bony films of pelvis and lower extremities as needed.

- Retrograde and antegrade bowel imaging to assess for any residual colonic length
- CXR
- Other imaging depending on findings

Pathological Findings

Histology not routinely done, but exstrophied bladders may have more type III collagen and fewer myelinated nerve fibers.

DIFFERENTIAL DIAGNOSIS

- Unique appearance makes it unlikely to confuse with other conditions.
- Classic exstrophy: Epispadias complex
- Patent urachus
- Giant omphalocele

TREATMENT

- Immediate management stabilization of the infant.
- Contact and involve the various specialists (see above) immediately.
- Cover the exposed hemi bladder and hindgut with plastic wrap to limit trauma.
- Gender assignment discussion should be initiated immediately:
  - Gender assignment is consistent with the karyotype if possible.

MEDICATION

- IV support
- Correction of metabolic imbalances particularly electrolytes

SURGERY/OTHER PROCEDURES

- For infants with a spinal anomaly, neurosurgical consultation and closure should be done as soon as it is medically feasible.
- Omphalocele closure should then be done to prevent rupture. Preserve the hindgut if possible.
- Hindgut will help with later fluid absorption issues. If the hindgut is not used with the bowel reconstruction, it should be saved and used with bladder or genital reconstruction.
- If possible at the time of omphalocele closure, assess if the bladder halves can be joined to create an exstrophy defect. Abdominal distention may then help expand the bladder plate for later repair.
- Osteotomies may be needed to close the abdomen and bony pelvis.
- Preserve Müllerian components for reconstruction.
- Modern approach:
  - Reapproximate bladder halves.
  - Mobilize bladder plate and posterior urethra and try to place deep into pelvis. Creates an incontinent bladder and urethra.

– Repair inguinal hernias at this time.
– Reconstruct external genitalia to match gender assignment if feasible.
– Pubic reapproximation usually requires osteotomies with fixation and traction for 6–8 wk.

- Later surgery to further improve continence and cosmetic appearance of the genitalia:
  – Bladder augmentation and construction of a catheterizable stoma or urethra are commonly done later.
- Single-stage approach similar to that used in classic exstrophy has been performed but requires careful patient selection.

ADDITIONAL TREATMENT

- Occupational and physical therapy depending on spinal and lower extremity conditions
- Short-gut patients may require hyperalimentation and nutritional supplementation.

ONGOING CARE

PROGNOSIS

In the past, considered fatal; since 1970, mortality has decreased to <50% and now survival out of the neonatal period is much higher, ~90%.

COMPLICATIONS

- Infection and breakdown of repair
- Short-gut syndrome:
  – Poor fluid absorption due to short functional and anatomic length of hindgut
  – Metabolic imbalances
  – Growth restriction

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Long-term monitoring of spinal repair
- Bowel function:
  – Regular electrolyte monitoring
- Other monitoring depends on nature of reconstruction, but life-long follow-up is to be expected.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Epispadias
- Exstrophy-Epispadias Complex
- Exstrophy, Bladder (Classic Extrophy)

CODES

ICD9

753.5 Exstrophy of urinary bladder

ABBREVIATIONS

- CT: Computed tomography
- MRI: Magnetic resonance imaging
- US: Ultrasound

FILLING DEFECT, UPPER URINARY TRACT

Jason C. Hedges, MD, PhD

Michael J. Conlin, MD

BASICS

DESCRIPTION

Radiolucency identified on excretory urogram, retrograde ureteropyelography, or contrast CT scan

RISK FACTORS

- Prior history of stones or transitional cell carcinoma
- UTI infection (bacterial, fungal)
- Diabetes, sickle cell, analgesic abuse
- Bleeding disorder

PATHOPHYSIOLOGY

Any radiolucent mass within the upper urinary tract will appear as a filling defect

COMMONLY ASSOCIATED CONDITIONS

None

DIAGNOSIS

HISTORY

- History of urinary calculi?
  - Especially uric acid and cysteine stones
- History of transitional cell carcinoma of the bladder?
  - 15–30% incidence of upper tract tumor development
- History of diabetes, analgesic abuse, or sickle cell disease?
  - Potential causes of sloughed papilla
- History of gross hematuria?
  - May indicate malignancy or blood clot as cause of filling defect
- History of inflammatory bowel disease, or long-term E. coli UTI?
  - Potential causes of air in the upper urinary tract
- History of urinary diversion?
  - Urinary diversion can be associated with urolithiasis, protein matrix production, and mucus within the upper urinary tract.
- History of fungal UTI?

PHYSICAL EXAM

Evidence of CVA tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and culture:
  - If the urine pH is >6.5, uric acid stones are unlikely.
  - Hematuria can indicate either malignancy or clot
  - Fungal elements on urinalysis raise the possibility of a fungus ball.
  - Mixed aerobic and anaerobic bacteria may indicate ureteroenteric fistula.
- Urine cytology:
  - Positive cytology would indicate possible TCC.
  - Negative cytology does not rule out TCC.
  - False negatives are common (up to 60%).

Imaging

- US:
  - US can usually distinguish stones from soft-tissue masses within the upper urinary tract. However, it is not as sensitive or specific as a CT scan.
- CT scan:
  - A CT scan with and without contrast will differentiate stones, tissue densities, and air. It will also rule out any parenchymal mass.

Diagnostic Procedures/Surgery

Ureteroscopy:

- Diagnosis can often be made by direct inspection alone.
- Ureteroscopic biopsy can also provide histologic confirmation.

Pathological Findings

See individual disease elsewhere in book.

DIFFERENTIAL DIAGNOSIS

- Malignant filling defect of ureter and renal pelvis:
  - TCC:

    The most common malignant cause of upper urinary tract filling defects
  - Squamous cell carcinoma
  - Rare malignant tumors: adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  - Renal cell carcinoma:

    Usually found in conjunction with renal mass on US or CT scan; has been reported without associated renal mass as a filing defect in the collecting system
- Benign filling defect of ureter and renal pelvis:
  - Air: Iatrogenic, infectious or due to fistula

- Blood clot
- Fibroepithelial polyp
- Fungus ball
- Hemangioma
- Inflammatory lesions: Granuloma, malakoplakia, tuberculosis
- Inverted papilloma
- Radiolucent calculus
- Rare benign tumors: leiomyoma, neurofibroma, cholesteatoma
- Renal papilla:

  Ectopic or “end on” renal papilla can be misidentified as a filling defect.
- Sloughed papilla:

  May be iatrogenic during retrograde pyelography, or due to ureteroenteric fistula, or emphysematous pyelonephritis
- Extrinsic compression on the ureter
- Mucus: Urinary diversion patients
- Protein matrix
- Pyelitis glandularis
- Ureteritis or pyelitis cystica
- Vascular impression

TREATMENT

- For urothelial cell carcinoma of the renal pelvic or ureter, surveillance of the contralateral renal unit and bladder is necessary
- Patients with upper urinary tract TCC are treated endoscopically:
  - Ureteroscopy has been shown to be more accurate than retrograde ureteropyelography, and should be performed every 6 mo once the patient is tumor-free.
  - Cystoscopic inspection of the bladder must also be included in the surveillance protocol, because of the relatively high frequency (39%) of asynchronous TCC of the bladder in these patients.
- Patients with radiolucent stones are the same as other urolithiasis patients. Metabolic evaluation is recommended.
- Patients with confirmed successful treatment of benign upper urinary tract tumors should not need any further imaging unless signs or symptoms return.

MEDICATION

- Uric acid calculi can often be dissolved medically
- Oral alkalinization therapy to maintain a urine pH of 6.5–7.0:

– May require several months to dissolve stone. Do not exceed pH 7 (stones of other composition can precipitate)

– Requires patient to self-monitor urine pH daily, with pH paper or Nitrazine paper

– Use Potassium citrate 30– 60 mEq/d (Polycitra-K or Urocit-K).

– Alternative: Sodium bicarbonate 650 mg q6–8h.

- For hyperuricemia or urinary uric acid secretion >1,200 mg/d:
  – Treat with allopurinol 100–600 mg/d in additional to oral alkalinization.
  – Allopurinol inhibits conversion of hypoxanthine and xanthine to uric acid:
    Side effects: Skin rash, fever, or acute attack of gout.

SURGERY/OTHER PROCEDURES

)[A]:

– Calculus: Appropriate treatment is initiated.

Uric acid calculus: Initially consists of urinary alkalinization

If this is unsuccessful, the stone can be treated with ESWL, ureteroscopy, or percutaneous nephrostolithotomy.

– Soft-tissue density is found within the collecting system; further evaluation with ureteroscopy and biopsy is recommended.

)[A]:

– Ureteroscopy, when needed, should consist of direct inspection of the lesion, lavage for cytology, and biopsy with 3-French biopsy forceps or a flat wire basket.

)[A]:

– However, ureteroscopic treatment and surveillance may be indicated in patients who cannot undergo nephroureterectomy because of comorbidities or renal insufficiency.

– Other benign tumors of the upper urinary tract, such as fibroepithelial polyps and inverted papillomas, can also be treated successfully ureteroscopically.

– Holmium laser is a useful tool for ureteroscopic treatment of soft-tissue lesions of the collecting system. It is very effective in ablating tissue, and its limited tissue penetration (0.4 mm) makes it very safe.

- Fungal UTIs should be treated prior to any endoscopic manipulation.

– Fungus balls, sloughed papilla, blood clot, mucus, and protein matrix can also be treated endoscopically during the initial ureteroscopic evaluation. Further endoscopic treatment from a percutaneous route may be necessary if the volume of these lesions is large.

- Endoluminal US during ureteroscopy can confirm the presence of an extrinsic vessel causing compression of the upper urinary tract.
- A ureteroenteric fistula usually requires open repair.

• Emphysematous pyelonephritis requires aggressive antibiotic treatment, and often nephrectomy.

ONGOING CARE

PROGNOSIS

Based on the primary cause

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Surveillance for urothelial carcinoma should include the contralateral renal unit and the bladder with imaging, cystoscopy, and urine studies such as cytologies.

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See Also (Topic, Algorithm, Electronic Media Element)

- Ureter and Renal Pelvic Tumors, General
- Ureter and Renal Pelvis, Inverted Papilloma
- Ureter and Renal Pelvis, Squamous Cell Carcinoma
- Ureter and Renal Pelvis, Urothelial Carcinoma (Transitional Cell Carcinoma and CIS)
- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General

CODES

ICD9

- 592.9 Urinary calculus, unspecified
- 599.0 Urinary tract infection, site not specified
- 793.5 Nonspecific abnormal findings on radiological and other examination of genitourinary organs

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle
- ESWL: Extracorporeal shock wave lithotripsy
- TCC: Transitional cell carcinoma
- US: Ultrasound
- UTI: Urinary tract infection

FLANK PAIN

Ivan Colon, MD

BASICS

DESCRIPTION

Flank pain refers to pain or discomfort in the side of the abdomen between the last rib and the hip.

EPIDEMIOLOGY

- True incidence is difficult to ascertain, as it is a common symptom associated with many medical conditions.
- It has been estimated that up to 12% of the adult US population will suffer from an attack of urolithiasis in their lives.
- Since many medical conditions can cause flank pain, the prevalence is also high.

Pregnancy Considerations

Flank pain during pregnancy may be a symptom of an obstructing ureteral stone or pyelonephritis.

GENERAL PREVENTION

- Depends on the etiology of the flank pain
- Recurrent stone disease can be a source of recurrent flank pain. Preventive strategies including dietary modification and medical management can reduce recurrent stone formation.
- Common dietary modifications include increasing fluid intake and reducing intake of sodium, animal protein, and oxalate-rich foods.
- Drugs such as citrate, allopurinol, and thiazide diuretics may be necessary depending on the underlying metabolic abnormality.

PATHOPHYSIOLOGY

- Flank pain caused by any renal pathology is usually due to sudden stretching of the renal capsule, generally from inflammation or obstruction.
- The severity of the pain is directly related to the acuity of the obstruction and not to its degree.
- Flank pain from renal inflammation has a gradual onset and is not as severe as renal colic due to acute obstruction from a stone.
- Flank pain from chronic obstruction is generally less severe, and in most cases, pain is absent.

DIAGNOSIS

HISTORY

- Age and sex of patient
- Pain characteristics:
  - Location: Flanks/abdomen
  - Quality: Dull/sharp
  - Duration: How long?
  - Severity: Use visual analogue pain scales
  - Timing: Constant/intermittent, onset (sudden vs gradual)
  - Radiation: Pain radiating from the flank down into the testicle or labia suggests renal colic caused by passage of stone or clot down the ureter.
  - Moderating factors: Medications, rest, position
  - Aggravating Factors: Movement, cough
  - Associated symptoms: Fever, chills, dysuria, nausea, vomiting
- Prior medical history:
  - History of nephrolithiasis (10% 1 yr, 35% 5-year, 50% 10-year stone recurrence rate).
  - Diabetes mellitus, patients have higher predisposition to papillary necrosis, infections, including XGP and emphysematous pyelonephritis.
  - GYN history (pregnancy/STDs)
- Prior surgical history:
  - General surgical and gynecological abdominal and pelvic procedures involving a potential risk of ureteral injury and obstruction (TAHBSO, vascular bypass, AAA repair, colectomy)
  - History of trauma (penetrating vs. blunt)
- Social history:
  - Smoking is a risk factor for development of TCC of renal pelvis or ureter
  - IV drug abuse patients are predisposed to renal abscess formation
- Family history (polycystic kidney disease)

PHYSICAL EXAM

- Vital signs:
  - Temperature: Fever is usually associated with infectious etiologies.
  - BP:

    Hypotension; suspect sepsis or hemorrhage (ie, ruptured angiomyolipoma); may need immediate intervention.

    Hypertension: May reflect response to pain. Rule out medical renal parenchymal disease, renal cystic or vascular disease.

- Abdominal exam:
  - Inspect for scars, skin changes, signs of trauma
  - Palpate abdomen and flank to evaluate for masses, organomegaly, and tenderness.
  - Fist percussion of flank: CVA tenderness suggests renal etiology.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: Initial diagnostic step in the management of flank pain.
- Ensure proper specimen collection: Clean catch or catheterized specimen.
- Presence of epithelial cells suggests contaminated sample
- Dipstick test is performed to evaluate for the presence of blood and/or infection. If abnormal, it is usually followed by microscopic analysis.
- Hematuria suggests injury to the urologic system.
- Urinary pH: PH >7.6 should raise suspicion for the presence of urea-splitting organisms. A pH <5 is often associated with the formation of uric acid calculi.
- Nitrate and/or leukocyte esterase–positive: Indicates infection.
- Urine culture and blood culture: Collect prior to institution of antibiotic therapy to ensure identification of pathogen, sensitivity, and appropriate coverage
- CBC: Elevated WBC suggests infectious/inflammatory process. Low hemoglobin suggests hemorrhage.
- Chemistry profile to assess renal function and electrolyte abnormalities: Elevated BUN, creatinine, and reduced creatinine clearance suggests renal insufficiency/failure. Elevated LFTs need to be evaluated to rule out metastatic process in liver.
- Other tests should be ordered depending on clinical presentation and judgment.

Imaging

- Plain radiographs:
  - A KUB film is usually the initial radiograph done for the evaluation of flank pain to rule out urolithiasis. However, a KUB film is unable to diagnose certain radiolucent calculi (eg, uric acid, indinavir).
- CT:
  - Non–contrast-enhanced spiral CT has become the standard imaging modality for the workup of acute flank pain from urolithiasis. It has been shown to be very sensitive and specific (97% and 96%, respectively) in detecting both ureteral calculi and ureteral obstruction.
  - It can detect calculi as small as 1 mm in diameter, secondary signs of obstruction (hydronephrosis, renal enlargement, perinephric stranding) and can also asses nonrenal

causes of flank pain (ie, appendicitis, pancreatitis, tubal pregnancy, etc.)

- US:
  - Less reliable at detecting small (<5 mm) ureteral and midureteral stones but can diagnose hydronephrosis with a sensitivity of 85–94% and a specificity of 100%
  - Disadvantages: Limited in obese patients, operator dependence
- Excretory urogram or IVP:
  - Once the standard for urologic evaluation of flank pain, IVP is very accurate, with the diagnosis of calculous disease able to be established in 96% of cases.
  - It can also quantify the presence and severity of obstruction.
  - Contraindications to the use of urographic contrast media for both CT and IVP include renal insufficiency and previous reaction to contrast material.
  - Its value is also limited by the complexity and length of time needed to perform the procedure.
- Nuclear scan: Helps evaluating split renal function, degree of obstruction, and presence of renal scaring.
- MRI is not usually considered as an initial diagnostic tool unless CT is contraindicated (ie, in the presence of a pacemaker). It can be helpful for evaluation of renal masses or in the evaluation of suspected spinal cord pathology.

Pathological Findings

Based on the etiology

DIFFERENTIAL DIAGNOSIS

- There are many causes of flank pain. It is useful to differentiate between urologic and nonurologic causes. Renal etiologies are usually the most common and those that usually require urologic intervention. Some of the most common causes are listed below.
- Urologic:
  - Stones: Mostly ureteral stones; however, renal pelvic stones and caliceal stones (obstructing infundibulum) can cause flank pain.
  - Acute cortical necrosis
  - Acute papillary necrosis
  - Dietl crisis (ptotic kidney)
  - Polycystic kidney disease
  - Acute/chronic pyelonephritis
  - Renal infarction
  - Renal cyst (especially hemorrhagic; benign cysts rarely cause flank pain)
  - Renal neoplasm

  - Renal trauma
  - Renal vein thrombosis
  - Retroperitoneal bleed or mass
  - Ureteropelvic junction obstruction
  - Calyceal diverticulum
  - Medullary sponge kidney
  - Ureteral obstruction from any cause (stone, blood clot, necrotic material, external compression, etc.)

- Nonurologic causes:
  - Appendicitis
  - Chest diseases (costochondritis, pleuritis, MI)
  - Diabetes
  - Diverticulitis
  - Herpes zoster
  - Musculoskeletal (muscle spasm, strain)
  - Pancreatitis
  - Peripheral nerve compression
  - Peripheral nerve trauma
  - Peripheral neuropathy
  - Vertebral or spinal cord/nerve root irritation (herniated disk, sciatica, vertebral body fracture or collapse)

TREATMENT

Based on etiology. Rest and physical therapy may be recommended for flank pain caused by muscle spasms. NSAIDs are excellent 1st-line agents to control pain secondary to inflammation, but caution must be used when prescribing them in the presence of acute ureteral obstruction or patients with advance renal disease, as they can decrease intrarenal blood flow.

MEDICATION

First line

- Acute pain control (morphine, NSAIDs)
- Antiemetics, antipyretics, antibiotics as appropriate
- IV fluids if sepsis/hypovolemia. May also help with passage of stone.

Second line

-Agonists and calcium channel blockers may help with expulsion of ureteral stones.

SURGERY/OTHER PROCEDURES

- Prior to any intervention, the patient must be stabilized.

• Surgical management may be required in some cases depending on the etiology and the patient's medical condition. Other sections of this book that refer to specific disease entities should be consulted.

• Percutaneous nephrostomy, ureteral stents, embolization, and nephrectomy are reasonable options depending on the situation, and clinical judgment should dictate management.

• Examples of surgical management: If the collecting system is infected and obstructed or dealing with abscesses, a percutaneous drainage and antibiotics are the mainstay of treatment. If dealing with a ruptured AML embolization should be considered. Renal tumors should be treated on an elective basis. Emergent nephrectomy for ruptured AML or XGP/emphysematous pyelonephritis may be necessary.

ONGOING CARE

• Follow-up for flank pain will also be dictated by the etiology and acuity of the clinical presentation. Repeat imaging and other laboratory 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, surgery).

PROGNOSIS

Depends on the etiology.

COMPLICATIONS

Longstanding ureteral obstruction can cause permanent loss of renal function.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Depends on the etiology. Periodic renal imaging, urinalysis, 24-hr urine for patients with stone disease.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult
- Renal Mass
- Urolithiasis, Adult, General

CODES

ICD9

- 583.9 Nephritis and nephropathy, not specified as acute or chronic, with unspecified pathological lesion in kidney
- 592.9 Urinary calculus, unspecified
- 789.09 Abdominal pain, other specified site

ABBREVIATIONS

- AAA: Abdominal aortic aneurysm
- AML: Antimyeloma lipoma
- BP: Blood pressure
- CT: Computed tomography
- CVA: Costovertebral angle
- GYN: Gynecologic
- IV: Intravenous
- IVP: Intravenous pyelography
- KUB: Kidney, ureter, bladder
- LFT: Liver function test
- MI: Myocardial infarction
- NSAID: Nonsteroidal anti-inflammatory drugs
- PCN: Percutaneous nephrostomy tube
- STD: Sexually transmitted disease
- TAHBSO: Total abdominal hysterectomy and bilateral salpingo-oophorectomy
- TCC: Transitional cell carcinoma
- WBC: White blood cell
- XGP: Xanthogranulomatous pyelonephritis

FOLEY CATHETER PROBLEMS (INSERTION AND REMOVAL)

David M. Albala, MD

Daniel A. Bazewicz, BS

BASICS

DESCRIPTION

- Foley catheter problems generally fall into 2 categories: Inability to insert or inability to remove. (Foley catheter-related infections are discussed in the section “Urinary Tract Infection (UTI), Catheter Related”
- Foley catheters are traditionally made of latex, with latex-free becoming more common due to concerns over latex allergy. Foley catheters are retained by means of a balloon at the tip, which is inflated with sterile water. The balloons typically come in 2 different sizes: 5, 10, and 30 mL.
- Catheters are made of various materials (latex rubber, silicone, polymers, plastic). Silver nano particles are now incorporated into many catheters to reduce the risk of infection.
- The relative size of a Foley catheter is described using French units (F): 1F is equivalent to 0.33 mm = .013 = 1/77 of diameter. Thus the size in French units is roughly equal to the circumference of the catheter in millimeters.
- The most common Foley sizes are 10F–28F. 3-way catheters (balloon, drainage, and irrigation channels) have smaller draining channels when compared to a standard 2-lumen Foley catheter.

RISK FACTORS

- Benign prostatic hypertrophy
- Bladder neck contracture
- Previous urethral or prostate surgery
- Urethral mass
- Urethral stricture
- Urethral trauma
- Bladder neck contracture

GENERAL PREVENTION

Attention to detail in proper Foley catheter placement and removal

PATHOPHYSIOLOGY

Indications for catheterization include monitoring fluid balance, overcoming outflow obstruction, urinary incontinence, and diagnostic purposes.

COMMONLY ASSOCIATED CONDITIONS

- Balanitis xerotica obliterans
- Benign prostatic hypertrophy
- Disorders of sexual development
- Hypospadias
- Meatal stenosis
- Obesity
- Posterior urethral valves
- Prostate cancer
- Urethral cancer
- Urethral diverticulum

DIAGNOSIS

HISTORY

- Age and sex of patient
- Onset/duration of symptoms
- Associated symptoms (frequency, nocturia, urgency, dysuria)
- History of trauma, prior surgery, or instrumentation
- Any history of STD
- Number of attempts made at catheter insertion
- Methods used in attempt to remove a retained catheter

PHYSICAL EXAM

- Abdomen: Palpable bladder, pain
- GU: Blood at meatus, phimosis, meatal stenosis, hypospadias
- Rectal: Floating prostate with urethral trauma; nodularity with cancer
- Bimanual exam: Abnormal anatomy, tumor

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urinalysis: Hematuria can suggest tumor, BPH, stone, or other foreign body. Pyuria can occur with stones, foreign bodies, and infectious processes.

Imaging

- Rarely needed acutely
- Urethrography: Retrograde, antegrade, and combined urethrograms can help diagnose the presence and extent of strictures, valves, false passages, and urethral trauma.

Diagnostic Procedures/Surgery

Cystoscopic exam in cases where a catheter or wire cannot be easily passed

DIFFERENTIAL DIAGNOSIS

- Common causes of difficult Foley placement:
  - Strictures: Primarily male patients (history of prior instrumentation, surgery, trauma, or STD)
  - BPH: Primarily elderly men
  - Cancer of the prostate: Primarily elderly men (obstructive symptoms usually present late in the disease)
  - Bladder neck contracture; late complication of prostate surgery
  - Meatal stenosis: Congenital or acquired (meatal instrumentation, balanitis xerotica obliterans, postcircumcision, STD)
  - Tight phimosis: Primarily diabetics, children, and elderly men
  - Buried penis: Short shaft length and/or a large suprapubic fat pad
  - Posterior urethral valves: Primarily male infants/children
  - Hypospadias: Smaller meatal opening with associated duplex urethras or false passages
  - Tumors: Prostate cancers and, rarely, bladder, penile, and urethral cancers can cause distortion of normal anatomy. Also, local spread of cancers of nearby structures (ie, vaginal, cervical, uterine, rectal)
  - Trauma: Intrinsic from instrumentation or extrinsic to the urethra and/or bladder can cause false passages, stricture, or complete transection of the urethra (ie, pelvic fracture).
  - Miscellaneous: A foreign body/stone in urethra/bladder or, rarely, a prolapsing ureterocele can cause obstruction.
- Difficult Foley removal:
  - Catheter malfunction (most common): To prevent this problem, test the catheter balloon prior to placement.
  - Obstruction of the balloon channel or balloon port from debris or crystals; sometimes caused by placement of solutions, other than the recommended sterile water, to inflate the balloon (ie, saline, sorbitol, contrast, etc.)
  - Long-term indwelling catheters can become encrusted by calcium.

TREATMENT

- Catheterization problems:
  - External sphincter spasm: Reassurance to patient, local anesthesia, distraction of patient, and patience
  - Suspected or known stricture: Retrograde urethrography can be carried out to assess the urethra. Filiform and followers to dilate stricture. Cystoscopic placement of guidewire

can be done at bedside with local anesthesia. In an impassible stricture, a suprapubic tube is indicated.

– Bladder neck obstruction: The Coude tip catheter or catheter stylette is useful and avoids risk of trauma.

– Trauma: Confirm via radiologic modalities. Percutaneous cystostomy is always a safe, reliable option. Direct visualization with flexible cystoscopy is also a viable option.

- Catheter placement:

– If necessary, use 2% lidocaine jelly for anesthesia.

– In females, with difficult anatomy, the hand may be placed into the vagina with gentle downward traction to allow better identification of the urethral meatus.

– In males, fill the urethra with lubricant jelly and maintain stretch on the penis to keep the urethra straight.

– If the catheter does not enter the bladder easily, the most likely causes are: Spasm of the external sphincter, stricture, or bladder neck obstruction. BPH rarely prevents the passage of a catheter.

– Blood on the tip of the catheter suggests a false passage.

– If urine is not obtained or if there is doubt regarding position of the catheter balloon, do not inflate the balloon (may cause urethral trauma or rupture). Hand irrigation with normal saline and catheter tip syringe can help check catheter position. If catheter can be irrigated in and withdrawn easily, it is most likely within the bladder and the balloon can be inflated safely. If not, continue to instill water and then withdraw. If again not successful, withdraw the catheter and reintroduce or try other options.

– Coude catheter with a curved hard tip is designed to guide the catheter over the prostate/bladder neck.

– Catheter stylettes: Malleable metal guides that, when placed into a Foley or other type of catheter, can be used to provide stiffness and a particular contour. Can be used following TURP to avoid undermining the bladder neck; should only be used by experienced operators.

- If stricture prevents placement:

– Van Buren sounds: Solid metal sounds curved in the shape of the male urethra (sizes 16F–30F), used for dilation in men

– Female sounds are short straight sounds. Useful also in men to dilate distal strictures or meatal stenosis

– Filiforms and followers: Thin, pliable, solid catheters for dilating urethral stricture (sizes 1F–6F). The tip may be straight, pigtailed, or Coude type. They have a female screw tip on the proximal end to allow attachment of the follower (sizes 12F–30F), which may be solid

or hollow.

– Laforte sounds: Similar to Van Buren sounds except for the presence of a male screw fitting on the end, permitting attachment to a filiform

– Coaxial dilators: Dilators that can be passed into the bladder over a flexible wire

– Council catheters: Similar to a Foley catheter except for a small perforation at its tip, which can engage a filiform or guidewire. Safest to place after difficult dilation

– Perform flexible/rigid cystoscopy to determine the nature of the problem and to pass a guidewire under direct vision

- Percutaneous cystostomy trocars:

– Used when the bladder cannot be entered through the urethra; bladder must be distended; verify with palpation or ultrasound. US guidance can be used to help with percutaneous cystostomy.

– Contraindications to percutaneous trocar placement includes: Prior lower abdominal surgery and the presence of surgical scars in the suprapubic area (small bowel may be interposed in the retropubic space)

– Stamey trocar: Malecot catheter into the bladder

– Argyle trocar: Foley-type can be used to irrigate.

– Cystocath: 8F or 12F simple tube retained in the bladder by skin glue and/or skin suture

– If the bladder is not distended sufficiently to permit blind cystostomy, a long spinal needle may be used to determine location of the bladder, and the bladder can be filled with saline through this needle (or distend the bladder by putting the catheter into the distal aspect of the urethra and introduce saline retrograde to fill the bladder). The trocar can then be passed into the bladder safely.

- Bladder irrigation for clots:

– Whistle-tip catheter: A straight catheter with a beveled opening at the tip and another opening in the side; provides better irrigation and drainage

– A large catheter will irrigate clots better than a 3-way catheter due to the larger lumen.

– A resectoscope sheath can be used to irrigate clots (in the OR).

- Children:

– Female children: Catheterization is similar to that for adult women, but smaller catheters are used (size 8F–12F).

– Male children: Some prefer to use an 8F feeding tube rather than a Foley because the Foley balloon is somewhat larger than the catheter itself and can be difficult to pass.

- Techniques for catheter removal:

– Deflate the balloon and test balloon channel before proceeding with any other procedure. The problem may be as simple as incomplete balloon deflation.

– Cut the distal port of the balloon channel. This aspect of the catheter may be the sole area that is blocked in the balloon channel, and cutting it may allow the fluid from the balloon to drain without obstruction.

– Balloon perforation: A stiff guidewire may be passed into the channel to try to clear the passage and perforate the balloon. Also a suprapubic technique for balloon perforation under US guidance can be utilized using a suprapubic needle. Blind needle placement is not recommended.

– Hyperinflation is not recommended (bladder injury and retained balloon segments within the bladder); remove these segments because they can become foci for stone formation and infection.

– External crystal formation: Bladder instillations of Renacidin or diluted vinegar (for struvite stones), or alkaline solutions (ie, k-citrate, NaHCO3) (for uric acid stones), have been used. ESWL may be required to disrupt stones.

Geriatric Considerations

A Foley catheter may be difficult to place in the elderly male population due to an enlarged prostate. In these cases, a Coudé catheter may be easier to place.

Pediatric Considerations

Correct sizing of catheters is especially important in the male child to avoid the development of strictures.

MEDICATION

Usually not indicated.

SURGERY/OTHER PROCEDURES

Cystourethroscopy: Direct visualization of urethra and bladder can help in both diagnosis and placement of catheter.

ONGOING CARE

COMPLICATIONS

- Bleeding/hematuria: Common following instrumentation; usually clears spontaneously within 24 hr. Maintain a high fluid intake to promote diuresis and prevent clot formation. Irrigation may sometimes be indicated.
- Perforation of the urethra: Can occur when excessive force is used. Diagnosis is made by retrograde urethrography. If minimal extravasation is present, antibiotic coverage and urinary drainage for 1–2 days is a reliable treatment. If major extravasation into the perineum or extraperitoneal extravasation occurs, drainage of fluid or surgery may be necessary.

- Infections: Range from simple bacteriuria to sepsis. Antibiotic prophylaxis and coverage is sometimes indicated.
- Encrustation/blockage: Occurs as a result of urease-producing bacteria, which is often the case in patients with long-term catheterization. Continual replacement of the catheter is the simplest solution.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow-up for retained catheter balloon that can serve a nidus for infection or bladder calculi

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Foley Catheter Problems Algorithm
- French Catheter Guide, Appendix
- Latex Allergy
- Urethra, Stricture

CODES

ICD9

V53.6 Fitting and adjustment of urinary devices

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- ESWL: Extracorporeal shock wave lithotripsy
- F: French units
- GU: Genitourinary
- $NaHCO_3$: Sodium bicarbonate
- STD: Sexually transmitted diseases
- TURP: Transurethral resection of the prostate

FOURNIER GANGRENE

Douglas E. Sutherland, MD

Thomas W. Jarrett, MD

BASICS

DESCRIPTION

- A progressive and life-threatening necrotizing fasciitis of the genitalia and/or perineum
- Originally described as idiopathic, an etiology can now be identified in >95% of cases.

ALERT

Fournier gangrene is a true urologic emergency that carries a high mortality rate unless prompt diagnosis and surgical management are instituted.

EPIDEMIOLOGY

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- Most common in the 5th and 6th decade of life, but can occur in all age groups.
- Male > Female (10:1)

RISK FACTORS

- Diabetes mellitus
- Alcoholism with cirrhosis
- IV drug abuse
- Genital skin trauma
- Recent penile, perineal, or perirectal surgery

PATHOPHYSIOLOGY

- Infection initially occurs in the perirectal skin, penile urethra, or scrotal skin folds.
- Aerobic and anaerobic organisms act synergistically to produce a progressive, obliterative endarteritis leading to thrombosis and ischemia.
- Resultant ischemia allows for local progression.
- The process extends down to Buck (penis) or Colles (perineum) fasciae, spreads along Dartos fascia in the penis and scrotum, and can extend to the abdominal wall and thighs via the Scarpa fascia.
- The most common organisms involved include E. coli, enterococci, Bacteroides.
- Streptococcus and Staphylococcus species are also very common, and predominate in pediatric patients.

COMMONLY ASSOCIATED CONDITIONS

- Urethral stricture
- Perianal abscess
- Immunosuppression

- Morbid obesity
- Paraplegia
- Malignancy

DIAGNOSIS

HISTORY

- Recent history of perineal trauma, urethral instrumentation for stricture disease, perirectal abscess management, or chronic exposure to urine extravasation
- Urinary symptoms include dysuria, urinary frequency, obstructed voiding, and urethral discharge.
- Prior STD that could result in a urethral stricture (N. gonorrhea)
- Anal fissure, fistulae, or hemorrhoids
- Alcohol or IV drug abuse
- Malignancy, diabetes, steroid use, and HIV
- Pressure ulcers associated with paraplegia

PHYSICAL EXAM

- Tachycardia, tachypnea, fever (>101°F/38.3°C) or hypothermia (<96°F/35.6°C), and altered mental status
- Cellulitis of the genital or perineal skin
- Pain out of proportion with the identifiable lesion
- Dark purple or necrotic skin
- Foul odor
- Evidence of crepitus within the genital and perineal skin
- Abdominal and leg extension can be identified by palpable crepitus and/or pain without evidence of erythema or cellulitis
- Rectal exam: Perirectal abscess or anal sphincteric involvement

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis or leukopenia, anemia
- Serum chemistry: Hyponatremia, hypocalcemia, elevated serum creatinine and BUN, hyperglycemia
- Coagulopathy may be present.
- Urinalysis: Glucosuria and pyuria
- Wound culture: Mixed flora, usually >4 organisms
- Urine and blood culture: Occasionally positive

Imaging

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- CT of the abdomen/pelvis can quickly document pelvic and intra-abdominal pathology and may demonstrate the nidus and extent of the infection. However, renal insufficiency may limit the use of IV contrast.
- US can be used to identify subcutaneous air, but is operator dependant.
- MRI can be used to define affected areas, but its use should not delay prompt surgical treatment.

Diagnostic Procedures/Surgery

Early biopsy of the ulcer with frozen section; pathologic review can confirm the diagnosis quickly.

Pathological Findings

Superficially intact epidermis with widespread dermal necrosis, vascular thrombosis, and evidence of acute PMN infiltrate.

DIFFERENTIAL DIAGNOSIS

- Balanitis
- Cellulitis
- Epididymitis/orchitis
- Hidradenitis suppurativa
- Hydrocele
- Pyoderma gangrenosum
- Strangulated inguinal hernia
- Testicular torsion

TREATMENT

- Admit to intensive care unit if patient is not stable prior to surgery.
- Aggressive fluid resuscitation with isotonic fluid
- Inotropic support is frequently necessary.
- Correct coagulopathy if possible.
- Obtain body weight and serum creatinine to adjust antimicrobial dosages as needed.
- Consider tetanus toxoid administration.

MEDICATION

First line

- Triple antibiotic therapy is given empirically and includes:
  - Penicillin G 3–5 million IU IV q6h: Gram-positive coverage
  - Imipenem 500–1,000 mg IV q6h: Polymicrobial coverage
  - Clindamycin 600–1,200 mg/d (divided dose): Anaerobic coverage if clostridia are suspected

- Add vancomycin 1 g IV b.i.d. if MRSA is suspected.

Second line

- Penicillin and clindamycin, OR
- Penicillin and gentamicin, OR
- 2nd-generation cephalosporin, gentamicin
- Change antibiotics when culture and sensitivity reported

SURGERY/OTHER PROCEDURES

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- Extent of debridement should include all affected tissue. Questionable involvement can be treated with incision and drainage and observation.
- Fascia and muscle are rarely involved and do not typically require wide resection.
- The testicles are rarely involved because of an independent blood supply, and are usually viable. They can be wrapped in moist fine-mesh gauze or placed in a subcutaneous abdominal or thigh pouch after debridement.

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- If a VAC closure is not possible, the wound should be packed with fine-mesh gauze soaked in normal saline, Dakin (25%) solution, or Clorpactin.
- If perirectal disease is identified, exam with proctoscopy under anesthesia is necessary.
- Consider a diverting colostomy if the anal sphincter is involved.
- Cystoscopy is necessary to rule out urethral involvement.
- Consider proximal urinary diversion (suprapubic tube, percutaneous nephrostomies) if the penis is extensively involved.
- Postoperative care:
  - If a VAC dressing is not used, wet-to-dry dressing changes are performed b.i.d.–t.i.d.
  - Repeat operative debridement q24–72h; may be necessary to remove newly necrotic tissue.
  - Follow cultures for sensitivities and adjust antibiotic therapy accordingly.
  - Nutritional support, preferably enteral over IV, should be instituted early to correct the resultant negative nitrogen balance associated with profound sepsis.
  - Reconstruction can be performed after the patient has stabilized and the wound demonstrates adequate granulation.
  - Various reconstructive techniques can be used, including skin grafting and myocutaneous flaps.

ADDITIONAL TREATMENT

- Daily whirlpool therapy following surgery acts to micro-débride the wound and keeps the surrounding tissues clean.

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- Silvadene cream can be applied during each dressing change.
- Retrograde (and antegrade if a suprapubic tube was placed) urethrography is used to help document the extent of stricture disease after resolution of the acute infection.

ONGOING CARE

PROGNOSIS

- Historically, Fournier gangrene carried a >50% mortality rate.

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COMPLICATIONS

- ARDS
- Death
- Infertility
- Multiorgan system dysfunction
- Urethral stricture

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Prolonged critical care is typically required.

REFERENCES

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3. Joseph E, Hamori CA, Bergman S, et al. A prospective randomized trial of vacuum-assisted closure vs. standard therapy of chronic non-healing wounds. Wounds 2000;12(3):60–67.

4. Mindrup SR, Kealey GP, Fallon B. Hyperbaric oxygen for the treatment of Fournier’s gangrene. J Urol 2005;173:1975–1977.

5. Gilbert DN, Moellering RC, Eliopoulos GM, et al. The Sanford Guide to Antimicrobial Therapy, 38th ed. Sperryville: Antimicrobial Therapy Inc., 2008.

ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Diabetes Mellitus, Urologic Considerations
- Urosepsis (Septic Shock)

CODES

ICD9

608.83 Vascular disorders of male genital organs

ABBREVIATIONS

- ARDS: Adult respiratory distress syndrome
- CT: Computed tomography
- MRI: Magnetic resonance imaging
- MRSA: Methicillin-resistant staphylococci aureus
- PMN: Polymorphonuclear leukocyte
- STD: Sexually transmitted disease
- US: Ultrasound
- VAC: Vacuum-assisted closure

FUNGAL INFECTIONS, GENITOURINARY

Raymond M. Bernal, MD

Michel A. Pontari, MD

BASICS

DESCRIPTION

Primary infection of the urinary tract is common with Candida, but uncommon with other fungi. When other fungal infections are found in the GU tract, systemic disease is assumed.

RISK FACTORS

- Urinary tract drainage catheter
- Prior antibiotics
- Diabetes/glucosuria
- Urinary tract pathology
- Malignancy
- Increased age
- Neonates
- Female sex
- Prior surgical procedures

GENERAL PREVENTION

- Remove unnecessary catheters/tubes
- Narrow antibiotic coverage
- Improve nutritional status
- Control hyperglycemia

PATHOPHYSIOLOGY

- Funguria to fungemia:
  - Can occur with obstruction, reflux, or instrumentation
- Fungemia to funguria:
  - Disseminated disease seeds GU tract
  - Multiple microabscesses develop in the renal cortex, with subsequent penetration into the glomeruli and shedding into the urine from the proximal tubules.

COMMONLY ASSOCIATED CONDITIONS

- Immunocompromised state:
  - Diabetes
  - AIDS
- Anatomic GU abnormalities:
  - Strictures

- Prostatic hypertrophy
- Diverticula
- Indwelling tubes
- Stones

DIAGNOSIS

HISTORY

- Immunocompromised state:
  - Fungi are ubiquitous in the environment and can overwhelm those with weakened immune systems: Those receiving chemotherapy, with AIDS, or afflicted with diabetes.
- Recent antibiotic use:
  - Risk of candiduria is 6 times after use of broad-spectrum antibiotics
- Indwelling GU tubes or prosthesis:
  - Risk of candiduria 12 times with catheterization
- GU tract abnormalities:
  - Risk of candiduria 6 times with abnormalities
- Occupation:
  - Exposure to aerosolized soil; spelunkers; bird handler
- Recent travel or recreation:
  - 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
  - Cryptococcus thrives with birds.
- UTI symptoms:
  - Only 4–14% with symptomatic candiduria: Treat. If asymptomatic, do not treat unless unable to vocalize or perceive symptoms.

PHYSICAL EXAM

- CVA tenderness
- Abdominal tenderness
- Boggy or firm prostate
- Firm testicular or epididymal masses
- GU tubes present
- Manifestations of disseminated disease

- Is proper urine collection possible

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Candida:
  - No studies have established the importance of pyuria or quantitative urine culture in diagnosing Candida UTI.
  - Presence of pyuria helpful in those without catheter, however, up to 25% with candiduria also have bacteriuria/pyuria
  - >10,000 CFU/mL could mean infection; 10,000–100,000 could mean colonization
  - Check urine microanalysis looking for casts containing yeast: Very specific, not sensitive.
- Aspergillosis:
  - Culture in Sabouraud medium or stain tissue with methenamine silver or PAS; can PCR
- Cryptococcosis:
  - Culture; stain tissue with India ink, PAS, methenamine silver; perform latex agglutination
- Phycomycosis:
  - Stain tissue
- Blastomycosis:
  - Stain tissue and visualize secretions.
- Coccidioidomycosis/histoplasmosis:
  - Culture and stain tissue.

Imaging

CT abdomen with contrast and delayed imaging vs. US may elucidate bezoars, perinephric pathology, renal destruction

Diagnostic Procedures/Surgery

- Cystoscopy/retrograde urogram
- Urine culture
- Tissue biopsy

Pathological Findings

Positive histology staining for fungi in tissue

DIFFERENTIAL DIAGNOSIS

- Clots
- Cystitis

- GU TB
- Nephrolithiasis
- SCC
- TCC

TREATMENT

Infectious Diseases Society of America recommends treatment of candiduria in:

- Infants with low birth weight
- Patients who will have GU procedures
- Neutropenic patients
- Symptomatic patients

MEDICATION

- Aspergillosis:
  - Amphotericin B 1–1.5 mg/kg/d 10 wk+ OR
  - Voriconazole 6 mg/kg q12h for 2 days, then 4 mg/kg q12h (IV or oral) for 10 wks+ or
  - Itraconazole 200 mg IV b.i.d. for 4 days, then 200 mg/d IV for 12 days, then 200 mg PO b.i.d. or 200 mg PO t.i.d. for 9 days, then 200 mg PO b.i.d. 10 wks+
- Blastomycosis:
  - Itraconazole 200 mg PO b.i.d. 6–12 mo OR
  - Amphotericin B 0.5–1 mg/kg/d 6–12 wk OR
  - Fluconazole 400–800 mg/d PO 6–12 mo
- Candidiasis:
  - Clotrimazole, miconazole, tioconazole, terconazole: Topical for 1 wk, or fluconazole 150 mg in 1 dose
- Candidemia (treat until 2 wk after afebrile & Cx negative):
  - Fluconazole 400–800 mg/d IV, then PO OR
  - Caspofungin 70 mg/d IV in 1 dose, then 50 mg/d
  - Amphotericin B 0.5–1 mg/kg/d
- Candiduria:
  - Fluconazole 200 mg/d IV/PO 1–2 wk OR
  - Amphotericin B 0.3–0.5 mg/kg/d IV 1–2 wk OR
  - Flucytosine 25 mg/kg/d PO 1–2 wk
- Coccidioidomycosis:
  - Itraconazole 200 mg PO b.i.d. 1 yr+
  - Fluconazole 400–800 mg/d PO 1 yr+

- Amphotericin B 0.5–0.7 mg/kg/d IV 1 yr+

- Cryptococcosis:
  - Amphotericin B 0.5–1 mg/kg/d IV + flucytosine 100 mg/kg/d PO 2 wk
  - Then fluconazole 400 mg/d PO for 8 wk OR
  - Then Itraconazole 200 mg PO b.i.d. for 8 wk
  - For cryptococcal suppression:
    Fluconazole 200 mg/d PO OR
    Amphotericin B 0.5–1 mg/kg IV every week
- Histoplasmosis:
  - Itraconazole 200 mg PO b.i.d. for 6–18 mo OR
  - Fluconazole 400–800 mg/d PO 6–18 mo OR
  - Amphotericin B 0.5–1 mg/kg/d IV for 10–12 wk
  - For histoplasmosis suppression:
    Itraconazole 200 mg/d or b.i.d. OR
    Amphotericin B 0.5–1 mg/kg IV every week
- Mucormycosis:
  - Amphotericin B 1–1.5 mg/kg/d IV for 6–10 wk

SURGERY/OTHER PROCEDURES

- Obstructions from fungal bezoars require drainage.
- Access to upper tracts can facilitate drainage, antifungal irrigation, and extraction if needed.
- Perinephric abscess can be drained percutaneously, but may require operative drainage if multiple loculations are present.
- Severe aspergillus kidney infections may require nephrectomy.

ADDITIONAL TREATMENT

- Amphotericin B GU tract irrigation: 50 mg in 1,000 mL water at 40 mL/hr (over 24 hr)
- In children, renal irrigation with 10–24 mg/d
- Irrigation may be necessary in aggressive infections when systemic medication is not excreted into the urine:
  - Removing catheter may eradicate funguria in 40% of cases

ONGOING CARE

PROGNOSIS

- Candiduria does not predict development of candidemia in most people. Rates 1.3–10.5%. No different in renal transplant population: 5%.
- Aspergillosis mortality 40–90% with treatment

• Phycomycosis (mucormycosis, zygomycosis) mortality 90% if untreated, 24% with nephrectomy and amphotericin B

COMPLICATIONS

- Bezoar formation
- Emphysematous pyelonephritis
- Obstruction, fungemia, death
- Papillary necrosis
- Perinephric abscess
- Renal scarring

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Surveillance cultures can be obtained to document clearance of infection.
- Prostate can be fungal reservoir for recurrent infection.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Candidiasis—Cutaneous, External Genitalia
- Cryptococcus, Genitourinary
- Histoplasmosis, Genitourinary
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

- 112.1 Candidiasis of vulva and vagina
- 112.2 Candidiasis of other urogenital sites
- 114.9 Coccidioidomycosis, unspecified

ABBREVIATIONS

- AIDS: Acquired immunodeficiency virus
- CFU: Colony-forming units
- CT: Computed tomography
- CVA: Costovertebral angle
- GU: Genitourinary
- PAS: Periodic acid–Schiff
- PCR: Polymerase chain reaction
- SCC: Squamous cell carcinoma
- TCC: Transitional cell carcinoma
- UTI: Urinary tract infection

GLOMERULONEPHRITIS, ACUTE

Matthew G. McIntyre, MD
Kelly E. Shaffer, MD

BASICS

DESCRIPTION

- Inflammation of the glomerulus mediated through humoral and cell mediated immune mechanisms including immunoglobins, complement, and circulating T cells usually in response to an infection (typically streptococcal).
- Poststreptococcal acute GN is the onset of GN after a preceding group A -hemolytic streptococcal infection, most commonly of the pharynx or skin.
- Synonym(s): Acute nephritic syndrome; Postinfectious glomerulonephritis

EPIDEMIOLOGY

- Poststreptococcal GN 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
- 20/100,000/yr

RISK FACTORS

Poststreptococcal GN occurs with infection of specific types of group A -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 following infection with type 12.
- Pyoderma is associated with types 2, 49, 55, 57, 60.

PATHOPHYSIOLOGY

- Tends to occur with impetigo in the late summer and with streptococcal pharyngitis in the winter.
- Note that cases of postinfective GN have also been reported from other bacteria (Pneumococcus, Staphylococcus, Meningococcus) and after viral infections (chickenpox, hepatitis).
- The exact mechanism of renal injury from poststreptococcal GN has yet to be fully elucidated. 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.
  - The antigen or antigens activate the alternative complement pathway and result in renal damage.

COMMONLY ASSOCIATED CONDITIONS

- Pharyngitis
- Hematuria
- Hypertension
- UTI
- Acute renal failure

Pediatric Considerations

Common in children ages 2–16.

DIAGNOSIS

HISTORY

- Recent episode of pharyngitis or skin infection
- Pharyngitis usually precedes renal disease by 1–3 wk
- Onset of gross hematuria, with easy fatigability
- Contacts with individuals complaining of similar symptoms
- Rare to have headaches, seizures, blurry vision, or coma

PHYSICAL EXAM

- Patients may have periorbital edema, peripheral edema, HTN
- Transient oliguria will be present in half of patients

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Hematuria 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 dysmorphic features is a highly sensitive test for glomerular disease.
  - Red blood cell cast present after acute pharyngitis episode is pathognomic for poststreptococcal GN.
- Proteinuria may also be present. Most cases of poststreptococcal GN have mild proteinuria, but some may have proteinuria to the nephrotic range. This may be evaluated with a spot urine protein-to-creatinine ratio with normal being <0.2 and nephrotic range being >2.0.
- Basic chemistry profile may reveal elevated BUN and creatinine consistent with ARF.
- Hyponatremia may be present due to volume overload.
- ESR will be elevated.
- Acidosis may be present
- Serum complement levels can be measured; in particular, C3 will be depressed early in the disease. This should return to normal within 6–8 wk. If this remains depressed, look for

other causes.

- Antistreptolysin-O and antihyaluronidase 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.

Pathological Findings

- IgG and C3 deposits are found at the capillary wall and in the mesangium on renal biopsy.
- Rapidly progressive GN is characterized pathologically by crescents forming from the cells of Bowman capsule:
  - Typically >50% of glomeruli should have crescents to be called rapidly progressive GN. This may result from any of the immunologically mediated types of GN, but most frequently occurs with antiglomerular basement membrane disease, antineutrophil cytoplasmic antibody GN, and Henoch-Schönlein purpura nephritis.

DIFFERENTIAL DIAGNOSIS

- Anaphylactoid purpura
- IgA nephropathy
- Membranoproliferative glomerulonephritis
- Other postinfective glomerulonephritis
- Rapidly progressive glomerulonephritis
- Systemic lupus erythematosus

TREATMENT

Restrict protein until azotemia clears.

MEDICATION

First-Line

Treatment is supportive for this condition and directed at the effects of renal insufficiency and HTN:

- Loop diuretics, calcium channel blockers, and vasodilators are mainstays in the treatment of resultant HTN.

- Sodium restriction is indicated in patients who show signs of fluid overload.

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 -hemolytic streptococci and treated if positive.

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 crescentic 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.
- Hypertensive retinopathy or encephalopathy
- Rapidly progressive glomerulonephritis
- Microhematuria may persist for years
- Nephrotic syndrome (10%)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Subsequent urinalysis to ensure hematuria has resolved
- Periodic BP monitoring

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Glomerulonephritis, Chronic

- Renal Failure, Acute (Chief Complaint)

CODES

ICD9

580.9 Acute glomerulonephritis with unspecified pathological lesion in kidney

ABBREVIATIONS

- ARF: Acute renal failure
- BP: Blood pressure
- CXR: Chest x-ray
- ESR: Erythrocyte sedimentation rate
- GN: Glomerulonephritis
- HTN: Hypertension

GLOMERULONEPHRITIS, CHRONIC

Stanley Zaslau, MD, MBA

Rocco A. Morabito, MD

BASICS

DESCRIPTION

- Disease of the glomeruli characterized by intraglomerular inflammation and cellular proliferation associated with hematuria
- Chronicity of disease associated with progressive loss of renal function
- May occur as a primary renal disease of manifestation of renal involvement in a systemic disease process

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- Most forms of GN present acutely with hematuria, proteinuria, elevated creatinine, and HTN. The progression from acute to chronic GN is variable.

EPIDEMIOLOGY

)[C]

- Accounts for up to 10% of patients on dialysis
- Most common cause of ESRD worldwide
- True incidence is unknown.

RISK FACTORS

- The causative agents in most forms of glomerulonephritis are unknown.
- Infection with Group A -hemolytic streptococci, viral infections (hepatitis C, HIV)
- Autoimmune diseases (SLE, Wegner granulomatosis)

GENERAL PREVENTION

No specific prevention measures; only close monitoring of BP, creatinine, and proteinuria

PATHOPHYSIOLOGY

- Anemia is the result of marked impairment of erythropoietin production.
- Hematuria characterized by dysmorphic red blood cells or red blood cell casts
- Characterized by irreversible and progressive glomerular and tubulointerstitial fibrosis
- 2 phases of glomerular damage: Acute and chronic
- Activation of mediators of tissue injury through immune reactions
- Complement activation generates chemotactic factors that lead to leukocyte recruitment, C5b-9 release, and up-regulation of coagulation factors.
- Causes direct damage to the glomeruli and deposition of fibrin along with crescent formation
- Local and systemic release of growth factors and cytokines also leads to injury of glomerular cells.

- Chronic phase results from response of glomerular cells themselves to the mediators.

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COMMONLY ASSOCIATED CONDITIONS

Autoimmune diseases (eg, SLE)

DIAGNOSIS

HISTORY

- Ask about previous upper respiratory infections, skin infections, drug use, episodic hematuria, subacute bacterial endocarditis (associated with SLE)
- Autoimmune disease
- Question about symptoms related to uremia and renal failure such as shortness of breath, fatigue, weakness, swelling, tremors, nausea and vomiting, itching

PHYSICAL EXAM

- HTN on vital signs
- Gross hematuria
- Lower-extremity edema
- Cardiac murmur

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Anemia is common with declining GFR.
- Serum creatinine and BUN are elevated.
- Hyperkalemia, hyponatremia, and low serum bicarbonate levels can be seen.
- Hypocalcemia, hyperphosphatemia, and high levels of parathyroid hormone (caused by impaired vitamin D3 production)
- Low serum albumin with poor nutrition or if the patient is nephrotic
- Urinalysis:
  - Dysmorphic RBCs, albumin, or RBC casts suggests glomerulonephritis.
  - Waxy or broad casts are seen.
  - Low urine-specific gravity: Loss of tubular concentrating ability, an early and sensitive finding
- Urinary protein excretion:
  - The degree of proteinuria (albuminuria) predicts prognosis. Patients with >1 g/d have an increased risk of progression to ESRD.
  - Estimate by calculating the protein-to-creatinine ratio on a spot morning urine sample. The ratio of urinary protein concentration (in mg/dL) to urinary creatinine (in mg/dL) reflects 24-hr protein excretion in grams. (Example: Spot urine protein is 450 mg/dL, creatinine is 150 mg/dL, then the ratio is 450/150 = 3. The 24-hr urine protein excretion is ~3 g.

• Creatinine clearance is used to assess and monitor the GFR. The creatinine clearance rate is also used to monitor response to therapy and to initiate dialysis access or transplantation evaluation.

• Various serologic studies (antibodies to streptococci, antinuclear antibodies, anti-GBM, ANCA, hepatitis C antibody, and complement) may assist in the further diagnosis and management in select cases.

Imaging

May perform renal US to evaluate size and cortical volume and to direct renal biopsy

Diagnostic Procedures/Surgery

Renal biopsy to confirm diagnosis; can help distinguish between the different glomerular diseases

Pathological Findings

• Usually see glomerular sclerosis and interstitial fibrosis along with tubular atrophy

• Renal biopsy can help determine the type of chronic GN and provide prognostic information. In the most advanced stages, the different etiologies are indistinguishable.

– Focal segmental glomerulosclerosis: 80% progress to ESRD in 10 yr; idiopathic or related to HIV infection.

– IgA nephropathy: 10% ESRD in 10 yr.

– Lupus nephritis: 20% progress to CRF and ESRD in 10 yr; some may have more rapid decline.

– Membranoproliferative glomerulonephritis: 40% ESRD in 10 yr.

– Membranous nephropathy: 20–30% ESRD in 10 yr.

– Poststreptococcal GN: 1–2% develop ESRD.

– Rapidly progressive GN or crescentic GN: 90% of patients progress to ESRD within weeks or months.

DIFFERENTIAL DIAGNOSIS

• Acute renal failure
• Glomerulonephritis, acute
• Glomerulonephritis, crescentic
• Glomerulonephritis, diffuse proliferative
• Glomerulonephritis, membranoproliferative
• Glomerulonephritis, membranous
• Glomerulonephritis, mesangial
• Glomerulonephritis, nonstreptococcal infectious
• Glomerulonephritis, poststreptococcal

- Glomerulonephritis, rapidly progressive

TREATMENT

- Dialysis an option for ESRD
- Follow BP and creatinine carefully

MEDICATION

First-Line

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- Data suggest the use of ACE inhibitors (Enalapril (Vasotec) and angiotensin II receptor blockers may slow the progression to ESRD in many patients.

Second line

- Can administer systemic steroids, immunosuppressive therapy, or cytotoxic agents (Cyclophosphamide)
- Some proven role with Bactrim in preventing relapses in patients with Wegener granulomatosis

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- Renal osteodystrophy in advanced renal failure is managed with vitamin D and phosphate binders.

SURGERY/OTHER PROCEDURES

- Vascular access for dialysis, usually when GFR drops below 20 mL/min; arteriovenous fistula preferred to graft due to improved long-term patency
- Peritoneal dialysis catheter placement
- Renal transplant for end-stage kidney disease
- Rarely, laparoscopic or open renal biopsy may be necessary to secure diagnosis.

ADDITIONAL TREATMENT

- Protein-restricted diets are controversial; may slow decline in the GFR and reduce hyperphosphatemia in patients with creatinine >4 mg/dL. Monitor these patients for signs of malnutrition, which may contraindicate protein restriction.
- Dietary counselling to help control hyperkalemia.
- Most dietary restrictions are no longer necessary with the initiation of renal replacement therapy.

ONGOING CARE

PROGNOSIS

- Consultation with nephrologist early in course can improve long-term outcome.
- Worldwide, is the leading cause of ESRD and 3rd most common cause in the US.
- Depends on how compliant patient is with follow-up appointments

- Excellent prognosis with conservative treatment; after renal transplant, patients have low risk of recurrence

COMPLICATIONS

- Can develop ESRD requiring dialysis or renal transplant
- Associated with increased cardiovascular complications; treat hyperlipidemia if present

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patients are to have serum creatinine, urinalysis (with level of proteinuria), and BP followed closely

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Chronic Kidney Disease
- Creatinine, Serum, Increased/Decreased
- Glomerulonephritis, Acute
- Nephrotic Syndrome
- Proteinuria

CODES

ICD9

582.9 Chronic glomerulonephritis with unspecified pathological lesion in kidney

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ANCA: Anti-neutrophil cytoplasmic antibodies
- BP: Blood pressure
- CRF: Chronic renal failure
- ESRD: End-stage renal disease
- GBM: Glomerular basement membrane
- GFR: Glomerular filtration rate
- GN: Glomerulonephritis
- HIV: Human immunodeficiency virus
- HTN: Hypertension
- NSAID: Nonsteroidal anti-inflammatory drug
- RBC: Red blood cell
- SLE: Systemic lupus erythematosus
- US: Ultrasound

GONORRHEA

Scott G. Hubosky, MD

BASICS

DESCRIPTION

A sexually transmitted disease caused by Neisseria gonorrhea, a gram-negative diplococcus:

- Can manifest as asymptomatic disease
- In men can cause urethritis, prostatitis, epididymitis
- In women can cause cervicitis, salpingitis, endometritis, PID
- Depending on sexual practices, either sex can get anorectal or pharyngeal infection.
- Purulent conjunctivitis can occur in neonates during vaginal delivery and can occur in adults due to autoinoculation.
- Monoarticular arthritis may occur in young adults with HLA-B27 genotype.

EPIDEMIOLOGY

- CDC estimates 700,000 new cases per year, only 1/2 of these reported
- In 2006, CDC reported the rate of gonorrheal infections to be 120.9 per 100,000 persons.
- Reported infections are most common in teenagers, young adults, and African Americans
- Infection rates decreased by 74% since the implementation of the national gonorrhea control program in the mid 1970s.

RISK FACTORS

- Sexual activity with an infected person
- Men have 10% chance and women have 40% chance of infection after having 1 exposure.

Genetics

Individuals with inherited or acquired deficiency of late complement components C5–C9 are susceptible to local Neisseria infections and bacteremia.

GENERAL PREVENTION

- Abstinence or monogamous relationship with uninfected partner.
- Latex condom use reduces gonorrhea transmission.

PATHOPHYSIOLOGY

- N. gonorrhea is not commensal flora to genitourinary tract
- Bacteria get introduced to mucosal surface after contact with infected person.
- Pili and Opa proteins are adherence ligands, which allow bacteria to attach to epithelial cells.

- These proteins demonstrate variation and may be mechanism for resistant strains.
- Brisk granulocyte response manifests in mucopurulent exudates and is responsible for mucosal damage and scarring.

COMMONLY ASSOCIATED CONDITIONS

- Always recommend testing for other STDs.
- Commonly associated with concomitant infection with Chlamydia trachomatis.

DIAGNOSIS

HISTORY

- Incubation period of 3–14 days
- 50% of infected women are asymptomatic; those with symptoms may have increased vaginal discharge, dysuria, urinary frequency, abdominal pain, and menstrual irregularity.
- 95% of infected men have symptoms; usually with urethral discharge and dysuria.
- Anorectal involvement may produce tenesmus, rectal bleeding, and discharge.
- Pharyngeal cases are usually asymptomatic but may present with sore throat.

PHYSICAL EXAM

- In women, pelvic exam with speculum may show mucopurulent cervical discharge.
- In men, mucopurulent urethral discharge may be seen if patient has not recently urinated.
- If indicated, anoscopy may show inflamed purulent rectal mucosa.
- Pharyngeal cases may show exudative pharyngitis and cervical adenitis.
- Infection of the conjunctiva manifests with severe purulent conjunctivitis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Gram stain and culture of urethral or endocervical discharge with swab
- Gram stain shows gram-negative diplococci found inside neutrophils.
- NAAT test may be performed on urine specimens but is less sensitive than intraurethral or endocervical swab.

Imaging

- Not indicated in uncomplicated cases
- CT or pelvic US if PID or pelvic abscess suspected
- RUG if urethral stricture suspected

Diagnostic Procedures/Surgery

Gram stain and culture make diagnosis.

Pathological Findings

Gram stain demonstrates gram-negative diplococci present in polymorphonuclear cells.

DIFFERENTIAL DIAGNOSIS

Urethritis/cervicitis:

- Chlamydia trachomatis
- Ureaplasma urealyticum
- Herpes simplex virus

TREATMENT

- Patients with active infection should abstain from sex with partners until adequately treated.
- Infected patients should notify sexual partners so they may also seek treatment.

MEDICATION

First-Line

- Uncomplicated urethral or endocervical infection (assume treatment for concomitant Chlamydia)
- For gonorrhea may choose from the following:
  - Ceftriaxone 125 mg IM in 1 dose
  - Cefpodoxime 400 mg PO in 1 dose
  - Cefixime 400 mg PO in 1 dose
- For Chlamydia may choose from the following:
  - Azithromycin 1 g PO in 1 dose
  - Doxycycline 100 mg PO b.i.d. for 7 days

Second line

Quinolones can be used if penicillin allergy, but resistant strains exist in Asia, Hawaii, and California; avoid in pregnancy:

- Ciprofloxacin 500 mg in 1 dose
- Levofloxacin 250 mg in 1 dose
- Ofloxacin 400 mg in 1 dose

Pregnancy Considerations

- Treatment options for pregnant patient:
  - Ceftriaxone 125 mg IM in 1 dose
  - Spectinomycin 2 g IM in 1 dose
  - Cefixime 400 mg PO in 1 dose
- Active infection in mother can cause vertical transmission to baby during vaginal delivery, resulting in neonatal conjunctivitis (ophthalmia neonatorum).
- Treatment for neonates:
  - Ceftriaxone 25–50 mg/kg/d IV (not to exceed 125 mg in a single dose)

SURGERY/OTHER PROCEDURES

Chronically, gonorrhea may result in urethral stricture disease and require dilation or incision.

ADDITIONAL TREATMENT

Encourage safe sex practices.

ONGOING CARE

PROGNOSIS

99% of uncomplicated cases are adequately treated with single IM dose of ceftriaxone.

COMPLICATIONS

- In males, may lead to urethral stricture or sterility.
- In females, ascending infection can cause PID, which may cause sterility, ectopic pregnancy, or chronic pelvic pain.
- Genital abscess in women may originate from Bartholin ducts; penile abscess may be seen in men.
- Fitz-Hugh-Curtis syndrome is gonococcal perihepatitis that can result from ascending infection in either sex.
- DGI is seen in >3% of mucosal infections and presents as either septic arthritis or arthritis-dermatitis syndrome

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Repeat cultures should be performed ~7 days after treatment to ensure negative cultures.

ADDITIONAL READING

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- Ryan KJ, Falkow S. Neisseria. In: Ryan KJ, et al. Sherris Medical Microbiology, 3rd ed. Norwalk: Appleton & Lange, 1994.
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See Also (Topic, Algorithm, Electronic Media Element)

- Sexually Transmitted Diseases, General
- Urethra, Discharge
- Urethritis

CODES

ICD9

- 098.0 Gonococcal infection (acute) of lower genitourinary tract
- 098.13 Gonococcal epididymo-orchitis (acute)

- 098.7 Gonococcal infection of anus and rectum

ABBREVIATIONS

- CDC: Centers for Disease Control and Prevention
- CT: Computed tomography
- DGI: Disseminated gonococcal infection
- NAAT: Nucleic acid hybridization
- PID: Pelvic inflammatory disease
- RUG: Retrograde urethrogram
- STD: Sexually transmitted disease
- US: Ultrasound

GROIN HERNIA, ADULT AND PEDIATRIC

Neil E. Fleshner, MD, MPH

BASICS

DESCRIPTION

- Groin hernias occur in a prone area defined by the rectus abdominus muscle medially, the inguinal ligament laterally, and the pubic ramus inferiorly.
- In adults, most hernias are acquired, and individuals with raised intra-abdominal pressure are at elevated risk (ie, physically active vs. sedentary)
- In children, most hernias are congenital and are due to the patency of the processus vaginalis.

EPIDEMIOLOGY

- Adult inguinal hernias carry a lifetime risk of 4–5%.
- 9–11% of premature infants
- 3.5–5% of full-term newborns have an inguinal hernia.

RISK FACTORS

- Adults:
  - Age: 1% risk <45 yr, 3–5% >45 yr
  - Raised intra-abdominal pressure: Heavy lifting, obesity, pregnancy, ascites, chronic cough/COPD, bladder outlet obstruction
  - Chronic muscle weakness: Malnutrition, systemic illness, smoking, steroids
  - Connective tissue disorders: Ehlers-Danlos, Marfan, Hunter-Hurler syndromes
- Children:
  - Gestation age: Higher in premature infants
  - Family history: 11% if an affected sibling
  - Increased intra-abdominal pressure: Ascites, V-P shunt

Genetics

- Testicular feminization syndrome (XY, phenotypic females)
- FBN1 and TGFBR2 (Marfan disease)
- ADAMTS2, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, PLOD1, and TNXB (Ehlers-Danlos)

GENERAL PREVENTION

Lifting techniques to minimize intra-abdominal pressure (ie, leg lifting)

PATHOPHYSIOLOGY

- Child:
  - Patency of the processus vaginalis at birth is a potential hernia but not all will develop a clinical hernia.

– Migration of abdominal contents through the patent processus causes a hernia.

– Incarceration and/or strangulation can occur.

– Most right sided, 10% are bilateral

– Up to 6 times more common in boys than girls

– 90% of hydroceles will resolve in the 1st few months of life; persistence suggests a concomitant hernia defect.

- Adult:

– Indirect hernias travel with the spermatic cord/round ligament (lateral to epigastrics); follow same path as the embryologically descending testicle and are covered by internal spermatic fascia.

– Direct hernias do not pass through the ring (via Hesselbach triangle) and are medial to epigastrics.

– Colon, small bowel, omentum, bladder, ovary, and fallopian tube can all be within hernia sacs.

– Femoral hernias travel below the inguinal ligament through the femoral canal. They are more common in women.

- If the hernia cannot be reduced, it is termed incarcerated.
- If the blood supply of the intestinal segment is compromised it is sometimes termed strangulated and is an urgent surgical problem.
- Richter hernia is strangulation in only 1 wall of the intestine hence no GI obstructive symptoms exist.

COMMONLY ASSOCIATED CONDITIONS

- Ambiguous genitalia (disorder of sexual development)
- Connective tissue diseases
- Continuous ambulatory peritoneal dialysis
- Cryptorchidism
- Exstrophy
- Hydrocele
- Hypospadias/epispadias

DIAGNOSIS

HISTORY

Many patients have no specific symptoms, and the defect is detected during routine physical exam:

- Groin bulge tends to disappear when lying down.
- Groin pain may be subtle or more severe.

- Nausea/vomiting if incarcerated with obstruction
- Acute abdomen if strangulated

PHYSICAL EXAM

- Adult:
  - Soft mass in groin
  - Enlarges with cough, strain
  - Examine with finger in the inguinal canal to feel an impulse
  - Bowel sounds in the scrotum confirms diagnosis
  - Scrotal transillumination of limited value
  - Direct vs. indirect is often hard to distinguish (unless the epigastrics are detectable)
- Child:
  - Bulge in inguinal region/scrotum/labia (if female)
  - Worse with crying
  - Often intermittent
  - Silk glove sign: Passing the fingers over the pubic tubercle may detect a patent processus vaginalis. The thickened cord of a hernia or hydrocele sac within the spermatic cord feels like of 2 fingers of a silk glove rubbing together.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Usually not necessary
- CBC may have elevated WBC if strangulation/pain
- Urinalysis may be abnormal if bladder is strangulated.

Imaging

- Generally a clinical diagnosis
- US with uncertain scrotal mass
  - CT, plain x-ray, sonography, or barium studies may demonstrate hernia

Diagnostic Procedures/Surgery

Massive herniation may sometimes involve the bladder in adults. Cystoscopy and evaluation for bladder outlet obstruction may be necessary

DIFFERENTIAL DIAGNOSIS

- Direct inguinal hernia
- Femoral hernia
- Indirect inguinal hernia
- Inguinal/femoral adenopathy

- Scrotal mass: tumor, hydrocele, spermatocele, varicocele

TREATMENT

- Manual reduction of a nonischemic trapped hernia can be attempted with analgesia and or sedation.
- General measures (if acute incarceration or strangulation) include fluid resuscitation, N/G tube, preoperative workup
- Incarcerated or strangulated hernias may require bowel resection at the time of emergency repair.

MEDICATION

No medical therapy can treat a groin hernia

SURGERY/OTHER PROCEDURES

- Adult:
  - Asymptomatic hernias continue to be a controversial topic regarding the need to treat.

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- Child:
  - No role for watchful waiting
  - Mesh repairs rarely performed in the pediatric age group
  - Laparoscopy not yet widely used
  - Simultaneous repair of hydrocele

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Use of binders and trusses is to be discouraged over primary repair.

ONGOING CARE

PROGNOSIS

1.5–3% recurrence rate

COMPLICATIONS

- Strangulated hernia can cause bowel perforation, peritonitis, and death. 60% of hernias in premature infants incarcerate within the 1st 6 mo after birth, therefore early repair is indicated.
- Surgical repair:
  - Hematoma
  - Ilioinguinal nerve damage/hyperesthesia/nerve entrapment
  - Infection

- Ischemic orchitis
- Mortality <0.001% for elective repair
- Recurrence
- Seroma
- Urine retention

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Mostly low-acuity outpatient surgery

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Herniation
- Groin/Inguinal Mass
- Hydrocele, Adult And Pediatric

CODES

ICD9

- 550.90 Unilateral or unspecified inguinal hernia, without mention of obstruction or gangrene
- 550.91 Recurrent unilateral or unspecified inguinal hernia, without mention of obstruction or gangrene
- 550.92 Bilateral inguinal hernia, without mention of obstruction or gangrene

ABBREVIATIONS

- CBC: Complete blood count
- COPD: Chronic obstructive pulmonary disease
- CT: Computed tomography
- N/G: Nasogastric tube
- US: Ultrasound
- V-P: Ventriculoperitoneal
- WBC: White blood cell

GROIN/INGUINAL MASS

Ahmed M. El-Zawahry, MD
J. Nathanial Hamilton, MD

BASICS

DESCRIPTION

It is a palpable bulge in the groin region. The groin has 2 distinct anatomic areas: The inguinal canal and the femoral triangle.

EPIDEMIOLOGY

- Hernia:
  - Estimated that ~5% of population will develop hernia at some point in their lifetime.
- Cryptorchidism: 3–5% in newborn and 0.7–1% by the end of 1st yr.

RISK FACTORS

- Hernia:
  - Low birth weights (<1,500 g)
  - Incidence increases with aging as well as complications.
  - Full-term newborn has 3.5–5% chance
- Cryptorchidism:
  - Low birth weights (<2,500 g)
  - Prematurity 30%
  - Factors that may lead to late testicular descent include black or Hispanic ethnicity; a family history, low birth weight, and preterm birth delivery; and cola consumption during pregnancy.

Genetics

Some connective tissue disorders are inherited and can be associated with a groin hernia (see “Groin Hernia, Adult and Pediatric”)

GENERAL PREVENTION

- Avoid chronic increase in intra-abdominal pressure.
- Avoid STDs.

PATHOPHYSIOLOGY

- The contents of the groin include skin, subcutaneous tissue, the inguinal canal and contents, femoral triangle and contents (including vessels, nerves and lymph nodes), and musculoskeletal structures.
- Lymphadenopathy:
  - Infection with STD, skin infection in the lower extremities
  - Malignancy such as melanoma, lymphoma, other

- Hernia:
  - Persistence of patent processus vaginalis.
  - Chronic increased intra-abdominal pressure.
  - Connective tissue disorder altering collagen formation can predispose to hernia.
  - Prematurity
- Cryptorchidism:
  - Endocrine abnormality
  - Absence or abnormalities of the gubernaculum
  - Reduced intra-abdominal pressure
  - Pronounced impairment in germ cell development

COMMONLY ASSOCIATED CONDITIONS

- Chronic increased intra-abdominal pressure.
- STDs associated with lymphadenopathy
- Penile cancer

DIAGNOSIS

HISTORY

- When mass was 1st noted and any associated symptoms
- Family history of cryptorchidism
- Symptoms of malignancy (fevers, weight loss)
- Birth history: Premature or low birth weight (for congenital hernia and cryptorchidism)
- History of presence or absence of testes in the scrotum, contralateral testis
- Alteration in the size of the mass with cough or abdominal straining suggests hernia or varicocele.
- Fever, a lesion on genitalia or lower extremity, and weakness may suggest infection and lymphadenitis.
- Surgical history of previous hernia repair

PHYSICAL EXAM

- General: Evidence of adenopathy elsewhere, to suggest more systemic disease such as lymphoma
- Groin: Patient should be examined in standing position as well as supine, and Valsalva maneuver should be done during exam.
  - A cough impulse usually suggests an inguinal hernia. Erythematous skin suggests infection or strangulated hernia. Pulsatile mass may suggest arterial aneurysm.
  - A finger in the external ring can help to differentiate direct and indirect hernia.
  - Groin tenderness: Likely infection is the etiology.

- Genitalia: Evaluate for masses, lesions, ulcers.
- Scrotum:
  - Absent testis points to undescended testes.
  - Tender testis suggests epididymitis, testicular torsion, and epididymitis.
  - Transillumination test, if positive, may suggest a hydrocele/hydrocele of the spermatic cord.
- Lower extremity exam:
  - Any source of infection or malignancy such as melanoma

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Blood tests:

- Full blood count and ESR.
- Renal function tests and electrolytes.
- Syphilis serology, if indicated
- HIV serology, if indicated.
- LGV serologic test, if suspected.
- Swab and culture the base of any lesions to diagnose genital herpes, syphilitic ulcer, chancroid (Haemophilus ducreyi).

Imaging

- US can confirm hernia and can help to see the testes within the inguinal canal. Not sensitive for intra-abdominal testis.
- Doppler US for vascular conditions (Valsalva maneuver should be performed during exam).
- CT/MRI can help to diagnose obscure hernias. Also can identify related lymphadenopathy.
- Arteriography may help diagnose femoral artery aneurysm.
- Venography or Doppler US will help diagnose saphenous varix.

Diagnostic Procedures/Surgery

- Laparoscopy: Can be diagnostic and therapeutic for hernia and intra-abdominal testes.
- Exploratory surgery is necessary in many cases for both diagnosis and treatment.
- Lymph node biopsy or FNA for definitive diagnosis of lymphadenopathy.
- Chromosomal and hormonal analysis in situation with bilateral undescended testes.

Pathological Findings

- Cryptorchidism:
  - Decreased number of Leydig and Sertoli cells

- Failure to develop primary spermatocyte
- Peritubular fibrosis

- Lymphadenopathy: Can identify neoplastic or inflammatory cause

DIFFERENTIAL DIAGNOSIS

The mnemonic MINT can be used to remember the possibilities:

- Malformations:
  - Hernia (inguinal or femoral), usually presents with a mass.
  - Hydrocele
  - Hydrocele of the canal of Nuck.
  - Cryptorchidism (undescended, maldescended, or retractile testicles)
  - Testicular torsion
  - Femoral artery aneurysm
  - Varicocele
  - Spermatocele
- Inflammatory lesions:
  - Inguinal lymphadenitis (a mass found during exam):

    Acute secondary to venereal disease (chancroid, gonorrhea herpes, or syphilis) or skin disease, infection in the groin area, drug reaction, and viral infections.

    Chronic secondary to TB
  - Cellulitis
  - Psoas abscess secondary to TB
  - Thrombophlebitis of the saphenous or femoral vein (especially postpartum)
  - Osteomyelitis
- Neoplasms:
  - Lymphadenopathy (penile cancer, melanoma, lymphoma, or metastatic tumor)
  - Skin tumor lipoma and sarcoma of the bone
- Trauma:
  - A perforation of the femoral vein or artery
  - Contusion and fracture, or dislocation of the hip

TREATMENT

Management is based on the cause of the mass and can vary from antibiotic therapy, biopsy, or further imaging for more extensive adenopathy.

MEDICATION

Lymphadenopathy:

- Infection requires treatment with the specific antibiotics. For STD-related adenopathy, see specific chapter.

- Malignancy with either requires chemotherapy or lymph node dissection based on the etiology. For penile cancer with lymphadenectomy a course of antibiotics is indicated

SURGERY/OTHER PROCEDURES

- Cryptorchidism:
  - Treatment started at 6–12 mo
  - Hormonal treatment efficacy is <20% and is dependent on testis location.
  - Surgery is the gold standard for management.
- Hydrocele:
  - Communicating hydrocele with patent processus vaginalis will require surgery.
- Testicular torsion:
  - Manual detorsion followed by orchiopexy.
- Hernias:
  - Congenital hernias are repaired by ligating the processus vaginalis at the internal inguinal ring (60% chance of having a contralateral defect).
  - Strangulated, incarcerated hernias require emergency intervention.
  - Elective surgical repair for hernia is recommended based on surgeon preference.

ONGOING CARE

- Lymphadenopathy: Requires follow-up for chronic infection, response to treatment.
- Cryptorchidism: Requires follow-up for:
  - Malignancy: Increased risk of malignancy in undescended testis, and patient is required to perform monthly self-exam for any abnormality (corrective surgery does not reduce the chances of malignancy).
  - Increased risk of trauma and torsion
  - Requires follow-up for fertility
- Hernia: Follow for recurrences and possible occurrence on the other side in young children.

PROGNOSIS

Depends on the etiology of the mass

COMPLICATIONS

- Cryptorchidism:
  - Infertility
  - Malignancy
  - Increased risk of trauma and torsion
  - Hernia
- Hernia:

  - Nonreducible and incarceration
  - Obstruction
  - Strangulation

- Lymphadenopathy can erode into femoral vessels and cause exsanguination and death.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Cryptorchidism:
  - Requires follow-up for fertility
  - Self-exam for testicular masses
- Hernia, for recurrence

ADDITIONAL READING

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- Shadbolt CL, Heinze SBJ, Dietrich BB, et al. Imaging of groin masses: Inguinal anatomy and pathologic conditions revisited. Radiographics 2001:S261.

See Also (Topic, Algorithm, Electronic Media Element)

- Cryptorchidism
- Groin Hernia
- Penis, Cancer General
- Sexually Transmitted Diseases, General

CODES

ICD9

- 550.90 Unilateral or unspecified inguinal hernia, without mention of obstruction or gangrene
- 603.9 Hydrocele, unspecified
- 752.51 Undescended testis

ABBREVIATIONS

- CT: Computed tomography
- ESR: Erythrocyte sedimentation rate
- FNA: Fine needle aspiration

- LGV: Lymphogranuloma venereum
- MRI: Magnetic resonance imaging
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

GYNECOMASTIA

Matthew G. McIntyre, MD
Kelly E. Shaffer, MD

BASICS

DESCRIPTION

- Benign enlargement of the male breast due to proliferation of ductal elements.
- Pseudogynecomastia/lipomastia is an increase in breast adipose tissue. This can be distinguished by careful physical exam of subareolar tissue and comparison to adjacent adipose tissue

ALERT

~2,000 cases of male breast cancer are diagnosed in the US annually

EPIDEMIOLOGY

30–65% of men have palpable breast tissue and at autopsy 40–55% of men have histologic evidence of gynecomastia.

RISK FACTORS

- Alcoholism
- Endocrinopathies
- Medications (see below)
- Obesity
- Renal failure

Genetics

- KS (47XXY) strongly associated with gynecomastia
- An increased risk of male breast cancer has been reported in families in which a BRCA2 gene mutation.

PATHOPHYSIOLOGY

- Male breast tissue has both androgen and estrogen receptors.
- Androgens inhibit breast development and estrogens stimulate it. Gynecomastia develops when there is an imbalance of these 2 influences (ie, estrogen excess or androgen deficiency) or lack of tissue response to them.

COMMONLY ASSOCIATED CONDITIONS

- Prostate cancer
- Testicular tumors
- Cirrhosis
- Renal failure

DIAGNOSIS

HISTORY

Detailed history should be obtained including:

- Age of patient and onset of symptoms (pubertal, gynecomastia of aging)
- Associated fevers or chills, breast trauma, nipple discharge
- Medical conditions (cirrhosis, chronic kidney disease, HIV, hyperthyroid)
- Medications/drugs as noted
- History of cryptorchidism
- Sexual history: Sexual maturation, changes in libido, erectile dysfunction, infertility

PHYSICAL EXAM

- General appearance, weight amount of adipose tissue containing aromatase capable of peripheral conversion
- Secondary sexual characteristics body hair distribution, phallus size
- Thyroid exam
- Breast exam: Special attention should be paid to distinguish true GM from pseudo-gynecomastia; unilateral vs. bilateral, firm and mobile vs. fixed, skin dimpling, any nipple discharge
  - Axillary lymph nodes
- Genitourinary exam with special attention to testicular exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Basic studies: Creatinine, LFTs, thyroid function testing, serum testosterone
- Further testing as needed:
  - Serum estrogens (estradiol, estrone)
  - LH, FSH, prolactin
  - Tumor markers AFP, -hCG
  - Adrenal androgens serum DHEA, urinary 17-ketostriods

Imaging

- Mammogram if suspicious for male breast cancer
- Breast US
- Testicular US if concerned for testicular tumor
- CT of chest, abdomen, and pelvis when looking for adrenal or extratesticular lesion

Diagnostic Procedures/Surgery

Needle biopsy of suspicious lesions

Pathological Findings

Benign GM consists of increased ducts and prominent stroma.

DIFFERENTIAL DIAGNOSIS

- Leydig cell tumors are rare tumors of the testis; 85–90% are benign. Most are nonpalpable. Leydig cells directly secrete estradiol. This increases estrogen levels and inhibits LH secretion, suppressing testicular production of testosterone.
- Sertoli cell tumor: Tumors overexpress the enzyme aromatase, which converts androgens to estrogen leading to a direct increase in circulating levels of estrogen.
- hCG-secreting tumors, such as choriocarcinoma, stimulate Leydig cells to preferentially secrete estradiol. Many hCG-secreting tumors also will take up steroid precursors such as DHEA and convert them to active estrogens.
- Feminizing 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.
- Increased peripheral aromatization to estrogens: Familial aromatase excess syndrome. The enzyme aromatase (P450 aroma, or CYP19A1) catalyses the conversion of steroid precursors to estrogens.
- Therapeutic administration of estrogens such as DES 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 transcutaneously by sexual intercourse with a partner that uses estrogen creams. Occupational exposure is also possible. Estrogens can be found in hair creams, embalming creams, and in the production of medicinal estrogen products.
- Primary hypogonadism: Testicular failure from any cause may result in GM. Testosterone deficiency leads to elevated LH, which increases estradiol production by remaining Leydig cells. Increased estrogens lead to elevated levels of SHBG, further decreasing free testosterone.
  - KS is the most common genetic disorder associated with hypogonadism and infertility in men. GM is present in 50–70% of cases. KS is the only cause of GM with an established increased risk of breast cancer, 20-fold compared to normal men
  - Defects in genes critical for testosterone production may also lead to decreased testosterone production.
- Deficient androgen action: 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.

• Pubertal GM results from the earlier rise of estrogens in early puberty. As the normal ratio of estrogen to testosterone is restored in later puberty the GM resolves:

– 50–70% of boys develop GM during puberty.

– 20% of men still have GM at 20 yr of age.

• GM of aging. The hypothalamic-pituitary-testis axis is variable in age-related decline. Some men will have elevated gonadotropins others will be normal:

– Adiposity increases with age, leading to peripheral conversion. SHBG levels rise with age, decreasing bioavailable testosterone.

– Medications may also play a part in GM in older men.

• Refeeding GM: 1st recognized after World War II when imprisoned men resumed normal diets and developed tender GM. Starvation is associated with a hypogonadotropic hypogonadism. With resumption of a healthy diet and regaining weight the hypothalamic-pituitary-testis axis returns to normal, resulting in a 2nd puberty with transient imbalance of estrogens to androgens. May explain the GM associated with several chronic illnesses.

• Renal failure and hemodialysis: Many men with chronic kidney disease develop GM upon initiation of hemodialysis. Before initiation of dialysis, men are often nauseated, anorectic, and on protein-restricted diets. The pathogenesis is thought to be similar to refeeding GM:

– Chronic kidney disease is associated with changes in the gonadal axis, which often results in defects in testicular steroidogenesis and spermatogenesis.

• Cirrhosis: It has been believed that men with liver disease and in particular cirrhosis have a higher prevalence of GM. However, studies have shown that the prevalence of GM in cirrhotics is no different than hospitalized age-matched controls. Hormonal changes in chronic liver disease may increase the risk of GM:

– Cirrhotics have decreased clearance of androstenedione, which provides more substrate for peripheral conversion.

– SHBG may also be increased, decreasing free testosterone.

– Alcohol has a direct toxic effect on the gonadal function, and cirrhotics may have testicular atrophy and hypogonadism.

• Hyperthyroidism: 10–40% of men with thyrotoxicosis may have GM. This is likely due to the increased peripheral conversion of androgens to estrogens. There is also an increase in SHBG in hyperthyroidism.

• Men with prostate cancer are at particular risk for development of GM. Androgen deprivation is often used and is associated with breast pain, tenderness, and enlargement. 4 methods of androgen deprivation are currently employed:

– Exogenous estrogen administration such as DES

– LHRH agonist such as goserelin
– Androgen receptor blockers nilutamide, flutamide, bicalutamide
– Orchiectomy:

Rates of GM in men with prostate cancer treated with androgen deprivation are 71%, 1–25%, 16–49%, and 10%, respectively.

Prophylactic radiation of breast tissue has been proven effective at decreasing the risk of developing GM with these agents.

• HIV/AIDS GM. Most likely multifactorial. Use of illicit drugs that may be associated with GM such as heroin or marijuana may also be seen in this group. Other chronic diseases may also be present such as Hep C, Hep B, and alcoholic liver disease. Some men on HAART therapy have hypogonadotropic hypogonadism for as-yet unknown reasons.

• Diabetic mastopathy presents as a discrete lump or diffuse nodularity. Histologically these lesions are composed of B-cell infiltration of mammary ducts and lobules with fibrosis and vasculitis. This condition can be seen in nondiabetics with Hashimoto thyroiditis and lupus.

• Drugs: May be responsible for 1 out of 4 new cases of GM in adults. Some drugs have clear mechanisms for formation of GM. Most drugs do not:

– Destruction of Leydig cells: Chemotherapeutic agents and cytotoxic agents
– Decreased testosterone or DHT production: Ketoconazole, metronidazole, spironolactone, finasteride, dutasteride
– Androgen receptor blocker: Flutamide bicalutamide, nilutamide, cimetidine, marijuana, spironolactone
– Increased serum prolactin: Antipsychotic agents, metoclopramide
– Possible: Refeeding GM, isoniazid, digoxin
– Unknown: HAART, human GH, amiodarone, calcium channel blockers, amphetamines, diazepam, antidepressants (tricyclic and SSRI)

• Breast cancer is rare in men. Symptoms are similar to female breast cancer: A hard fixed mass, ulceration, lymphadenopathy, or bloody nipple discharge should raise suspicion:

– Suspicious lesions should be biopsied.
– GM, except for KS, does not increase the risk of breast cancer.

TREATMENT

• Removal of offending drug agent if possible
• Remove source of exogenous estrogens.

MEDICATION

• SERMs have been used to block effects of an estrogen excess on breast tissue. Tamoxifen (10 and 20 mg/d for 3–9 mo with 90% resolution). Raloxifene and clomiphene cit-

rate have also been used.

- Aromatase inhibitors such as testolactone and anastrazole have been used but not proven as effective as tamoxifen.

SURGERY/OTHER PROCEDURES

- With longstanding GM or those that refuse medical treatment cosmetic surgical excision and reconstruction may be performed.
- Testicular cancer radical orchiectomy
- Adrenal tumors; perform radical adrenalectomy

ADDITIONAL TREATMENT

- Prophylactic breast irradiation has been used prior to initiation of estrogens or androgen blockade for prostate cancer patients.
- Radioactive iodine ablation or propothyuricil for hyperthyroidism

ONGOING CARE

COMPLICATIONS

Psychologic stress

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

For benign GM no follow-up is usually needed. Consider breast self-exams.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Gynecomastia Algorithm
- Infertile Male Syndrome
- Testis, Leydig Cell Tumor
- Testosterone, Decreased (Hypogonadism)
- XXY Syndrome (Klinefelter Syndrome)

CODES

ICD9

611.1 Hypertrophy of breast

ABBREVIATIONS

- AFP: Alpha-fetoprotein
- AIDS: Acquired immunodeficiency syndrome
- CT: Computed tomography
- DES: Diethylstilbestrol

- DHEA: Dehydroepiandrosterone
- DHT: Dihydrotestosterone
- FSH: Follicle-stimulating hormone
- GH: Growth hormone
- GM: Gynecomastia
- HAART: Highly active antiretroviral therapy
- hCG: Human chorionic gonadotropin
- HIV: Human immunodeficiency virus
- KS: Klinefelter syndrome
- LFT: Liver function test
- LH: Luteinizing hormone
- LHRH: Luteinizing hormone-releasing hormone
- SERM: Selective estrogen receptor modulators
- SHBG: Sex hormone binding globulin
- SSRI: Selective serotonin reuptake inhibitor
- US: Ultrasound

HEMATOSPERMIA

David F. Penson, MD, MPH

BASICS

DESCRIPTION

- Defined as the presence of visible blood (fresh or altered) in the ejaculate
- 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

- Represents 1% of all urologic symptoms
- In men <40, cause is almost always due to an inflammatory or infectious process.

RISK FACTORS

- Recent prostate biopsy
- Prostatitis, bacterial

PATHOPHYSIOLOGY

- Often occurs in isolation
- Pathophysiologic causes include:
  - Inflammation and infection
  - Ductal obstruction and cysts of the accessory sexual glands
  - Neoplasms
  - Vascular abnormalities
  - Systemic factors
  - Iatrogenic factors

COMMONLY ASSOCIATED CONDITIONS

- Nonmalignant prostatic disease (26%)
- HTN (5%)
- Genital TB (1%)
- Prostate cancer (1%)

DIAGNOSIS

HISTORY

- Duration and amount of bleeding
- Sexual history/frequency:
  - Hematospermia often associated with long periods of abstinence
- Associated voiding complaints

- Systemic symptoms:
  - Fever
  - Weight loss
- Travel history to endemic areas:
  - TB
  - Schistosomiasis
- Medications:
  - Aspirin
  - Oral anticoagulants
- Recent trauma, surgery, or infection:
  - TRUS biopsy
  - Brachytherapy
  - Microwave hyperthermia
  - Cryoablation
  - Radiation therapy
  - High-intensity focused ultrasound
- Medical conditions:
  - Hypertension
  - Liver diseases
  - Bleeding disorders

PHYSICAL EXAM

- Assess BP
- Abdominal exam for masses
- Penis/urethra
  - Urethral lesions/masses
  - Discharge
  - Condylomata
  - Meatus should be checked for bloody discharge after rectal exam
- Scrotum, epididymis and testes:
  - Palpate vas deferens:
    Induration may indicate TB
    Absence may explain infertility
  - Assess for masses
  - Tenderness?
- Prostate/seminal vesicles:

- Nodularity. Tenderness, masses
- Palpate for midline cystic structures
- SV fullness can be associated with schistosomiasis (egg burden).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and cultures:
  - Urine culture for acid-fast bacilli and parasites, if indicated
- Serum leukocyte and platelet count, PT/PTT:
  - CBC if systemic blood dyscrasia suspected
- Tuberculin skin test should be considered, particularly in patients with exposure history
- Semen analysis can be used to confirm diagnosis and, in cases of schistosomiasis, eggs may be noted. If performed, semen culture should also be sent.
- In older patients (>40):
  - PSA test
  - Urine cytology

Imaging

- TRUS of the prostate:
  - To evaluate the prostate, seminal vesicles and possible Müllerian duct remnants
  - Identified etiology in ~95% of cases (51 of 54 cases)
    Prostatic calcifications (43%)
    Ejaculatory duct calculi (39%)
    BPH (33%)
    Dilated ejaculatory ducts (33%)
    Seminal vesicle calcifications (11%)
    Dilated seminal vesicles (22%)
    Ejaculatory duct cyst (11%)
    Prostatitis (11%)
  - Facilitates diagnostic procedures such as cyst puncture, etc.
  - Should be 1st imaging study for hematospermia
- MRI:
  - Abnormal signal intensity may represent subacute hemorrhage.
  - Should be used if TRUS is not helpful or further clarification of TRUS is needed.

Diagnostic Procedures/Surgery

- Prostate biopsy (see above)
- Cystourethroscopy:

- Allows visualization of urethral inflammation and opening of ejaculatory ducts
- Critical for ruling out urothelial carcinoma

DIFFERENTIAL DIAGNOSIS

- Inflammation/infection:
  - Calculi of seminal vesicles, prostate, and urethra
  - Prostatitis
  - Urethritis
  - Seminal vesiculitis
  - Viral:
    Herpes simplex
    Cytomegalovirus
    Human papilloma virus/condylomata
  - Bacterial:
    TB
    Chlamydia trachomatis
    Gonorrhea
    Syphilis
  - Parasitic:
    Schistosomiasis
    Hydatid disease (echinococcus)
- Ductal obstruction and cysts of accessory glands:
  - Ejaculatory duct cyst
  - Seminal vesicle diverticulum
  - Urethral stricture
  - Utricular cysts
  - Wolffian duct cysts
  - Prostatic cysts
- Neoplasms:
  - BPH
  - Leiomyoma of the seminal vesicle
  - Prostate cancer
  - Testicular cancer
  - Urothelial carcinoma
  - Sarcoma of the prostate and seminal vesicle
  - Prostatic lymphoma

  - Urethral tumor
- Vascular abnormalities:
  - AV malformations
  - Prostatic varicosities
  - Hemangioma
- Systemic factors:
  - Hematologic conditions:
    Hemophilia
    Von Willebrand disease
  - HTN
  - Chronic liver disease
  - Amyloidosis of the seminal vesicles
- Iatrogenic causes:
  - Prostate biopsy
  - GU instrumentation
  - Brachytherapy (occurs in 28% of seed cases)
  - Prostate radiation
  - HIFU
  - Post vasectomy
  - Post orchiectomy

TREATMENT

- Hematospermia is usually a benign and self-limited condition, particularly in younger men.
- Will often resolve spontaneously.
- Underlying condition should be treated if identified.

MEDICATION

- If an underlying cause is identified (ie, bleeding disorder, GU TB, schistosomiasis), initiate appropriate medical management.
- In men <40 without an obvious cause of hematospermia after workup:
  - Watchful waiting
  - Empiric antibiotic therapy with doxycycline or fluoroquinolone
- While a similar approach can be taken in men >40, diagnostic workup should be more exhaustive and prostate biopsy should be considered if PSA or DRE indicates.

SURGERY/OTHER PROCEDURES

- Prostatic calculi: Transurethral incision if patient symptomatic.

- Cystoscopic resection of any lesions seen on this exam
- Cyst puncture and drainage should be considered in selected cases when indicated.

ONGOING CARE

PROGNOSIS

- Patients should be reassured, as should their partners.
- A significant number of cases remain idiopathic even after full workup.
- Hematospermia following prostate biopsy may take several months to clear.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow PSA in older patients, as per prostate cancer screening recommendations
- Semen analysis can be repeated if need be.

ADDITIONAL READING

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CODES

ICD9

608.82 Hematospermia

ABBREVIATIONS

- AV: Anteriovenous
- BP: Blood pressure
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- DRE: Digital rectal exam
- GU: Genitourinary
- HIFU: High-intensity focused ultrasound
- HTN: Hypertension
- MRI: Magnetic resonance imaging
- PT: Prothrombin time
- PTT: Partial thromboplastin time
- PSA: Prostate-specific antigen

- SV: Seminal vesicle
- TB: Tuberculosis
- TRUS: Transrectal ultrasound

HEMATURIA, GROSS AND MICROSCOPIC, ADULT

Edmund Chiong, MBBS

H. Barton Grossman, MD

BASICS

DESCRIPTION

- Hematuria may be gross (visible) or microscopic.
- It can originate from any part of the urinary tract.

ALERT

- Hematuria of any degree should not be ignored, as it may be a sign of serious renal or urologic disease, including malignancy (up to 20%).

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EPIDEMIOLOGY

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RISK FACTORS

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GENERAL PREVENTION

- Adequate fluid intake, especially for patients with history of calculi
- Avoid/decrease tobacco smoking.
- Treat/prevent underlying cause.

PATHOPHYSIOLOGY

RBCs in the urine: RBCs that are isomorphic and have smooth, round membranes and even hemoglobin distribution; suggests urologic disease. RBCs that are dysmorphic with irregular shapes and uneven hemoglobin distribution; suggests glomerular disease.

COMMONLY ASSOCIATED CONDITIONS

Neoplasms, UTI, urolithiasis, and BPH are major causes of hematuria.

DIAGNOSIS

HISTORY

- Age and sex: In men >50, bladder cancer is most common cause. GU cancer is more common in males; females may have vaginal bleeding.
- Timing during urinary stream:
  - Initial hematuria: Anterior urethral pathology.
  - Terminal hematuria: Bladder neck area or prostatic urethra inflammation/pathology.
  - Hematuria throughout the stream: Vesical or upper-tract origin

- Associated pain: Painless gross hematuria suggests bladder cancer. Flank pain, gross hematuria, and abdominal mass is pathognomonic of renal cell carcinoma. Ureteral colic can be caused by calculi (most common), tumor, or blood clot. UTI or prostatitis 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 are of bladder and prostatic origin. Vermiform (wormlike) clots indicate upper tract origin.
- Lower urinary tract symptoms (frequency, urgency, etc.): BPH may cause hematuria. Incomplete bladder emptying predisposes to infection and/or bladder stones.
- Activity: Exercise-induced hematuria should be excluded
- Trauma: Significant crush injury or burn may result in myoglobinuria; abdominal or pelvic trama may cause urinary tract injury.
- Recent URTI: Associated with GN or IgAN.
- Medical or surgical history: Record history of renal or urologic disease or surgery. STDs or recent urethral instrumentation (including catheterization); a history of TB; pelvic irradiation; history of autoimmune disease and bleeding diatheses.
- Current medications: Anticoagulants
- History of tobacco use: Risk of TCC
- Menstrual history: Vaginal bleeding can be mistaken for hematuria.
- Family history: Primary renal disease, HTN, adult polycystic disease, Alport syndrome, urolithiasis, or GU cancers.
- Occupational risk factors: Exposure to chemicals or dyes (aromatic amines, benzenes) in rubber, petroleum and dye industries, risk of TCC.

PHYSICAL EXAM

- HTN: Renal parenchymal disease, renal failure, renal cystic disease, or renal vascular disease
- Pallor: Anemia may be associated with SLE, hemolytic anemia, and renal failure.
- Rashes: Henoch-Schönlein purpura, SLE, and vasculitis
- Generalized edema: Nephrotic syndrome or renal failure
- Hearing loss: Alport syndrome
- Heart murmurs: Subacute bacterial endocarditis
- Palpable abdominal or flank masses: Hydronephrosis, renal cystic disease, renal tumors, and distended bladder
- Flank tenderness: Pyelonephritis or urolithiasis
- Flank lacerations, contusions, or rib fractures: Underlying renal injury

• DRE: Boggy, tender, warm prostate with acute prostatitis; nodularity suggests cancer; floating prostate suggests urethral disruption if pelvic fracture

• Pelvic exam: Urethral caruncle or vaginal prolapse, vaginal bleeding

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• Urine analysis: Must include the standard urine dipstick and microscopic evaluation:

) [C]

– Color: Bright red with urologic/anatomic causes; brown or tea-colored urine suggests GN or old clots.

– Dipstick:

Specific gravity: Poorly concentrated urine (low specific gravity) suggests hydronephrosis with renal impairment or intrinsic renal disease. Proteinuria: If heavy (3–4+), suggests GN or renal disease. Leukocyte esterase and/or nitrite positive; pyuria: Suggests infection.

False-positive dipsticks for blood: Oxidizing agents (hypochlorite, povidone, bacterial peroxidases), myoglobinuria, hemoglobinuria (microscopic analysis is negative). False-negative dipsticks for blood: Reducing agents (high-dose vitamin C), urine pH <5.1.

– Microscopy: Pyuria suggests infection. Red cell casts are pathognomonic of glomerular bleeding. Crystalluria suggests urolithiasis.

• Phase-contrast microscopy of urinary sediment: Differentiates glomerular and non-glomerular bleeding based on the presence of distorted RBCs (80%) in glomerular bleeding; sensitivity of 95% and specificity 100%

• Urine culture: If urinalysis suggestive of infection

)[C]; detects high-grade TCC; less effective with well-differentiated TCC. Atypical cells can be seen with calculi or inflammation (NMP22 and UroVysion are alternatives).

• Renal function tests (creatinine and BUN): Renal impairment associated with underlying pathology

• CBC: Anemia may be due to gross hematuria or chronic renal disease. Elevated white count with a left shift suggests infection.

• Coagulation profile studies: Coagulopathy.

• Other laboratory tests as clinically indicated:

– Streptozyme (antistreptolysin-0 titer), serum complement and ANA, total serum proteins, and albumin: Globulin ratios (for GN)

– Urinary calcium: Creatinine ratio (for hypercalciuria), peripheral smear (for sickle cell disease/trait), TB skin test and urinary mycobacterial cultures (for TB).

Imaging

) [C] but is being replaced by CT. May detect renal masses; collecting system filling defects may signify tumors or stones. (contraindicated if serum creatinine is >2 mg/dL).

- Abdominal US: More sensitive for renal masses than ExU. Poor in diagnosing filling defects in upper tract unless due to stones. Useful in children and when radiation is contraindicated (eg, Pregnancy).
- Abdominal CT or MRI: If US or ExU suggests mass. Noncontrast spiral CT for rapid evaluation of suspected urolithiasis.
- Nuclear renal scans, arteriography, retrograde urethrogram, cystogram as clinically indicated.

Diagnostic Procedures/Surgery

- Cystoscopy: Identifies lower urinary pathology and bleeding site; not recommended in children
- Retrograde pyelograms (if contrast allergy) and ureteroscopy needed to evaluate upper tracts
- Renal biopsy: US guided; for suspected GN.

Pathological Findings

Based on primary cause

DIFFERENTIAL DIAGNOSIS

- Pseudohematuria: Drugs (eg, Pyridium); vegetables, dyes, or pigments; myoglobin and free hemoglobin); menstrual periods; and dysfunctional uterine bleeding.
- Congenital/inherited:
  - Cystic renal disease: Polycystic kidney disease, medullary sponge kidney, medullary cystic disease.
  - Benign familial hematuria or TMN.
  - Alport syndrome
  - Inherited renal tubular disorders: Renal tubular acidosis type I, cystinuria, and oxalosis can cause stones.
- Hematologic abnormalities: Bleeding dyscrasias and sickle hemoglobinopathies
- Anatomic: Urethral and ureteric strictures, phimosis, posterior urethral valves, diverticula, UPJ obstruction, and vesicoureteric reflux
- Vascular malformations: Hemangiomas
- Traumatic:
  - Abdominal and pelvic injury: Can cause GU injury; degree of hematuria is a poor indicator of injury severity.

- Iatrogenic trauma after abdominal, pelvic or urinary tract surgery
- Exercise-induced hematuria
- Foreign bodies: Foley catheter, stents, etc.
- Inflammatory:
  - UTI and specific infections (eg, schistosomiasis, TB, etc.)
  - GN: IgAN most common (4%)
  - Radiation: Radiation nephritis and cystitis
- Metabolic: Urinary calculi, hypercalciuria, and hyperuricosuria
- Neoplastic: Any benign or malignant GU lesion. Cancer is found in 20–40% with gross hematuria and in 5.1% of microscopic hematuria.
- Miscellaneous:
  - Drugs: Nephrotoxic drugs, analgesic abuse, cyclophosphamide (hemorrhagic cystitis), overanticoagulation, etc.
  - BPH
  - Renal vessel disease: Arterial emboli or thrombosis, or renal vein thrombosis etc.
  - Obstructive uropathy: Hydronephrosis
  - Endometriosis of the urinary tract: Female with cyclic hematuria
  - Benign essential hematuria

TREATMENT

MEDICATION

Not normally treated by medications primarily. Occasionally bleeding is caused by prostatic blood vessels can be treated by finasteride or dutasteride

SURGERY/OTHER PROCEDURES

Used in the management of specific conditions such as bladder tumor or renal cell carcinoma

ADDITIONAL TREATMENT

General-Measures

- The standard urologic evaluation of hematuria (gross and microscopic) has been ExU, cystoscopy, and cytology. Workup is undergoing refinement to determine the most cost-effective approach.
- Additional testing based on clinical findings
- Consider medical causes of hematuria (eg, GN, IgAN) based on presentation, lab data, or if evaluation for anatomic lesion is negative.
- Gross hematuria:
  - Often requires urgent evaluation to prevent/treat clot retention

– Clot retention: Irrigate clots from the bladder using 3-way Foley catheter (24F–26F) and continuous bladder irrigation. Large bore, 2-way Foley or rigid catheter may be more effective to clear clots (larger lumen). For difficult clots, cystoscopy is best.

- Microscopic hematuria:
  – Workup is usually elective unless associated with traumatic injury.

ONGOING CARE

PROGNOSIS

Based on etiology of the hematuria

COMPLICATIONS

Hypotension and anemia may result based on degree and chronicity of blood loss

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Monitor hemodynamic status if severe persistent gross hematuria or associated with trauma.

REFERENCES

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Hematuria Algorithm
- Hematuria, Gross and Microscopic, Pediatric
- Hematuria, Traumatic Algorithm
- Hemorrhagic Cystitis
- Urine, Abnormal Color

CODES

ICD9

- 189.9 Malignant neoplasm of urinary organ, site unspecified
- 599.71 Gross hematuria
- 599.72 Microscopic hematuria

ABBREVIATIONS

- ANA: Antinuclear antibody
- BPH: Benign prostatic hyperplasia
- CT: Computed tomography
- DRE: Digital rectal exam
- ExU: Excretory urography
- GN: Glomerulonephritis
- GU: Genitourinary
- HPF: High-power field
- HTN: Hypertension
- IgAN: Immunoglobulin A nephropathy
- MRI: Magnetic resonance imaging
- RBC: Red blood cell

- SLE: Systemic lupus erythematosus
- STD: Sexually transmitted disease
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- TMN: Thin basement membrane nephropathy
- UPJ: Ureteropelvic junction
- URTI: Upper respiratory tract infection
- US: Ultrasound
- UTI: Urinary tract infection

HEMATURIA, GROSS AND MICROSCOPIC, PEDIATRIC

Paul F. Austin, MD

BASICS

DESCRIPTION

Hematuria can be gross (visible) or microscopic:

- Common pediatric urology referral
- Approached differently in pediatric population than adults:
  - Less risk for malignancy
  - Medical causes more frequent than surgical

EPIDEMIOLOGY

- Microscopic hematuria more frequently encountered than gross hematuria
- Microscopic hematuria:
  - 4.1% (41 in 1,000 pediatric visits)
  - More frequent in girls:
    3.2% girls
    1.4% boys
- Macroscopic hematuria
  - 0.13% (1.3 in 1,000 pediatric visits)
  - More frequent in boys:
    80% of case in males and 20% in girls
- Exact prevalence is unknown.

RISK FACTORS

- Alport syndrome
- Anaphylactoid purpura
- Benign familial hematuria
- Calculi
- Cystinuria
- Dysfunctional voiding
- Glomerular bleeding
- Glomerulonephritis
- Hemophilia
- Henoch-Schönlein purpura
- Recent upper respiratory illness
- Renal papillary necrosis
- Sexual abuse

- Sickle cell disease or trait
- SLE
- Trauma
- UTI
- Vigorous exercise

Genetics

- Benign familial hematuria is autosomal dominant.
- Sickle cell anemia is autosomal recessive:
  - Short arm of chromosome 11
- Alport syndrome is X-linked.

GENERAL PREVENTION

Understanding the etiology of the hematuria and tailoring prevention accordingly

PATHOPHYSIOLOGY

Depends on the source of bleeding:

- Interstitial sources
- Vascular sources
- Urinary tract sources
- Glomerular sources

COMMONLY ASSOCIATED CONDITIONS

- Depends on the etiology of the hematuria
- Benign conditions associated with hematuria:
  - Loin pain hematuria syndrome
  - Idiopathic urethrorrhagia
  - Benign familial hematuria

DIAGNOSIS

HISTORY

- Age and timing of onset:
  - Poststreptococcal GN occurs 7–14 days after the onset of the sore throat.
  - IgA nephropathy hematuria develops at the time of or shortly after the respiratory infection.
  - Hematuria secondary to Henoch-Schönlein purpura develops 1–3 mo after the rash.
- Determine the duration of hematuria and whether episodes of gross hematuria are followed by periods of microscopic hematuria or resolve completely.
- Characterize the pattern of hematuria:

– Gross suggests a urologic cause and microscopic suggests a nephrologic cause.

– Initial or terminal hematuria suggests a lower urinary tract source whereas total hematuria suggests upper tract bleeding.

– Idiopathic urethrorrhagia presents in prepubertal boys with blood spotting at the end of voiding.

– Blood clots or blood that is not persistent throughout voiding is suggestive of non-glomerular bleeding.

- Any precipitating events that would suggest conditions associated with hematuria:
  – Onset of hematuria after a respiratory illness, skin infection, or viral illness directs the evaluation toward postinfectious GN.
- LUTS associated:
  – Frequency, urgency, dysuria, hesitancy, incomplete emptying.
- Flank or abdominal pain:
  – Suggests urologic cause eg stones or dysfunctional elimination.
- Oliguria, symptomatic HTN, and symptoms of systemic disease (eg, arthritis, arthralgias, rash or respiratory problems) are suggestive of glomerular disease.
- Obstructive symptoms suggest posterior urethral valves, urethral strictures, or polyps.
- Trauma, strenuous exercise (eg, long distance runners), foreign bodies, and sexual abuse.
- Family history of specific renal diseases, stones, end-stage renal disease, neurosensory hearing loss, and UTIs may focus laboratory and radiologic evaluation.
- Any history of free bleeding or blood dyscrasias
- Current medications

PHYSICAL EXAM

- BP:
  – Make sure to use an age-appropriate BP cuff.
  – Obtain >1 BP measurement, as elevated pressures may be situational.
  – High BP is suggestive of renal glomerular disease, as is the presence of edema.
- Look for evidence of SLE, Wegener granulomatosis, Goodpasture syndrome, etc.
- Hearing loss suggestive of Alport disease.
- Presence of palpable abdominal or flank mass, bruit, or tenderness.
- Eyes should be examined for evidence of acute or long-standing HTN.
- Rashes and arthritis can occur in Henoch-Schönlein purpura and SLE.
- Examine the genitalia for meatal stenosis, urethral prolapse, ureterocele, trauma, or sexual abuse.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Significant hematuria requires 5 RBCs per high powered field on microscopic urinalysis of spun urine.
- Persistent hematuria is defined as 3 positive urinalyses, based on a test strip and microscopic exam, over a 2–3-wk period:
  - False-negative results occur in samples with high specific gravity or with high ascorbic acid concentrations.
  - False-positive results occur in the presence of myoglobin, free hemoglobin, and oxidizing agent's (ie, household bleach).
- Urinalysis:
  - Determines if patient is able to acidify and concentrate urine
  - Detects presence of proteinuria
  - Microscopic analysis show casts, crystals, or WBCs
  - RBCs eumorphic or dysmorphic:

    Dysmorphic red cells predict glomerular bleeding with a sensitivity of 93–95% and a specificity of 95–100%.
- Concomitant proteinuria, cellular casts, and brown, tea-, or cola-colored urine suggests glomerular causes of bleeding.
- Urine culture:
  - If infected, repeat the urinalysis after treating the infection.
- Other laboratory tests: Serum creatinine, blood urea nitrogen, CBC with differential, C3/C4 levels (may be lowered in cases of SLE or GN), ANA, plasma lgA levels (may be Increased with IgA nephritis or Henoch-Schönlein purpura), antistreptlysin-0-titer (indicative of post-streptococcal GM), urine calcium-to-creatinine ratio
- Urine calcium-to-creatinine ratio should be <0.18. If >0.18, usually indicates that the 24-hr excretion of calcium is >4 mg/kg/d.

Imaging

- Renal and bladder sonography:
  - Evaluate for renal parenchymal disease, stones, tumors, or anatomic abnormalities
- VCUG:
  - Evaluate for vesicoureteral reflux, posterior urethral valves, other anomalies.
- CT:
  - Selectively used in pediatric populations secondary to radiation exposure.

– Noncontrast stone protocol CT is useful for working up older child/adolescent with suspected stone disease.

- MR or CT angiography:
  - Detect suspected arteriovenous malformation

Diagnostic Procedures/Surgery

- Renal biopsy:
  - Open or closed, heavy proteinuria, or worsening renal function are the main indications for biopsy. It should only be done if the results will alter therapy.
- Cystoscopy:
  - Rarely indicated in children
  - Examine bladder mucosa
  - Inspect efflux from each ureteral orifice to lateralize source of bleeding
  - Consider retrograde ureteropyelogram:

    Fibroepithelial polyp
- Hearing test:
  - Alport syndrome

Pathological Findings

Depends on etiology and diagnosis

DIFFERENTIAL DIAGNOSIS

- Divided into categories, depending on the source of bleeding:
  - Interstitial sources
  - Vascular sources
  - Urinary tract sources
  - Glomerular sources
- Interstitial:
  - Pyelonephritis
  - Renal TB
  - Nephrocalcinosis
  - Interstitial nephritis
  - Metabolic (eg, Fabry disease)
  - Nephrotoxins (eg, analgesics, NSAIDs)
  - Cystic disease
  - Hydronephrosis
  - Tumors
  - Acute tubular necrosis

- Vascular sources:
  - Trauma
  - Sickle cell disease/trait
  - Renal vein thrombosis
  - Renal artery thrombosis:
    ~20% of gross hematuria occurring in the 1st months of life
  - Arteriovenous malformation
  - Nutcracker syndrome
  - Vasculitis:
    C3 arteriolar deposition
  - Coagulopathy:
    Hemolytic uremic syndrome (hemolytic anemia, renal failure, and thrombocytopenia)
  - Thrombocytopenia
- Urinary tract sources:
  - Infection:
    Dysfunctional voiding and elimination
    Papillary necrosis, infections (eg, TB)
    HIV, hepatitis
    Infestations (eg, schistosomiasis)
  - Hemorrhagic cystitis:
    Viral, chemical or radiation
  - Urethritis
  - Nephrolithiasis
  - Hypercalciuria
  - Obstruction/reflux
  - Fibroepithelial polyp
  - Tumor
  - Drug induced cystitis
  - Menstruation
  - Foreign bodies (eg, catheters)
  - Exercise
  - Anatomic:
    Urethral prolapse, caruncle, meatal stenosis, ureterocele, etc.
- Glomerular sources:

– Postinfectious GN: Edema, HTN, and oliguria. Usually follows a group A - hemolytic streptococcal sore throat or pyoderma. Positive ASO titers and decreased serum complement (C3) are usually present.

– Henoch-Schönlein purpura (rash on the dependent parts of the body that is heralded by a prodrome of malaise, arthralgia, and/or abdominal pain)

– Neoplasm

– IgA nephropathy or Berger disease (recurrent, gross, painless hematuria, often following a mild fever, viral respiratory infection, or exercise)

– Membranoproliferative glomerulonephritis

– Lupus nephritis

– Goodpasture syndrome (pulmonary hemorrhage associated with severe and progressive GN)

– Familial benign hematuria (hematuria in patient and 1st-degree relatives without hearing loss or renal insufficiency)

– Nail-patella syndrome (dystrophic fingernails and toenails, absence of 1 or both patellae, iliac crest horns, and renal disease)

– Alport syndrome (microhematuria, proteinuria, progressive renal insufficiency, high-frequency hearing loss)

TREATMENT

Establish diagnosis and treat any acute medical problems accounting for the hematuria

MEDICATION

Based on clinical diagnosis and etiology

SURGERY/OTHER PROCEDURES

Based on clinical diagnosis and etiology

ONGOING CARE

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- The current recommendation of the American Academy of Pediatrics is to perform a screening urinalysis at age 5 yr. Conduct dipstick urinalysis for leukocytes annually for sexually active male and female adolescents.
- Annual measurements of height and weight and annual BP measurement after age 3 yr.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Cystitis, Hemorrhagic (Infectious, Noninfectious, Radiation)
- Hematuria Algorithm
- Hematuria, Gross And Microscopic, Adult
- Hemorrhagic Cystitis
- Hematuria Traumatic Algorithm
- Urine, Abnormal Color

CODES

ICD9

- 599.71 Gross hematuria
- 599.72 Microscopic hematuria

ABBREVIATIONS

- ANA: Antinuclear antibodies
- ASO: Antistreptolysin O
- BP: Blood pressure
- CBC: Complete blood count
- CT: Computed tomography
- GN: Glomerulonephritis
- HIV: Human immunodeficiency virus
- HTN: Hypertension
- IgA: Immunoglobulin A
- LUTS: Lower urinary tract symptoms
- NSAIDs: Nonsteroidal anti-inflammatory drugs
- RBC: Red blood cell
- SLE: Systemic lupus erythematosus
- TB: Tuberculosis
- VCUG: Voiding cystourethrogram
- WBC: White blood cell

HEMORRHAGE POST-TURP

Grant I. S. Disick, MD

Ravi Munver, MD

BASICS

DESCRIPTION

Significant gross hematuria with or without clot retention that occurs following TURP

EPIDEMIOLOGY

)[B]

)[A]

)[A]

RISK FACTORS

- Excessive valsalva/straining/constipation
- Inadequate hemostasis/coagulation of bleeding vessels
- Infection
- Medications (aspirin, clopidogrel, warfarin, heparin, enoxaparin, dalteparin, etc.)
- Trauma
- Undermining of bladder neck

Genetics

Patients with deficiencies in the clotting cascade (eg, 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.

)[B]

- Gentle postoperative catheter traction

)[B]

PATHOPHYSIOLOGY

- Anesthetic technique (regional or general) appears to have no impact on TURP-related bleeding.
- Inadequate hemostasis/coagulation of bleeding vessels
- Narcotics may cause constipation and increased intra-abdominal pressure.
- Due to sloughing of necrotic tissue in prostatic fossa or bleeding at the bladder neck

)[B]

- Studies suggest that there is transient change in platelet count, prothrombin time, and fibrinogen and serum sodium concentrations postoperatively, which can be explained on the basis of dilution of the blood.

- Prostate cancer is known to trigger DIC, and this should be kept in mind when performing resection in the face of known advanced prostate cancer.
- In the absence of prostate cancer up to 6% of patients undergoing TURP may develop mild subclinical intravascular coagulopathy.
- Urinary fibrinolysis is a normal physiologic process. Plasminogen is converted to plasmin by plasminogen activators.
- The presence of clot in the bladder causes the release of additional plasminogen activators. This evacuation of clot in the bladder is essential to stopping the bleeding.

COMMONLY ASSOCIATED CONDITIONS

BPH

DIAGNOSIS

HISTORY

- Color of urine; presence of clots
- Patient is not able to void (clot retention)
- History of TURP: 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

Lab

- CBC
- Serum chemistry, evaluate creatinine level
- 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

Diagnostic Procedures/Surgery

Bladder drainage and irrigation with large caliber hematuria catheter

DIFFERENTIAL DIAGNOSIS

- Bleeding from lower GU tract source: Urethra, prostate, bladder
- Bleeding from upper GU tract source: Ureter, renal pelvis, kidney

TREATMENT

- Limit physical activity, encourage bed rest
- Limit Valsalva and avoid constipation through stool softeners
- Catheter traction
- Adequate hydration
- Bladder drainage and clot evacuation with large caliber hematuria catheter
- 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
- PRBC transfusions if necessary, vitamin K and/or FFP if coagulopathic
- IV fluid resuscitation

)[B]

- Aminocaproic acid (Amicar) antifibrinolytic
- CBI with intravesical alum or silver nitrate
- These are reported but rarely necessary:
  - Hyperbaric oxygen
  - Hormonal manipulation: LHRH agonists
  - Urinary diversion with bilateral PCNs

)[A]

  - Salvage radical prostatectomy

MEDICATION

- Antibiotics if infected
- Stool softeners
- 5-Reductase inhibitors such as finasteride or dutasteride (although will not have an acute effect)

SURGERY/OTHER PROCEDURES

- Transurethral clot evacuation with fulguration and cauterization (laser or electrocautery) of prostate if bleeding does not subside within a reasonable time frame.
- Findings: Visibly bleeding arterial vessel or discrete/nondiscrete venous bleeding

ONGOING CARE

PROGNOSIS

- The mortality rate for hemorrhage after TURP 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 seems advisable.

COMPLICATIONS

Severe anemia and/or hypovolemic shock can lead to syncope and/or MI.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Can be managed on the floor setting with staff that is accustomed to managing catheters and CBI
- Serial CBCs, blood transfusions as necessary
- Monitor coagulation profile, FFP if needed

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See Also (Topic, Algorithm, Electronic Media Element)

- Hematuria Evaluation Algorithm
- Hemorrhagic Cystitis
- Traumatic Hematuria Evaluation Algorithm
- Urine, Abnormal Color

CODES

ICD9

- 602.1 Congestion or hemorrhage of prostate
- 998.11 Hemorrhage complicating a procedure

ABBREVIATIONS

- BPH: Benign prostatic hyperplasia
- CBC: Complete blood count
- CBI: Continuous bladder irrigation
- CT: Computed tomography
- DIC: Disseminated intravascular coagulation
- FFP: Fresh frozen plasma
- GU: Genitourinary
- IV: Intravenous
- LHRH: Luteinizing hormone-releasing hormone
- MI: Myocardial infarction

- PCN: Percutaneous nephrostomy tube
- PRBC: Packed red blood cells
- PT: Prothrombin time
- PTT: Partial thromboplastin time
- SAPE: Selective arterial prostatic embolization
- TURP: Transurethral resection of prostate
- US: Ultrasound

HERPES SIMPLEX, GENITAL

Steven P. Petrou, MD
David D. Thiel, MD

BASICS

DESCRIPTION

- An STD from HSV. Virus may be shed from open skin, mucosal lesions, or intact mucus membranes. HSV-2 is the most common cause of genital herpes, with HSV-1 usually associated with CNS and nasopharyngeal infection, as well as genital infection. Most patients with genital herpes are asymptomatic and will intermittently shed virus.
- Lifelong recurrent viral infection
- Women tend to have more severe symptoms than men.

EPIDEMIOLOGY

- 0.5–1 million new cases of genital herpes per year in the US
- ~45 million people in the US have genital herpes.
- Genital herpes has a higher incidence in females (1:4) than in males (1:5).

ALERT

Most patients are asymptomatic.

RISK FACTORS

- Sexual contact with an infected person
- Unprotected sexual intercourse
- Nonmonogamous sexual partners
- Immune system compromise
- Illness
- Stress and fatigue
- Skin microabrasion or friction associated with sexual contact

Genetics

HSV-1 and HSV-2 are herpes virus types associated with genital herpes.

GENERAL PREVENTION

- Abstain from all sexual activity (oral/genital/anal) with the onset of prodromal symptoms or during active herpetic lesion outbreak.
- Use condoms.
- Monogamous sexual lifestyle with uninfected partner

PATHOPHYSIOLOGY

- Transmission occurs through sexual contact. Pharmacotherapy and condom use may reduce though not eradicate transmission of virus. Patients are highly contagious when active ulceration is present.

• Majority of viral infections are transmitted by patients who are asymptomatic and unaware of their infected status.

• Prior orolabial HSV-1 protects against genital HSV-1 but not HSV-2.

• Viral transmission infection occurs through sexual contact: Oral/vaginal/anal.

• Staging:

– Primary genital herpes: Initial episode of herpetic genital infection in a patient with no pre-existing outbreak of either HSV-1 or HSV-2.

– Asymptomatic HSV infection: Patients with HSV who are unaware of their infection secondary to its subclinical status or do not recognize presenting signs or symptoms.

– Recurrent genital herpes: Reactivation of latent HSV, either HSV-1 or HSV-2

– 1st episode nonprimary infection: HSV-2 infection in a person who has HSV-1 or vice versa.

COMMONLY ASSOCIATED CONDITIONS

• Those patients infected with HSV-2 have a marked increased risk of being infected with HIV through sexual contact.

• Uninfected patients in a monogamous relationship with an infected partner may remain uninfected for an extended period of time (years) despite potential repeat contact.

• Recurrences may be triggered by physical or mental stress, immune system insult, illness, and fatigue.

DIAGNOSIS

HISTORY

• Recent sexual contact

• Age range between 2nd and 4th decades of life.

PHYSICAL EXAM

• 1st episode:

– Flulike syndrome including fevers, malaise, myalgia, body aches, lymphadenopathy.

– Clusters of fluid filled lesions (<5 mm) involving:

Genitals, anus, buttocks, rectum, vulva, vagina, neighboring skin

– Atypical symptoms: Dysuria, itching, abdominal and bladder pressure, urethral discharge, vaginal discharge, localized tenderness, meningitis

• Primary infection can last up to 3 wk.

• Recurrences usually last <10 days.

• Symptoms may be frequent, with variable severity (usually milder than the primary infection):

- Symptoms may vary from hours to days before appearance of lesions.
- Outbreaks occur on the average of 4–5 times a year (HSV-2 > HSV-1).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Viral cultures (high specificity)
- Rapid shell vial cell culture assay: Requires maintenance of active virus during specimen transport
- Rapid PCR: Gold standard for detection of HSV (12–22% improvement over culture)
  - Rapid PCR advantages: Can differentiate between HSV-1 and HSV-2; results may be obtained same day; PCR assays do not cross-react (no false-positive results) with other herpes virus gene targets (eg, cytomegalovirus, Epstein-Barr virus)

Diagnostic Procedures/Surgery

- Tzanck preparation: An intact vesicle is unroofed with a tuberculin syringe. The base of the vesicle is scraped and examined under PAS or H&E stain.
- Multinucleated giant cells is a positive result.
- Cannot differential HSV-1, HSV-2, or Varicella Zoster virus.

DIFFERENTIAL DIAGNOSIS

- Behçet's syndrome ulcer
- Carcinoma
- Chancroid
- Erythema multiforme
- Lymphogranuloma venereum
- Scabies
- Syphilitic chancre
- Trauma

TREATMENT

- Suppressive therapy may be considered in patients who have >6 recurrences per year.
- Use of condoms
- Appropriate local wound care during periods of outbreak
- Judicious and frequent handwashing with wound care

MEDICATION

First Line

- For 1st clinical episode: Acyclovir or famciclovir or valacyclovir (therapy usually 7–10 days but may have to be extended if healing not complete)
- Reduces period of signs and symptoms; no effect on subsequent outbreaks:

– Acyclovir (Zovirax) 200 mg PO 5 times daily or 400 mg t.i.d.

– Valacyclovir (Valtrex) 1 g PO b.i.d. for 10 days, preferably beginning within 48 hr of onset

– Famciclovir (Famvir) 250 mg PO t.i.d.

Second Line

• Suppressive therapy (acyclovir or famciclovir or valacyclovir) may reduce frequency/severity of genital herpes outbreaks by up to 80%. Reduces duration of signs and symptoms of episode:

– Acyclovir 400 mg b.i.d. or 200 mg 3–5 times daily; re-evaluate after 12 mo

– Valacyclovir 500 mg to 1 g/d

– Famciclovir 250 mg b.i.d. for up to 1 yr

• Episodic therapy for herpes recurrence

• (acyclovir or famciclovir or valacyclovir):

– Initiate therapy during prodromal stage or within 1 day of lesion outbreak

– Reduces duration of signs and symptoms of episode:

Acyclovir 400 mg PO t.i.d. or 800 mg PO b.i.d. for 5 days or 800 mg PO t.i.d. for 2 days

Famciclovir 125 mg PO b.i.d. for 5 days or 1,000 mg PO b.i.d. for 1 day

Valacyclovir 500 mg PO b.i.d. for 3 days or Valacyclovir 1 g PO once a day for 5 days

ADDITIONAL TREATMENT

If recurrent outbreaks are mild: Mild analgesic agents and abstinence from sexual activity

COMPLEMENTARY AND ALTERNATIVE MEDICINE

• Systemic therapy more effective than local topical therapy

• No scientific evidence that nutritional or herbal therapies are effective

ONGOING CARE

PROGNOSIS

• Frequency of recurrent episodes may lessen with time.

• Research shows that acyclovir has been safely used long-term for up to 6 yr and valacyclovir or famciclovir for 1 yr.

• 90% can reactivate within 12 mo of initial outbreak.

• Genital herpes is a lifelong condition.

• Vaccine therapy is noneffective currently.

COMPLICATIONS

• Women who are pregnant and have genital herpes should inform their healthcare provider.

• Noninfected pregnant women should abstain from sexual relations during the 3rd trimester with infected men and should avoid genital exposure during this trimester to partners who are infected with HSV-1 (oral or genital infection).

ADDITIONAL READING

• Board of the Australian Herpes Management Forum. Managing Genital Herpes: Guidelines for Clinicians 2008. Accessed March 2009 at http://www.ahmf.com.au/health_professionals/guidelines/managing_gh.htm.

• Centers for Disease Control and Prevention (http://www.cdc.gov/std/)

• Corey L, Wald A, Patel R, et al. Once daily valacyclovir to reduce transmission of genital herpes. N Engl J Med 2004;250:11–20.

• Geretti AM, Brown DW. Genital herpes. Sex Transm Infect 2006;82(Suppl 4).

• Sen P, Barton SE. Clinical review: Genital herpes and its management. BMJ 2007;334:1048–1052.

See Also (Topic, Algorithm, Electronic Media Element)

• Genital Ulcers Algorithm

• Penis, Lesion, General

• Sexually Transmitted Diseases (STD), General

CODES

ICD9

• 054.10 Genital herpes, unspecified

• 054.11 Herpetic vulvovaginitis

• 054.12 Herpetic ulceration of vulva

ABBREVIATIONS

• CNS: Central nervous system

• H&E: Hemolysin & eosin

• HIV: Human immunodeficiency virus

• HSV: Herpes simplex virus

• PAS: Periodic-acid Schiff

• PCR: Polymerase chain reaction

• STD: Sexually transmitted disease

HESITANCY AND INTERMITTENCY

David F. Penson, MD, MPH

BASICS

DESCRIPTION

- Hesitancy is defined as a delay in the start of micturition.
- Intermittency is defined as the involuntary stopping and starting of the urinary stream during voiding.
- Both symptoms are part of the constellation of urinary symptoms commonly referred to as obstructive (emptying) symptoms which, in addition to hesitancy and intermittency include:
  - Post-void dribbling
  - Straining to void
  - Decreased force of stream
  - Incomplete emptying

EPIDEMIOLOGY

- Community-based studies indicate that the incidence of obstructive urinary symptoms is highly correlated with age.
- Incident symptom reporting is also influenced by sociodemographic and cultural factors.
- Hesitancy and intermittency occur much more commonly in men, as they are primarily associated with BPH.
- Community-based studies estimate the age-stratified prevalence of moderate to severe LUTS in men, including hesitancy and intermittency, as follows:
  - 40–50 yr old: ~20%
  - 50–60 yr old: ~30%
  - 60–70 yr old: ~40%
  - 70–80 yr old: ~56%

RISK FACTORS

- Bladder outlet obstruction:
  - In men, may be due to benign prostatic enlargement, prostate cancer, bladder neck contracture, bladder stones, urethral valves, and urethral stricture disease
  - In women, may be due to pelvic floor prolapse/large cystocele, bladder stones and stricture disease (rarely)
- Detrusor hypocontractility:
  - Idiopathic
  - Neurogenic in origin:

Diabetes

Parkinson disease

– Non-neurogenic (dysfunctional voiding)

- Obesity is associated with a higher incidence of LUTS
- ED appears to be associated with LUTS.

PATHOPHYSIOLOGY

- Bladder outlet obstruction: Increased resistance to urinary flow due to various etiologies (BPH, stricture, etc.) requires the bladder to generate higher voiding pressures which delays the initiation of micturition and may cause intermittency.
- Inadequate detrusor contraction due to various etiologies delays the start of voiding and may cause intermittency.

COMMONLY ASSOCIATED CONDITIONS

ED

DIAGNOSIS

HISTORY

- Quantification of lower urinary tract symptoms:
  - AUA/IPSS symptom index should be used
  - Other obstructive voiding symptoms should be assessed.
  - Concurrent presence of irritative symptoms should be noted as this may alter differential diagnosis and workup.
- Consider voiding diary if history is unclear.
- Assess for underlying cystitis/prostatitis. Prostatitis can present with acute, severe obstructive symptoms.
- History of hematuria
- History of urologic or prior pelvic surgery:
  - Predisposes to stricture formation and possible bladder stones
  - Certain pelvic procedures can result in detrusor hypocontractility.
- Other medical conditions:
  - Certain neurologic conditions and diabetes can cause detrusor hypocontractility.
  - Prior pelvic irradiation can affect bladder contractility.
  - History of STD may predispose to stricture disease.
- Family history of prostate disease
- Medications:
  - Certain OTC medications for colds or sinusitis may exacerbate LUTS:

    Inhaled and oral phenylephrines

- OTC and prescribed medications with anticholinergic effects

PHYSICAL EXAM

- Abdominal exam:
  - Palpate for distended bladder
- Focused neurologic exam should be performed. The following should be assessed:
  - General mental status
  - Ambulatory status
  - Lower extremity neuromuscular function
  - Anal sphincter tone
- In men:
  - Urethra should be examined for meatal stenosis.
  - DRE should be performed:

Prostatic nodularity, if present, may be a sign of prostate cancer and should be worked up accordingly

Size should be assessed, although DRE tends to underestimate size

Bogginess or tenderness are consistent with prostatitis

- In women:
  - Pelvic exam should be performed to assess for masses, pelvic floor prolapse, and/or cystocele.
  - Urethral lesions should also be assessed

Pediatric Considerations

Meatal stenosis should be considered in young boys who present with hesitancy and intermittency.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis by dipstick testing or microscopic exam of the sediment should be performed to screen for hematuria and UTI.
- Urine culture should be performed if urinalysis suggestive of infection.
- Serum PSA should be assessed in men with at least a 10-yr life expectancy
- Renal function tests (BUN and creatinine), are NOT recommended in the initial evaluation of men with LUTS, such as hesitancy of intermittency according to the 2003 AUA BPH guidelines

Imaging

- Upper tract evaluation (CT scan, IVP, or US) are not recommended as part of the initial work-up of hesitancy and intermittency unless warranted by history, exam, or laboratory evaluation.

- If urethral stricture disease is suspected, retrograde urethrography is useful.
- Transrectal US should be reserved for patients with an increased suspicion of prostate cancer undergoing prostate needle biopsy.

Diagnostic 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.
- Catheterized or scanned PVR should also be considered:
  - May be helpful in detecting bladder dysfunction
  - Will indicate which patients need immediate catheterization for acute urinary retention
- Cystourethroscopy should be considered in certain patients.
- Urodynamics study should be considered in certain patients with complicated histories that imply neurologic disease.

Pathological Findings

Patients with hesitancy and intermittency due to BPH usually have proliferation of the stromal and epithelial elements of the prostate on pathologic evaluation.

DIFFERENTIAL DIAGNOSIS

- Bladder outlet obstruction (more common cause of hesitancy and intermittency in men):
  - BPH
  - Bladder neck contracture
  - Urethral stricture disease
  - Bladder stone
  - Foreign body
  - Cancer (prostate, bladder, urethral)
  - Prostatitis
  - UTI
  - Bladder neck dyssynergia
  - Detrusor-sphincter dyssynergia
  - Pelvic floor prolapse or large cystocele
- Detrusor hypocontractility (more common cause of hesitancy and intermittency in women):
  - Diabetes mellitus

– Parkinson disease
– Multiple sclerosis
– Interstitial cystitis
– Radiation cystitis
– Spinal cord injury
– Lumbosacral disk disease

TREATMENT

• Patients with mild hesitancy and intermittency may be best treated with watchful waiting.

• Limiting fluid intake and avoiding certain substances that have a diuretic effect and may irritate the bladder (ie, coffee, alcohol) may also be of some use.

MEDICATION

• For men with hesitancy and intermittency presumably due to BPH/BOO:

– -Adrenergic antagonists (alfuzosin, doxazosin, tamsulosin, terazosin, silodosin) 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 syncope, orthostasis, retrograde ejaculation, asthenia, and nasal congestion.

– 5-Reductase inhibitors (finasteride 5 mg/d and dutasteride 0.5 mg/d) 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 with symptoms who do not have an enlarged prostate.

– Combination therapy: The MTOPS 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).

• For patients with evidence of infection, appropriate antibiotic therapy should be initiated.

SURGERY/OTHER PROCEDURES

• Urethral stricture disease and/or bladder neck contractures should be addressed using appropriate endoscopic or open procedures.

• Cystocele and/or pelvic floor prolapse should be addressed surgically if indicated.

• For men with hesitancy and intermittency presumably due to BPH/BOO who do not respond to medical management:

– TURP remains the gold standard surgical approach to BPH.

– Transurethral microwave heat treatment is a minimally invasive therapy that appears to be somewhat effective in the treatment of LUTS due to BPH.

– Transurethral laser vaporization/prostatectomy is also effective.

– Simple open prostatectomy is reserved for patients with large prostates (>100 cc) who do not respond to medical management.

ADDITIONAL TREATMENT

Behavioral interventions, such as timed voiding or double voiding, may be helpful.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Saw palmetto (Serenoa repens) has been reported to improve LUTS due to BPH/BOO. Randomized clinical studies have produced contradictory results.

ONGOING CARE

PROGNOSIS

- 25% of untreated patients with moderate to severe LUTS, such as hesitancy or intermittency, presumably due to BPH/BOO experience clinical progression within 5 yr.
- Randomized clinical trials of patients receiving -blocker therapy indicate that >1/2 will report a >25% improvement in symptoms within 3 mo of initiating treatment.
- 5–10% of men with moderate-severe LUTS 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 RECOMMENDATIONS

Patient Monitoring

- After appropriate treatment has been initiated and patients report improvement, annual follow-up should include:
  – History and physical, urinalysis, PSA
- Additional tests should be ordered based on patient clinical status.

ADDITIONAL READING

- AUA Guideline on the Management of Benign Prostatic Hyperplasia, 2003. Accessed July 2008 at http://www.auanet.org/guidelines/bph.cfm.
- McConnell JD, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 2003;349:2387–2398.

• Roehrborn CG, McConnell JD. Benign prostatic hyperplasia: Etiology, pathophysiology, epidemiology and natural history. In: Wein, et al. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

• Rosenberg MT, Staskin DR, Kaplan SA, et al. A practical guide to the evaluation and treatment of male lower urinary tract symptoms in the primary care setting. Int J Clin Pract 2007;61:1535–1546.

• Takeda M, Araki I, Kamiyama M, et al. Diagnosis and treatment of voiding symptoms. Urology 2003:62;11–19.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Outlet Obstruction (BOO)
- Lower Urinary Tract Symptoms (LUTS)
- Prostate, Benign Hypertrophy
- Prostatitis, General

CODES

ICD9

- 600.91 Benign localized hyperplasia of prostate with urinary obstruction and other lower urinary tract symptoms (LUTS)
- 788.61 Splitting of urinary stream
- 788.64 Urinary hesitancy

ABBREVIATIONS

- AUA: American Urological Association
- BOO: Bladder outlet obstruction
- BPH: Benign prostatic hypertrophy
- CT: Computed tomography
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- IPSS: International prostate symptom score
- IVP: Intravenous pyelography
- LUTS: Lower urinary tract symptoms
- MTOPS: Medical Therapy of Prostatic Symptoms
- OTC: Over-the-counter
- PSA: Prostate-specific antigen
- PVR: Postvoid residual volume
- STD: Sexually transmitted disease
- TURP: Transurethral resection of the prostate

- US: Ultrasound
- UTI: Urinary tract infection

HIV/AIDS, UROLOGIC CONSIDERATIONS

Michel A. Pontari, MD

BASICS

DESCRIPTION

- HIV disease results from the acquired deficiency of cellular immunity caused by the human immunodeficiency virus.
- A hallmark of the disease is the reduction of the helper T-lymphocytes in the blood and the lymph nodes, the development of opportunistic infections (Pneumocystis carinii pneumonia, CMV infections, TB, candida infections, cryptococcosis, others); and the development of malignant neoplasms (non-Hodgkin lymphoma and Kaposi sarcoma).
- A spectrum of human immunodeficiency virus infections range from asymptomatic seropositivity, through ARC, to AIDS.
- Urologic manifestations of HIV/AIDS include bacterial and nonbacterial infections, urolithiasis, increased risk of malignancy, renal impairment, and voiding dysfunction

EPIDEMIOLOGY

- 2.5 million new cases in 2007 worldwide; 40–50,000 new cases per year in US
- 2.1 million deaths due to HIV/AIDS in 2007
- 33.2 million people worldwide with HIV/AIDS
- 0.5% of US adults <50 are infected
- 2.6% of African American men and 1.5% of African American women were HIV positive 1999–2006.

RISK FACTORS

- Unprotected intercourse, anal or oral sex
- IV drug abuse and needle sharing
- Transfusion of blood products
- Concomitant STD
- Uncircumcised phallus
- Transmission from mother to child at birth or via breast milk
- Transmission to health workers: Risk for HIV after percutaneous exposure to HIV infected blood is 0.3%; after mucous membrane exposure 0.09%:
  - Urine carries low HIV titers, no documented seroconversions to infected urine exposure.

Genetics

- 3 groups of HIV viruses identified: M, N, and O.
- Most infections are by class M. 9 subtypes of M exist, with 15–20% genetic variation between viruses.

GENERAL PREVENTION

- Barrier protection during sex
- Avoid high-risk sexual behavior
- Male circumcision
- Use of precautions by health workers
- Treating STDs

PATHOPHYSIOLOGY

- HIV-1 binds to cells expressing CD4, leading to decline in CD4 cells and immune function.
- Immunosuppression allows opportunistic/unusual infections, decreases host defense against malignancy.
- HIV nephropathy is associated with FSGS on renal biopsy.

COMMONLY ASSOCIATED CONDITIONS

- UTI: Greater if CD4 count <500/mm3. Associated with typical bacteria (E. coli, Enterococcus) and atypical pathogens such as fungi, mycobacteria, and viruses
- Epididymitis/orchitis: Chlamydia, Gonorrhea, Salmonella, toxoplasmosis
- Fournier gangrene
- Prostatitis: Up to 14% in patients with AIDS. Greater risk of prostatic abscess.
- Urolithiasis: Risk with use of indinavir or from metabolic abnormalities
- Malignancies: Non-Hodgkin lymphoma—usually B cell. May involve kidneys in 6–12% AIDS patients. Kaposi sarcoma in up to 20% of untreated patients. Testicular tumors up to 50 times more common usually seminoma. Up to 8-fold risk of renal cell carcinoma in infected patients compared to noninfected individuals.
- HIVAN: Nephrotic disease with proteinuria >3.5 g/d and edema, HTN. Progress to dialysis in <10 mo.
- Voiding dysfunction: Can be retention, detrusor overactivity, and sphincter dyssynergia

DIAGNOSIS

HISTORY

- Voiding history: Dysuria, frequency, incontinence, urethral discharge, pelvic or testicular pain, flank pain
- Neurologic history: Numbness, dysesthesias
- Social history: Sexual history, IV drug use, blood product transfusions
- ROS: Constitutional symptoms, skin lesions, confusion, urticaria
- Generalized lymphadenopathy, fever, weight loss, and chronic diarrhea are common symptoms.

PHYSICAL EXAM

- General: Skin lesions, adenopathy
- Neurologic exam: Numbness, alterations in sensation
- GU exam: Urethral discharge, testicular/epididymal exam for masses, prostate exam for nodule or tenderness
- Penile lesions of Kaposi sarcoma present as red/brown/purple nodules macules or patches

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- HIV testing: Screening HIV-1 antibody titer. If positive, need confirmation by Western blot or immunofluorescence. Need separate consent for HIV testing.
- Urinary symptoms: UA, urine C+S:
  - Urinalysis may show rectangular crystals from indinavir
  - Common bacterial pathogens in HIV-infected patients are E. coli, Enterobacter (enterococci), Pseudomonas aeruginosa, Proteus spp., Klebsiella, Acinetobacter, Staphylococcus aureus, group D Streptococcus, Serratia, and Salmonella spp.
  - If UTI suspected and C&S negative, consider atypical organisms: Fungi, parasites, viruses
- CBC
- BUN, creatinine
- Specific testing for STD if urethral discharge

Imaging

- With flank pain: Noncontrast CT
  - Indinavir stones may not show on CT: Consider contrast study or retrograde pyelogram if renal impairment.
- Scrotal US for palpable lesions
- Prostate abscess: CT scan

Diagnostic Procedures/Surgery

- Measure PVR urine
- Urodynamics for voiding dysfunction or retention. Distinguish bladder outlet obstruction from acontractile bladder if in retention. Common urodynamic findings: Hypo- and hyperreflexia, acontractile hypoactive bladder, and detrusor-sphincter dyssynergia. Bladder hypocontractility was seen in 35–45% at time of urinary retention.

Pathological Findings

- Testicular tumors: Usually seminoma

- Lymphoma: B-cell NHL
- Penile lesions: Kaposi sarcoma from lymphatic endothelial cells vs. SCC

DIFFERENTIAL DIAGNOSIS

- Other systemic disease that cause fatigue: CFS
- Salmonella epididymitis pathognomonic for HIV

TREATMENT

- Refer to neurology, nephrology, infectious diseases when appropriate
- Patient education about risk factors, transmission
- Use of universal precautions

MEDICATION

- HAART: Combination therapy to combat the ability of HIV to generate drug-resistant mutants
- HIV therapy should be started in patients with AIDS, CD4 count <350/mm3, pregnant women, patients with HIV nephropathy, or coinfection with HBV regardless of CD4 count.
- General urologic conditions such as UTI, voiding symptoms, calcium stones treat as per general practice.
- Salmonella epididymitis: 2–4 wk of Doxycycline 100 mg PO b.i.d. plus Cipro 500 mg PO b.i.d.; if difficult to eradicate may need lifelong suppression.
- Kaposi sarcoma: If focal, local radiation, cryosurgery, or retinoids. If disseminated use chemotherapy (doxorubicin) or immunotherapy with interferons.

SURGERY/OTHER PROCEDURES

- Indinavir stones: Stop indinavir, hydration, stent if necessary. Stones are soft and may pass after stenting.
- Surgical drainage of prostatic abscess
- Stenting for ureteral obstruction from retroperitoneal NHL

ADDITIONAL TREATMENT

Health care workers exposed to infected blood from non-AIDS or acute HIV: Zidovudine plus lamivudine. For increased risk exposure, use 3-drug regimen including protease inhibitor (lopinavir and ritonavir).

Additional Therapies

Can be used for Kaposi sarcoma

ONGOING CARE

PROGNOSIS

Much improved prognosis leading to longer life expectancies, primarily due to newer drug combination therapies. Will need treatment for age-related conditions same as general population.

COMPLICATIONS

- Antiretroviral therapy: Risk of nephrotoxicity, crystal precipitation leading to stones, hypocalcemia
- ED and decreased libido (caused by increased estradiol) may be associated with HAART therapy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

CD4 counts, serum creatinine

ADDITIONAL READING

- Cohen MS, Hellmann N, Levy JA, et al. The spread, treatment and prevention of HIV-1: Evolution of a global pandemic. J Clin Invest 2008;118:1244–1254.
- Lebovitch S, Mydlo JH. HIV-AIDS: Urologic considerations. Urol Clin North Am 2008;35(1):59–68; vi.
- von WV, Yerly S, Boni J, et al. Emergence of HIV-1 drug resistance in previously untreated patients initiating combination antiretroviral treatment: A comparison of different regimen types. Arch Intern Med 2007;167:1782–1790.
- www.aidsinfo.nih.gov

See Also (Topic, Algorithm, Electronic Media Element)

- Kaposi Sarcoma, Urologic Considerations
- Urolithiasis, Indinavir

CODES

ICD9

- 041.9 Bacterial infection, unspecified, in conditions classified elsewhere and of unspecified site
- 042 Human immunodeficiency virus (HIV) disease
- 599.0 Urinary tract infection, site not specified

ABBREVIATIONS

- AIDS: Acquired immunodeficiency syndrome
- ARC: AIDS-related complex
- BUN: Blood urea nitrogen
- CBC: Complete blood count
- CFS: Chronic fatigue syndrome
- CMV: Cytomegalovirus
- CT: Computed tomography
- ED: Erectile dysfunction

- FSGS: Focal segmental glomerulosclerosis
- HIV: Human immunodeficiency virus
- HIVAN: HIV-associated nephropathy
- HTN: Hypertension
- GU: Genitourinary
- HAART: Highly active antiretroviral therapy
- NHL: Non-Hodgkin lymphoma
- PVR: Postvoid residual
- ROS: Review of symptoms
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- TB: Tuberculosis
- UA: Urinalysis
- US: Ultrasound
- UTI: Urinary tract infection

HOT FLUSHES (VASOMOTOR INSTABILITY)

Manlio A. Goetzl, MD

J. Brantley Thrasher, MD

BASICS

DESCRIPTION

- Typically experienced as a feeling of intense heat with associated flushing, sweating, and rapid heart rate.
- Common side effect of androgen ablation therapy in men with metastatic or locally advanced prostate cancer

EPIDEMIOLOGY

- Occurs in 50–80% of men on androgen ablation therapy
- >50% of men who develop hot flushes seek treatment.
- ~25% say hot flushes are greatly distressing.
- In some patients, symptoms persist for many years after castration.
- No relationship to race or disease stage

RISK FACTORS

- Men with hot flushes tend to be younger than those without hot flushes
- Little correlation between development of hot flushes and precastration testosterone levels
- Common triggers:
  - Changes in body position
  - Ingestion of warm liquids, alcoholic beverages, caffeinated beverages
  - Changes in room temperature
  - Exercise, smoking

GENERAL PREVENTION

- Limit intake of warm beverages, alcohol, and caffeine
- Monitor room temperature
- Quit smoking
- Identify unique triggers and modify behavior

PATHOPHYSIOLOGY

- Exact mechanism unknown; majority of theories based on studies in postmenopausal women
- Hot flushes in prostate cancer patients result from decreased feedback of testosterone to the hypothalamus.
- Central control of thermoregulation is preoptic/anterior area in the brain.

• Increases in internal and/or skin temperature sensed in the anterior pituitary results in cutaneous vasodilatation (flushing) and sweating.

• Thermoregulatory zone is disrupted:

– Reduced thermoneutral zone between an upper threshold for sweating and a lower threshold for shivering

• Alterations in glucose transport across blood–brain barrier theorized to be a trigger:

– Hot flushes are counterregulatory attempts to increase cerebral blood flow and cerebral glucose levels.

• Decreased plasma sex hormones results in loss of negative feedback, thus increasing hypothalamic norepinephrine levels.

• Norepinephrine decreases thermo neutral zone:

– Thermoregulatory center in hypothalamus is anatomically close to the GnRH-secreting neurons.

– These neurons are stimulated by norepinephrine to secrete GnRH.

– Increased GnRH stimulation, by being in close proximity to the thermoregulatory center, might activate heat-losing mechanisms (flushing, sweating).

COMMONLY ASSOCIATED CONDITIONS

• Osteopenia, osteoporosis
• Erectile dysfunction
• Metabolic syndrome (Increasing fat mass, increased cholesterol, glucose intolerance)
• Gynecomastia
• Normocytic, normochromic anemia

DIAGNOSIS

HISTORY

• Abrupt onset of warmth, frequently followed by profuse sweating requiring change of clothes

• Sensation usually felt in the face, upper body

)[C]

• Can occur occasionally or multiple times daily:

– Majority of patients have daily episodes

• Frequently experienced at night

• Onset is typically seen within the 1st yr after androgen ablation:

– 1/3 of men will develop symptoms within the 1st mo.

PHYSICAL EXAM

• During acute episode, facial flushing common

- Sweating frequently present
- Mild tachycardia secondary to vasodilation or anxiety
- Slight increase in oral and forehead temperature
- Usually normal exam in between hot flush episodes
- May have gynecomastia, increased fat mass secondary to androgen deprivation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No routine laboratory evaluation is indicated.
- No pattern of characteristic changes in testosterone, FSH, LH or prolactin

DIFFERENTIAL DIAGNOSIS

- Systemic illness:
  - Carcinoid syndrome
  - Pheochromocytoma
  - Medullary thyroid tumors
  - Pancreatic islet-cell tumors
  - Renal cell carcinoma
- Other illness:
  - Rosacea
- Medications:
  - Any vasodilatory agent
  - Calcium channel blockers
  - Opiates
  - Tamoxifen
  - Cephalosporins
- Dietary:
  - Ethanol ingestions
  - Monosodium glutamate

TREATMENT

- Reassurance if symptoms mild
- Avoid daily lifestyle triggers.
- Keep environment cool.
- Many men will experience resolution after several years without therapy.

MEDICATION

)[B]:

  - 83% reported some improvement

  - Side effects include breast swelling, nipple tenderness
- DES: 0.30–1 mg/d:
  - 70–90% of men achieve excellent results
  - Side effects include painful gynecomastia.
  - At low doses, thromboembolic events are not a significant problem.
  - Generic drug, inexpensive though difficult to obtain in the US.
- Megestrol acetate (Megace) 20 mg/d:
  - Synthetic derivative of progesterone
  - Complete resolution in 70% of patients, partial response in 20%
  - Side effects include chills, weight gain, nausea, carpal-tunnel-like syndrome
- Medroxyprogesterone acetate 400 mg/d IM:

)[B]

  - 46% have complete response as defined as total elimination of hot flushes.
  - Side effects could include weight gain, congestive heart failure exacerbation, loss of bone mineral density.
- Clonidine (Catapres) 0.1–1.0 mg/d (PO or patch formulations):
  - -Adrenergic agonist used for treatment of HTN
  - 1/3 of men will report a partial response although similar to placebo.
  - Side effects include hypotension, dry mouth, skin irritation from patches.
- Venlafaxine (Effexor) 12.5 mg/d PO:
  - Antidepressant of the SNRI type
  - Median weekly hot flush scores decreased 54% from baseline after 1 mo
  - 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 SSRI class

)[B]

  - Side effects include sexual dysfunction, somnolence
- EBP: 1 tablet PO b.i.d.:
  - Ergot alkaloid used primarily to treat migraine headache
  - 45% achieve a partial response
  - Use with caution with patients on MAOIs, CNS depressants, anticholinergic agents

ADDITIONAL TREATMENT

Behavioral therapy: Slow, deep breathing may reduce frequency of hot flushes.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Acupuncture
- Vitamin E:
  - 30% reduction compared to 22% of patients receiving placebo in 1 study
- Soy products:
  - Contain phytoestrogens which might decrease severity of hot flushes
  - Also have shown benefit with regards 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

ONGOING CARE

PROGNOSIS

Most men have symptom improvement with medical or complementary therapy.

COMPLICATIONS

Some men have side effects from medicines taken to alleviate hot flushes.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Ask patients on androgen deprivation at each follow-up clinical evaluation about the presence and severity of hot flushes:

- Inquire about side effects from therapy
- Intermittent cessation of treatment can be used if side effects become bothersome.

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See Also (Topic, Algorithm, Electronic Media Element)

- Andropause (Late-Onset Hypogonadism)
- Menopause, Urologic Considerations
- Testosterone, Decreased (Hypogonadism)

CODES

ICD9

- 257.2 Other testicular hypofunction
- 782.62 Flushing

ABBREVIATIONS

- CNS: Central nervous system
- DES: Diethylstilbestrol
- EBP: Ergotamine/belladonna/phenobarbital
- FSH: Follicle-stimulating hormone
- HTN: Hypertension
- LH: Leuteinizing hormone
- MAOIs: Monoamine oxidase inhibitor
- SNRI: Serotonin-norepinephrine reuptake inhibitor
- SSRI: Selective serotonin reuptake inhibitor

HYDROCELE, ADULT AND PEDIATRIC

Costas D. Lallas, MD

BASICS

DESCRIPTION

- A collection of serous fluid in some part of the processus vaginalis, usually in the tunica. Can be congenital or acquired
- Translucent swelling in the scrotum or inguinal canal or both
- Apart from congenital hydrocele, it is possible to get examining fingers above the swelling.
- Demonstrated fluctuation in size in congenital hydrocele (also called communicating hydrocele)
- Usually not painful
- Sensation of heaviness or discomfort in the scrotum
- Positive pinch test in a secondary hydrocele (ability to pinch the tunica)

EPIDEMIOLOGY

- More common in childhood
- 1% of adult males; prevalence: 1,000 in 100,000
- No racial predilection

RISK FACTORS

- The hydrocele is produced by:
  - Connection with the peritoneal cavity (PPV); also known as congenital hydrocele
  - Defective absorption of fluid by tunica vaginalis; eg, primary hydrocele (common in adults)
  - Excessive production of fluid within the sac; eg, secondary hydrocele (epididymitis, bleeding, etc.)
  - Lymphatic obstruction; eg, filariasis, scrotal surgery (varicocele), renal transplantation, pelvic radiation, malignancy
  - Migration of ventriculoperitoneal shunt
- Prematurity, low birth weight are risk factors

GENERAL PREVENTION

None other than repair of indirect hernia defect in infants/children

PATHOPHYSIOLOGY

- Congenital: The PV does not close after testicular descent.
- 4 anatomic variants:
  - Vaginal (PV around the testis)

  - Infantile (PV around testis and cord)
  - Congenital communicating (PV communicates with the peritoneal cavity)
  - Hydrocele of the cord (PV patent with obliteration above and below)
- Acquired: Can be primary (idiopathic) or secondary to disease of the testis. Secondary hydroceles may present acutely or chronically.
- The hydrocele of the canal of Nuck is comparable in females. The cyst is in relationship with the round ligament and located in the inguinal canal.
- 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

COMMONLY ASSOCIATED CONDITIONS

- Ehlers-Danlos syndrome
- Exstrophy of the bladder
- Indirect inguinal hernia
- Hydrocephalus (with ventriculoperitoneal shunt)
- Peritoneal dialysis
- Testicular tumors or epididymo-orchitis in secondary hydrocele
- Undescended testicle with PPV
- Varicocele surgery

DIAGNOSIS

HISTORY

- Symptoms of epididymitis, UTI, or acute pain:
  - Secondary hydrocele with infection, torsion, and trauma usually painful
- Change in size of the swelling (ie, size varies throughout day):
  - Suggests congenital communicating hydrocele
- Birth history:
  - Hydrocele more common in premature and low-birth-weight infants
- Medical or surgical history:
  - Varicocelectomy, renal transplant, VP shunt, trauma to the genitalia can be causes

PHYSICAL EXAM

- Transilluminate scrotum:
  - If transilluminates, favors simple hydrocele, but is not diagnostic

- Palpation of testes bilaterally:
  - Especially in children, need to rule out undescended testicle. Adults, attempt to feel for testicular mass
- Examine the groin for inguinal hernia.
- Lymphedema of external genitalia or lower extremities:
  - Tissue edema can be mistaken for the hydrocele.
- On abdominal exam, concomitant presence of a mass may indicate an abdomino-scrotal hydrocele.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture if epididymo-orchitis suspected
- Tumor markers (bhCG, AFP) if tumor suspected

Imaging

- Transscrotal US in adults with hydrocele to detect underlying testicular abnormality (ie, tumor) and confirm the nature of the mass as a hydrocele.
- Nuclear scan or Doppler US exam in cases of torsion

Pathological Findings

Fibrous wall lined by mesothelial single layer cuboidal or flattened mesothelial cells; may contain benign mesothelial proliferations

DIFFERENTIAL DIAGNOSIS

- Inguinal hernia
- Epididymo-orchitis
- Spermatocele
- Traumatic injury to the testis (hematocele)
- Varicocele (large)
- Torsion (testis or appendix testis)
- Testicular or paratesticular tumors
- Lymphedema of the external genitalia

TREATMENT

- Adults: No treatment is necessary unless the hydrocele causes discomfort or cosmetic concerns or there is a significant underlying cause patent, such as a tumor.
- Children: Most will resolve in 1st yr of life. Persistence suggests the presence of a patent indirect hernia sac that should be repaired.

SURGERY/OTHER PROCEDURES

- Children:

– Inguinal incision between internal and external rings.

– High ligation of the processus vaginalis and excision of the sac.

– In hydrocele of the cord, the sac can be completely removed. It is imperative that the hydrocele sac be opened when the anatomy is confusing or the sac is very thickened. Failure to do so may result in disastrous consequences if bowel, bladder, or ovary is contained in the sac and not recognized.

- Adults:

– Scrotal approach with drainage of the hydrocele and resection of the tunica vaginalis; drain for 24–48 hr

- Bottle procedure (thin hydrocele sac: Incise anteriorly, wrap sac back around testicle
- Jaboulay-Winkelman procedure (thick hydrocele sac): Hydrocele sac resected and edge wrapped posteriorly around cord structures (resected edges can also simply be oversewn)
- Lord procedure (thin hydrocele sac): Radial sutures used to gather sac posterior to testis

ADDITIONAL TREATMENT

- Aspiration of the hydrocele, with or without the injection of sclerosing agents, should be discouraged. May dissect hernia defect in infants/children due to high recurrence rates compared to surgery.
- Aspiration may have a role in postoperative hydroceles.

ONGOING CARE

PROGNOSIS

Many hydroceles do not enlarge and can be observed if confirmed that there is no underlying pathology (using US).

COMPLICATIONS

- Rupture: Usually traumatic
- Hernia of the hydrocele sac: Tension causes herniation through the Dartos muscle.
- Calcification of the wall: May occur with longstanding cases
- Hematocele: Following trauma or aspiration, or presents chronically simulating a neoplasm
- Infection
- Postoperative:

– Testicular atrophy or infarction after repair due to damage to vascular supply to the testicle

– Infection

– Recurrence

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Periodic follow-up (baseline US) suggested if managed by observation; return for any acute changes in symptoms
- Parents of a newborn 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 READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Canal of Nuck Hydrocele and Cyst (Female Hydrocele)
- Hydrocele of the Spermatic Cord
- Scrotum and Testicle, Mass

CODES

ICD9

- 603.0 Encysted hydrocele
- 603.1 Infected hydrocele
- 603.8 Other specified types of hydrocele

ABBREVIATIONS

- AFP: -Fetoprotein
- bhCG: -Human chorionic gonadotrophin
- PPV: Patent processus vaginalis
- UTI: Urinary tract infection
- VP: Ventriculoperitoneal

HYDROCOLPOS AND HYDROMETROCOLPOS

Michael J. Cox, MD

Paul F. Austin, MD

BASICS

DESCRIPTION

Congenital anomaly 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
- Hydrometrocolpos: Gross distension of the vagina and uterus. May also be associated with vaginal or cervical atresia, stenosis
- Can be an infrequent cause of an abdominal mass in a newborn female

EPIDEMIOLOGY

0.1–3.8% of female live births

RISK FACTORS

- Imperforate hymen
- High transverse vaginal septum
- Urogenital sinus/cloacal abnormality

Genetics

Rare familial syndromes:

- McKusick-Kaufman syndrome
- Bardet-Biedl syndrome

GENERAL PREVENTION

Early diagnosis may prevent hydronephrosis and upper tract damage.

PATHOPHYSIOLOGY

Congenital obstruction of the female genital tract leading to accumulation of vaginal secretions and distension of the vagina:

- Increasing intravaginal pressure causes distension of the uterus (HMC)
- Imperforate hymen or extrinsic compression of the urethra can lead to urinary retention and hydronephrosis

COMMONLY ASSOCIATED CONDITIONS

Cloacal anomalies

Pediatric Considerations

Prenatal diagnosis may be difficult, and careful exam of the neonate is mandatory. The diagnosis should also be considered in the pubertal female with amenorrhea.

DIAGNOSIS

HISTORY

- Sonolucent mass on prenatal US
- Difficulty/inability to void due to bladder outlet obstruction
- Amenorrhea in pubertal females if the problem was not diagnosed before menarche. In these rare cases, chronic 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

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Usually not helpful

Imaging

- Abdominal US:
  - Large sonolucent mass displacing bladder anteriorly and rectum posteriorly
  - May see layering of debris
  - Hydronephrosis may be present
- IVP:
  - May see hydroureteronephrosis and a distended bladder
- VCUG:
  - May see an anteriorly displaced bladder
- MRI:
  - May be useful for further delineation of pelvic anatomy when ultrasound is equivocal

DIFFERENTIAL DIAGNOSIS

- Mucocolpos
- Prolapsed urethra:
  - Donut-shaped urethral meatus in the center of a normal vaginal introitus
- Periurethral cyst:
  - Eccentric smooth mass displacing urethral meatus
- Prolapsed ureterocele:
  - May see necrotic tissue
- Ovarian cyst

- Dermoid cyst
- Rhabdomyosarcoma:
  - Cluster of grapelike masses protruding from vaginal introitus
- HMC:
  - Accumulation of menstrual blood products in vagina and uterus

TREATMENT

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 HC.

SURGERY/OTHER PROCEDURES

Simple incision of the imperforated hymen. A cruciate incision with resection of excess tissue tags as necessary

ONGOING CARE

PROGNOSIS

Excellent, especially with early diagnosis and treatment

COMPLICATIONS

- 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 RECOMMENDATIONS

Patient Monitoring

Usually none necessary

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See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal

CODES

ICD9

623.8 Other specified noninflammatory disorders of vagina

ABBREVIATIONS

- HC: Hydrocolpos
- HMC: Hydrometrocolpos
- IVP: Intravenous pyelography
- MRI: Magnetic resonance imaging
- US: Ultrasound
- VCUG: Voiding cystourogram

HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), ADULT

Grant I. S. Disick, MD
Ravi Munver, MD

BASICS

DESCRIPTION

)[C]:

– HN: The presence of dilation of the renal pelvis and calyces. The term does not refer to the etiology of the dilatation, as hydronephrosis can occur without obstruction

– Hydroureteronephrosis: Dilation of the renal pelvis, calyces, and ureter

– Obstructive uropathy: Functional or anatomic impedance to the flow of urine anywhere along the urinary tract

– Obstructive nephropathy: Damage to the renal parenchyma from obstruction anywhere along the urinary tract

- HN common causes: Obstructive uropathy or VUR
- Obstruction can occur at the level of the kidneys, ureter, bladder outlet, prostate, or urethra; progressive renal damage may occur.
- Urinary infection and sepsis may be superimposed.

EPIDEMIOLOGY

)[C]

- Disease-specific

RISK FACTORS

Congenital anomalies (eg, VUR, UPJO) urinary calculi, urothelial cancer, retroperitoneal process, BPH, prostate cancer, neurogenic bladder, urinary strictures, trauma, iatrogenic secondary to previous abdominal/pelvic surgery

Genetics

Siblings of those with VUR have a higher risk of the condition than those without

GENERAL PREVENTION

Disease-specific

PATHOPHYSIOLOGY

- Elevated ureteral pressure and decreased renal blood flow
- Impairment of renal function
- Gradual destruction of renal parenchyma
- Oliguria or anuria may occur with acute obstruction

COMMONLY ASSOCIATED CONDITIONS

- Bladder outlet obstruction (BPH, prostate cancer, urethral strictures)
- Vesicoureteral reflux
- Pregnancy

ALERT

A unilaterally obstructed, infected kidney in a septic patient requires immediate drainage

DIAGNOSIS

HISTORY

- Symptoms vary from acute flank pain to chronic vague flank discomfort or fullness.
- Can be asymptomatic
- If HN is due to obstruction, the symptom complex will vary according to:
  - Time interval over which obstruction has occurred (acute or chronic)
  - If the obstruction is unilateral or bilateral
  - The etiology of the obstruction (intrinsic vs. extrinsic)
  - Whether the obstruction is complete or partial
- Age and sex of the patient:
  - Diagnosis by prenatal US, association with posterior urethral valves in male neonates
  - Calculi most common in middle-aged men
  - Pregnancy and physiologic dilation
- Hematuria:
  - Usually noted with urinary tract malignancies and may be painless; may be associated with flank pain when caused by calculi or blood clots in ureter
- Associated pain:
  - Acute ureteral obstruction produces severe flank pain, but chronic obstruction may be asymptomatic
- History of voiding difficulty:
  - BPH, prostate cancer, and urethral strictures in older men; neurogenic bladders in children with myelodysplasia and in adults with diabetes or neurologic disorders
- Symptoms of urinary obstruction:
  - BPH, prostate cancer, and urethral strictures in men
- History of GI disorders:
  - History of regional enteritis, granulomatous colitis, intestinal malignancy, pancreatic tumors, or pancreatic pseudocysts
- Medical or surgical history:

- Pelvic surgical history with potential ureteral injury
- Gynecologic history:
  - Association with endometriosis, benign and malignant pelvic masses
- Family history:
  - Stones, prostate cancer
- Occupational risk factors:
  - Association of smoking with urothelial malignancies

PHYSICAL EXAM

- HTN:
  - Can be caused by reflux nephropathy.
- Pallor:
  - Anemia associated with chronic renal failure from HN.
- Abdominal or flank mass:
  - HN is the most common etiology in neonates.
  - HN with UPJ obstruction may produce a palpable flank mass.
- Flank tenderness:
  - Calculi, pyelonephritis, pyonephrosis, retroperitoneal or tubo-ovarian abscess
- Pelvic mass:
  - Gynecologic causes
- Vaginal exam:
  - Uterine prolapse, urethral prolapse, prolapse of ureterocele through urethra
- Digital rectal exam:
  - Enlarged prostate associated with BPH, nodularity suggestive of prostate cancer

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis (UA) for UTI or hematuria
- Urine culture: If UA suggestive of infection
- Renal function tests (BUN and creatinine):
  - Assessment of severity of obstruction
- CBC:
  - Anemia is associated with chronic renal insufficiency, and elevated white blood cell count with infection
- Serum chemistry (especially hyperkalemia)
- Serum PSA
- Urinary cytology for urothelial carcinoma

Imaging

- US:
  - Useful 1st study, noninvasive
  - Differentiates ureteropelvic junction obstruction from multicystic dysplastic kidney in neonates and children
  - Hydroureters may be detected
  - Assess extrinsic retroperitoneal or pelvic mass, abscess
  - Aides placement of nephrostomy tube when indicated

)[B]

  - RI = ([peak systolic velocity] – [lowest diastolic velocity])/[peak systolic velocity]
  - RI >0.7 suggestive of obstruction

)[A]:

  - Often delineates point of obstruction
  - Assess extrinsic retroperitoneal and abdominal disorders
  - CT-guided percutaneous procedures and biopsies when indicated

)[B]:

  - May provide additional information to CT when a vascular anomaly is involved
  - Cannot detect calcifications or urinary calculi

- Radionuclide imaging (diuretic renogram):
  - Useful in determining renal function and diagnosing obstruction; assessment of significance of UPJ obstruction
- IVU:
  - If serum creatinine is not significantly elevated (should be <2 ng/dL); used for identification of obstructive uropathy and in determining location of obstruction

Diagnostic Procedures/Surgery

- Cystoscopy: Evaluates lower urinary tract
- Retrograde pyelography: If imaging fails to identify location or extent of obstruction
- Ureteroscopy: Evaluates upper urinary tract
- Whitaker test: To evaluate dilated upper tract

Pathological Findings

Findings depend on HN etiology

DIFFERENTIAL DIAGNOSIS

- In adults, calculi, urinary neoplasms, extrinsic retroperitoneal process, BPH, prostate cancer, and voiding dysfunction are major causes. In children, vesicoureteral reflux, congenital ureteropelvic obstruction, neurogenic bladder, and posterior urethral valves are common causes.

)[A]:

– Usually diagnosed before adulthood (see the chapters on Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric Adult/Intrinsic

– Urinary calculi

– Malignant ureteral or bladder tumors (urothelial carcinoma in the majority)

– Renal cell carcinoma with invasion of the urinary collecting system

– Fibroepithelial polyp of the ureter

– Trauma to renal pelvis and ureter

– Neurogenic bladder (with or without VUR)

– BPH with bladder outlet obstruction

– Prostate cancer: May obstruct bladder outlet or ureters by direct extension

– Retained ureteral stent

– Ureteral stricture

– Infectious (TB, schistosomiasis)

• Adult/extrinsic:

– Vascular lesions (abdominal aortic or iliac aneurysm, aberrant arterial anomalies), obstruction of the ureter after arterial repair or replacement, venous obstruction (ovarian vein syndrome, postpartum ovarian vein thrombophlebitis)

– Benign pelvic masses (pregnancy, extrauterine pregnancy, mass lesions of the uterus and ovary, ovarian remnants, Gartner duct cyst)

– Pelvic conditions (tubo-ovarian abscess, endometriosis, periureteral inflammation associated with contraceptives, uterine prolapse, imperforate hymen)

– Trauma (ureteral ligation and intraoperative ureteral injury)

– GI diseases (granulomatous ileitis, granulomatous colitis, appendicitis, diverticulitis, pancreas cancer or pseudocyst, acute pancreatitis, splenic cyst, fecal impaction)

– Retroperitoneal processes (retroperitoneal fibrosis, radiation fibrosis, TB, lymphangitis, extravasation of medical materials such barium, retroperitoneal hemorrhage, abscess, or inflammation)

– Retroperitoneal masses (primary retroperitoneal tumors; metastases to the retroperitoneum, usually from prostate, bladder, or cervix; lymphocele; pelvic lipomatosis)

TREATMENT

)[C]:

– Initial management depends on clinical circumstances and determining the etiology for the HN

• Placement of retrograde ureteral stent or percutaneous nephrostomy are the most common methods for immediate drainage.

– Calculi in a noninfected patient may be initially managed therapeutically with ESWL or ureteroscopy with lithotripsy, depending on location.

– Vascular lesions (aortic aneurysm) may require urgent management.

– Renal failure and electrolyte abnormalities should be corrected in conjunction with drainage.

– Hemodialysis in the acutely ill patient

– Treatment may be limited (an obstructed kidney in a terminally ill patient with a normal opposite kidney and satisfactory serum creatinine and electrolytes may require no intervention).

• After initial drainage and stabilization, the location and cause of obstruction should be determined.

• Nature of surgical intervention that may be required depends largely on the etiology for the HN. A permanent form of urinary drainage may be necessary in some patients

ONGOING CARE

PROGNOSIS

Cause-specific

COMPLICATIONS

• If due to VUR, renal scarring and HTN can occur (reflux nephropathy)

• If due to obstruction, proximal infection and sepsis can occur. Progressive renal deterioration can be expected (obstructive nephropathy).

• In some cases, HN will have an indolent course

• Postobstructive diuresis: Usually seen only with bilateral obstruction or obstruction of a solitary functioning kidney.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

The etiology for the HN will dictate the appropriate surveillance regimen.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis, Pediatric
- Hydronephrosis, Prenatal

CODES

ICD9

- 591 Hydronephrosis
- 599.60 Urinary obstruction, unspecified
- 753.29 Other obstructive defect of renal pelvis and ureter

ABBREVIATIONS

- BPH: Benign prostatic hyperplasia
- CBC: Complete blood count
- CT: Computed tomography
- ESWL: Extracorporeal shock wave lithotripsy
- HN: Hydronephrosis
- HI: Hydronephrosis index
- HTN: Hypertension
- IVU: Intravenous urography/urogram
- PSA: Prostate-specific antigen
- RI: Resistive index
- TB: Tuberculosis
- UA: Urinalysis
- UPJO: Ureteropelvic junction
- US: Ultrasound
- UTI: Urinary tract infection
- VUR: Vesicoureteral reflux

HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PEDIATRIC

Erica J. Traxel, MD

Paul H. Noh, MD

BASICS

DESCRIPTION

- Dilation of the collecting system.
- Can be isolated to a particular portion of the collecting system:
  - HDN: Dilation of the renal pelvis (pelviectasis) ± calyces (caliectasis)
  - Hydroureter: Dilation of the ureter only
  - Hydroureteronephrosis: Dilation of the entire upper tract.

EPIDEMIOLOGY

- True incidence unknown, as asymptomatic cases may go undetected

)[A]

- Cannot determine, as HDN is a dynamic process, owing to acute vs. chronic causes.

RISK FACTORS

- Neurologic conditions: Myelomeningocele, SCI, tethered cord

)[B]

- Family history of HDN

Genetics

Not 1 specific genetic cause of HDN, as it is the final common result of many pathologies, but is associated with a number of genetic diseases.

GENERAL PREVENTION

Once a disease process that leads to HDN has been identified, can take measures against underlying pathology to prevent or stabilize HDN:

- For instance, can decrease intravesical pressures and consequent HDN in NGB with anticholinergics and intermittent catheterization.

PATHOPHYSIOLOGY

- Must discern physiologic from pathologic HDN.
- Physiologic HDN:
  - Dilation present but renal function and drainage preserved
  - Thought to be due to transient obstruction in utero that later resolved spontaneously
  - Can also be residual dilation following intervention to relieve the pathology

– Megacalycosis is congenital nonobstructive dilation of calyces in setting of an otherwise normal collecting system:

Thought to be X-linked, partially recessive, as bilateral cases only in males and segmental unilateral cases only in females. Male > Female (6:1)

Mild decrease in concentrating ability, but otherwise no functional sequelae.

No long-term progression or deterioration.

- Pathologic HDN due to obstruction:
  - UPJO:

    Most common cause of HDN in children.

    Typically detected on antenatal US

    Primary: Due to intrinsic obstruction: Stenotic segment of ureter at the UPJ that lacks smooth muscle and peristalses poorly.

    Primary: Due to extrinsic obstruction: Most commonly from a lower pole-crossing vessel.

    Secondary: Due to a very dilated and tortuous system in which the primary pathology is distal to the UPJ.
  - UVJO:

    Primary: Due to stenotic aperistaltic distal segment of ureter lacking smooth muscle.

    Secondary: Due to a more distal abnormality resulting in a thickened and poorly compliant bladder wall, as in NGB or PUV.
  - Ectopic ureteral insertion:

    More commonly associated with the upper pole of duplicated systems.

    Closely related to Wolffian development.

    In males, typically insert into bladder neck, prostatic urethra, less commonly into vas deferens, seminal vesicle, ejaculatory duct. Insertion still proximal to sphincter, so remain continent.

    In females, typically insert into bladder neck, urethra, vestibule, less commonly into vagina, uterus. Insertion usually distal to sphincter, so often incontinent.
  - Ureterocele:

    In females, most commonly subtends upper pole ureter of duplicated system.

    In males, most commonly subtends a single system.

)[B]

  - PUV:

    Congenital obstruction of the urethra resulting in high intravesical pressure and proximal HDN, often with VUR.

Asymmetry of HDN in VURD syndrome: PUV, VUR, unilateral renal dysplasia. This portends a better prognosis for renal function.

– Other causes of urethral obstruction:

Urethral atresia, typically in prune belly syndrome.

Anterior urethral valves, rare

Congenital urethral stricture, rare

- Pathologic HDN due to VUR:
  - Can be primary due to inherent deficiency in UVJ or secondary due to distal obstruction.
  - Can have significant VUR without HDN.
- Pathologic HDN due to NGB:
  - High storage and voiding pressures are transmitted retrograde to the upper tracts.

)[A]

- Pathologic HDN due to increased urine production:
  - Diabetes insipidus; psychogenic polydipsia.
- Pathologic HDN due to behavioral disorder:
  - Hinman syndrome: Extreme voiding dysfunction with excessive holding and detrusor-sphincter discoordination.
  - Increased bladder pressures transmitted to upper tracts resulting in HDN
- Pathologic HDN due to infection:
  - Bacterial toxins and resultant inflammatory cascade inhibit effective smooth muscle peristalsis

COMMONLY ASSOCIATED CONDITIONS

HDN is the final common pathway of a number of disease processes, as noted above.

DIAGNOSIS

HISTORY

- May present with renal colic:
  - Intermittent flank pain, nausea/vomiting.
- May have a history of UTIs:
  - A history of unexplained febrile illnesses can suggest previously undiagnosed UTIs.
- Systemic presentations of underlying renal disease, potentially due to HDN:
  - HTN, failure to thrive, dehydration.
- Family history renal disease may be present.

PHYSICAL EXAM

- In acute setting of renal colic, CVA or abdominal tenderness may be present.
- Palpable flank or abdominal mass may be present.
- Paucity of bowel sounds on auscultation may be present on side of HDN due to displacement of bowel.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

No screening laboratory test for HDN; however, lab abnormalities may be present.

- Urinalysis: May show hematuria or findings consistent with UTI
- Renal profile: May show azotemia and electrolyte abnormalities

Imaging

- Plain film: Displaced bowel gas pattern
- US: 1st-line diagnostic study:
  - Most pediatric cases of HDN now diagnosed on prenatal US.
- VCUG: Rule-out VUR, urethral and bladder pathology
- Diuretic nuclear renal scan: Provides functional information:
  - Technetium-99m-MAG3 Lasix renal scan is study of choice
  - Delayed renal uptake and excretion of isotope, as well as delayed drainage from collecting system suggest obstruction.
  - Considered a provocative study, as administration of diuretic can stimulate a Dietl crisis.
- Excretory urography: Provides anatomic and functional information:
  - Can see diminished concentration of contrast as a delayed nephrogram
  - Can see actual level of obstruction
- CT useful in complicated cases with extra-urologic pathology
- MR urogram helpful in cases of ureteral ectopia

Diagnostic Procedures/Surgery

- Endoscopy with cystoscopy and ureteroscopy can visualize pathology directly:
  - Retrograde pyelogram at time of endoscopy can delineate upper tract abnormality.
- Whitaker perfusion test:
  - Simultaneous measurement of intrarenal pressures via percutaneous nephrostomies and bladder pressure via Foley catheter.
  - Initial opening pressures measured, and then subsequent filling pressures measured while saline or contrast is instilled into collecting system at rate of 10 mL/min.
  - <15 cm H20 normal; >20 cm H2O obstructed.

DIFFERENTIAL DIAGNOSIS

Conditions that mimic HDN:

- Extrarenal pelvis
- Peripelvic renal cysts
- Multicystic dysplastic kidney
- Neonatal kidney with hypoechoic renal sinus

TREATMENT

Attempt to relieve the obstruction promptly and prevent further damage with therapeutic or prophylactic antibiotics.

MEDICATION

- Antibiotics: May be needed as treatment or as prophylaxis:
  - This does not treat the HDN itself but helps to prevent the sequelae of infection while investigating the cause of the HDN or while observing the condition, as in VUR.
- Anticholinergics helpful in cases of NGB causing HDN as an adjunct to other treatment.
- -Blockers to treat behavioral disorders like dysfunctional voiding.

SURGERY/OTHER PROCEDURES

- Necessary when the HDN is due to obstruction or when the cause of the HDN threatens renal function.
- Temporary relief of obstruction may be needed with nephrostomy tube, ureteral stent, or Foley catheter.
- Definitive surgery depends upon pathology:
  - Pyeloplasty for UPO
  - Ureteral reimplantation for UVJO
  - Ureteral reimplantation for ureteral ectopia
  - Ureteral reimplantation with excision of ureterocele for ureterocele
  - Transurethral incision of PUV and/or vesicostomy for PUV
  - Ureteral reimplantation (± ureteral tapering) vs. observation for VUR
  - Bladder augmentation in cases of NGB not effectively managed with medical therapy
  - If renal moiety affected no longer functions, then ablative surgery, such as nephrectomy, may be appropriate

ADDITIONAL TREATMENT

- Clean intermittent catheterization may be necessary in NGB.
- Behavioral modification therapy and biofeedback may aid in cases of severe voiding dysfunction.

ONGOING CARE

PROGNOSIS

Directly related to underlying cause of HDN

COMPLICATIONS

Ongoing pathologic HDN leads to:

- Infection
- Calculi
- HTN
- Impaired renal function:
  - Acidosis
  - Sodium and electrolyte imbalance
  - Abnormal water homeostasis
  - Altered production of erythropoietin and vitamin D
  - Diminished GFR, often the last excretory function to be affected

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- For cases in which observation is selected, it is incumbent upon the urologist to follow the patient very closely, typically with serial US and nuclear renal scans.
- As soon as deterioration in renal function or sequelae such as infection or calculi occur, intervention should be entertained.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

Hydronephrosis, Prenatal

CODES

ICD9

- 591 Hydronephrosis
- 593.5 Hydroureter
- 753.29 Other obstructive defect of renal pelvis and ureter

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle
- GFR: Glomerular filtration rate
- HDN: Hydronephrosis
- MR: Magnetic resonance
- NGB: Neurogenic bladder
- PUV: Posterior urethral valves
- UPJO: Ureteropelvic junction obstruction
- US: Ultrasound
- UTI: Urinary tract infection
- UVJO: Ureterovesical junction obstruction
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

HYDRONEPHROSIS/HYDROURETERONEPHROSIS (DILATED URETER/RENAL PELVIS), PRENATAL

Anthony J. Casale, MD

BASICS

DESCRIPTION

- In utero US detection of fetal renal dilation, pelviectasis, or hydronephrosis
- May represent a normal developmental variant or a pathologic anomaly
- Hydronephrosis may be observed early in pregnancy but the diagnosis usually cannot be made with certainty until 18 wk of gestation

EPIDEMIOLOGY

1 in 100 fetuses are observed to have urinary dilation, and 1 in 500 have a significant urologic anomaly.

RISK FACTORS

- Family history of renal abnormalities or vesicoureteral reflux
- Previous fetal loss due to urinary tract causes

PATHOPHYSIOLOGY

- Transitional hydronephrosis (most common, physiologic dilation of the ureter is seen in up to 84% of cases of hydronephrosis)
- Ureteropelvic junction obstruction (most common pathophysiology)
- Ureterovesical obstruction (megaureter, obstructed and nonobstructed)
- Bladder outlet obstruction (posterior urethral valves, urethral atresia)
- Nonobstructive processes: Vesicoureteral reflux, nonrefluxing nonobstructed megaureter, and prune belly syndrome
- Severe with oligohydramnios may cause pulmonary hypoplasia

COMMONLY ASSOCIATED CONDITIONS

Congenital hydronephrosis is associated with many syndromes.

DIAGNOSIS

HISTORY

- Timing of prenatal detection; earlier detection implies more severe condition
- Renal pelvic dilation vs. pathologic hydronephrosis: Renal pelvic AP diameter >10 mm by 32 wk gestation requires postnatal evaluation.
- Presence of calyectasis 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: Suggests severe comprise of renal function:
  - Associated with severe obstructive uropathy due to posterior urethral valves, congenital urethral stricture, or ureterocele obstructing bladder outlet
  - Associated with pulmonary hypoplasia and fetal or neonatal death

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Maternal -feto protein may be elevated in some cases of fetal renal anomalies
- Assessment of pulmonary maturity in patients with oligohydramnios (lecithin-to-sphingomyelin ratio)
- Amniotic fluid studies:
  - Volume: Composed mostly (90%) of fetal urine after the 16th wk of gestation
  - Correlates with fetal renal function
- Fetal karyotype (may indicate gender or important genetic information)
- Assessment of fetal urinary electrolytes:
  - Good prognosis: Sodium <100 mg/dL; osmolarity <210 mOsmol/dL; chloride <90 mg/dL (remember dilute urine is better in the fetus)
- Postnatal serum electrolyte assessment:
  - Nadir creatinine (<0.8 mg/dL in 1st yr holds good prognosis)
  - CO2: Acidosis has a bad prognosis.
- Urinalysis and urine culture

Imaging

- Prenatal: Serial fetal US. Assessment of urinary tract considered standard part of antenatal fetal US testing
- Postnatal assessment: Unilateral hydronephrosis:
  - Delay initial renal/bladder ultrasound until 48 hr of age to avoid underestimating degree of hydronephrosis due to newborn dehydration.
  - VCUG at 14 days
  - Diuretic nuclear renal scan (MAG-3) at 30 days
- Postnatal assessment: Bilateral hydronephrosis
  - Male: Early postnatal assessment with US and VCUG to exclude posterior urethral valves
  - Female: Early postnatal assessment with US and VCUG to exclude ureterocele obstructing the bladder outlet or ectopic ureter

Diagnostic Procedures/Surgery

- Fetal urinary electrolyte bladder aspiration in cases of oligohydramnios
- Whitaker test (postnatal): May be helpful to determine if hydronephrosis is obstructive

DIFFERENTIAL DIAGNOSIS

- Urinary conditions:
  - Transitional hydronephrosis (transitory)
  - UPJ obstruction
  - Duplication anomalies
  - Vesicoureteral reflux
  - UVJ obstruction
  - Prune-belly syndrome
  - Megacystis-megaureter microcolon syndrome
  - Multicystic dysplastic kidney
  - Autosomal recessive polycystic kidney disease
- Intestinal disorders:
  - Intestinal duplication
  - Mesenteric cysts
  - Imperforate anus
  - Duodenal atresia
- Persistent cloaca
- Cloacal exstrophy
- Ovarian cysts
- Tumors:
  - Neuroblastoma
  - Congenital mesoblastic nephroma

TREATMENT

- Prenatal management: Assessment of hydronephrosis, oligohydramnios:
  - Unilateral cases: Serial fetal US every 4 wk; deliver at term
  - Bilateral cases:

    No oligohydramnios: Observation, deliver at term

    Oligohydramnios: Termination, early delivery, prenatal treatment for pulmonary immaturity
- Fetal intervention (bilateral cases only):
  - Tapping of fetal bladder
  - Percutaneous shunting: Vesicoamniotic drain
- Postnatal management:

- Pulmonary support if respiratory compromise
- Antibiotic prophylaxis: Amoxicillin (20 mg/kg/d in a single dose)
- Bilateral hydronephrosis: Place catheter to drain bladder
- All hydronephrosis: US, VCUG, MAG-3 renal scan as indicated

MEDICATION

- No specific antenatal medications exist
- See above, prophylactic antibiotics
- Surfactant to assist lung function after birth with pulmonary hypoplasia

SURGERY/OTHER PROCEDURES

- Intrauterine intervention is highly controversial.
- 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.

ONGOING CARE

PROGNOSIS

- Most neonates have an excellent prognosis. Prognosis depends on etiology of the dilated system and other associated anomalies.
- Severe bilateral hydronephrosis is associated with obstruction and oligohydramnios early in gestation predicts an adverse outcome.
- Fetuses with bilateral hydronephrosis, a distended bladder, and oligohydramnios are at highest risk of neonatal demise or pulmonary complications.

COMPLICATIONS

- Pulmonary hypoplasia with severe oligohydramnios
- Renal impairment

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Based on initial evaluation, subsequent imaging may be necessary

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric

CODES

ICD9

- 591 Hydronephrosis
- 655.83 Other known or suspected fetal abnormality, not elsewhere classified, affecting management of mother, antepartum condition or complication
- 753.29 Other obstructive defect of renal pelvis and ureter

ABBREVIATIONS

- UPJ: Ureteropelvic junction
- UVJ: Ureterovesical junction
- VCUG: Voiding cystourethrogram

HYPERALDOSTERONISM, PRIMARY (ALDOSTERONISM, CONN SYNDROME)

Michael O. Koch, MD
Helen J. Kuo, MD

BASICS

DESCRIPTION

- Conn syndrome refers to an aldosterone-producing adenoma that is usually small (<3 cm), unilateral, and renin-unresponsive.
- Characterized by HTN, hypokalemia, mild hypernatremia, metabolic alkalosis, and suppressed renin, due to excess production of aldosterone.
- APA subtype of primary hyperaldosteronism accounts for 30–60% of primary hyperaldosteronism.
- Secondary hyperaldosteronism is usually related to HTN and/or edematous states disorders such as CHF, cirrhosis, and nephrotic syndrome.
- Pseudohypoaldosteronism can be due to ingestion of large amounts of licorice or Liddle syndrome

EPIDEMIOLOGY

- 5–12% of hypertensive population (recent increased prevalence of primary aldosteronism due to improved diagnostic testing)
- Adrenal adenoma is more common in women.
- Peak incidence during 4th and 5th decades
- 20% primary aldosteronism in resistant hypertensives (elevated BP despite 3 antihypertensive medications)

RISK FACTORS

Genetics

- Hereditary pattern for more common APAs unclear
- A rare form of autosomal dominant primary hyperaldosteronism is GRA.
- 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 during Na depletion.
- Autonomous aldosterone secretion leads to inappropriate Na and water reabsorption from the cortical collecting tubule:
  - Electrical gradient created favors secretion of potassium (K), resulting in hypokalemia.

- ECF volume causes mild HTN.

- Renal escape limits Na retention and prevents significant edema:
  - Occurs after ~1.5 kg of ECF is absorbed, or a weight gain of ~3 kg.
  - Spontaneous diuresis then occurs, lowering the ECF.
  - Increased ANP, decreased thiazide-sensitive Na-Cl co-transporter, and pressure natriuresis are factors that may contribute to renal escape.

COMMONLY ASSOCIATED CONDITIONS

- Adrenal cancer (rare)
- Essential HTN

DIAGNOSIS

HISTORY

- HTN, often resistant to therapy
- Headaches related to HTN
- Nocturia, polyuria, muscle cramps, tetany, or paresthesias related to hypokalemia:
  - Milder symptoms if normokalemic
  - Symptoms better with low-salt diet in some patients
- Family history of HTN not important.

PHYSICAL EXAM

- No specific findings
- Mild to moderate HTN, not usually distinguishable from essential HTN
- Malignant HTN rare
- Lack of edema

DIAGNOSTIC TESTS & INTERPRETATION

- Consider screening the following patients:
  - Hypertensive and hypokalemic:

    HTN with K <3.0 highly suspicious of an APA.

    Hypokalemia is thought to be a late manifestation of aldosterone excess.

    If patient is on restricted Na diet, severe hypokalemia often absent; only test patients if adequately salt loaded.

    Hypokalemia can be induced with oral sodium loading.

    20% of patients with hyperaldosteronism are normokalemic; more often seen in adrenal hyperplasia.
  - Inappropriate kaliuresis on initiation of diuretic
  - HTN resistant to multi-drug treatment
  - Family history of early HTN or stroke

– Adrenal incidentaloma

Lab

- Hypernatremia, hypokalemia, metabolic alkalosis, impaired glucose tolerance
- PRA low in primary hyperaldosteronism; if plasma renin >1, diagnosis unlikely
- Screening: PAC/PRA in the upright position; obtain when K is corrected. Positive if:
  - PAC/PRA >20 with PAC 15 ng/dL OR
  - PAC/PRA >40 with PRA >0.2 ng/mL/h
  - Diuretics, ACE inhibiters, ARBs can falsely elevate PRA.
- Confirmatory studies:
  - Na-loading test with:

    Saline infusion: PAC at baseline and 4 hr (positive test PAC >10 ng/dL)

    Oral sodium: 24-hr urine Na and aldosterone on days 3 and 4 (positive if aldosterone <12 mg/d) and (Na >200 mmol/d)

    Fludrocortisone suppression
  - Captopril-suppression test is used in patients when salt loading is contraindicated.
- All confirmatory tests should be used with care in patients with compromised left ventricular cardiac function.

Imaging

- CT with thin cuts through the adrenals is the preferred noninvasive test:
  - Used to identify surgically curable disease and differentiate the subtypes once primary aldosteronism is confirmed
  - APAs usually uniform, round, and hypodense with Hounsfield unit 10
  - 6% probability of identifying an adrenal mass on CT
  - Lacks 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 scintigraphy using 131I-6-iodomethyl-19-nor-cholesterol is rarely available in the US, cumbersome to perform, and depends heavily on the size of the adenoma.

Diagnostic Procedures/Surgery

- AVS for aldosterone 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 after corticotrophin infusion
  - 44% of patients with bilateral renal masses had a unilateral source of aldosterone secretion.

– Cure also reported after adrenalectomy in patients with AVS-proven unilaterality despite normal adrenals on CT scan.

- Postural tests, historically used to distinguish adenoma from bilateral hyperplasia have become less useful with the discovery of angiotensin-responsive APAs.

Pathological Findings

- Solitary, 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 non-neoplastic uninvolved adrenal gland
- Histopathology: Foamy lipid-laden clear cells, in sheets or nests

DIFFERENTIAL DIAGNOSIS

- Other causes of HTN. In Cushing 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:
  - Over ingestion of licorice
  - Use of chewing tobacco
  - Hyper-deoxycorticosterones
- Other subtypes of primary hyperaldosteronism:
  - Bilateral adrenal hyperplasia: Idiopathic
  - Glucocorticoid-remediable aldosteronism due to aldosterone-producing, renin-responsive adenoma. Familial hyperaldosteronism type I, autosomal dominant
  - Familial occurrence of aldosterone-producing adenoma or bilateral idiopathic hyperplasia or both
  - 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

- Treatment selected based on etiology of hyperaldosteronism
- Control HTN.
- Diagnosis may be difficult in those with normal serum K levels and those being treated with antihypertensives or diuretics.

MEDICATION

- 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. Can cause gynecomastia, sexual dysfunction, menstrual irregularities

– Eplerenone: No active metabolites, shorter half-life than spironolactone, 50–75% as potent as spironolactone but less adverse effects

- Amiloride, an epithelial Na-channel blocker and K-sparing diuretic, may also be used, especially if spironolactone or eplerenone are intolerable. More often used in conjunction with the above.
- Thiazide diuretics, ACE inhibitors, calcium channel antagonist, angiotensin blockers

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 PAC after surgery to confirm cure
- Monitor K closely postoperatively

ADDITIONAL TREATMENT

Emerging therapies include developing drugs that inhibit actions of aldosterone synthase enzyme, encoded on the CYP11B2 gene

ONGOING CARE

PROGNOSIS

- Patients with PA have higher rates of prior stroke (12.9% vs. 3.4%) compared to those with essential HTN.
- Nonfatal MI (4% vs. 0.6%)
- Atrial fibrillation (7.3% vs. 0.6%)

COMPLICATIONS

- Those due to HTN (left ventricular hypertrophy, coronary artery disease, heart failure, stroke, intracerebral hemorrhage, etc.)
- Those due to low K (tetany, headache, arrhythmias, etc.)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

BP and serum electrolytes should be evaluated postoperatively and following medical therapy.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Aldosteronism (Hyperaldosteronism, Conn Syndrome) Algorithm
- Hypertension, Urologic Considerations

CODES

ICD9

- 255.10 Hyperaldosteronism, unspecified
- 255.11 Glucocorticoid-remediable aldosteronism
- 255.12 Conn’s syndrome

ABBREVIATIONS

- ANP: Atrial natriuretic peptide
- APA: Aldosterone producing adenoma
- ARB: Angiotensin receptor blocker
- AVS: Adrenal vein sampling
- BP: Blood pressure
- CHF: Congestive heart failure
- CT: Computed tomography
- ECF: Extracellular fluid
- GRA: Glucocorticoid remediable aldosteronism
- HTN: Hypertension
- MI: Myocardial infarction
- PA: Primary aldosteronism

- PAC/PRA: Plasma aldosterone concentration-to-plasma renin activity
- PAC: Plasma aldosterone concentration
- PRA: Plasma renin activity
- US: Ultrasound

HYPERPROLACTINEMIA, UROLOGIC CONSIDERATIONS

Roger S. Rittmaster, MD

BASICS

DESCRIPTION

- HPRL refers to serum prolactin levels that exceed the normal range <25 mg/L (~500 mIU/L) in women and <20 mg/L (~400 mIU/L) in men.
- It is a rare but important cause of ED and hypogonadism in men.
- Most common causes are pregnancy, medications, PCOS, and prolactin-secreting pituitary tumors (prolactinomas)

EPIDEMIOLOGY

- Limited data. In 1 series of 850 men presenting with sexual dysfunction: 10 had marked HPRL (1.1%) of whom 6 cases were associated with a pituitary adenoma.
- 10–25% of women with amenorrhea
- 75% of women with amenorrhea and galactorrhea
- Prolactinomas:
  - 90% occur in reproductive-aged women
  - Common and diagnosed early in women because of amenorrhea and galactorrhea; usually present as microadenomas (tumors <10 mm in diameter).
  - Uncommon in men: Present often as hypogonadism or ED or visual field defects
  - 10% in autopsy or MRI series
  - 40% of all pituitary tumors are prolactinomas
  - About 100 per million adults

RISK FACTORS

- Female sex (prolactinomas, pregnancy)
- Medications (antipsychotics, antidepressants, verapamil, opiates, GI motility drugs, estrogens)
- MEN-1

Genetics

Prolactinomas are most often sporadic:

- 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

GENERAL PREVENTION

Discontinuation of mediation causing symptomatic hyperprolactinemia (asymptomatic prolactin elevations need not be treated)

PATHOPHYSIOLOGY

- Prolactin is produced in the anterior pituitary.
- Physiologically, primary function is in breast development and lactation; it is a normal physiologic response in pregnancy.
- Secretion is pulsatile and can increase with stress and sleep.
- Dopamine acts through the D2 receptor to tonically suppress prolactin levels:
  - Most medications that raise prolactin levels do so by inhibiting dopamine secretion or action.
  - Prolactinomas: Pituitary microadenomas (<10 mm) and macroadenomas (>10 mm) can be seen in some patients as the cause of the elevated levels.
  - Rarely, chest wall injury can increase prolactin levels.
  - Macroprolactinemia is caused by an abnormal binding of the molecule to circulating IgG.
  - Elevated prolactin can suppress GnRH, with subsequent reductions in LHRH, FSH, and testosterone levels.

COMMONLY ASSOCIATED CONDITIONS

- Amenorrhea and/or galactorrhea in women
- Hypogonadism and or ED in men
- Hypothyroidism: Increased thyrotropin-releasing hormone can stimulate prolactin secretion.
- Renal failure can result in reduced clearance.
- Cirrhosis
- Herpes zoster (particularly involving the chest wall)

DIAGNOSIS

HISTORY

- In males, the typical complaint is some type of sexual dysfunction:
  - Decreased libido
  - ED
  - Galactorrhea
  - Gynecomastia
  - Headache
  - Visual-field defects
- In females, menstrual irregularities, infertility, and galactorrhea are common complaints:
  - Pregnancy history including infertility

- Amenorrhea
- Galactorrhea
- Headaches
- Visual field defects

- Psychiatric history and antipsychotic medication use
- Alcohol abuse
- Medication use:
  - The following have been reported to cause hyperprolactinemia mediated through the dopamine axis: Antipsychotics: Butyrophenones (eg, haloperidol), phenothiazines (eg, chlorpromazine), thioxanthenes (eg, thiothixene), risperidone and others: Metoclopramide, sulpiride, pimozide, methyldopa, reserpine
  - Others reported: Antiandrogens, cimetidine, cyproheptadine, danazol, estrogens, INH, tricyclic antidepressants, opiates, verapamil

PHYSICAL EXAM

- Breast exam for gynecomastia, galactorrhea
- Evidence of chest wall trauma or herpetic lesions
- Signs of hypogonadism or in men
- Signs of hypothyroidism
- Visual field abnormalities

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Unless pregnancy is impossible, females 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.
- Repeat prolactin level, waiting at least 1 hr after last meal or period of exercise.
- 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 done in all cases where prolactin is persistently elevated and no cause is apparent.
- DEXA scanning to evaluate for possible bone mineral density problems
- Females, pelvic US to assess for uterine or ovarian pathology

Diagnostic Procedures/Surgery

Formal visual field assessment should be done in patients with macroadenomas.

DIFFERENTIAL DIAGNOSIS

- Hypothyroidism
- Laboratory error or macroprolactinemia (abnormal prolactin molecule)
- Medication-induced
- Non–prolactin-secreting pituitary or hypothalamic tumor
- PCOS
- Pregnancy
- Prolactinoma
- Renal failure

TREATMENT

- In females, rule out pregnancy 1st
- In men, usually detected as part of workup for ED or hypogonadism

MEDICATION

- Asymptomatic HPRL does not need to be treated.
- Treat underlying cause or stop offending drug, if possible.
- Cabergoline or bromocriptine (dopamine agonists):
  - Usually will lower prolactin levels, regardless of cause, and shrink prolactinomas
  - 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/wk is rarely 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 b.i.d.–t.i.d.).

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 macroadenomas in whom previous mass effects may recur if tumor enlarges.

- Significant enlargement of microadenomas is uncommon during pregnancy.
- Lactation: Dopamine agonists will inhibit lactation.

SURGERY/OTHER PROCEDURES

- Often performed trans-sphenoidally
- For microadenomas, generally reserved for patients intolerant of drug therapy. Tumors may recur.
- Only indicated for pituitary macroadenomas when medical therapy is ineffective, including persistent visual field abnormalities:
  - Usually not curative.

ADDITIONAL TREATMENT

Radiotherapy

Usually only indicated for pituitary macroadenomas that have failed medical therapy, and where response to surgery is inadequate or surgery is contraindicated.

Additional Therapies

In men, ED or persistent hypogonadism may require additional therapy.

ONGOING 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 RECOMMENDATIONS

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.

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See Also (Topic, Algorithm, Electronic Media Element)

- Erectile Dysfunction
- Gynecomastia

CODES

ICD9

253.1 Other and unspecified anterior pituitary hyperfunction

ABBREVIATIONS

- DEXA: Dual energy x-ray absorptiometry

- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- GnRH: Gonadotropin-releasing hormone
- HPRL: Hyperprolactinemia
- INH: Inhibin
- LHRH: Luteinizing hormone-releasing hormone
- MEN: Multiple endocrine neoplasia
- MEN1: Multiple endocrine neoplasia type 1
- MRI: Magnetic resonance imaging
- PCOS: Polycystic ovary syndrome

HYPOSPADIAS

Jared Cox, MD

C. D. Anthony Herndon, MD

BASICS

DESCRIPTION

- Common congenital defect of the male external genitalia characterized by an incompletely formed ventral radius of the penis, with an ectopic meatal opening which located anywhere from the glans penis to the perineum.
- Associated conditions (not present in all cases):
  - Abnormal curvature of the penis (chordee), especially with more proximal meatus
  - Abnormal distribution of foreskin with excess dorsally (hood) and deficiency ventrally
- May be an isolated defect or may be associated with a significant underlying abnormality
- Classification:
  - Anterior (distal): 50%
- Glandular
- Megameatus intact prepuce
- Coronal
- Subcoronal:
  - Middle (shaft): 30%
- Distal
- Midshaft
- Proximal:
  - Posterior (proximal): 20%
- Penoscrotal
- Scrotal
- Perineal

EPIDEMIOLOGY

- 1 in 250–300 live male births
- 1 in 80–100 if family history of hypospadias exists

RISK FACTORS

- 5 times higher in IVF compared to controls
- Environmental:
  - Suspected because of possible increased incidence over last several decades

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- Phytoestrogens and other environmental substances with estrogenic activity

- Genetics (see below)

Genetics

- <5% of cases have genetic cause
- Seen in various types of isolated and syndromic genetic abnormalities
- Occurs in mutations of genes affecting penile development or determination of the male gonad (eg Homeobox, FGF, and Sonic hedgehog genes)
- 5-Reductase mutations
- Familial propensity:
  - 10% have affected 1st-, 2nd-, or 3rd-degree relative
  - 14% male siblings affected
  - 27% concordance in monozygotic twins

GENERAL PREVENTION

Generally not possible; avoidance of contact with 5-reductase inhibitors or estrogenic compounds by women during pregnancy

PATHOPHYSIOLOGY

- Normal penile development:
  - Urogenital folds form on either side of the cloacal membrane, 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 the urethra from proximal to distal
  - Canalization of the glans occurs distally, fusing with the urethra
  - Process complete by 20th wk of gestation
- Glandular hypospadias likely represents failure of distal canalization
- More proximal types due to failure of fusion of the genital folds
- Scrotal or perineal types may result in cleft scrotum

COMMONLY ASSOCIATED CONDITIONS

- Growth restriction (low birth weight and length, small head circumference) has been associated with hypospadias.
- Associated anomalies more common in those with more severe hypospadias:
  - Cryptorchidism: 7–9%
  - Inguinal hernia and/or hydrocele: 9–16%

– Syndromes:

49 in which hypospadias is frequent or occasional

78% of these have associated micropenis, cryptorchidism and/or a scrotal abnormality

Intersex state, especially when cryptorchidism present

15% with hypospadias and palpable undescended gonad

50% with hypospadias and nonpalpable undescended gonad

DIAGNOSIS

HISTORY

- Family history of hypospadias
- Any associated anomalies
- Exposure of parents to any drugs or chemicals (eg, 5-reductase inhibitors)

PHYSICAL EXAM

- Evaluate location of meatal opening.
- Determine the presence of chordee.
- Skin proximal to meatus should be examined for health.
- Inguinal and scrotal exam for cryptorchidism, hydrocele, or hernia
- Severe proximal hypospadias may be associated with bifid scrotum and/or penoscrotal transposition.
- Signs of other anomalies

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Karyotype and endocrine evaluation in cases of severe hypospadias and cryptorchidism to rule out intersex state

Imaging

- Genitogram can be performed during intersex evaluation when deemed appropriate.
- Literature does not support routine imaging of upper urinary tract.

TREATMENT

ALERT

With any suspicion of hypospadias, neonatal circumcision should not be performed.

Do not perform circumcision in any newborn suspected of having hypospadias or disorder of sexual development.

MEDICATION

- No primary medical therapy for hypospadias
- Preoperative hormonal therapy treatment (testosterone injections or topical creams, or hCG injections), can be used promote penile growth in cases of a short phallus. Some have

expressed concern that the use of androgens before puberty may limit normal pubertal genital growth.

SURGERY/OTHER PROCEDURES

- Indications:
  - Distal defects usually repaired for cosmetic purposes as normal function is maintained for the most part.
  - More proximal hypospadias usually treated to provide the ability to:
  - Micturate in the standing position without deflection of urinary stream
  - Have sexual intercourse
  - Effectively inseminate
- Timing of repair best at early age:
  - Anesthetic risks optimal after 4 mo of age
  - Best at 6–18 mo (preferably 6–12 mo, as genital awareness occurs after 18 mo)
  - Operative amnesia most prominent prior to age 2
  - Less surgical complications as a child than as an adult

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- Based on:
  - Meatal location
  - Degree of penile curvature
  - Tissue availability
- Any curvature should be assessed 1st, and orthoplasty (penile straightening) performed
- Distal:
  - MAGPI
  - Tubularization
- Thiersch-Duplay: Used with deep glanular groove and sufficient width of urethral plate
- TIP or Snodgrass: Similar to Thiersch-Duplay but longitudinal midline relaxing incision made in urethral place for decreased tension in neourethra
- Permeatal-based flap (Mathieu)
- Midshaft:
  - Tubularization/TIP
  - Mathieu
  - OIF
- Proximal:
  - 1-stage

- Tubularization
- OIF:
  - 2-stage
- 1st stage includes orthoplasty (phallus reconstruction) and repositioning of prepuce ventrally

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  - Hypospadias revision
- Meatoplasty
- Closure of fistula
- Inlay procedure using buccal or bladder mucosa

ADDITIONAL TREATMENT

Psychosocial support for family and long term for patient if necessary

ONGOING CARE

PROGNOSIS

- Fistula may develop in 10% (simple repair) and in up to 40% with complex repair
- See “Complications.”
- Most patients have satisfactory sexual function
- Fertility and androgen function usually not affected

COMPLICATIONS

- Early surgical:
  - Bleeding/hematoma: Compression or re-exploration
  - Infection: Antibiotics/incision and drainage
  - UTI
  - Wound breakdown: Revision
- Later surgical:
  - Residual or recurrent chordee
  - Meatal stenosis: Meatal dilation/meatoplasty
  - Urethral stricture
- Urethrotomy: 50% success; reserved for short, thin strictures
- Free graft patch
- Flap-only urethroplasty:
  - Urethrocutaneous fistula: Fistula excision and urethral repair
  - Diverticulum: Excision and urethral repair
  - Hair in urethral repair; avoid the use of hair-bearing skin in initial repair; cystoscopic depilation using a laser or cautery; if severe, excise and redo-repair

  - Lichen sclerosis or balanitis xerotica obliterans
- Requires complete excision with insertion of buccal or other type of graft

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow for penile development and the complications noted above

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Bifid Scrotum
- Disorder of Sexual Development (DSD)
- Penoscrotal Transposition

CODES

ICD9

752.61 Hypospadias

ABBREVIATIONS

- hCG: Human chorionic gonadotropin
- IVF: In vitro fertilization
- MAGPI: Meatal advancement and glanuloplasty
- MRI: Magnetic resonance imaging
- OIF: Onlay island flap
- TIP: Tubularized incised plate
- UTI: Urinary tract infection

INCONTINENCE, URINARY, ADULT FEMALE

Anil A. Thomas, MD
Sandip P. Vasavada, MD

BASICS

DESCRIPTION

- Involuntary loss of urine that is objectively demonstrable and is of social and hygienic concern.
- Stress incontinence: Associated with increased intra-abdominal pressure such as coughing, sneezing, or exertion
- Urge incontinence: Sudden uncontrollable urgency, leading to leakage of urine (also known as OAB)
- Mixed incontinence: Loss of urine from a combination of stress and urge incontinence
- Overflow incontinence: High residual or chronic urinary retention leads to urinary spillage from bladder overdistention
- Functional incontinence: Loss of urine due to deficits of cognition and mobility
- Total incontinence: Continuous leakage of urine

EPIDEMIOLOGY

- Affects 30–50% of adult women
- Stress urinary incontinence is the most common (49%), followed by mixed (29%) and urge (21%) incontinence

RISK FACTORS

Advanced age, obesity, menopause, pregnancy, vaginal childbirth, pelvic surgery or radiation, urethral diverticula, genital prolapse, smoking, COPD, cognitive impairment

GENERAL PREVENTION

Weight loss, pelvic floor exercises, smoking cessation

PATHOPHYSIOLOGY

- Stress incontinence: Occurs with increased intra-abdominal pressure without uninhibited detrusor contraction. 2 types:
  - Anatomic: Due to urethral hypermobility from lack of pelvic support
  - Theory 1: Normally, during increased intra-abdominal stress, equal pressure transmission occurs to the proximal urethra, which lies within the abdomen above the plane of fascia and the muscle separating the abdomen from the pelvis. A hypermobile urethra due to loss of pelvic support descends below the plane. The normal pressure transmission mechanism is lost, causing stress incontinence
  - Theory 2: Hammock theory: Normally, the suburethral support contributed by the endopelvic fascia and anterior vaginal wall provides a stable backboard against which the ur-

ethra is compressed while intra-abdominal pressure rises. When this suburethral support layer is lax and mobile, any effective compression is not achieved, causing leakage.

– ISD: Impairment of various intrinsic factors is responsible for the normal coaptation and closure of the urethra. Urethral mucosal seal and inherent closure from collagen, fibroelastic tissue, smooth and striated muscles, etc., may be lost secondary to surgical scarring, radiation, or hormonal and senile changes

• Urge incontinence: Detrusor overactivity (may be secondary to detrusor myopathy or neuropathy)

• Overflow incontinence: Urinary retention (usually from lower motor paralytic neurogenic bladder)

• Total incontinence: Constant loss of urine in epispadias–exstrophy complex due to absence of bladder neck and urethra. Ectopic ureters in females usually open in the urethra distal to the sphincter or in the vagina, causing continuous leakage

COMMONLY ASSOCIATED CONDITIONS

Genitourinary prolapse, UTI, COPD, diabetes mellitus, neurologic disease

DIAGNOSIS

HISTORY

• Age: Stress incontinence is more common in elderly postmenopausal women. Incontinence dating from childhood indicates congenital causes such as ectopic ureter, epispadias, etc.

• Childbirth: Weakness of the pelvic floor is more likely in multiparous women.

• Amount and nature of leakage: Severity of leakage should be graded by the number of pads used in 24 hr.

• Stress incontinence: Occurs in small spurts. Patients typically remain dry at night in bed.

• Urge incontinence: Sudden urge followed by leakage of large amounts, usually associated with frequency and nocturia.

• Continuous slow leakage in between regular voiding indicates ectopic ureter, urinary fistula, etc.

• Pain: Suprapubic pain with dysuria implies urinary infection, interstitial cystitis, etc.

• Medical history:

– Cerebrovascular accidents, parkinsonism, multiple sclerosis, myelodysplasia, diabetes, spinal cord injury (can cause neurogenic incontinence)

– Radiation to pelvic and vaginal areas: Causes ISD, vesical irritative urgency, and low bladder compliance

– A history of smoking and chronic obstructive pulmonary disease can aggravate incontinence.

- Medications:
  – Sympatholytic -blockers (terazosin, prazosin, doxazosin, clonidine, etc.) can cause or worsen incontinence.
  – Sympathomimetic and tricyclic antidepressants such as ephedrine, imipramine, etc., can cause retention with overflow incontinence.
- Surgical history: Pelvic and vaginal surgeries can weaken the pelvic floor support. Prior anti-incontinence surgeries can also lead to recurrent incontinence from ISD.

PHYSICAL EXAM

- General neurologic exam:
  – Mental status, speech, intellectual performance
  – Motor status: Gait, generalized or focal weakness, rigidity, tremor
  – Sensory status: Impairment of perineal-sacral area sensation helps localize the level of neurologic deficit
  – Reflex: A bulbocavernous reflex implies contraction of the anal sphincter in response to squeezing the clitoris. This reflex tests the integrity of S2–S4 spinal cord segments
- Urologic exam:
  – Abdomen: Visible exstrophy-epispadias; incisional scars of previous surgeries
  – Suprapubic tenderness: May indicate cystitis
  – Palpable bladder: Chronic urinary retention
- Pelvic exam:
  – Vaginal exam with empty bladder to check pelvic organs
  – Vaginal exam with comfortably full bladder
  – The patient is asked to cough or strain to reproduce incontinence.
  – Cystocele, if evident, is staged.
  – Urethral hypermobility
  – Gauged by palpation of the descent of the proximal urethra on straining
  – Q-tip test: A lubricated Q-tip is inserted to proximal urethra and the patient is asked to strain. A resting or straining angle of >30 degrees is indicative of hypermobility of the urethra.
  – Exam of the vaginal vault and posterior vaginal wall for enterocele or rectocele

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:

  - Specific gravity: Low specific gravity implies renal impairment.
  - Dipstick: Blood, protein, nitrites, leukocyte esterase
  - Crystalluria: Suggests urinary calculus disease
- Urine culture: If tests suggest infection
- Creatinine/BUN: Impairment from associated pathologies

Imaging

- Excretory urography: Determines status of upper urinary tract, duplicated systems for ectopic ureters, and associated pathologies (indicated only when upper-tract issues are suspected)
- Cystogram and VCUG: Preferably done under fluoroscopic monitoring and in combination with videourodynamic studies. Determines presence of trabeculations, diverticula, vesicoureteric reflux, integrity of the sphincteric mechanism, degree and type of incontinence, and associated cystocele

Diagnostic Procedures/Surgery

Urodynamic studies:

- Cystometric study of detrusor function: Determines bladder compliance, sensations, and detrusor responses to filling
- Useful in patients with history of urgency and urge incontinence, cystometric documentation of detrusor hyperreflexia, or detrusor instability; has important therapeutic and prognostic implications.
- Urinary flow rate: Good flow rate with minimal PVR may suggest sphincteric incontinence
- Valsalva leak point pressure: Determines the intra-abdominal pressure at which leakage is observed at the meatus or by fluoroscopy; low leak point pressure implies ISD.
- Videourodynamic studies: Sophisticated combination of fluorocystourethrography and urodynamic studies mentioned above

DIFFERENTIAL DIAGNOSIS

- Stress incontinence: Due to urethral hypermobility or ISD, although in the majority it is mixed or due to both of the factors.
- Urge incontinence: Can be due to urinary infection, interstitial cystitis, carcinoma in situ, bladder calculi, detrusor overactivity, or neurogenic detrusor hyperreflexia. Most often idiopathic.
- Nocturnal enuresis: Idiopathic, neurogenic, cardiogenic, or obstructive causes
- Continuous leakage: Ectopic ureter, urinary fistulas, exstrophy–epispadias complex
- Postvoid dribbling: Urethral diverticulum, idiopathic, iatrogenic, surgical

TREATMENT

- Treat correctable causes (UTI, etc.)
- Encourage weight loss in obese patients

MEDICATION

First Line

- Stress incontinence: Activation of -adrenergic receptors in the internal urethral sphincter increases the urethral resistance to urinary flow with sympathomimetic drugs, estrogen, and tricyclic agents (not used commonly due to side effects and interaction concerns and potential limited efficacy).
- Urge incontinence: Anticholinergic, antispasmodic, and tricyclic antidepressant medications have been used to treat overactive bladder symptoms.

Second Line

Nonsurgical management (helps ~50–65% patients with milder symptoms):

- Behavioral therapy: Voiding at progressively increasing predetermined intervals
- Biofeedback and pelvic floor exercises (Kegel exercise)
- Electrical stimulation of pelvic floor muscles
- Occlusive and supportive devices, urethral plugs

SURGERY/OTHER PROCEDURES

- Surgical management: Provides more successful and sustained outcome
- Periurethral injection of bulking agents: Collagen, carbon beads, hyaluronic acid
- Vesicourethral suspension procedures: Aim at repositioning and retropubic fixation of bladder neck and proximal urethra:
  - Provide high initial success rate, especially as the initial operation. At long-term follow-up, the continence rate seems to decline.
- Abdominal approaches: Marshall-Marchetti-Krantz cystourethropexy, Burch colposuspension, laparoscopic colposuspension
- Vaginal needle suspension: Raz, Stamey, etc. (not used commonly today)
- Slings:
  - Suburethral compression surgeries:

    Pubovaginal sling suspension: Used for coaptation and compression of the incontinent urethra, using autologous fascia or xenograft or allograft materials

    Proven useful especially for ISD patients

    Lately being recommended for both urethral hypermobility and ISD patients

    Postoperative de novo urgency, urge incontinence, voiding difficulty, and urinary retention, necessitating intermittent self-catheterization or take-down of the suspension, remain as concerns in up to ~20% of patients.

- TVT or TOT commonly used now to manage most cases of stress urinary incontinence
- Artificial urinary sphincter placement (not approved by FDA for female stress incontinence at present)
- Refractory overactive bladder (failed 1st- and 2nd-line therapies including anticholinergics):
  - Sacral neuromodulation: Efficacy in 70–80% of patients who have failed other treatments
  - Percutaneous tibial nerve stimulation: Office-based therapy for urge, frequency, and urge incontinence
  - Botulinum toxin (intravesical injection) has an emerging role in management of urge incontinence but currently not FDA-approved

ADDITIONAL TREATMENT

Dietary and fluid intake modification: Reduction or avoidance of spicy foods, citrus, or chocolate; limiting excessive fluid intake and caffeine can improve symptoms of urinary incontinence.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Biofeedback in selected cases

ONGOING CARE

PROGNOSIS

Excellent prognosis for many patients with improvement in awareness of this condition, combined with advances in diagnosis and management to minimize associated morbidity of this condition

COMPLICATIONS

- Prolonged exposure to urine causes skin breakdown and dermatitis, which may lead to ulceration and secondary infection.
- Catheter-related complications can result from long-term indwelling catheters, such as recurrent UTIs, skin infections, and urethral erosion.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Initial postoperative assessment: Evaluate voiding function with estimation of PVR and need for intermittent catheterization.
- Urgency and urge incontinence: Anticholinergics after elimination of UTI
- Periodic long-term follow-up with outcome-based questionnaire surveys

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Areflexia (Detrusor Areflexia)
- Incontinence, Adult Female Algorithm
- Overactive Bladder

CODES

ICD9

- 625.6 Stress incontinence, female
- 788.31 Urge incontinence
- 788.33 Mixed incontinence (male) (female)

ABBREVIATIONS

- BUN: Blood urea nitrogen
- COPD: Chronic obstructive pulmonary disease
- ISD: Intrinsic sphincteric deficiency
- OAB: Overactive bladder
- PVR: Post void residual
- TOT: Transobturator tape procedures
- TVT: Tension-free vaginal tape
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

INCONTINENCE, URINARY, ADULT MALE

Patrick J. Shenot, MD

BASICS

DESCRIPTION

As defined by the International Continence Society, urinary incontinence refers to the involuntary loss of urine that presents a social or hygienic problem.

EPIDEMIOLOGY

- Large studies have indicated a 3–11% overall prevalence rate of incontinence in the male population

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- Stress incontinence in men is rare unless attributable to prostate surgery, neurologic disease, or trauma.
- Reported rates of incontinence after prostatectomy range from 1% after transurethral resection to 2–57% after radical prostatectomy.
- Incontinence in men of all ages is ~1/2 as prevalent as it is in women.

RISK FACTORS

- Age
- Neurologic disease
- Prostate surgery
- Pelvic trauma

GENERAL PREVENTION

Proper management of conditions such as symptomatic bladder outlet obstruction due to BPH early in the course may prevent continence problems later in life.

PATHOPHYSIOLOGY

- Incontinence secondary to bladder abnormalities:
  - Detrusor overactivity results in urge incontinence
  - Detrusor overactivity is commonly associated with bladder outlet obstruction from BPH
- Incontinence secondary to outlet abnormalities:
  - Sphincteric damage secondary to pelvic surgery or radiation
  - Sphincteric dysfunction secondary to neurologic disease
- Mixed incontinence is due to abnormalities of both the bladder and the outlet.

COMMONLY ASSOCIATED CONDITIONS

- Neurologic disease (Parkinson, multiple sclerosis)

- Pelvic radiation
- Pelvic trauma
- BPH
- Prostate surgery

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, such as neurologic disease
- Medication use: Diuretics
- Alcohol and drug use including caffeine
- Radical pelvic surgery or radiation:
  - Abdominoperineal resection
  - Prostatectomy

PHYSICAL EXAM

- Abdominal exam:
  - Suprapubic mass suggests retention.
  - Suprapubic tenderness suggests UTI.
  - Surgical scars suggesting pelvic surgery
  - Skin lesions associated with neurologic disease (such as neurofibromatosis and café au lait spots)
- External genitalia
- Prostate
- Spine/back
- Skeletal deformities
- Scars from previous spinal surgery
- Sacral abnormalities may be associated with neurogenic bladder dysfunction:
  - Cutaneous signs of spinal dysraphism:

Subcutaneous lipoma

Vascular malformation, tuft of hair, or skin dimple on lower back

– Cutaneous signs of sacral agenesis:

Low, short gluteal cleft

Flattened buttocks

Coccyx not palpable

- Focal neurologic exam:
  - Motor function:

    Inspect muscle bulk for atrophy

    Tibialis anterior (L4–S1): Dorsiflexion of foot

    Gastrocnemius (L5–S2): Plantarflexion of foot

    Toe extensors (L5–S2): Toe extension
- Sensory function
- Reflexes:
  - Anal reflex (S2–S5):

    Gently stroke mucocutaneous junction of circumanal skin

    If visible contraction (wink) absent, suggests peripheral nerve or sacral (conus medullaris) abnormality
  - Bulbocavernosus reflex (BCR) (S2–S4):

    Elicited by squeezing glans to cause reflex contraction of anal sphincter

    Absence of BCR suggests sacral nerve damage.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Creatinine if significant retention suspected
- Urinalysis to check for glucosuria, infection

Imaging

Routine imaging is not indicated

Diagnostic Procedures/Surgery

Urodynamics is useful for confirming bladder outlet obstruction as a possible cause of detrusor overactivity.

DIFFERENTIAL DIAGNOSIS

- Urge incontinence
- Stress incontinence
- Mixed incontinence
- Overflow incontinence

TREATMENT

- Bladder diaries are invaluable in helping patients understand patterns of incontinence.
- Time voiding to avoid significant bladder distention

MEDICATION

First Line

- Urge incontinence:
  - Oxybutynin 5 mg PO t.i.d.
  - Tolterodine LA 4 mg/d PO
- Stress incontinence:
  - No generally accepted drug therapy
  - Tricyclics sometimes used:
    Imipramine 10–25 mg PO b.i.d.–t.i.d.

Second Line

- Urge incontinence:
  - Tricyclic antidepressants:
    Imipramine 10–25 mg PO b.i.d.–t.i.d.
  - DDAVP for nocturnal symptoms:
    0.1–0.5 mg PO or intranasal q.h.s.
  - Intradetrusor botulinum toxin injections

Geriatric Considerations

- Anticholinergics and tricyclics may result in significant cognitive impairment in elderly patients.
- DDAVP should be avoided in patients with known or potential cardiac disease.

SURGERY/OTHER PROCEDURES

- Urge incontinence:
  - Sacral neuromodulation
  - Augmentation cystoplasty
- Stress incontinence:
  - Urethral bulking agents

)[B]

)[A]

ADDITIONAL TREATMENT

- Pelvic floor exercise (Kegels) may significantly improve both stress and urge incontinence in male patients.
- Timed voiding is a useful therapy in patients with urge incontinence.

- Overflow incontinence is usually due to poor bladder contractility with urinary retention:
  - Indwelling catheter
  - Intermittent catheterization
  - Evaluate for outlet obstruction.

ONGOING CARE

PROGNOSIS

Continence can be improved in almost all patients

COMPLICATIONS

- Dermatitis
- Candidiasis
- Skin breakdown

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Must monitor PVR volume in patients on anticholinergic medications

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Areflexia (Detrusor Areflexia)
- Incontinence, Urinary, Following Radical Prostatectomy
- Incontinence, Urinary, with Orgasm

CODES

ICD9

- 788.30 Urinary incontinence, unspecified
- 788.31 Urge incontinence
- 788.32 Stress incontinence, male

ABBREVIATIONS

- BCR: Bulbocavernous reflux
- BPH: Benign prostatic hyperplasia
- DDAVP: Desmopressin
- PVR: Post void residual
- UTI: Urinary tract infection

INCONTINENCE, URINARY, FOLLOWING RADICAL PROSTATECTOMY

Herbert Lepor, MD

BASICS

DESCRIPTION

- PPI is a well-recognized complication of RP performed openly (perineal retropubic) or laparoscopically with or without robotic assistance.
- The definition of continence in the literature varies widely, with the strictest definition of continence being no pads used.

EPIDEMIOLOGY

- 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.

RISK FACTORS

- No preoperative factors have consistently been associated with a greater risk for developing PPI.
- Older age and deliberate wide excision of the cavernous nerves have inconsistently been reported to be predictors of PPI.

GENERAL PREVENTION

- Achieving a bloodless surgical field following anatomic ligation of the dorsal venous complex is required to meticulously divide the prostatourethral junction.
- Maximal preservation of the rhabdosphincter is felt to minimize PPI.
- Encourage Kegel exercises.

PATHOPHYSIOLOGY

- PPI results primarily from injury to the rhabdosphincter resulting in SUI.
- Preexisting detrusor instability is a less likely etiology of PPI.
- An anastomotic stricture may be the cause, or exacerbate PPI.

COMMONLY ASSOCIATED CONDITIONS

- Anastomotic stricture/bladder neck contracture
- DI

- OAB
- Sphincteric incompetence

DIAGNOSIS

HISTORY

- Assess the severity of LUTS and incontinence preoperatively.
- Inquire about the use of -blockers because these agents may exacerbate PPI.
- It is important to ascertain if the PPI is exacerbated by physical activity.
- The severity of PPI should be determined by: Number of pads, degree of bother, and frequency of incontinent episodes.
- The severity of LUTS should also be assessed.
- Inquire if PPI is improving, stable, or deteriorating:
  - Deterioration of continence together with increasing voiding symptoms suggests an anastomotic stricture.

PHYSICAL EXAM

- Observe for skin excoriation secondary to PPI.
- 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

Lab

Urinalysis to exclude urinary tract infection

Imaging

US PVR

Diagnostic Procedures/Surgery

- Uroflowmetry
- 24-hr pad test to quantify PPI
- Pressure flow urodynamics evaluation with or without fluoroscopy will help define the etiology for PPI.
- Pressure flow study must be performed prior to pursuing any surgical intervention.

DIFFERENTIAL DIAGNOSIS

- Anastomotic stricture
- DI
- SUI

TREATMENT

- Kegel exercises should be encouraged as soon as urinary catheter removal.

- Discontinue -blockers
- Limitation of fluid intake
- Timed voiding
- Voiding before strenuous activity
- Counsel patient that incontinence following RP is the norm and that with time most patients will improve.

MEDICATION

First Line

- -Agonists generally not effective for SUI
- Anticholinergic agents may improve PPI secondary to DI.

Second Line

Periurethral bulking agents (bovine glutaraldehyde cross-linked collagen polydimethyl-siloxane elastomer) are costly; they require multiple injections and have limited durable success in this setting.

SURGERY/OTHER PROCEDURES

- Surgical intervention should not be pursued until at least 1 yr PPI 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 prior to embarking on surgical correction of SUI.
- Surgical options:
  - Male slings
  - AUS
  - The specific surgical procedure is dictated by severity of PPI.
  - More severe cases best managed with an AUS.
  - In many cases, surgery achieves marked improvement in PPI but some degree of SUI may persist

ADDITIONAL TREATMENT

RADIOTHERAPY

While there is no role in the treatment of post RP incontinence, data suggest that radiation administered in the adjuvant setting following RP may not worsen incontinence but may limit resolution of continence particularly if the radiation is administered before continence returns.

Additional Therapies

- Urethral dilation should be performed if evidence of bladder outlet obstruction and anastomotic stricture.

• Transurethral incision of the stricture may be required if stricture reoccurs despite multiple dilation(s).

COMPLEMENTARY AND ALTERNATIVE MEDICINE

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 worse prognosis exists for cases with severe refractory anatomic strictures who must 1st be made totally incontinent with subsequent placement of an artificial urinary sphincter.

• PPI secondary to DI likely to improve with anticholinergic agents.

COMPLICATIONS

• Dermatitis
• Diminished self-esteem:
• Limitation of physical activity
• Withdrawal from sexual activity
• Complications of treatment for PPI

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Pad use
• Impact of PPI on quality of life

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Bladder Neck Contracture

• Incontinence, Urinary, Adult Male

CODES

ICD9

• 788.39 Other urinary incontinence

• 997.5 Urinary complications, not elsewhere classified

ABBREVIATIONS

• AUS: Artificial urinary sphincter

• DI: Detrusor instability

• LUTS: Lower urinary tract symptoms

• OAB: Overflow incontinence

• PPI: Postprostatectomy urinary incontinence

• PVR: Post void residual

• RP: Radical prostatectomy

• SUI: Stress urinary incontinence

• US: Ultrasound

INCONTINENCE, URINARY, PEDIATRIC

Steve J. Hodges, MD
Anthony Atala, MD

BASICS

DESCRIPTION

- Incontinence: Involuntary loss of urine due to an underlying anomaly.
- Enuresis: Involuntary wetting with no underlying anatomic or functional abnormality
- A “wet child” is the most common problem seen by pediatric urologists. Most wetting children will be enuretic, and the majority improves spontaneously. Hard to discern incontinent from enuretic child.
- Nocturnal enuresis implies nighttime wetting alone; diurnal implies both night and day wetting.
- Primary enuresis: Child has never been dry
- Secondary enuresis: Dry for at least 6 mo before wetting again.

EPIDEMIOLOGY

- Occurs in 10–15% of 4–6-yr-old children:
  - Resolution of 15% per year
- At 12 yr of age, 4% of children are incontinent at least 1 once per week, and at 15, 2%; more common in girls

RISK FACTORS

- Spinal dysraphism/CNS anomalies
- Urinary tract anomalies
- Developmental delay
- Family history of enuresis
- Attention deficit disorder
- Constipation

GENERAL PREVENTION

- Nonneurogenic incontinence: Delay toilet training until after 3 yr, treat constipation; timed voiding
- Neurogenic incontinence: Routine pediatric urology care, CIC, and anticholinergics if needed

PATHOPHYSIOLOGY

- Daytime control attained before nighttime
- 15–20% of 5-yr-olds have nocturnal enuresis; 15% attain continence each year.
- 20% of enuretics are diurnal; 10–20% also have constipation/encopresis.

• Normal bladder control involves 3 basic components: Intact neurologic system, normal anatomy, and a motivated child.

• Normal urinary control occurs in stages:

– Infantile voiding (0–6 mo): Low-pressure filling, reflex detrusor contraction; simultaneous relaxation of external sphincter; complete emptying, uninhibited/frequent voids

– Transitional voiding: Conscious sensation of bladder filling at 1–2 yr; continence achieved by controlling the external sphincter. Decreased voiding frequency due to increasing capacity (60 cc at birth +30 cc/yr to age 12).

– Adult voiding: Supraspinal inhibition of voiding reflex; voluntary inhibition/initiation of voiding

COMMONLY ASSOCIATED CONDITIONS

See “Risk Factors.”

DIAGNOSIS

HISTORY

• Child’s age: 15% of 5-yr-olds have nocturnal enuresis; 1% of adolescents wet bed.

• Child’s sex: Bedwetting is more common in boys than in girls (3:2); daytime frequency and wetting is more common in girls.

• When did symptoms begin; what is the pattern and severity? Bed wetting > once a night suggests polyuria. Pure nocturnal enuresis does not warrant aggressive investigation.

• Secondary enuresis implies an acquired disorder.

• Primary enuresis implicates an unmasked congenital anomaly that should be sought after.

• Dribbling upon standing in a girl may suggest labial adhesions.

• Associated daytime voiding symptoms (diurnal enuresis, urgency, frequency, weak or intermittent stream, or infrequent voiding)

• 39% of patients with both day and night wetting had symptoms suggestive of bladder instability.

• May suggest a small bladder capacity, bladder instability, acquired voiding dysfunction, or a UTI

• Intermittent stream may indicate detrusor sphincter dyssynergia or urethral obstruction.

• A partially suppressed sudden urge to void suggests bladder instability

• Frequency of bowel movements: Enuretic children with severe diurnal voiding often have chronic constipation and/or encopresis. May signal underlying voiding dysfunction/neuropathy.

• Relevant psychosocial history: Recent stresses (eg, arrival of new sibling, a move, a new school, or a family death) may contribute.

- Environmental/socioeconomic factors
- Any tricks used to prevent getting wet: Many girls will squat down and sit on the heel of 1 foot (Vincent curtsy), seen in unstable bladder.
- Some children cross their legs or jump around, and some boys hold their penises.
- Family history, medical or surgical history: Familial pattern of inheritance with enuresis.
- UTIs may lead to wetting; VUR has been associated with uninhibited bladder contractions.
- Nearly all children with myelodysplasia have diurnal incontinence. Secondary incontinence in a myelodysplastic child may indicate cord tethering.

PHYSICAL EXAM

- Mental status, level of development
- Abdominal exam: Masses can cause extrinsic compression of the bladder, causing incontinence.
- A palpable, low-lying, midabdominal mass could be a distended bladder.
- Back exam: Dimples, short sacrum, spinal defects, or hairy patches (dysraphism).
- Flattened buttocks, low gluteal cleft, or nonpalpable coccyx suggest sacral agenesis.
- GU exam: Assess genital and perineal sensation if neuropathy suspected. Contusions and bruises with abuse. Missed hypospadias and epispadias may present as incontinence.
- Vaginal vault: Labial adhesions in a child with a history of pooling of urine in the vagina.
- Ectopic ureteral orifice in the perineum is a cause of constant perineal wetness (only in girls).
- Rectal exam: Can confirm hard stool in vault or absence of anal sphincter tone
- Extremity exam: Observe walking; assess symmetry, coordination, atrophy, and leg muscle strength and size to rule out neuropathy.
- Neurologic exam: Reserved for cases of suspected neuropathy
- Observe voiding: Assess stream force, caliber, straining, character, and duration

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: May suggest renal disease:
  - Microhematuria or proteinuria; endocrinopathy:
  - Glucosuria; specific gravity >1.022 signifies normal concentrating ability. Polyurics have much lower values.
- Urine culture: Although uncommon, infection is a clinically important cause of incontinence.

Imaging

- KUB with lateral spine film:
  - May detect spinal anomalies or constipation
- Renal and bladder US:
  - Useful in child with daytime incontinence; finding of major anomaly uncommon
  - Recommended with history of UTI, urgency, dysuria, or outlet obstructive symptoms
  - Noninvasive study reassures physician, patient, and family of normal urinary tract
- VCUG:
  - Indicated with febrile UTI or hydronephrosis
  - Allows evaluation of urethra; rules out stricture, diverticulum, or valve
- MR urography: When duplicated system, ectopic ureters suspected
- Radioisotope scan: Assess of renal function, particularly in duplex kidneys when upper moiety heminephrectomy is being considered.

Diagnostic Procedures/Surgery

- Urodynamics: Seldom necessary with nonneurogenic voiding dysfunction. Advised with bony vertebral anomalies, neurogenic bladder, or neurologic or neurosurgical history
- Cystoscopy: If VCUG demonstrates endoscopically treatable anomaly (eg, posterior urethral valves); no role in evaluation of uncomplicated pediatric enuresis

Pathological Findings

- Incontinence classified as structural, neurogenic, uncomplicated, or complicated enuresis
- Structural incontinence: Anatomic abnormality leading to incontinence (see “Differential Diagnosis”)
- Neurogenic: Spinal dysraphism leading to incontinence (see “Differential Diagnosis”)
- Uncomplicated enuresis: Monosymptomatic, no other pathology, self-limited:
  - Isolated nocturnal enuresis, normal exam, and negative urine culture (very common)
  - Incidence of organic pathology no different than population at large
  - Radiographic imaging, UDS, and cystoscopy unnecessary
- Complicated enuresis: Collectively known as functional voiding disorders:
  - No obvious neurologic disorder; serious symptoms present (diurnal enuresis, constipation/encopresis, UTI, slow or intermittent stream, urgency and frequency)
  - Should be evaluated with KUB, renal and bladder US (full and empty)
  - Use of urodynamics varies; reserved for cases of associated upper tract and/or deterioration or after empiric therapy fails

– Lazy bladder syndrome (infrequent voider):

Usually older girls; present with recurrent UTIs; void only 2–3 times daily

Detrusor becomes hyporeflexia, capacity increases, decreased fullness sensation, due to misuse of the voluntary sphincter.

May have stress or overflow incontinence and associated encopresis/constipation

– Small-capacity, hypertonic bladder:

Similar to detrusor hyperreflexia but without a neurologic lesion

Etiology similar to infrequent voider; forceful constriction of external sphincter during uninhibited contraction

Voluntary sphincter dyssynergia produces bladder outlet obstruction and increased intravesical pressures.

Urodynamically, a small-capacity bladder with increased filling pressures noted; results in severe urgency and urge incontinence

External sphincter may relax incompletely; results in outflow obstruction and incomplete emptying.

VUR may also be present; particularly in patients with UTIs.

- Hinman-Allen syndrome (nonneurogenic neurogenic bladder)
- Daytime frequency syndrome:
  – Presents as acute onset of isolated daytime frequency in a previously toilet-trained child without UTI or uropathology: can be associated with new life stressor
- Giggle incontinence (enuresis risoria):
  – Complete/partial loss of bladder control with laughing or giggling while awake
  – No known specific cause; suggestions of imbalance between cholinergic and monoaminergic systems proposed
  – No associated organic disease; begins before puberty and resolves with time
- Unstable bladder:
  – Most common cause of daytime incontinence in children. Most frequent symptom is urgency with or without urge incontinence
  – Renal and bladder ultrasound and VCUG typically normal; UDS demonstrates uninhibited contractions during filling
  – Characteristic posturing to prevent leakage is common (eg, Vincent curtsy).
  – Unlike in a small-capacity bladder, complete relaxation of sphincter occurs, allowing complete emptying during voiding.
  – Associated with constipation/encopresis, UTIs, and VUR

DIFFERENTIAL DIAGNOSIS

- Structural incontinence:
  - Ureteral duplication with ectopia
  - Exstrophy–epispadias complex
  - Posterior urethral valves
  - Urethral duplication
  - Vesical fistula
  - Fibrotic bladder (postop or postradiation)
  - Labial adhesions
  - Urogenital sinus
  - Imperforate anus
- Neurogenic:
  - Myelodysplasia (meningocele, etc.)
  - Occult dysraphisms
  - Intradural lipoma, diastematomyelia
  - Tight filum terminale, dermoid cyst/sinus
  - Anterior sacral meningocele, cauda tumor
  - Sacral agenesis, spine trauma, cerebral palsy
- Isolated nocturnal enuresis
- Complicated enuresis:
  - Lazy bladder syndrome (infrequent voider)
  - Hinman-Allen syndrome
  - Daytime frequency syndrome
  - Giggle incontinence (enuresis risoria)
  - Unstable bladder

TREATMENT

- Behavioral modification: Timed voiding
- Treat constipation
- Biofeedback: Relaxation of external sphincter
- Dietary modification: Avoid caffeine, irritants
- Improve perineal hygiene with appropriate voiding techniques or CIC

MEDICATION

- Voiding dysfunction/detrusor overactivity:
  - Anticholinergics: Oxybutynin chloride 0.2 mg/kg, Ditropan XL 5 mg/d, hyoscyamine sulfate 0.03 mg/kg b.i.d., methantheline bromide 0.5 mg/kg b.i.d., tolterodine tartrate 0.02 mg/kg b.i.d., Detrol LA 2 mg/d

– -Adrenergic antagonists: Tamsulosin 0.4 mg q.h.s., Alfuzosin 10 mg q.h.s., Doxazosin 0.5 mg q.h.s., Terazosin 1 mg q.h.s.

- Constipation: MiraLax 17 g, lactulose 15 mL/d, mineral oil 1–2 tbsp p.r.n., docusate sodium, glycerin suppository, Senna

SURGERY/OTHER PROCEDURES

- Structural: To alleviate structural anomaly
- Neurogenic: Low-compliance bladder may need enterocystoplasty, urethral dilation, neural stimulation, or botulinum toxin injection
- Complicated enuresis: Surgery rarely indicated, reports of benefits of botulinum toxin injection or urethral dilation in cases of DSD

ONGOING CARE

PROGNOSIS

With urologic care, the prognosis is excellent.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Structural and neurogenic incontinence requires routine evaluation to rule out upper-tract deterioration and to monitor progress.
- Only refractory cases in the functional voiding dysfunction group need routine follow-up; the rest will likely spontaneously resolve.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Hinman Syndrome (Hinman-Allen Syndrome)
- Incontinence, Urinary, Adult Female
- Incontinence, Urinary, Adult Male
- Sacral Agenesis
- Spinal Dysraphism

CODES

ICD9

  - 788.30 Urinary incontinence, unspecified
  - 788.36 Nocturnal enuresis
  - 788.91 Functional urinary incontinence

ABBREVIATIONS

- CIC: Clean intermittent catheterization
- CNS: Central nervous system
- DSD: Detrusor sphincter dyssynergia
- GU: Genitourinary
- KUB: Kidney, ureters, bladder
- UDS: Urodynamic study
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

INFERTILITY, UROLOGIC CONSIDERATIONS

Craig S. Niederberger, MD

Hector Pimentel, MD

BASICS

DESCRIPTION

- Infertility is the inability of a couple to conceive within 1 yr of unprotected intercourse:
  - Primary infertility: Never fertile
  - Secondary infertility: Previously fertile and now infertile
- Normal couples will achieve conception at a rate of 20–25%/mo. By 6 mo, 75% will achieve pregnancy, and 90% will do so by 1 yr.

EPIDEMIOLOGY

15% of couples have infertility.

RISK FACTORS

Varicocele, family history of infertility and miscarriages, frequent hot baths, history of torsion, drug use, GU tract infections, endocrine disorders, chromosomal abnormalities, neurologic disease, radiation and chemotherapy, bilateral cryptorchidism, testicular trauma, hypospadias, inguinal, spinal, and retroperitoneal surgery, and cystic fibrosis

Genetics

- Important in 15% of azoospermic, 4% of oligospermic, and 1% of normospermic patients
- Most common genetic disorders are Y chromosome microdeletions, karyotype abnormalities, and CFTR gene mutations.

GENERAL PREVENTION

Avoidance of radiotherapy, chemotherapy, hot baths, or steam rooms

PATHOPHYSIOLOGY

3 categories:

- Pretesticular: Endocrine disorders
- Testicular: Abnormal sperm production
- Posttesticular: Abnormal sperm transport

COMMONLY ASSOCIATED CONDITIONS

- Pretesticular:
  - Hypogonadotropic hypogonadism: Low FSH, LH, and testosterone, with normal prolactin.
  - Medications: Exogenous testosterone, antipsychotic drugs, and LHRH agonist or antagonists.

– Renal failure

– Hypothyroidism

– Estrogen excess: Caused by tumors, hepatic dysfunction, or morbid obesity in men.

– Kallmann syndrome: X-linked defect, absent GnRH secretion, absent puberty, and anosmia

– Complex congenital syndromes: Laurence-Moon-Bardet-Biedl causes polydactyly and retinitis pigmentosa; Prader-Willi causes mental retardation, small hands, and hypotonicity.

– Pituitary/cranial trauma

– Prolactin excess: Hypogonadotropic hypogonadism, galactorrhea, gynecomastia, erectile dysfunction, and decreased libido

- Testicular:

– Varicocele: Affects up to 40% of infertile men and typically produces abnormalities in multiple semen parameters. Only palpable varicoceles are significant.

– Idiopathic: Found in 25% of patients.

– Gonadotoxins: Radiation, chemotherapy, and medications.

– Immunologic: Antisperm antibodies, testicular mumps causes seminiferous tubule scarring, febrile infections can decrease sperm production for several months.

– Cryptorchidism: Spermatogenesis not recovered if orchiopexy performed after puberty.

– Testicular cancer: Associated with decreased sperm production

– Sertoli-cell only syndrome: Absence of germ cells. Normal LH and testosterone levels.

– Maturation arrest: Can present with azoospermia or oligospermia; ART usually only treatment option.

– Genetic disorders/chromosomal abnormalities:

Klinefelter: 47XXY small firm testes, azoospermia, elevated estradiol levels, with sclerosis of seminiferous tubules; XYY syndrome males have azoospermia, and tall stature; XX males can have gynecomastia and azoospermia.

Y chromosome micro deletions

Deletions of DAZ and RBM genes

Ultrastructural sperm defects: Immotile cilia syndrome associated with situs inversus and frequent respiratory infections.

Androgenization defects: Caused by defects in testosterone, DHT enzyme, and androgen receptor synthesis.

Myotonic dystrophy: Testicular atrophy with normal LH and testosterone levels.

Noonan syndrome: Infertility with cryptorchidism

- Posttesticular:
  - Vasal or epididymal obstruction:
  - CBAVD associated with CFTR gene mutations. Female partners must be tested for CFTR gene mutations. Semen volume often normal and renal US used to evaluate for renal anomalies; acquired (vasectomy); and iatrogenic injury
  - Ejaculatory dysfunction: Anejaculation typically caused by retroperitoneal surgery, -blockers, and neuropathic disorders; retrograde ejaculation
  - Transurethral prostate surgery, bladder neck surgery, and the same causes as anejaculation
  - Both associated with low-volume ejaculate
  - Ejaculatory duct obstruction: Associated with low-volume ejaculate and caused by müllerian cysts and infectious scarring of GU tract

DIAGNOSIS

HISTORY

- Pneumonic TICS:
  - Toxic: Varicocele, chemical or radiation exposure, chemotherapy, hot baths, torsion, testicular injury, cigarette, alcohol, recreational drug use, anabolic steroid use, major medical illness, medications
  - Infectious: Mumps as child, STD, TB, recent febrile infections
  - Congenital: Cryptorchidism, bladder surgery, relatives with cystic fibrosis or difficulty conceiving
  - Sexual: Length of time trying to conceive, previous pregnancies with partner (or another partner), partner's previous pregnancies, fertility treatments, frequency of intercourse, use of lubricants, erectile dysfunction, timing of puberty. Ask about partner's history of endometriosis, fertility treatments, gynecologic infections, or irregular menses.

PHYSICAL EXAM

- Abnormal body habitus and hair distribution can suggest genetic abnormality such as Klinefelter syndrome.
- Genitourinary: Evaluate for hypospadias, penile curvature/plaques, absent vas (suggests CFTR mutation), varicoceles, epididymal lesions, seminal vesicle enlargement, and prostate tenderness (suggest infection).
  - Measured testis size: Distinguishes OA from NOA. Small size strongly correlated with NOA if azoospermia is present.

• Neurologic: Anal sphincter tone and neuropathy may indicate complex syndrome or possible ejaculatory dysfunction.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• SA: Minimal of 2 specimens. Preferably collected >7 days apart and with 3–7 days of abstinence prior to collection. Masturbation preferred method, and SA should be analyzed as soon as possible.

– Volume: >1.5 mL normal. If low, then a post ejaculatory urinalysis needed to distinguish between retrograde ejaculation and ejaculatory obstruction.

– Concentration/total: >20 × 106/mL and >40 × 106 per ejaculate normal. Varicocele most common cause for oligospermia.

– Azoospermia: Distinguish between obstructive (CBVAD, postvasectomy, müllerian cyst) and nonobstructive (testicular failure, hypogonadotropic hypogonadism). FSH and testicular size can reliably distinguish between OA and NOA. See “Diagnostic Procedures.”

– Motility: >50%. Consider cilia defects, antisperm antibodies, ejaculatory duct obstruction. Commonly associated with other abnormal semen parameters.

• Specialized semen analysis testing:

– Antisperm antibodies for IgA and IgG on head are clinically significant.

– WBC staining to evaluate for GU tract infection

– Vitality: Asses cell membrane integrity and distinguish necrospermia from immotile sperm.

• Endocrine workup: Serum testosterone and FSH indicated in all patients. LH and prolactin also needed if the exam indicates a pretesticular cause, severe oligospermia/azoospermia, or if testosterone and FSH is abnormal.

• Genetic screen: With findings suggestive of a genetic disorder, counsel on karyotype and other genetic testing. Patients with absence of the vas should have female partner tested for cystic fibrosis mutations to aid counselling.

Imaging

• Transrectal US: With low-volume ejaculate, when there is concern of OA. Look for seminal vesicle dilatation (>1.5 cm) or ejaculatory duct dilatation. Partial obstruction suggested by normal pH (>7.2) and small amounts of sperm.

• Renal US: Recommended in patients with unilateral absent vas and CBAVD to evaluate for renal abnormalities.

• MRI of brain: Used to evaluate for prolactinoma in patients with visual changes, headaches, and elevated prolactin.

Diagnostic Procedures/Surgery

)[B]

- Testis biopsy is typically unnecessary

Pathological Findings

While testis biopsy is typically not necessary, if performed findings include:

- Normal spermatogenesis which indicates OA.
- NOA patients may show maturation arrest, Sertoli-only syndrome, sclerosis of seminiferous tubules (Klinefelter), tumor, or signs of previous trauma.

DIFFERENTIAL DIAGNOSIS

See “Commonly Associated Conditions.”

TREATMENT

Initial goal should be to fix underlying problem to allow conception through intercourse. Female evaluation by reproductive specialist and coordinated care is crucial to ensure optimal outcomes.

MEDICATION

- Endocrine deficiencies:
  - Hypogonadotrophic hypogonadism: Treat with clomiphene citrate as exogenous testosterone will decrease fertility. For failures use hCG/or recombinant FSH.
  - Prolactinomas: Initially treated with bromocriptine or cabergoline.

)[C]

- Retrograde ejaculation: Pseudoephedrine 60 mg q.i.d., ephedrine 25 mg q.i.d., imipramine 25 mg b.i.d., or phenylpropanolamine 75 mg b.i.d..
- Antisperm antibodies: Steroids have been employed with minimal success.

SURGERY/OTHER PROCEDURES

)[A]; repair contralateral grade 2 or 3 varicoceles as well.

)[B] If absent sperm in vas then vasoepididostomy should be performed by microscopic specialist.

- Electroejaculation requires general anesthesia and allows sperm retrieval in men with neurologic lesions above the ejaculatory reflex. Men with lower spinal lesions should undergo penile vibratory stimulation initially.
- EDO surgery: Transurethral resection of ejaculatory ducts.
- OA: Reconstruction, if not possible, then TESE, TESA, or PESA with the option of cryopreservation.
- NOA: Micro-TESE, Multiple TESE/TESA.

ADDITIONAL TREATMENT

- ART: See “Prognosis” section
- Donor insemination and adoption are the final options for partners unable to conceive with ART.

ONGOING CARE

PROGNOSIS

ART:

)[B]

- In vitro and ICSI: 20–37% pregnancy rate per cycle, respectively.

COMPLICATIONS

- Scrotal and inguinal surgery: Bleeding, bruising, and pain
- Electroejaculation: Risk of autonomic dysreflexia
- ART: Increased risk of multiple gestations, low birth weight, and birth defects

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- SA should be acquired 3 mo after initiation of treatment.
- Age of female partner critical in dictating the length that treatments are attempted. Men with older female partners may appropriately choose to proceed more quickly to ART and donor insemination.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Azoospermia
- Oligoasthenoteratospermia
- Oligospermia
- Varicocele

CODES

ICD9

- 606.0 Azoospermia
- 606.1 Oligospermia
- 606.9 Male infertility, unspecified

ABBREVIATIONS

- ART: Assisted reproductive techniques
- CBAVD: Congenital bilateral absence of vas deferens
- CFTR: Cystic fibrosis transmembrane conductance regulator
- DAZ: Deleted in azoospermia
- DHT: Dihydrotestosterone
- EDO: Ejaculatory duct obstruction
- FSH: Follicle-stimulating hormone
- GnRH: Gonadotropin-releasing hormone
- GU: Genitourinary
- hCG: Human chorionic gonadotropin
- ICSI: Intracytoplasmic sperm injection
- IUI: Intrauterine insemination
- IVF: In vitro fertilization
- LH: Luteinizing hormone
- LHRH: Luteinizing hormone-releasing hormone
- MRI: Magnetic resonance imaging
- NOA: Nonobstructive azoospermia
- OA: Obstructive azoospermia
- PESA: Percutaneous epididymal sperm aspiration

- RBM: RNA binding motif
- SA: Semen analysis
- SPA: Sperm penetration assays
- STD: Sexually transmitted disease
- TB: Tuberculosis
- TESA: Testicular sperm aspiration
- TESE: Testicular sperm extraction
- US: Ultrasound
- WBC: White blood cell

INTERSTITIAL CYSTITIS

Nadya M. Cinman, MD
Robert M. Moldwin, MD

BASICS

DESCRIPTION

- Pelvic pain, pressure, or discomfort related to the bladder
- Typically, persistent urge to void or urinary frequency, in the absence of infection or other pathology
- Wide spectrum of symptom severity
- Nomenclature evolving: Common terms include IC/PBS, PBS/IC, BPS syndrome/IC
- 2 variants:
  - Classic (5%): Associated with Hunner ulcers: Focal regions of panmural inflammation
  - Nonclassic (95%): No gross inflammation seen upon office cystoscopy
- Diagnosis is 1 of exclusion
- Most care performed as outpatient

EPIDEMIOLOGY

- Female > Male (5–10:1)
- Average age of onset: 3rd–4th decade
- May be seen in childhood and in the elderly
- Symptom duration to diagnosis: Average 3–5 yr
- Estimated 20–70 cases/100,000 women: Prevalence increases when less strict criteria applied for diagnosis
- Hospitalization rarely necessary, but may be used for pain control of aggressive surgical care (ie, cystectomy)
- 1.3 women/100,000 and 0.2/100,000 men hospitalized for IC in 2000
- National expenditure increased by 29% between 1994 and 2000 to $66 million

RISK FACTORS

17-fold risk of IC in 1st-degree relatives

PATHOPHYSIOLOGY

- No specific causative factors known.
- Various etiologies include:
  - Abnormal epithelial permeability of lower urinary tract
  - Symptom initiation: Dysfunction of the GAG-containing mucous layer, which protects the bladder from caustic agents

– Antiproliferative factor: A frizzled 8 protein-related sialoglycopepide produced by urothelium; profoundly inhibits normal urothelial growth. High levels in IC patients; 90% sensitivity and specificity for IC; assay not commercially available

– Nerve upregulation (peripheral +/or central)

– Infection

– Autoimmune

– IC may be part of multisystem pain syndrome in view of its numerous comorbid conditions.

COMMONLY ASSOCIATED CONDITIONS

- Allergies
- Sensitive skin
- IBS
- Migraine headaches
- Fibromyalgia
- Vulvodynia
- PFD
- Sjögren syndrome

DIAGNOSIS

- NIDDK (1988) criteria for IC
- Originally developed for research purposes. Identifies patients with more severe disease and not recommended for use in clinical practice:

– Inclusion criteria:

Pain associated with urinary urgency and on bladder filling, that is relieved by bladder emptying

Suprapubic, pelvic, urethral, vaginal, or perineal pain

Glomerulations (epithelial hemorrhages) or bladder mucosal lesions (Hunner' ulcers) elicited by bladder hydrodistention

– Exclusion criteria:

Symptoms <9 mo

Age <18 yr old

Urinary frequency: <8 times/d while awake

Absence of nocturia

Bladder capacity >350 mL while awake

Absence of intense urge to void when filling bladder with 150 mL during cystometry

Phasic involuntary bladder contractions on cystometry, with filling rate of 30–100 mL/min

Urologic malignancy: Uterine, cervical, vaginal, urethral, or bladder tumors

Bladder/ureteral calculi

Vaginitis

Active genital herpes

Urethral diverticulum

Cyclophosphamide/chemical cystitis

TB cystitis

Bacterial cystitis or prostatitis within 3 mo

Pelvic radiation/radiation cystitis

Symptoms that are relieved by antibiotics, anticholinergics, or antispasmodics

HISTORY

- Onset and duration of symptoms: May vary from acute, subacute, intermittent
- Prior diagnosis of bacterial cystitis, overactive bladder, endometriosis, prostatitis
- Urinary problems during childhood, such as nocturnal enuresis, urethral stenosis, UTI
- Pattern of voiding: Discomfort/pain associated with bladder filling or emptying, frequent urination, >8 times/d; sensation of complete emptying; nocturia; difficulty initiating urine flow; difficulty emptying bladder
- Symptom failure with anticholinergics or antispasmodics; antibiotics
- Pain worsens with restrictive clothing; stress; certain foods/beverages (coffee, spicy food, acidic drinks, alcohol)
- Dyspareunia (may be bladder based or PFD)
- Constipation (associated with PFD or IBS)

PHYSICAL EXAM

- Abdominal exam usually unremarkable
- Pelvic exam: Rule out GU/GYN malignancy, infection, herpetic lesions, urethral diverticulum
- Pelvic exam often reveals pain to palpation of anterior bladder wall in region of bladder neck/fundus
- Levator tenderness and/or vulvar tenderness: Very common (levator tenderness present in ~70% of IC patients)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture: Rule out infection

- Urine cytology recommended for patients with higher risk for bladder cancer (ie, older age, smoking history)

Imaging

Routinely, no imaging studies are necessary

Diagnostic Procedures/Surgery

- Bladder hydrodistention under anesthesia:
  - Distend under cystoscopic exam (80–100 cm H_2O), then release irrigant; inspect bladder for glomerulations/Hunner ulcers
  - Assess bladder capacity: Typically <800 cc
  - Gold standard for IC diagnosis; however, recent data suggests poor sensitivity and specificity, especially in patients early in course of the condition
  - Bladder biopsy: Not recommended, unless, abnormality of the bladder wall (ie, Hunner ulcer)
- PST: Intravesical saline administered as control, then intravesical instillation 0.4 M KCl solution: Increased irritative voiding symptoms and/or pain with KCl solution suggest bladder hyperesthesia. Limited sensitivity and specificity
- Anesthetic challenge: Sodium-channel blocker (lidocaine, bupivacaine) alkalinized or nonalkalinized instilled into bladder. Decrease in pelvic pain suggests bladder source
- Urodynamics: Not routinely indicated in the initial evaluation; various complaints may warrant this evaluation (poor urine flow, urinary retention, or urinary incontinence)
- Commonly employed questionnaires:
  - Useful for monitoring patient symptoms
  - No questionnaire can accurately diagnose interstitial cystitis; use as screening tool is controversial:

    The University of Wisconsin IC scale

    O'Leary-Sant IC symptom index and IC problem index

    Pelvic Pain and Urgency/Frequency scale

Pathological Findings

Pathognomonic Hunner ulcers seen in classic variant of IC (5%)

DIFFERENTIAL DIAGNOSIS

- UTI (dysuria, frequency, hematuria, back pain)
- Chronic urethral syndrome
- Overactive bladder syndrome (painless sudden urgency without warning)
- Endometriosis
- Vulvodynia

- Prostatitis

TREATMENT

MEDICATION

First Line

Only 2 medications currently FDA-approved for IC treatment:

- Pentosan polysulfate sodium (Elmiron): 100 mg PO t.i.d.; augments protective GAG layer of bladder to minimize irritative effects
- 50% DMSO (RIMSO-50), weekly intravesical instillation for 6 wk, often used as cocktail with triamcinolone, heparin sodium, $NaHCO_3$:
  - All other medications are off-label
  - Efficacy studies vary widely relative to level of evidence.
- Intravesical agents may be used as 1st-line therapy or in conjunction with oral agents upon physician discretion.

Second Line

- Amitriptyline (Elavil): TCA; 75 mg PO q.h.s.
- Hydroxyzine (Atarax/Vistaril): H1 histamine receptor blocker; 25–75 mg/d PO
- PPS, 100 mg t.i.d.
- Antiseizure: Gabapentin
- Narcotics: To be discouraged
- Cimetidine: 300 mg PO b.i.d.
- Cyclosporine (rare use; adverse events)
- Urinary anesthetics: Pyridium, methylene blue
- Intravesical:
  - Dimethylsulfoxide (DMSO) solution
  - Alkalinized lidocaine +/ heparin sodium
  - Other intravesical agents: Clorpactin, silver nitrate (resiniferatoxin and BCG found ineffective)

SURGERY/OTHER PROCEDURES

- Bladder hydrodistention, fill for 2–5 min, pressure 80–100 cm H_2O; assess symptomatic relief 3 wk postoperatively
- Transurethral resection/fulguration of Hunner ulcers
- If severe disease and all other therapeutic options have failed (rare):
  - Supratrigonal cystectomy + enterocystoplasty (primarily useful for classic IC with severe pain and significant decrease bladder capacity); patients must understand potential need for intermittent catheterization postoperatively.

– Urinary diversion +/ total cystectomy

ADDITIONAL TREATMENT

- During symptom flare-ups, 1st rule out UTI.
- Refrain from consumption of potentially symptom-inciting foods and beverages.
- Treat comorbid conditions that may worsen pelvic pain: Constipation (cathartics, change in diet), pelvic floor dysfunction (topical heat application, muscle relaxants, physical therapy), vaginitis (depends on cause, but may include topical estrogens, steroids, antifungal agents, etc.)
- The least invasive therapy is recommended, which may include watchful waiting.

General Measures

Patient education:

- Spend extra time during initial encounter
- Patient should understand there is no known cure; treatment is for symptom control
- Interstitial Cystitis Association: www.ichelp.org
- Stress reduction, exercise, and diet modification may be helpful

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Biofeedback/pelvic floor rehabilitation
- Neuromodulation: Direct sacral nerve stimulation
- TENS
- Acupuncture and hypnosis
- Hyperbaric oxygen
- Physical therapy

ONGOING CARE

PROGNOSIS

Not life-threatening; morbidity is variable, based upon wide spectrum of symptom severity

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Depends on symptomatology

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Overactive Bladder
- Potassium Sensitivity Testing

CODES

ICD9

595.1 Chronic interstitial cystitis

ABBREVIATIONS

- BCG: Bacillus Calmette Guérin
- BPS: Bladder pain syndrome
- DMSO: Dimethylsulfoxide
- GAG: Glycosaminoglycogan
- GU: Genitourinary
- GYN: Gynecological
- IBS: Irritable bowel syndrome
- IC: Interstitial cystitis
- NIDDK: National Institute of Diabetes, Digestive, and Kidney Diseases
- PBS: Painful bladder syndrome
- PFD: Pelvic floor dysfunction
- PPS: Pentosan polysulfate sodium
- PST Potassium sensitivity test
- TB: Tuberculosis
- TCA: Tricyclic antidepressant
- TENS: Transcutaneous electrical nerve stimulation
- UTI: Urinary tract infection

LATEX ALLERGY, UROLOGIC CONSIDERATIONS

Mark Horowitz, MD

Brian K. Marks, MD

Rosalia Misseri, MD

BASICS

DESCRIPTION

- Local or systemic allergic reaction to NRL-based products
- Rapid demand for gloves and other products to prevent blood-borne pathogens such as HIV led to a rapid expansion of factories producing latex products. This was associated with a rapid rise in the incidence of latex allergies in the 1980s, thought to be due to impurities in poorly processed natural latex rubber.

EPIDEMIOLOGY

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ALERT

Use caution when examining any child for dysfunctional voiding especially if the child has neurologic symptoms or suspected spina bifida.

RISK FACTORS

- Atopic dermatitis history
- Food allergies: Banana, kiwi, avocado, passion fruit, chestnut
- Occupational including healthcare, food service, rubber manufacturing
- Spina bifida, GU or GI congenital malformations:

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- Spinal cord injury
- Intermittent catheterization

GENERAL PREVENTION

- Prevent early sensitization to latex allergens through use of nonlatex alternatives or limit contact with latex products especially in high-risk populations.
- Use of latex-free gloves and other products in people with known NRL allergy.

PATHOPHYSIOLOGY

- Sensitization occurs after contact with the allergen and is the 1st required step:
  - Increased likelihood with moisture and repeated mechanical damage or friction.

– Increased likelihood when there is disruption of the epidermal barrier (ie, dermatitis or abrasions)

- Immediate hypersensitivity reaction, type I:
  - Less common mechanism, but most life-threatening
  - Sensitization to latex proteins
  - Pre-formed IgE from prior sensitization is bound to mast cells.
  - Antigen binding releases pre-formed vasoactive compounds and initiates the generation of secondary mediators.
  - Generates nearly immediate local and systemic reactions (anaphylactic).
- Delayed hypersensitivity reaction, type IV:
  - Most common mechanism
  - Cell-mediated response to accelerants and other residual compounds from production.
  - Mediated by CD4 cells
  - Presents as a contact dermatitis within 24–48 hr of exposure
- Some potential items that may contain latex in the healthcare setting include: Gloves, stethoscopes, IV tubing, syringes, drains, tourniquets, BP cuffs, respirator circuits, oxygen masks, catheters (Foley, red rubber).

COMMONLY ASSOCIATED CONDITIONS

- Spina bifida
- Congenital GU or GI anomalies
- Spinal cord injury

DIAGNOSIS

HISTORY

- Detailed history of surrounding events:
  - Latex gloves
  - Foley catheter or Texas catheter
  - Latex balloon use
- History of the aforementioned risk factors
- Allergy history
- Symptoms:
  - Dizziness
  - Dyspnea
  - Pruritus
  - Rhinitis

  - Tearing

PHYSICAL EXAM

- Use nonlatex exam gloves
- Mucocutaneous manifestations:
  - Erythema
  - Edema
  - Papules, macules, urticaria
  - Allergic rhinitis
  - Allergic conjunctivitis
  - Angioedema
- Cardiopulmonary manifestations:
  - Tachypnea
  - Stridor, wheezing
  - Tachycardia
  - Hypotension
  - Shock

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[B]:

  - Immunoassay of serum IgE antibodies to latex allergens
  - Unaffected by concurrent therapy

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Diagnostic Procedures/Surgery

)[B]:

- Latex protein is diluted in solution, dripped on forearm, and pricked with a lancet.
- Most sensitive for type I and type IV reactions
- Dangerous due to risk of anaphylaxis.
- Rarely used

Pathological Findings

Biopsy of skin lesions (type IV hypersensitivity):

- Perivascular cuffing of CD4 cells identified using anti-CD4 antibody stain
- Vesicular dermatitis with dermal and epidermal mononuclear infiltrates

DIFFERENTIAL DIAGNOSIS

- Allergic rhinitis
- Asthma
- Atopic dermatitis (ie, eczema)
- Cardiogenic shock
- Conjunctivitis
- Contact dermatitis to other allergens (ie, nickel products)
- Septic shock
- Systemic allergic reaction to another allergen, including medications or food products.

TREATMENT

- There is no cure for latex allergy.
- Personal avoidance of latex for health care workers and patients
- Reducing unnecessary exposure to latex in healthcare setting
- Avoid latex gloves during physical and mucosal exam of patients. Use latex-free products like vinyl or nitrile gloves and silicone catheters, latex-free masks and intubation equipment.
- Label charts of latex allergic patients.
- Medical allergy bracelets
- Consider scheduling procedure as 1st case of day to prevent exposure to aerosolized latex.

MEDICATION

- Antihistamines
- Corticosteroids
- IV fluid challenge
- Topical steroids (in type IV reaction)
- Epinephrine injections may be required in severe reactions or anaphylactic reactions.

ADDITIONAL TREATMENT

- Corticosteroids and H1 and H2 antagonists as pretreatment, sublingual desensitization, subcutaneous injection protocols, immunotherapy with T-cell epitope peptide
- Most health care facilities have banned latex helium-filled balloons.
- Many facilities are striving to become latex-free.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

No evidence for specific herbal or alternative medications

ONGOING CARE

PROGNOSIS

- Depends on the severity of the reaction and the timely identification of the causative agent

- Generally good if proper precautions are used
- Type I hypersensitivity: Risk of fatal anaphylaxis, and/or respiratory compromise

COMPLICATIONS

- Anaphylactic shock
- Concomitant bacterial suprainfection in the region of contact dermatitis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Inpatient admission may be necessary until cardiopulmonary risk is reduced.
- Allergy identification band, Medi-Alert bracelet
- Avoid foods with cross-reactivity:
  - Banana, kiwi, chestnut, avocado

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Dysfunctional Voiding
- Myelodysplasia (Myelomeningocele, Spinal Dysraphism), Urologic Considerations
- Spina Bifida/Spina Bifida Occulta, Urologic Considerations

CODES

ICD9

V15.07 Allergy to latex

ABBREVIATIONS

- BP: Blood pressure
- GI: Gastrointestinal
- GU: Genitourinary
- HIV: Human immunodeficiency virus
- IgE: Immunoglobulin E
- IV: Intravenous
- NRL: Natural rubber latex
- RAST: Radioallergosorbent test

LIBIDO, DIMINISHED

Mohamad W. Salkini, MD
James F. Donovan, MD

BASICS

DESCRIPTION

- Libido (sexual drive) is mediated by the cerebral cortex and limbic system.
- 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.

Geriatric Considerations

Loss of libido increases with advancing age. Women may experience decreased libido with menopause.

Pediatric Considerations

Loss of libido can start at a young age without being noticed, especially when there is a congenital syndrome.

Pregnancy Considerations

Loss of libido is seen more often in pregnancy and that is attributed to hormonal, emotional, and physical factors.

EPIDEMIOLOGY

- 10–15% of men
- 20–25% of women

RISK FACTORS

- Therapy for prostate cancer
- Congenital absence of the testicles
- Inflammatory insults to the testicles
- Surgical injury or removal of the testicles

Genetics

Loss of libido may be associated with some of the genetic disorders/syndromes listed below.

PATHOPHYSIOLOGY

- Psychological:
  - 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:
  - Hypogonadism: Androgen deficiency, particularly testosterone, whether primary (testicular defect) or secondary to hypothalamic-pituitary dysfunction
  - Hyperprolactinemia with and without pituitary lesion.
  - Thyroid: Both hyper- and hypothyroidism can lead to diminished sexual desire.
- Drugs: -Blockers, clonidine, diuretics, lithium, major tranquilizers, methyldopa, sedatives, ketoconazole, -blockers, DHT-inhibitors, cimetidine, antiandrogens, androgen analogues, SSRIs.
- Prostatitis
- Temporal lobe epilepsy
- Chronic and serious diseases can lead to loss of libido through psychological or physiologic effects.

COMMONLY ASSOCIATED CONDITIONS

- ED and infertility may be associated with loss of libido and vice versa.
- Hypothyroidism
- Alcoholism
- Syndromes that manifest by testicular failure such as:
  - 17-Hydroxylase deficiency
  - Anorchia
  - Autoimmune polyendocrine syndrome
  - Inactivating mutations of the LH-receptor gene
  - Klinefelter syndrome
  - Mutations of the steroid 5-reductase gene

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
  - Patients with hypogonadism may note decreased or absent ejaculation.
  - If semen volume is normal, it is unlikely that endocrine factors are responsible for loss of libido.
- History of psychiatric illness
- Symptoms to suggest decreased testosterone: ED, increased irritability or depression, fatigue, reduced muscle mass and strength, inability to concentrate, decreased bone dens-

ity/osteoporosis

- Previous/current medication
- History of endocrine disorder
- Therapy for prostate cancer
- Chronic alcoholism may result in decreased serum testosterone, testicular atrophy, and decreased libido.

PHYSICAL EXAM

- Assessment of secondary sexual characteristics. Absence of secondary sexual characteristics suggests hormonal etiology.
- Detailed exam of external genitalia for abnormalities
- Assessment of testicular volume

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum testosterone
- Serum prolactin
- If any disturbances in the above, then serum FSH and LH measurements

Imaging

MRI of brain: If prolactin is elevated

DIFFERENTIAL DIAGNOSIS

- Psychiatric disturbances
- Hormonal disturbances
- Drug-induced
- Chronic and serious diseases

TREATMENT

- Determine the cause and correct it if possible.
- Identify potential medications causing libido issues.
- Psychiatric consultation/sex function therapist
- Endocrinology consultation

MEDICATION

- Decreased testosterone: Hormonal supplementation. See chapter “Testosterone, Decreased (Hypogonadism)” for replacement dosing
- Patient interested in sustaining fertility: Avoid exogenous testosterone; stimulate endogenous testosterone with hCG
- If sexual dysfunction is identified as the cause: sildenafil, vardenafil, and tadalafil are potentially useful 1st-line therapies

- Bromocriptine for prolactin-secreting pituitary adenoma

SURGERY/OTHER PROCEDURES

Only useful for pituitary adenomas causing hyperprolactinemia

ADDITIONAL TREATMENT

Postmenopausal women with decreased libido who are not receiving estrogen therapy have modest success using an experimental testosterone patch delivering 300 g/d testosterone.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

L-arginine, yohimbine are touted but not proven

ONGOING CARE

PROGNOSIS

The prognosis is good when there is a treatable underlying cause for the loss of libido. Otherwise it can be permanent.

COMPLICATIONS

Loss of libido can result in depression, infertility, and ED.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Men treated with androgens should be followed closely with DRE and PSA every 6 months.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Erectile Dysfunction
- Female Hypoactive Sexual Desire Disorder

CODES

ICD9

- 302.71 Hypoactive sexual desire disorder
- 799.81 Decreased libido

ABBREVIATIONS

- DHT: Dihydrotestosterone
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- hCG: Human chorionic gonadotropin
- LH: Luteinizing hormone
- PSA: Prostate-specific antigen
- SSRI: Selective Serotonin Reuptake Tnhibitor

LYMPHADENOPATHY, INGUINAL

Michelle J. Kim, MD

Ihor S. Sawczuk, MD

BASICS

DESCRIPTION

Palpable inguinal lymph nodes secondary to infectious, inflammatory, or neoplastic processes.

EPIDEMIOLOGY

)[A]:

- Inguinal lymph nodes are most common site of metastasis.
- Metastasis is stepwise from superficial inguinal to deep inguinal to pelvic nodes with low rates of skin lesions.
- Metastasis can be bilateral.
- 50% of patients present with palpable inguinal nodes.
- 50% of patients with palpable nodes have metastatic disease.
- 20% of patients without palpable nodes have nodal metastasis.

)[A]:

- Chancroid: 33 cases reported
- Herpes: 20% seropositive rate in general population, 371,000 new office visits
- LGV: Rare
- Syphilis: 36,935 cases
- HIV: 1.1 million cases

- 14% of all presentations of palpable lymphadenopathy are inguinal

RISK FACTORS

- Genital hygiene:

)[A]

- Low rates of penile cancer in ethnicities that practice neonatal circumcision

- Trauma
- Infections of the perineum, perianal, perirectal, or urethral
  - HPV is associated with penile cancer
- Neoplasia:
  - For penile carcinomas, corporal invasion, high-grade disease, and vascular invasion are at high risk for lymph node metastasis

GENERAL PREVENTION

- STD counseling and education

)[A]

- Genital hygiene

PATHOPHYSIOLOGY

- Inguinal nodes act as drainage for the penis, urethra, lower extremities, lower abdominal wall up to the umbilicus, gluteal regions, and anal canal
- Superficial inguinal nodes lie above the fascia lata within the femoral triangle:
  - Femoral triangle is bound by the inguinal ligament, sartorius and adductor longus muscles
  - Drain the lower extremity, preputial, penile, and scrotal skin
  - Drain the glans penis and corpora
- Deep inguinal nodes:
  - Lie deep to the fascia lata and include Cloquet node, which is at the apex of the femoral canal

DIAGNOSIS

HISTORY

- Age:
  - Neoplasias more common in older patients.
  - Penile cancer most commonly presents in 6th decade.
  - Infections more common in younger patients.
- Sex
- History of trauma
- Sexual history
- Occupational history:
  - Scrotal cancer has higher incidence in chimney sweeps.
- Ethnicity:
  - Penile cancer more common in South America and Africa

PHYSICAL EXAM

- Vital signs:
  - Fever may be a sign of infection
- General appearance:
  - Signs of systemic disease
  - Cachexia or weight loss
- Noninguinal nodal exam:
  - For evidence of generalized lymphadenopathy
- Abdominal exam

- Inguinal node exam:
  - Look for extent of involvement, size, tenderness, fluctuance, purulence, overlying erythema, possible involvement of femoral vessels.
- Genitalia exam:
  - Examine for penile, scrotal, preputial lesions.
  - Look for erythema, fluctuance, or purulence.
  - Painful ulcers with herpes or chancroid
  - Painless ulcers with granuloma inguinale, syphilis, or neoplasias
- Digital rectal exam:
  - Examine for presence of infection, erythema, tenderness, or purulence.
- Lower extremity exam:
  - Inspect for lesions, erythema, phlebitis, purulence, scaling of skin.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[A]:

- Chancroid: Haemophilus ducreyi on special culture; only 80% sensitive.
- Herpes: Viral culture for HSV-1 and -2
- LGV: Culture positive in only 30–50%; complement fixation titers or immunofluorescence confirms diagnosis.
- Syphilis: Darkfield microscopy of ulcer bed, nontreponemal tests (VDRL and RPR), treponemal tests (FTA-ABS)
- HIV: ELISA with Western blot confirmation

Imaging

- Inguinal US:
  - May help identify invasion into surrounding structures (ie, femoral vessels)
- CT of the abdomen and pelvis:
  - Sensitivity/specificity 36%/100%
- Lymphangiogram:
  - Neoplastic lesions appear irregular and display filling defects
  - Older exam, rarely performed

Diagnostic Procedures/Surgery

- Biopsy of primary lesions
- Culture of primary lesion
- Lymph node biopsy: Open or needle

Pathological Findings

- Infectious:
  - Superficial infections of the lower extremities usually are due to staph
  - Chancroid:

H. ducreyi; combination of painful genital ulcer with tender suppurative adenopathy

  - Herpes: HSV I and 2, can have painful, firm nodes.
  - LGV:

Chlamydia trachomatis, unilateral tender lymphadenopathy with self-limited genital ulcer

  - Syphilis:

Treponema pallidum, secondary infection leads to firm nodes

  - HIV: As part of generalized lymphadenopathy
- Neoplastic:
  - Penile carcinoma
  - Scrotal carcinoma
  - Distal urethral carcinoma
  - Vaginal or vulvar carcinomas
  - Cutaneous carcinomas (melanoma or squamous cell carcinomas)
  - Anal carcinomas
  - Lymphomas

TREATMENT

- Penile carcinoma:
  - Observation reasonable for low-risk patients without palpable nodes (low grade, no vascular invasion, stages Tis, Ta, or T1).
- Due to high rates of coinfection of STDs, so if no response to proper therapy, consider diagnosis of a secondary infection.
- Appropriate antibiotics for STD

MEDICATION

- Antibiotics for penile cancers:
  - Treat for 4–6 wk with cephalexin 500 mg PO t.i.d., then reassess node status
- Chancroid: Azithromycin PO 1 g in one dose, or ceftriaxone 250 mg IM in 1 dose, or ciprofloxacin 500 mg PO b.i.d. for 3 days, or erythromycin base 500 mg PO t.i.d. for 7 days
- Herpes: Acyclovir 400 mg PO t.i.d. for 7–10 days, or acyclovir 200 mg PO 5 times a day for 7–20 days, or famciclovir 250 mg PO t.i.d. for 7–10 days, or valacyclovir 1 g PO b.i.d. for 7–10 days
- LGV: Doxycycline 100 mg PO b.i.d. for 21 days, or erythromycin 500 mg PO q.i.d. for 21 days

- Syphilis: Benzathine penicillin G 2.4 million units IM in 1 dose
- HIV: Multidrug cocktail of reverse transcriptase inhibitors
- Lymphoma usually treated with systemic chemotherapy

SURGERY/OTHER PROCEDURES (4)[A]

- Incision and drainage if abscess is present
- Sentinel lymph node biopsies:
  - Up to 0–20% false-negative rates even with addition of dynamic scintigraphy
- Prophylactic inguinal LAD:
  - For nonpalpable lymph nodes
  - 70–80% false-negative rates
  - Recommended for stage T2 or greater, high-grade tumors, or vascular invasion
- Superficial inguinal LAD:
  - Removal of nodes superficial to fascia lata
  - Indicated for prophylactic LAD
  - If positive nodes on frozen section, complete total LAD on that side.
- Modified inguinal LAD:
  - Can perform removal of superficial and deep nodes
  - Smaller skin incision, excludes area lateral to femoral artery, preservation of the saphenous vein, thicker skin flaps, no sartorius muscle transposition
- Radical inguinal lymphadenectomy:
  - Larger skin incision, saphenous vein ligation, sartorius flap

ADDITIONAL TREATMENT

Radiotherapy

For penile cancer associated LAD, may be used for palliation:

- Risk of skin ulceration or breakdown, lymphedema
- Role of monotherapy is questionable

Additional Therapies

Chemotherapy for penile cancer:

- Use in combination with surgery for bulky metastasis from penile carcinoma or as monotherapy for unresectable disease
- Single agents include bleomycin, methotrexate, and cisplatin.
- Combination therapy includes cisplatin with 5-fluorouracil, cisplatin/bleomycin/methotrexate, or vincristine/bleomycin/methotrexate.

ONGOING CARE

PROGNOSIS

Extent of lymph node metastasis is most important factor in determining survival from penile cancer.

COMPLICATIONS

- Infection
- Bleeding:
  - Erosion into femoral vessels
- Lymphedema

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow-up 6 wk after initiating therapy.

REFERENCES

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- HIV/AIDS Urologic Considerations
- Herpes Simplex, Genital
- Sexually Transmitted Diseases, General
- Penis, Cancer, General.

CODES

ICD9

- 091.4 Adenopathy due to secondary syphilis
- 187.4 Malignant neoplasm of penis, part unspecified
- 785.6 Enlargement of lymph nodes

ABBREVIATIONS

- HIV: Human immunodeficiency virus
- HPV: Human papilloma virus
- LAD: Lymphadenectomy
- LGV: Lymphogranuloma venereum
- STD: Sexually transmitted disease

LYMPHADENOPATHY, PELVIC AND RETROPERITONEAL

Neil E. Fleshner, MD

Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Presence of enlarged nodal tissue in the pelvis and/or retroperitoneum
- Definitions can vary but a solitary node from 1.0–1.5 cm in short axis or multiple nodes >1.0 cm are considered to be pathologically enlarged in the pelvis and/or retroperitoneum.
- Often discovered when imaging performed for staging of tumors
- Usually a nonacute but potentially life-threatening condition

EPIDEMIOLOGY

Lymphoma is the most frequent malignant tumor in the retroperitoneum and the most common cause of lymphadenopathy there.

RISK FACTORS

- Tumor-associated syndromes: Von Hippel Lindau, cryptorchidism
- Patients with primary tumors of the genitourinary system (renal, prostate, testicular, penile, cervical, ovarian)
- Immunosuppressed patients (eg, HIV)
- Patients with inflammatory conditions of the pelvis

PATHOPHYSIOLOGY

Usually 1 of 3 causes: Neoplastic, infectious (including granulomatous inflammation), or inflammatory (reactive)

DIAGNOSIS

HISTORY

- Most adenopathy incidental
- Constitutional: Weight loss, night sweats (especially with lymphoma), fatigue, fever
- Local compressive symptoms: Bowel obstruction, hydronephrosis/pyelonephritis/uremia, lower limb edema (vascular/lymphatic compromise)
- Severe infection on perineum/pelvis (often with associated inguinal adenopathy)
- Constitutional symptoms
- Primary GU, GI, or gynecological tumor
- Lymphadenopathy elsewhere is possible
- Paraneoplastic syndromes (eg, breast tenderness, anemia, etc.)

PHYSICAL EXAM

- Determine the presence of palpable lymphadenopathy (neck, supraclavicular, inguinal, axillary)

- Skin for signs of melanoma
- Chest:
  - Clear breath sounds
  - Breast tissue or tenderness
- Abdominal exam: Palpable mass, bruits, thrills
- Pelvic exam in case of possible gynecologic malignancy
- Scrotal exam: Testicular mass, right-sided varicocele
- Penile exam for lesions
- Digital rectal exam for prostate nodule and fecal occult blood testing
- Perineum: Cellulitis, abscess
- Lower extremity edema

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC, ESR, exam of peripheral smear
- Creatinine (for imaging and to check renal function)
- Urinalysis for hematuria
- Urine cytology
- Tumor markers:
  - PSA: Prostate cancer
  - AFP, -hCG, LDH: Testicular cancer
  - CA-125: Ovarian cancer
  - CEA: Colon cancer

Imaging

- May diagnose the cause of the adenopathy (eg, renal mass)
- US:
  - Can pick up larger masses
  - False negatives are significant
- CT/MRI:

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  - Nodes <7–10 mm considered reactive
  - CT generally considered best test (use MRI if contrast contraindicated)
- PET:
  - May be helpful to determine fibrosis from metabolically active nodes (especially post chemotherapy testicular cancer)

)[C]

– Some studies have shown that PET scanning can define testicular relapse sites before CT scanning.

Diagnostic Procedures/Surgery

- Basic principle is nodal tissue exam unless diagnosis is clear (ie, testicular or prostate tumor)
- CT-guided biopsy:
  - Best way to obtain nodal tissue
  - Not always feasible if close proximity to major vessels
- Laparoscopic biopsy in selected cases
- Always ask for lymphoma testing for markers if suspicion is high.
- Bone marrow biopsy with cytogenetic analysis for some cases of lymphoma
- Cystoscopy, and/or ureteroscopy with biopsy if bladder cancer suspected
- TRUS prostate biopsy if prostate cancer suspected
- Cervical biopsy for cervical cancer

Pathological Findings

Numerous, depends on cause (see below)

DIFFERENTIAL DIAGNOSIS

- Tumor:
  - Primary lymphatic: Lymphoma (non-Hodgkin and Hodgkin, others)
  - Secondary: Renal, GI (carcinoid, lymphomas), urothelial, prostate, melanoma, penile, germ cell, cervical, ovarian, uterine, colorectal
- Infectious/Inflammatory:
  - Granulomatous: TB, sarcoidosis, histoplasmosis, lymphogranuloma venereum, Castleman disease, etc.
  - Nongranulomatous: Viral, bacterial (if abscess in local areas), sinus histiocytosis, retroperitoneal fibrosis
- Others: Neoplastic, non-neoplastic and cystic retroperitoneal masses (lymphocele, urinoma, hemorrhage), aneurysms

TREATMENT

MEDICATION

As necessary, based on the diagnosis of the primary disease

SURGERY/OTHER PROCEDURES

- Open or laparoscopic nodal sampling may be required in some cases.
- Lymphadenectomy is often considered therapeutic in some cases of testicular and bladder cancer.

ADDITIONAL TREATMENT

General Measures

- Underlying cause must be treated appropriately.
- Wide variety from no treatment to chemotherapy/surgery and/or radiotherapy

Radiotherapy

For certain causes such as seminoma

Additional Therapies

- In some borderline cases, reimaging for signs of growth or assessing therapeutic response to therapy (eg, hormonal therapy in prostate cancer) is best overall approach.

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ONGOING CARE

PROGNOSIS

Widely variable

COMPLICATIONS

Severe lymphadenopathy can result in lower extremity edema

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Based on primary disease process

REFERENCES

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Groin/Inguinal Mass
- Individual Disease Entities
- Retroperitoneal Mass and Cysts

CODES

ICD9

785.6 Enlargement of lymph nodes

ABBREVIATIONS

- AFP: -Fetoprotein
- CBC: Complete blood count
- CEA: Carcinoembryonic antigen
- CT: Computed tomography
- ESR: Erythrocyte sedimentation rate
- GI: Gastrointestinal
- GU: Genitourinary
- hCG: Human chorionic gonadotropin
- HIV: Human immunodeficiency virus
- LDH: Lactate dehydrogenase
- MRI: Magnetic resonance imaging
- PET: Positron emission tomography
- PSA: Prostate-specific antigen
- TB: Tuberculosis
- TRUS: Transrectal ultrasonography
- US: Ultrasound

LYMPHOCELE, PELVIC

Stephen E. Strup, MD
Bradley W. Warner, MD

BASICS

DESCRIPTION

- A localized encapsulated collection of lymphatic fluid created by disruption of lymphatic vessels
- A collection of lymph fluid in a cavity that is not lined by epithelium
- Generally occurs following extraperitoneal surgery such as lymphadenectomy or renal transplantation

EPIDEMIOLOGY

- Incidence: 0.6–18% after renal transplant
- Incidence: 0.7–15% after pelvic lymphadenectomy; can be up to 10–27% if all patients are imaged with US

RISK FACTORS

- Recent pelvic surgery (ie, PLND, open or laparoscopic), renal transplant, RPLND, gynecologic procedures:
  - Extended PLND > conventional PLND
  - Extraperitoneal > transperitoneal procedures
- Prior radiation or chemotherapy
- Anticoagulation may increase risk

GENERAL PREVENTION

Meticulous lymphadenectomy with clips on proximal end of lymphatic vessels; standard electrocautery may not adequately seal lymph channels

PATHOPHYSIOLOGY

- Lymphatic fluid collects in the extraperitoneal space due to continued lymphatic leakage.
- Transperitoneal pelvic lymphadenectomy is unlikely to be associated with the development of a lymphocele.

COMMONLY ASSOCIATED CONDITIONS

- Prostate cancer
- Bladder cancer
- Penile cancer
- Renal transplantation
- Gynecologic malignancy

DIAGNOSIS

HISTORY

- Recent pelvic surgery, particularly involving lymphadenectomy
- Prior chemotherapy or pelvic radiation
- Timing of onset of symptoms:
  - Abscess, hematoma, and urinoma tend to occur earlier in the postoperative period
- Urinary frequency (if compressing bladder)
- Constipation
- Flank pain
- Lower extremity pain/swelling

PHYSICAL EXAM

- Palpable abdominal mass
- Lower extremity/genital edema; painful leg swelling suggests DVT

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum creatinine, BUN (especially to follow renal function in transplant patient)
- Aspirated fluid creatinine and BUN, Gram stain and culture
- Lymphatic fluid typically contains protein, BUN, creatinine, electrolytes, and, occasionally, lipids as serum
- In contrast, urinoma, markedly elevated creatinine; lymphocele creatinine usually equal to serum creatinine

Imaging

- Key to diagnosis, but cannot distinguish between lymphocele and urinoma
- US:
  - Pelvic: To identify fluid collection that is separate from bladder, adjacent to renal allograft
  - Retroperitoneal: To evaluate hydronephrosis, if suspected
  - Duplex study of lower extremities: To evaluate for DVT
- Pelvic CT: Best definition of size and location of lymphocele
- IVP: May show displacement of ureter and compression of bladder, but is seldom necessary

Diagnostic Procedures/Surgery

Lymphangiography/lymphoscintigraphy: If other studies unclear, may aid diagnosis

Pathological Findings

Lymph fluid in a fibrous cavity not lined by epithelium containing lymphatic fluid

DIFFERENTIAL DIAGNOSIS

- Abscess
- Hematoma
- Lymphocele
- Urinoma

TREATMENT

- Treat DVT if present.
- Foley catheter in bladder if patient has significant voiding dysfunction
- Asymptomatic lymphoceles should be monitored.

MEDICATION

Systemic antibiotics (with percutaneous drainage) if lymphocele is infected

SURGERY/OTHER PROCEDURES

- Open marsupialization (internal drainage) into the peritoneum is the historic gold standard:
  - A window of peritoneum is excised, allowing the lymph to be reabsorbed by the peritoneum.
  - Omentoplasty may decrease recurrence by keeping the window patent. Success: 75–100%
- Laparoscopic marsupialization is equally effective and less invasive:
  - 3 transperitoneal ports provide access for excision of the peritoneal window and optional omental wick placement to keep peritoneal window open. Success: 77–100%
- Open external drainage is an historic procedure only, with prolonged drainage and high infection rates (25%).

ADDITIONAL TREATMENT

- Needle aspiration: Good for differentiating between lymph and urine, but high recurrence rate; success <20% with multiple aspirations.
- Percutaneous drainage: Minimally invasive but requires prolonged treatment (up to 4 mo), with risk of infection, especially in immunocompromised (transplant) patients; success: 70%

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- 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.
- Contraindicated for complex multiseptated lymphoceles: Incomplete drainage and inability to introduce sclerotic agent into all chambers.
- Sclerotherapy is best avoided when the ureter contacts 1 of the walls of the lymphocele (periureteral fibrosis, ureteral obstruction).

- Infected lymphoceles should not be treated by sclerosis.
- Requires prolonged treatment (3–5 wk), and may need to be repeated. The intense inflammatory response may be worrisome around the renal allograft; successful in 70–90%.

ONGOING CARE

PROGNOSIS

- Most asymptomatic lymphoceles resolve spontaneously.
- >90% success with marsupialization

COMPLICATIONS

- DVT/PE
- Lymphostasis of lower extremity
- Infection
- Ureteral obstruction
- Bowel obstruction

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Repeat imaging 2–4 mo after treatment to detect recurrence.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Edema, External Genitalia
- Urinoma (Peri-Nephric Pseudocyst)

CODES

ICD9

457.8 Other noninfectious disorders of lymphatic channels

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CT: Computed tomography
- DVT: Deep venous thrombosis
- IVP: Intravenous pyelography
- NS: Normal saline

- PE: Pulmonary embolism
- PLND: Pelvic lymph node dissection
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound

MEDULLARY CYSTIC KIDNEY DISEASE (MCKD)

Florian R. Schroeck, MD
Judd W. Moul, MD

BASICS

DESCRIPTION

- Rare renal cystic disease characterized by structural defects in the renal tubules, which lead to a reduction of urine concentrating ability and a decrease in sodium conservation
- Often considered part of nephronophthisis complex because they have similar clinical and histopathologic features
- 2 clinical MCKD variants described, types 1 and 2

)[C]

EPIDEMIOLOGY

)[C]

RISK FACTORS

Positive family history

Genetics

- Autosomal dominant inheritance
- Mapped gene defects:

)[C]

)[C]

PATHOPHYSIOLOGY

It is unclear how the genetic changes lead to the clinical phenotype.

COMMONLY ASSOCIATED CONDITIONS

- MCKD with hyperuricemia and gout

)[C]

DIAGNOSIS

HISTORY

- Polyuria
- Polydipsia
- If renal insufficiency:
  - Nausea, anorexia, weakness
- Family history for MCKD

PHYSICAL EXAM

- Usually unremarkable
- Many patients are hypertensive in the later stages

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis is not helpful.
- May show decreased urinary concentrating ability
- In later stages, progressive renal insufficiency, anemia, and metabolic acidosis

Imaging

- Cysts on imaging, typically <2 cm
- US:
  - Hyperechogenic kidneys of slightly reduced or normal size
  - Increased echogenicity
  - Loss of corticomedullary margin
- CT:
  - Most sensitive technique, can detect cysts as small as 5 mm
  - However, lack of cysts does not exclude a diagnosis of MCKD.

Diagnostic Procedures/Surgery

Diagnosis can be confirmed by histology after renal biopsy.

Pathological Findings

- Clinically and pathologically similar to nephronophthisis
- Macroscopically:
  - Diffuse contraction of both kidneys due to shrinking of both the cortex and the medulla
  - Cysts of variable size primarily at the corticomedullary junction and in the medulla
- Microscopically:
  - Chronic diffuse interstitial nephritis with few inflammatory cells
  - Focal areas of tubular atrophy and segmental zones of interstitial fibrosis
  - Glomeruli often normal

DIFFERENTIAL DIAGNOSIS

- Nephronophthisis:
  - Also characterized by bilateral small corticomedullary cysts
  - Differentiated from MCKD by inheritance patterns, age of onset
  - Typically presents in childhood
  - Often accompanied by extrarenal manifestations (MCKD usually has no extrarenal findings)
- Medullary sponge kidney
- Polycystic kidney disease

- Other diseases causing chronic progressive tubulointerstitial disease without glomerular abnormalities:
  - Chronic pyelonephritis (scarring on DMSA scan)
  - Urinary tract obstruction (hydronephrosis on US)
  - Polycystic kidney disease (bilateral cysts with enlarged kidneys on US)

TREATMENT

MEDICATION

- With progressive renal insufficiency, avoid and treat complications.
- Treat anemia and metabolic acidosis.
- Correct electrolyte, acid–base, and water-balance disturbances.

First Line

No specific medical therapy until renal insufficiency develops

Second Line

- MCKD progresses toward end-stage renal failure and patients generally require dialysis or transplantation.
- Type 1 typically develop ESRD around age 60
- Type 2 typically develop ESRD around age 30

SURGERY/OTHER PROCEDURES

After renal transplantation, the disease does not recur in the transplanted kidney.

ONGOING CARE

PROGNOSIS

Most patients will ultimately require dialysis or transplantation.

COMPLICATIONS

Typically only related to the complications of ESRD

REFERENCES

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See Also (Topic, Algorithm, Electronic Media Element)

- Nephronophthisis (Juvenile, Infantile, and Adolescent)
- Polycystic Kidney Disease, Autosomal Dominant
- Polycystic Kidney Disease, Autosomal Recessive

CODES

ICD9

753.16 Medullary cystic kidney

ABBREVIATIONS

- CT: Computed tomography
- DMSA: Dimercaptosuccinic acid
- ESRD: End-stage renal disease
- MCKD: Medullary cystic kidney disease
- US: Ultrasound

MEDULLARY SPONGE KIDNEY (MSK)

Margaret S. Pearle, MD, PhD

BASICS

DESCRIPTION

MSK is characterized by ectatic or dilated collecting ducts and associated cysts and diverticulas that give the appearance of a paint brush on IVU.

EPIDEMIOLOGY

- Identified in 1 in 200 IVUs
- Estimated at 1 in 5,000–1 in 20,000 in the general population

)[B]

RISK FACTORS

Genetics

Most cases occur sporadically:

- Few cases of autosomal dominant or autosomal recessive inheritance
- Has been reported in association with hemihypertrophy, Beckwith-Wiedemann syndrome, Ehlers-Danlos syndrome

PATHOPHYSIOLOGY

- Dilated collecting ducts and small cysts
- Dilated ducts and cysts may be filled with calcium apatite
- No associated cysts in other organs

COMMONLY ASSOCIATED CONDITIONS

- Renal calculi
- UTI

DIAGNOSIS

HISTORY

- Often asymptomatic and diagnosed incidentally on radiographic imaging studies
- Renal colic or flank pain common (50–60% of patients)
- Recurrent UTI
- Recurrent renal calculi
- Gross hematuria

PHYSICAL EXAM

- May be completely unremarkable
- May have associated flank tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• Electrolytes are typically normal except when associated renal tubular acidosis, in which serum bicarbonate is low

• Hypercalcemia present in 1/3–1/2 of patients

• Parathyroid hormone may be elevated.

• Urinalysis may reveal microhematuria, pyuria, bacteria.

• 24-hr urine collecting for stone risk factors most commonly reveals hypercalciuria but may also demonstrate hypocitraturia and/or high urine pH.

Imaging

• IVU:

– Classic paint brush appearance of ectatic collecting ducts that may appear as a bunch of grapes or as linear striations

– Nephrocalcinosis, representing calcifications in dilated ducts, may be present on scout film and calcifications appear to lie outside collecting system in the papillae

– Typically involves both kidneys, but may occur unilaterally or in a single renal pyramid.

• CT useful only if calcifications are present in the collecting ducts or collecting system

• Renal sonography not diagnostic in adults, but in children hyperechoic renal papillae may be identified

Diagnostic Procedures/Surgery

)[B]

Pathological Findings

Dilated intrapapillary collecting ducts and small medullary cysts give the kidney the typical sponge appearance:

• Calcium apatite concretions may be found in the cysts and dilated collecting ducts.

DIFFERENTIAL DIAGNOSIS

• Primary hyperparathyroidism

• Renal tubular acidosis

• Autosomal recessive polycystic kidney disease

TREATMENT

• Observe asymptomatic patients.

• Maintain a high fluid intake.

• Treat infections appropriately.

• Medical management of any abnormality (ie, hypercalcuria)

MEDICATION

• Antibiotics only for treatment of associated UTI:

– Suppressive antibiotics may be useful in patients with recurrent UTIs

• Thiazide diuretics are used to treat patients with stones and hypercalciuria.

)[B]

SURGERY/OTHER PROCEDURES

• SWL generally reserved for treatment of collecting duct stones that can be distinguished from nephrocalcinosis:

)[B]

• Ureteroscopy and percutaneous nephrostolithotomy can be used to treat collecting system stones and to unroof accessible collecting duct stones:

– Benefit of removing collecting duct stones is unproven.

ONGOING CARE

PROGNOSIS

• Progression to renal failure distinctly uncommon

• Recurrent UTIs and stones remain a significant risk but can be controlled with medical therapy

COMPLICATIONS

• Stone formation

• UTI

• Obstruction from stones

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Frequent urine cultures in patient with known recurrent UTIs

• Periodic imaging in stone formers to identify new stones or growth of existing stones (ie, KUB every 6–12 mo)

• Regular 24-hr urine collections for stone risk factors to monitor correction of urinary abnormalities with diet and medication (every 6–12 mo) and blood work depending on specific medications used

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See Also (Topic, Algorithm, Electronic Media Element)

- Hypercalcuria
- Medullary Cystic Kidney Disease (MCKD)
- Nephrocalcinosis
- Polycystic Kidney Disease, Autosomal Dominant
- Polycystic Kidney Disease, Autosomal Recessive
- Urolithiasis, Adult, General

CODES

ICD9

753.17 Medullary sponge kidney

ABBREVIATIONS

- CT: Computed tomography
- IVU: Intravenous urogram
- KUB: Kidneys, ureters, bladder
- MSK: Medullary sponge kidney
- SWL: Shock wave lithotripsy
- UTI: Urinary tract infection

MEGAURETER, CONGENITAL

David A. Bloom, MD
Lindsay A. Hampson, MD

BASICS

DESCRIPTION

- A ureter with increased diameter, generally in the range of 7 mm, with or without concomitant dilation of the upper collecting system

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EPIDEMIOLOGY

- Primary obstructed megaureter: 1 per 10,000
- Unclassified megaureter: 20% of cases of neonatal hydronephrosis:
  - 2–4 times more common in males
  - More common on the left side
  - 10–20% bilateral

RISK FACTORS

Genetics

)

PATHOPHYSIOLOGY

- The terminology can be confusing, and most pathophysiologic causes of megaureter are primary or secondary in origin:
  - Primary: Deficient peristalsis in 1 segment of the ureter, usually at UVJ, prevents outflow of urine into the bladder and causes proximal dilation
  - Secondary: Due to infection, calculus, neuropathic bladder, tumor, polyuria, extrinsic compression, bladder outlet obstruction. Once the causal process is resolved, secondary megaureter may or may not persist.
- Obstructed megaureter:
  - Primary: Adynamic segment of ureter with failure of effective propagation of urine outflow
  - Secondary: Functional obstruction due to elevated bladder pressures caused by urethral obstruction (posterior urethral valves), neuropathic bladder, tumor, calculus, inflammation, fibrosis, or extrinsic compression
- Refluxing: Transmission of pressure from bladder to ureter can result in increased collagen deposition in ureteral wall, causing decreased ureteral compliance and associated reflux:
  - Primary: Associated with deficient longitudinal muscle of intravesical ureter or a short intravesical ureter segment

– Secondary: Due to bladder outlet obstruction or bladder dysfunction causing elevated bladder pressures and subsequent failure of the UVJ. Surgical alteration of the UVJ can cause reflux.

- Refluxing-obstructed:
  – Primary: Ectopic implantation of ureter resulting in reflux when bladder is relaxed and obstruction when bladder contracts
  – Secondary: Any of the causes of secondary obstructed or refluxing megaureter as listed above
- Nonrefluxing-nonobstructed:
  – Primary: A diagnosis of exclusion, seen in many cases of neonatal megaureter
  – Secondary: Due to polyuria, diabetes insipidus, infection, postobstructive dilatation, prune belly syndrome
- Synonym(s): Wide ureter; megaloureter

COMMONLY ASSOCIATED CONDITIONS

- Primary refluxing megaureter is commonly associated with prune belly syndrome.
- Secondary refluxing megaureter may occur in boys with posterior urethral valves.

DIAGNOSIS

HISTORY

- Antenatal presentation (50% of cases):
  – Usually asymptomatic
- Postnatal presentation (50% of cases):
  – Can present with infections (UTI, pyelonephritis), hematuria, calculus, abdominal mass or pain, uremia (rarely)

PHYSICAL EXAM

Usually nonfocal; rarely, a palpable abdominal mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture to assess for infection
- Serum electrolytes, creatinine, and BUN to assess renal function

Imaging

- Renal and bladder US to evaluate upper and lower urinary tract:
  – Upper: Renal parenchymal evaluation, presence of hydronephrosis, ureteric duplication, degree of ureteric dilation
  – Lower: Bladder wall thickness, presence of ureterocele, posterior urethral dilatation
- VCUG to evaluate lower urinary tract for vesicoureteral reflux, ureterocele, bladder trabeculation/neuropathic bladder, posterior urethral valves

• Diuretic nuclear renography establishes differential renal function and assesses obstruction

• Excretory urography (IVP) has been generally replaced by US and nuclear renography and is less commonly used, but can be used to define anatomy and assess obstructed by delayed films.

Diagnostic Procedures/Surgery

• Urodynamic studies (flow study, cystometrogram):
  – Useful to assess voiding dysfunction and neuropathic bladder
• Endoscopic procedures (cystoscopy, retrograde pyelogram):
  – For direct visualization of the upper or lower urinary tract
  – Uncommonly indicated
• Pressure-perfusion studies (Whitaker test):
  – Requires percutaneous renal access
  – Useful to evaluate obstruction when other tests are equivocal

Pathological Findings

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DIFFERENTIAL DIAGNOSIS

• Differentiation among types of megaureter
• Other causes of dilated ureter (ie, reflux, obstruction, posterior urethral valves, etc.)

TREATMENT

Nonoperative treatment using routine imaging surveillance:

• Useful in primary refluxing megaureter in infancy if reflux is not high-grade and can be continued if improvement is seen on follow-up

MEDICATION

Antibiotics:

• Treat acute UTI
• Consider antibiotic prophylaxis for children with megaureter associated with reflux.

SURGERY/OTHER PROCEDURES

• Indications for surgery (case-development):
  – High-grade reflux with no improvement upon observation
  – Decreased renal function in follow-up or severely decreased renal function on presentation
  – Recurrent breakthrough febrile infections
  – Symptomatic
• Ureteral reimplantation to create tunnel under urothelium for ureter:

– Approach: Intravesical, extravesical, combined

– Ureteral remodeling may be necessary to achieve good length-to-diameter ratio (5:1); required for reimplantation to be successful:

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– Complications:

Reflux (10%): Mild reflux likely to resolve with time; if moderate/severe or associated with complications, reoperative reimplantation

Ureteral obstruction (2–5%): In postop period, usually due to postop edema and will likely resolve; if persistent, usually due to ischemia of a segment of ureter that must be excised

Stricture of distal ureter

Diverticula

- Endoscopic subureteric injection has a limited role in high-grade refluxing megaureter, although a few centers have reported success.

ADDITIONAL TREATMENT

Temporizing measures (necessary only rarely):

- Temporary cutaneous vesicostomy
- Temporary end-cutaneous ureterostomy
- JJ stent insertion in the megaureter

ONGOING CARE

PROGNOSIS

- Nonoperative treatment for primary obstructed megaureter:

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– This is most likely successful in asymptomatic infants with antenatally detected megaureter.

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COMPLICATIONS

Decreased renal function, continued obstruction or reflux, UTI, pain, urolithiasis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Nonoperative treatment: Routine radiologic surveillance:

– Urine analysis and culture, blood work to evaluate renal function, and US every 3–6 mo

  - Diuretic nuclear renography periodically
- Operative treatment:
  - Renal (and bladder) US at 3–6 mo following procedures:
  - VCUG usually around 6 mo following procedure

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See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal

CODES

ICD9

- 593.89 Other specified disorders of kidney and ureter
- 753.22 Congenital obstruction of ureterovesical junction

ABBREVIATIONS

- IVP: Intravenous pyelography
- US: Ultrasound
- UTI: Urinary tract infection
- UVJ: Ureterovesicular junction
- VCUG: Voiding cystourethrogram

MESOBLASTIC NEPHROMA, CONGENITAL (BOLANDE DISEASE)

Ahmed M. El-Zawahry, MD
Avi C. Weiss, MD

BASICS

DESCRIPTION

- CMN is a solid renal tumor that arises from renal mesenchyme and is usually benign.
- Accounts for ~3–6% of all childhood renal tumors
- Rarely reported to demonstrate invasion

EPIDEMIOLOGY

- CMN is the most common solid renal tumor in early infancy between 0 and 3 mo.
- 50–75% of cases occur in young infants.
- It occurs mostly in males.
- It is almost always unilateral.

Genetics

ETV6–NTRK3 gene fusion is found in most of the cellular forms. This gene results from the translocation t(12;15) (p13;q25). This fusion is also found in congenital fibrosarcoma.

PATHOPHYSIOLOGY

Mesoblastic nephroma is classified into 5 stages:

- Stage I: Tumor limited to the kidney with a healthy capsule
- Stage II: Tumor invading the renal capsule and possible extension into the perinephric fat or the IVC, but the tumor is still surgically resectable
- Stage III: Not completely resectable
- Stage IV: Hematogenous metastases
- Stage V: Bilateral tumors

COMMONLY ASSOCIATED CONDITIONS

- Polyhydramnios
- Hydrops fetalis

DIAGNOSIS

HISTORY

- Newborn infant with an abdominal mass
- Clinical features in the perinatal period include polyhydramnios (70%), hematuria, anemia, HTN, abdominal pain, hypercalcemia, and elevated renin levels.
- History of prenatal US with a unilateral solid renal mass

PHYSICAL EXAM

- Polyhydramnios (prenatal)
- Palpable abdominal mass
- Hypertension, hematuria, and jaundice

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood count and electrolytes
- Serum creatinine
- Calcium level
- Urinalysis

Imaging

- Findings on imaging are often nonspecific, other than demonstrating a renal mass.
- Abdominal US:
  - Typically exam of 1st choice
  - A hypoechogenic mass with an echogenic rim (the ring sign), mostly in classic forms.
  - A homogenous or heterogenous solid mass in cellular forms
- CT: Typically nonenhancing, without calcifications
- MRI: Signal similar to normal renal parenchyma

Pathological Findings

- CMN is a solitary hamartoma.
- It resembles leiomyoma on the cut surface.
- There are 3 histologic forms:
  - Classic form: Typical or leiomyomatous form usually occurs in infants <3 mo and is characterized by rare mitoses and absence of necrosis. Dilated vessels and entrapped nephrons are sometimes seen at the periphery of the tumor.
  - Cellular or atypical CMN: More aggressive type, characterized by a high mitotic index, hypercellularity, and an atypical growth pattern

In cellular type, age and positive surgical margins may be related to a higher risk of recurrence and metastasis

DIFFERENTIAL DIAGNOSIS

- Solid renal mass:
  - Wilms tumor
  - Autosomal recessive polycystic kidney disease
  - Diffuse nephroblastomatosis

  - Beckwith-Wiedemann syndrome
  - Compensatory hypertrophy with absence of the contralateral kidney
  - Crossed-fused ectopia
- Adrenal mass (eg, neuroblastoma, hemorrhage)

TREATMENT

Immediate delivery if hydrops fetalis is associated with CMN

MEDICATION

Adjuvant chemotherapy should be offered to patients with advanced-stage cellular types, positive surgical margins, or patients of 3 mo.

SURGERY/OTHER PROCEDURES

Nephrectomy is considered the 1st line.

ADDITIONAL TREATMENT

May be required for HTN and hypercalcemia

ONGOING CARE

PROGNOSIS

- Generally cured by nephrectomy
- Classical form is favorable.
- Rare local recurrence or metastasis in cellular forms

COMPLICATIONS

- During pregnancy: Polyhydramnios, preterm labor, hydrops fetalis, intrauterine fetal death.
- At birth: Hemodynamic instability, respiratory distress syndrome, and HTN.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

For 1 yr in all patients, and long-term monitoring for cellular variant

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Mass
- Renal Mass Algorithm

CODES

ICD9

236.91 Neoplasm of uncertain behavior of kidney and ureter

ABBREVIATIONS

- CMN: Congenital mesoblastic nephroma
- CT: Computed tomography
- HTN: Hypertension
- MRI: Magnetic resonance imaging
- US: Ultrasound

MICROPENIS (MICROPHALLUS)

Julian Wan, MD

David A. Bloom, MD

BASICS

DESCRIPTION

- A penis that is <2.5 standard deviations below the mean in length
- Normal full-term newborn penis should be at least 1.9 cm long.
- The penis is normally formed but small.
- Diameter is usually proportional to length.
- Scrotum usually normal but can be smaller.
- Testicles may be small or undescended.

Pediatric Considerations

A condition that deserves consultation and evaluation in the neonatal period

EPIDEMIOLOGY

- ~ 1.4/10,000
- Estimated between 1:10,000–1:60,000 based on prevalence of Kallmann syndrome

RISK FACTORS

- Associated with Down, Klinefelter, polysomy X syndromes, and major chromosome abnormalities
- Advanced maternal age: Nondisjunction during meiosis can lead to Down and Klinefelter syndrome
- Maternal exposure to antiandrogen medications during pregnancy:
  - No known environmental factors

Genetics

- Several modes of occurrence and inheritance noted
- 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
  - Polysomy X (eg, Klinefelter)
  - Translocation, deletion, trisomy of chromosome 8, 13, and 18
  - Androgen-insensitivity syndrome

GENERAL PREVENTION

Avoid maternal exposure to antiandrogens

PATHOPHYSIOLOGY

- Normal penile growth and development is both androgen dependent and independent.
- 1st trimester: Maternal hCG stimulates testicular Leydig cells to produce T. T is converted to DHT by 5-reductase in genital tubercle. Penis and urethra are completely formed by end of 1st trimester.
- 2nd trimester: Fetal hypothalamus and pituitary drive T production by fetal testis.
- Micropenis believed to be due to inadequate T stimulation during 2nd and 3rd trimester.
- Inadequate stimulation due to poor T secretion or poor response.
- Growth in puberty due to surge in serum T.

COMMONLY ASSOCIATED CONDITIONS

- Hypogonadotropic hypogonadism:
  - Most common cause of micropenis
  - Kallmann syndrome: Anosmia, deficit in GnRH secretion, 10% linked to KAL1 gene defect on Xp22.3, 10% autosomal dominant mutation on KAL2 gene of chromosome 8p12, 70% are autosomal dominant with no known gene defect.
  - Prader Willi syndrome: Short stature, obese, diabetes mellitus, behavior problems, lack of expression or missing 7 genes on chromosome 15 of paternal origin.
  - Laurence-Moon-Biedl syndrome
- Primary testicular failure:
  - Hypergonadotropic hypogonadism
  - Gonadal dysgenesis
  - Partial androgen insensitivity (Xq11–12 mutation)
- Chromosome anomalies:
  - Polysomy X syndromes (eg, Klinefelter)
  - Translocation, deletion, or trisomy of chromosomes 8, 13, and 18.
- Idiopathic form:
  - Normal hypothalamic-pituitary-testicle axis
  - Hypothesized to be due to delayed onset of fetal gonadotropin stimulation

DIAGNOSIS

HISTORY

- History may suggest genetic transmission
- Maternal history: Medications during pregnancy, antenatal US, prior stillbirths, decreased fetal activity or floppiness at birth

- Family history: Genitourinary anomalies, hypospadias, cryptorchidism, infertility, major congenital anomalies

PHYSICAL EXAM

- Face: Facies suggestive of midline cranial defect, mental retardation:
  - Microcephaly, hypertelorism, low-set ears, small mouth, high-arched palate
- Hands and feet are small or exhibit polydactyly or syndactyly
- Weight and body habitus: Prader-Willi syndrome, growth hormone abnormality
- Skin: Nevi, ichthyosis
- Hearing: Deafness
- Smell: Anosmia suggests Kallmann syndrome
- Retinal pigment changes on funduscopic exam
- Penis:
  - Always depress fat pad during exam
  - Prepuce, meatus location, general appearance
  - Stretched penile length: Measure from tip of glans to pubic symphysis
  - Use physiologic age, NOT chronologic age when comparing results with standard nomograms
  - Penile girth usually normal and proportional to length
- Scrotum: Size, symmetry, and appearance
- Palpate gonads: Size, shape, and position

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Differentiate between a central hypothalamic-pituitary vs. gonadal hormone deficiency
- All patients:
  - Karyotype
  - Genetic testing if history of Prader-Willi, Klinefelter, or other known syndromes
  - Anterior pituitary assessment: ACTH, GH, TSH
  - Gonadotropic studies: LH, FSH, T
  - Elevated levels of LH, FSH, T are normal during 1st 6 months of life. Low T suggests testicular failure. Confirm with hCG stimulation test. LH, FSH should elevate but T will remain low in testicular failure.
  - hCG stimulation test: Measures testicle for T biosynthesis: 1000 U of hCG IV or IM for 3 days, measure serum T and DHT levels on day 0 and 4. If T at day 4 >100 ng/dL, response is normal. If no response, suggests no functional testicular tissue.
  - From 6 month to puberty, levels of LH, FSH, and T are usually low. To check testicular function with hCG stimulation test: LH, FSH elevate 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.

– If testicular function is intact, assess for hypothalamic-pituitary function.

- Androgen insensitivity assessment:
  - Increased LH, FSH, and T after puberty
  - Confirm with genital fibroblasts for AR gene mutation

Imaging

All patients:

- MRI of head: Assess hypothalamus, pituitary, brain, craniofacial anomalies, optic chiasm, 4th ventricle, corpus callosum
- Renal imaging: Assess kidneys and bladder; VCUG and MAG3 renal scan if US suggest renal or bladder anomaly or ectopia

Diagnostic Procedures/Surgery

- Laparoscopy is used to assess nonpalpable undescended testicles, look for Müllerian duct structures, biopsy any dysgenetic tissue
- Genitogram is indicated if dysgenetic gonads, ovotestis, Müllerian duct structures are found or if androgen insensitivity is suspected.

Pathological Findings

- Newborn penis is proportional but <2 cm full stretched; with growth, remains <2.5 standard deviations below the mean.
- Kallmann syndrome: Anosmia, GnRH deficiency: 10% KAL1 gene defect on Xp22.3, 10% KAL2 on 8p12, 70% autosomal dominant with no identified gene defect
- Prader-Willi syndrome: Short stature, obesity, mental retardation, diabetes, poor muscle tone, behavioral problems; lacking expression of gene SNRPN or necdin on 15q of paternal origin.
- Laurence-Moon-Biedl syndrome: Obesity, retardation, pigmented retinopathy, polydactyly

DIFFERENTIAL DIAGNOSIS

- Concealed penis:
  - Large suprapubic fat pad
- Webbed penis:
  - Penoscrotal web can mimic micropenis

- Postcircumcision cicatrix:
  - Residual foreskin after circumcision can scar above the glans tip
- Hypospadias with and without chordee
- Chordee
- Disorders of sex differentiation:
  - Female pseudohermaphroditism: Congenital adrenal hyperplasia, gonads not palpable in labia/scrotum
  - Male pseudohermaphroditism
- Hypothalamic-pituitary axis dysfunction (50% of cases):
  - Syndromes: Kallmann, Prader-Willi, Laurence-Moon-Biedl, Rud
- Isolated hormone deficiency:
  - GnRH deficiency without Kallmann syndrome
  - LH deficiency
  - GH deficiency or growth hormone receptor defect (Laron dwarfism)
- Primary testicular failure:
  - Hypergonadotropic hypogonadism (25% of cases)
  - Testicular dysgenesis (Klinefelter syndrome, 47XXY)
  - Laurence-Moon-Biedl syndrome
  - Polysomy X syndromes
  - Vanishing testicle syndrome; intrauterine testicular torsion
- 5-Reductase deficiency
- Androgen insensitivity
- CNS abnormalities:
  - Anencephaly, congenital pituitary aplasia, agenesis of corpus callosum, malformation of fourth ventricle.
- Chromosome defects:
  - Polysomy X syndromes
  - Translocation, deletion, and trisomy of chromosomes 8, 13, and 18.
- Rare syndromes: Rud, Robinow, Martsolf, Fanconi anemia, Smith-Lemli-Opitz syndromes
- Idiopathic: Normal hypothalamic pituitary axis:
  - Virilize normally at puberty

TREATMENT

Correct any metabolic disturbances

MEDICATION

- Hypoglycemia: Give IV dextrose infusion
- Adrenal insufficiency: Treat with hydrocortisone supplementation and IV saline to correct hypovolemia
- Testosterone therapy: Diagnostic and therapeutic: 25–50 mg testosterone enanthate IM
- Long-term cortisol replacement, growth hormone and thyroid hormone if panhypopituitarism present
- For gonadal deficiency: Induce puberty later in life with T IM injection or transdermal patch/gels
- For central deficiency: Administer hCG injection or GnRH therapy

SURGERY/OTHER PROCEDURES

- Manage cryptorchidism with orchiopexy, orchiectomy (if dysgenetic), and laparoscopy as needed
- Orchiopexy for undescended testicles that are normal; 2 stage Fowler-Stephens for intra-abdominal testicles
- Penile surgery for length or bulk has NOT been shown to be effective.

ADDITIONAL TREATMENT

- Familial genetic counseling and screening
- Prenatal care:
  - Amniocentesis or chorionic villous sampling for chromosomal anomalies and sex determination
  - Fetal US to look for genitourinary and central nervous anomalies

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Gender reassignment: Rarely done anymore
- Usually reserved for true cases of disorders of sex differentiation and not for true cases of micropenis

ONGOING CARE

PROGNOSIS

In general good; long-term effects depend on underlying cause

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 penile growth does not affect ultimate penile length

- Psychosocial issues:
  - Most micropenis patients develop stable male gender.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Psychological support and psychiatric therapy as needed:
  - Reassure concerns about penile size, function, gender, potency
  - Address behavioral and psychosocial problems
- Hormone biochemical monitoring:
  - Follow pituitary and gonadal hormone therapy
  - Assess growth, vital signs, electrolytes, serum glucose, renin, ACTH, GH, LH, FSH, and T.
- Physical monitoring: Serial penile measurements

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See Also (Topic, Algorithm, Electronic Media Element)

- Ambiguous Genitalia (Disorders of Sexual Development) Algorithm
- Disorders of Sexual Development (DSD)
- Penis, Buried (Concealed, Trapped, or Hidden)
- Penis, Length, Normal
- Penis, Webbed

CODES

ICD9

752.64 Micropenis

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- DHT: Dihydrotestosterone
- FSH: Follicle stimulating hormone
- GH: Growth hormone
- HCG: Human chorionic gonadotropin
- LH: Luteinizing hormone
- T: Testosterone
- TSH: Testosterone stimulating hormone

MULTICYSTIC DYSPLASTIC KIDNEY

Benjamin J. Scoll, MD
Jack H. Mydlo, MD

BASICS

DESCRIPTION

- Congenitally nonfunctional, dysplastic kidney with cysts, associated with changing morphology
- Renal cortex replaced by multiple variable sized cysts with co-connection to the collecting system
- Usually unilateral; bilateral is incompatible with life
- 2nd most common cause of abdominal mass in neonate (hydronephrosis is 1st)

EPIDEMIOLOGY

- 1 in 2,400–4,300 live births
- Male > Female (2.4:1)
- Left > Right (56% vs. 44%)
- Bilateral 19–34% (Potter syndrome), incompatible with life

RISK FACTORS

Genetics

- No known genetic association with unilateral disease
- Bilateral disease may be related to chromosomal abnormalities.

PATHOPHYSIOLOGY

Atresia of the ureter or renal pelvis vs. failed union between the ureteric bud and the metanephric blastema

COMMONLY ASSOCIATED CONDITIONS

- Dilated nonobstructed contralateral renal pelvis (common)
- Contralateral UPJ obstruction (3–12%)
- Contralateral vesico-ureteral reflux (18–43%)
- Ipsilateral atresia of ureter or renal pelvis (common)
- Wilms tumor (rare)

DIAGNOSIS

HISTORY

- Typically detected prenatally on screening US (sensitivity 80–100%)
- In the past was often diagnosed in older children or adults, but the use of antenatal US has reduced this occurrence

PHYSICAL EXAM

- Abdominal mass palpable in 13%
- BP

DIAGNOSTIC TESTS & INTERPRETATION

Lab

No lab tests are useful

Imaging

- US: Multiple noncommunicating cysts of variable size, scant or no renal parenchyma
- Increased areas of solid component increases risk for malignancy
- Renal scan (DMSA): Confirms no function, or rarely minimal function

Diagnostic Procedures/Surgery

)[B]

Pathological Findings

- Variable/changing morphology:
  - Large kidney with large cysts
  - Smaller kidney, more solid, with small cysts
  - Often involutes into nubbin
- Dysplastic elements
- No functional renal parenchyma can usually be identified
- Microscopic communication between cysts
- 3 variants described:
  - Classic: Multiple cysts of variable sizes separated by thin, dysplastic parenchyma
  - Hydronephrotic: A dilated but identifiable renal pelvis
  - Solid cystic dysplasia: Smaller cysts and more predominant stroma

DIFFERENTIAL DIAGNOSIS

- Acquired renal cysts
- Cystic congenital mesoblastic nephroma
- Cystic Wilms tumor
- Cysts of the medulla
- Hydronephrosis
- Multilocular cystic nephroma
- Neuroblastoma
- Polycystic kidney disease
- Renal cysts, isolated or associated with syndromes (tuberous sclerosis, von Hippel-Lindau, others)
- UPJO

- VUR

TREATMENT

- Generally controversial, with some advocating nephrectomy due to risk of malignant degeneration
- Most today suggest observation and nonoperative management.

MEDICATION

Unless necessary to treat HTN

SURGERY/OTHER PROCEDURES

)[B]:

  - 60–89% involute or regress
  - 2–37% remain stable
  - 0–18% increase in size

- Indications for nephrectomy:
  - Large size or symptomatic

)[B]

  - Concern for malignancy (functional elements) such as Wilms tumor has been rarely reported.

ONGOING CARE

PROGNOSIS

- Excellent in unilateral disease
- Bilateral disease not compatible with life

COMPLICATIONS

- Wilms tumor (4–5 times risk of general population) in observed patients
- HTN

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

)[C]

- Solitary kidney precautions (ie, avoidance of contact sports)

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See Also (Topic, Algorithm, Electronic Media Element)

- Potter Syndrome/Potter Facies
- Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)
- Renal Dysplasia, Hypodysplasia and Hypoplasia

CODES

ICD9

753.19 Other specified cystic kidney disease

ABBREVIATIONS

- BP: Blood pressure
- DMSA: Dimercaptosuccinic acid
- HTN: Hypertension
- MCDK: Multicystic dysplastic kidney
- UPJ: Ureteropelvic junction
- UPJO: Ureteropelvic junction obstruction
- US: Ultrasound
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

MULTIPLE SCLEROSIS, UROLOGIC CONSIDERATIONS

Douglas F. Milam, MD

BASICS

DESCRIPTION

- MS is neurologic disease causing focal demyelination of white matter in the brain and spinal cord
- These areas visible as plaques on 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.
- Neurologic impairment can vary from mild to profound.
- Urologic manifestations can include urinary frequency, incontinence, sexual dysfunction; urgency and urge incontinence are frequent urinary symptoms.
- DSD, detrusor hyperreflexia, and bladder outlet obstruction are common dysfunctions noted on urodynamic studies.

Geriatric Considerations

MS is typically a disease of middle age. Improved care for the sequelae such as urologic manifestations now permits many patients to live into older age.

EPIDEMIOLOGY

- Most commonly presents between 20–45
- Females have 1.5–3 times greater incidence than males
- Increased risk if MS is present in a 1st-degree relative
- Identical twin: 300 times increased risk if other twin develops MS
- Unknown pattern of inheritance
- 1 in 1,000 people per year in the US
- 250,000–300,000 in the US have MS
- Marked variations in worldwide prevalence

RISK FACTORS

- Primary relative with MS confers 20 times risk
- Monozygotic twins have 30% concordance rate
- Upper urinary tract deterioration and renal insufficiency prevention through urologic monitoring, as above

PATHOPHYSIOLOGY

- Autoimmune attack of the CNS myelin:
  - Focal demyelination with relative axon sparing
  - Histopathology shows perivenular lymphocytic infiltrates, macrophages within the white matter, gliosis, and scarring.

- GU pathophysiology:
  - MS affects the cervical spinal cord in the pyramidal and reticulospinal tracts, affecting innervation of the bladder and external urethral sphincter, causing detrusor hyperreflexia and DSD.
  - MS can affect the sacral cord and may lead to bladder areflexia and large PVRs.

COMMONLY ASSOCIATED CONDITIONS

- Detrusor sphincter dyssynergia leading to urinary retention, recurrent UTI, and renal functional loss
- Bladder and renal stones due to urinary stasis from incomplete bladder emptying and chronic infection

DIAGNOSIS

- Most common: Weakness, visual disturbances, ataxia, diplopia, and sensory disturbances
- Urologic manifestations: Presenting complaint in 2.0– 2.5% of MS patients:
  - In patients with MS >10 yr, 90% will have urologic symptoms
  - Detrusor hyperreflexia with urge incontinence is the most common GU symptom present in 78% of patients with voiding dysfunction.
  - DSD present in 30–65%: Leads to poor emptying and possible upper tract damage.
  - Impotence: Up to 80% of males
  - Detrusor hypocontractility and poor bladder emptying are seen in some patients, usually as a late finding.

HISTORY

- Presence of neurologic symptoms:
  - Blurry vision, balance problems, numbness, or tingling, and muscle weakness
- Urinary history: All patients with MS should be screened for urologic problems.
- Recurrent UTI or incontinence should prompt urologic specialty evaluation:
  - Incontinence due to MS: Urgency-related or urge incontinence
  - Hematuria may indicate the presence of infection, stones, or cancer.
  - Current medications
  - Previous pelvic surgery

PHYSICAL EXAM

- GU exam:
  - Testicular and prostate exam in male to rule out neoplasm or infection
  - Pelvic exam in female to assess pelvic support, rule out urethral or vaginal pathology

– Bulbocavernosus reflex to assess function of sacral nerves (although absent in up to 30%)

- Focused neurologic exam:
  – Deep tendon reflexes, proprioception, Babinski reflex, and cranial nerve exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: Concomitant infection or hematuria
- CSF for initial MS diagnosis (oligoclonal IgG bands)

Imaging

- MRI:
  – The most useful tool for diagnosing MS; diagnostic in 70–95% of cases
  – Increased signal intensity on T2-weighted images in areas of demyelination
- Upper-tract imaging:
  – Rule out presence of hydronephrosis
- Renal US is a good screening test:
  – Important in patients with known DSD or in patients with indwelling catheters
- Lower-tract imaging less commonly performed:
  – Lateral voiding cystourethrogram in female helps exclude reflux and calculi as well as assess anatomic support of the bladder and urethra
- Special studies:
  – Video-urodynamics done by urologic specialists to assess bladder capacity, compliance (elasticity), contraction:

Absolutely necessary to characterize voiding dysfunction to allow for proper management

Predicts patients at risk for upper-tract deterioration (elevated storage and voiding pressures or high-amplitude involuntary bladder contractions)

Demonstrate presence of DSD

May suggest diagnosis of MS in patient with few other neurologic symptoms

Need follow-up urodynamics, as patterns of voiding dysfunction may change

Diagnostic Procedures/Surgery

With respect to urologic diseases:

- Bladder instability due to infection, inflammatory conditions, CIS
- Detrusor hyperreflexia due to other neurologic causes (ie, CVA, tethered cord, herniated disc)
- Sexual dysfunction due to medications or coexisting disease

- Detrusor areflexia due to diabetes, medications, or obstruction

TREATMENT

- Remissions can occur spontaneously, making management difficult.
- Physical therapy and exercise to help prevent muscle atrophy, loss of postural tone, osteoporosis, and deep venous thrombosis
- Avoid stressors
- Disease-modifying medications can reduce relapses and control some symptoms. These include interferon -1a (Avonex) and interferon -1b (Betaseron)
- Urologic medical treatment:
  - To decrease the frequency and force of involuntary bladder contractions. (see “Medications”)
  - CIC: Cornerstone of treatment for patients with hypocontractility or DSD and poor bladder emptying; protects upper urinary tracts
  - Avoid indwelling Foley catheters.
  - Appropriate treatment of UTIs, as MS patients at risk for recurrent UTIs and pyelonephritis
  - Patients on intermittent catheterization should not be treated with antibiotics for asymptomatic bacterial colonization of the urinary tract.
- Artificial urinary sphincter or male sling is uncommonly used for patients with normal bladder compliance, but insufficient urinary sphincter function.
- Injection of bulking agents such as collagen, Coaptite, or Duraspheres for treatment of urinary sphincter dysfunction (uncommon in MS)
- Sexual function in both men and women has been reported to improve with the use of agents such as sildenafil.

MEDICATION

First Line

- 20–80% of patients respond for symptoms of bladder overactivity; however, there is a high attrition rate due to side effects and lack of durable efficacy.
- There are many medication choices. Individual response is idiosyncratic, so several medications must be tried before finding the optimal 1 based on response and side effects.
- Medication options include:
  - Oxybutynin 5 mg b.i.d.–t.i.d.
  - Oxybutynin XL 10–15 mg/d
  - Tolterodine 2–4 mg/d
  - Trospium XR 60 mg/d

- Solifenacin 5–10 mg/d
- Hyoscyamine extended release 0.375 mg b.i.d.
- Transdermal oxybutynin patch 3.9 mg/d

Second Line

Botulism toxin injection:

- Decreases the force and frequency of involuntary bladder contraction
- Office-based therapy performed under local anesthesia; well tolerated
- Cystoscopic injection of 50–300 U of botulism toxin into 10–25 sites within the bladder muscle
- Treatment effect lasts 4–8 mo
- Occasional patients develop temporary total urinary retention and require self-intermittent catheterization q.i.d.

SURGERY/OTHER PROCEDURES

- Suprapubic cystotomy:
  - If unable to perform self-intermittent catheterization; avoids urethral erosion; allows for better hygiene; reduces incidence of epididymitis and prostatitis
  - Drawbacks include risk of bladder calculi and development of squamous cell carcinoma (usually in >10 yr).
- Sphincterotomy for the male patient with DSD and inability to catheterize:
  - Requires use of condom catheter for urinary collection.
  - 15–50% failure rate requiring revision sphincterotomy; uncommonly performed in MS patients.
- Augmentation cystoplasty: When conservative management of incontinence from involuntary bladder contraction or decreased bladder compliance has failed and the patient can catheterize per urethra without difficulty
- Urinary diversion either through ileal conduit, ileovesicostomy, or catheterizable diversion

ONGOING CARE

PROGNOSIS

With proper urologic follow-up, renal function can be preserved in most patients.

COMPLICATIONS

Urologic complications:

- Hydronephrosis due to elevated bladder storage or voiding pressure
- Renal insufficiency due to elevated storage or voiding pressures, recurrent infections, and poor emptying (more common in men)

- Bladder and upper urinary tract stone formation due to urinary stasis and infection
- Recurrent UTIs and pyelonephritis
- Urethral erosion from indwelling catheters left in for long periods of time

FOLLOW-UP RECOMMENDATIONS

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. Continence, 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:
  - High-risk patients: Incontinence, recurrent infections, DSD, elevated storage pressures >40 cm H2O, indwelling catheters
  - Follow closely for upper-tract deterioration, development of squamous cell carcinoma of the bladder, and other problems associated with long-term indwelling catheters.
  - Low-risk patients: Those with normal continence, no UTIs, and complete bladder emptying. These patients do not require frequent upper-tract imaging.
- All patients should undergo periodic urodynamic testing, especially if there is a change in symptoms, an increase in infections, or an overall worsening of the MS.

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See Also (Topic, Algorithm, Electronic Media Element)

- Detrusor Sphincter Dyssynergia
- Neurogenic Bladder, General

CODES

ICD9

- 340 Multiple sclerosis
- 788.39 Other urinary incontinence
- 788.41 Urinary frequency

ABBREVIATIONS

- CIS: Clean intermittent self-catheterization
- CNS: Central nervous system
- CSF: Cerebrospinal fluid
- CVA: Costovertebral angle
- DSD: Detrusor sphincter dyssynergia
- GU: Genitourinary
- MRI: Magnetic resonance imaging
- MS: Multiple sclerosis
- PVR: Post void residual
- US: Ultrasound
- UTI: Urinary tract infection

MYASTHENIA GRAVIS, UROLOGIC CONSIDERATIONS

Doron S. Stember, MD
Neil H. Grafstein, MD

BASICS

DESCRIPTION

- MG is a chronic autoimmune disorder characterized by weakness and early fatigability of the skeletal muscles due to antibody-mediated loss of nicotinic acetylcholine receptors
- Involvement of the external striated urethral sphincter is rare but may be vulnerable to dysfunction after TURP, explaining the relatively high incidence of post-TURP incontinence in this group.
- Although smooth muscle is generally not affected, there are rare reports of detrusor areflexia.

EPIDEMIOLOGY

- Published estimates of 2–21 cases per million people per year
- 20:100,000
- In patients <40 yr:
  - Female > Male (7:3)
- In the 5th decade, new cases of MG are evenly split between the genders.
- After the 5th decade:
  - Male > Female (3:2)

RISK FACTORS

Thymic hyperplasia is observed in 65–75% of patients

Genetics

- Congenital myasthenia syndromes, a subset of MG, stem from genetic mutations resulting in abnormal neuromuscular transmission.
- HLA types B8 and DR3 are associated with MG.

PATHOPHYSIOLOGY

- Autoantibodies develop against Ach nicotinic postsynaptic receptors.
- 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 is 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.

COMMONLY 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 extraocular muscles and eyelids.

DIAGNOSIS

HISTORY

- Reduced exercise tolerance that improves with rest and worsens with warm temperature (eg, after a hot bath)
- The natural history of MG usually follows a characteristic pattern that initially involves weakness of eyelids and extraocular 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

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serology tests demonstrate anti-ACh receptor antibodies in ~90% of patients
- ~50% of patients who test negative for anti-ACh receptor antibodies have antibodies against the MuSK protein.

Diagnostic Procedures/Surgery

- Edrophonium chloride test: Positive for MG if IV administration unequivocally yields improved strength
- Repetitive nerve stimulation
- Single-fiber electromyography
- Chest CT to rule out thymoma
- Complete urodynamic evaluation if urologic symptoms are present
- Urodynamics:
  - If bladder dysfunction present, resembles lower motor neuron pattern with variable areflexia or atonia

DIFFERENTIAL DIAGNOSIS

- Lambert-Eaton syndrome
- Botulism
- Acute inflammatory demyelinating polyradiculoneuropathy

TREATMENT

- Intermittent catheterization for rare cases of refractory detrusor areflexia
- Adjust mealtimes to take advantage of daily periods of relative strength.
- Install railing in household places where they'll likely be needed for support in rising, such as adjacent to 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 with 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.

MEDICATION

First Line

- Ach inhibitors 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.
- IV 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.

SURGERY/OTHER PROCEDURES

- If surgical intervention for bladder outlet obstruction secondary to 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

ADDITIONAL TREATMENT

-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.

• Thymectomy 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

• Multiple complicating effects may result from chronic steroid use, including poor wound healing and opportunistic infection.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patients with MG should be followed by a neurologist with urology referral as needed.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

Neurogenic Bladder, General

CODES

ICD9

– 358.00 Myasthenia gravis without (acute) exacerbation

– 788.39 Other urinary incontinence

ABBREVIATIONS

• Ach: Acetylcholinesterase

• BPH: Benign prostatic hypertrophy

- CT: Computed tomography
- IgG: Immunoglobulin
- IV: Intravenous
- MG: Myasthenia gravis
- TURP: Transurethral resection of prostate

MYELODYSPLASIA, UROLOGIC CONSIDERATIONS

Clifford Georges, MD
Mark Horowitz, MD
Rosalia Misseri, MD

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.
- This includes a group of developmental abnormalities that can be open (meningocele, myelomeningocele, lipomyelomeningocele) or closed (spina bifida occulta, posterior meningoceles, lipomyelomeningocele, and myelocystocele).
- Primary functional deficits 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.

ALERT

Patients with myelodysplasia have a high incidence of latex allergy.

EPIDEMIOLOGY

- Open spinal dysraphism:
  - 1 in every 1,000 births in US
  - 2.5 times more common in whites than blacks
  - Incidence decreasing over past 20 yr
  - 60,000 cases estimated in US
- Spina bifida occulta:
  - 5–10% of the general population
  - Most of these cases are found incidentally.

RISK FACTORS

- Maternal folate deficiency during pregnancy
- Family history
- Intrauterine exposure to valproate, carbamazepine
- Pregestational maternal diabetes
- Chromosome trisomies 13 and 18, triploidy, and single gene mutations.
- Geographic regions of lower socioeconomic status

Genetics

- 2–8% incidence of myelodysplasia when a older sibling has spina bifida

- Incidence doubles when >1 family member is affected.
- Genes involved in folate-homocysteine metabolism and transport

GENERAL PREVENTION

- Folic acid 4.0 mg/d, 3 mo preconception, in women with family history or other risk factors

PATHOPHYSIOLOGY

- Increased maternal blood AFP at 16 wk can indicate the presence of an NTD.
- Spinal cord begins normal development on day 18 of gestation:
  - The canal closes in a cephalocaudal direction, with complete closure by day 35 of gestation.
  - Exact mechanism of dysraphism remains undefined
- Myelodysplastic 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 (cord may be attached to vertebral column or subcutaneous tissues by a thickened filum terminale, fibrous band, dermal sinus trac, etc.) and often associated with a low-lying conus (below L2–L3); usually detected by plain x-ray, demonstrating open vertebral bodies
  - Posterior meningoceles, myelocystocele and lipomyelomeningocele are closed defects associated with a skin-covered back mass.
  - Meningocele: The meninges or dural sac, but no neural elements, extend beyond the confines of the vertebral canal. Most have normal lower extremity.
  - Myelomeningocele: The nerves and spinal cord are exposed through an opening in the spinal column, meninges, and skin. Neural tissue has evaginated with the meningocele. Significant neurologic defects (paralysis, urinary incontinence) are usually associated.
  - Lipomyelomeningocele: Fatty tissue along with cord structures extend with the protruding sac.
- Myelomeningocele account for 90% of spinal dysraphism and can also be associated with a solitary kidney or ureteral anomaly:
  - Arnold-Chiari malformation in 85% of children with myelomeningocele:

    Cerebellar tonsils herniate through foramen magnum.

    The 4th ventricle is obstructed, hydrocephalus develops unless ventricular-peritoneal shunting is performed.
- Varying neurologic deficits; may not be directly related to level of lesion. Milder forms such as spina bifida occulta may be totally asymptomatic or present later in life.
- Urologically, bladder contractility and activity of external urinary sphincter are often affected.

- Bladder may be hypercontractile, poorly compliant, or atonic.
- Sphincter activity may be synergic or dyssynergic.
- May lead to upper urinary tract abnormalities and chronic urinary incontinence

COMMONLY ASSOCIATED CONDITIONS

- Hydrocephalus/Arnold-Chiari malformation
- Imperforate anus
- Sacral agenesis
- VACTERL syndrome
- Various musculoskeletal, neurologic, and cognitive defects
- Latex allergy

DIAGNOSIS

HISTORY

- Review medical and developmental history
- Patients commonly present with incontinence:
  - Primary vs. secondary
  - Stress vs. urge
  - Nocturnal vs. diurnal
- Check for neurologic symptoms:
  - Change in bowel habits or gait
  - Onset of leg or back pain
  - Onset of seizures or other neurologic symptoms
- Voiding (catheterization) history most important:
  - How often patient voids or catheterizes, and leakage between.
  - Typical voided/catheterized volumes and at what volume patient leaks.
  - Size catheter used: Larger caliber catheters drain faster and lead to better patient compliance.

PHYSICAL EXAM

- Assess general appearance, body habitus, gait, dexterity, muscular, and neurologic development.
- Genitalia:
  - Hypospadias
  - Cryptorchidism
  - Labiovulvar abnormalities
- Rectal exam:
  - Perianal sensation

- Rectal tone
- Check for fecal impaction.

- Back exam for open (obvious exposed neural tissues) or closed defects. Stigmata that may be associated with spina bifida occulta include:
  - Dimples or sinuses
  - Subcutaneous mass
  - Skin tags
  - Hemangiomas
  - Abnormal hair patches or pigmentation
- Neurologic exam:
  - Gait
  - Balance
  - Muscular development
  - Muscle tone

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis
- Urine cultures
- Basic metabolic panel
- Urine 24-hr creatinine

Imaging

- Plain abdominal x-rays:
  - May show structural vertebral anomalies (hemivertebra, butterfly vertebra, incomplete fusion of posterior elements) or evaluate for partial or complete sacral agenesis
  - Widened interpedicular distance
  - Rule out stone disease and fecal impaction in the older child
- Renal US:
  - Determine baseline of urinary tract
  - Access for hydronephrosis, bladder wall thickness and PVR if patient voids.
- VCUG:
  - Usually done at time of urodynamics
- MRI/CT:
  - Access spinal cord and vertebral anomalies

Diagnostic Procedures/Surgery

Urodynamic studies:

- Often with video
- Performed 1–2 times a year
- Best objective measurement of bladder status
- Assesses leak point pressure, bladder capacity, volume and pressure at leakage, volume and pressure when reflux is seen, uninhibited contractions
- Used to assess response to therapy
- Performed with latex precautions
- Catheter in bladder and rectum to measure vesical and abdominal pressure that, when subtracted, gives detrusor pressor

DIFFERENTIAL DIAGNOSIS

- Other causes of neurogenic bladder (see Neurogenic Bladder)
- Tethered cord syndrome

TREATMENT

- Urgent neurosurgical intervention is critical for open defects to treat hydrocephalus.
- Temporary vesicostomy may be needed until CIC can be begun
- Urologically achieving continence is a goal:
  - CIC therapy alone
  - CIC and anticholinergic therapy
  - Multidrug regimen of anticholinergics and sympathomimetics

MEDICATION

Anticholinergics:

- Decrease bladder contraction thereby increasing compliance and functional capacity
- Titrate up over time as tolerated.
- Side effects include headaches, dry mouth, flushing of skin, abdominal discomfort, blurred vision
- Ditropan, Levsin, Oxytrol, Detrol, Enablex
- Available in liquid, pills, patches; should be initiated early in life to prevent sequelae
- Almost always used in conjunction with intermittent catheterization
- Antibiotics used in some patients who have recurrent infections, but must be kept in mind that all patients on catheterization have colonized urine
- -Blockers to decrease tone at bladder neck

SURGERY/OTHER PROCEDURES

When conservative management fails, consider any of the following procedures, which are often performed in combination with some or all of the others.

- Bladder augmentation with creation of continent catheterizable stoma

- Antireflux procedure
- Incontinence surgery:
  - Usually wait until the child is 5 yr old
  - Bladder neck reconstructions:
    Young-Dees, Leadbetter, Kropp, Pippi-Salle modification
  - Fascial sling
  - Artificial urinary sphincters
- Early experience with intrauterine surgery to correct spinal defect
- Tissue-engineered bladder augmentation (experimental)
- Artificial somatic–autonomic reflex pathway procedure (experimental)

ONGOING CARE

PROGNOSIS

- Independence in ADLs is likely for children without associated hydrocephalus.
- >95% of children with myelomeningocele continue to have normal renal function with proper management.

COMPLICATIONS

- Incontinence
- Renal failure
- Paralysis
- UTIs
- Skin ulceration from incontinence
- Hydrocephalus and meningitis if myelomeningocele not treated early in life
- Seizure disorders
- Musculoskeletal problems (scoliosis, club foot, others)
- Latex allergy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Close follow-up with pediatric urology and neurology from infancy
- Yearly US is acceptable monitoring in child with normal voiding and normal studies.
- Yearly sonograms and urodynamic studies in patients with bladder/sphincter dysfunction.
- Maintain detrusor storage pressure 40 cm H_2O to avoid upper-tract deterioration.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Neurogenic Bladder, General
- Tethered Cord Syndrome

CODES

ICD9

- 596.54 Neurogenic bladder nos
- 741.90 Spina bifida, unspecified region, without mention of hydrocephalus
- 742.59 Other specified congenital anomalies of spinal cord

ABBREVIATIONS

- ADL: Activities of daily living
- AFP: -Fetoprotein
- CIC: Clean intermittent catheterization
- KUB: Kidneys, ureters, bladder
- MRI: Magnetic resonance imaging
- NTD: Neural tube defect
- PVR: Post void residual
- US: Ultrasound
- UTI: Urinary tract infection
- VACTERL: Vertebral anomalies, anal atresia, cardiovascular anomalies, tracheoesophageal fistula, renal anomalies, limb anomalies
- VCUG: Voiding cystourethrogram

NEPHROCALCINOSIS

Ivan Colon, MD

BASICS

DESCRIPTION

- A kidney disorder involving deposition of calcium and oxalate or phosphate in the renal tubules and interstitium. It may be classified as either microscopic or macroscopic.
- Nephrocalcinosis (macroscopic) can also be differentiated radiographically into:
  - Medullary nephrocalcinosis is the most frequent form and is characterized by the exclusive involvement of the medullary pyramids.
  - Cortical nephrocalcinosis: Rarer and involves all the renal parenchyma. Frequently associated with severe metabolic defects (ie, primary hyperoxaluria).

Pediatric Considerations

Nephrocalcinosis is rare in pediatric patients. It has been recognized in neonates and premature babies. Recognition is therefore important to prevent renal failure and long-term effects.

Pregnancy Considerations

Symptoms may be present in pregnancy as urolithiasis or flank pain in pregnancy. See chapters related to those topics.

EPIDEMIOLOGY

Macroscopic nephrocalcinosis is a radiographic diagnosis and may not be associated with any symptoms. Microscopic nephrocalcinosis is a common incidental finding at post mortem exams:

- Histologic classification
- Radiographic classification:
  - Medullary nephrocalcinosis: Calcification in the medullary interstitium or renal tubular lumen.
  - Cortical nephrocalcinosis: Calcification is predominantly in the renal cortex.

RISK FACTORS

- Depends on etiology
- Hypercalcemia: Structural abnormality
- Hypercalcemia: Shock, sepsis, ischemia (chronic recovery from)

GENERAL PREVENTION

- Based on etiology; the goal of treatment is to reduce symptoms and prevention.
- Treat the underlying cause.
- Osteoporosis: Discontinue medications that enhance calcium loss (loop diuretics).

ALERT

DO NOT GIVE vitamin D and calcium to correct bone loss if nephrocalcinosis is secondary to type 1 RTA as it may worsen the condition.

PATHOPHYSIOLOGY

- Cortical nephrocalcinosis:
  - Acute renal cortical necrosis: Causes include infection, ESWL, and HUS:
  - Primary and secondary oxalosis
  - Chronic glomerulonephritis
  - Chronic pyelonephritis
  - Renal graft rejection
- Medullary nephrocalcinosis:
  - Hypercalcemic state: Hyperparathyroidism, excess vitamin D, bone metastases, bone loss from chronic immobilization and severe osteoporosis, sarcoidosis, idiopathic hypocalcemia of infancy (William disease).
  - Hypercalciuric state: Distal RTA, idiopathic hypercalciuria, hypothyroidism, inherited tubular disorders (eg, Bartter syndrome and familial magnesium-losing nephropathy), and may follow intensive loop diuretic treatment in premature infants. Hypercalciuria is also seen as part of the Fanconi syndrome and proximal RTA.
  - Absence of factors in urine (eg, citrate) that help to maintain calcium salts in solution (eg, in conditions causing chronic hypokalemia, such as primary hyperaldosteronism)
  - Medullary sponge kidney

COMMONLY ASSOCIATED CONDITIONS

Renal stones

DIAGNOSIS

HISTORY

- Nephrocalcinosis is usually found incidentally on radiographic studies for another underlying cause, or in the workup of renal stones.
- Patients are usually asymptomatic.
- If symptoms are present, patients may experience symptoms that are related to the causative etiology: Hematuria, renal colic, nausea or vomiting (obstructing ureter stone), frothy or foamy urine, weakness (hypercalcemia, renal failure), muscle aches, weight loss, fluid retention (renal failure), edema (renal failure), mental status changes, easy bruising, sleep disturbances, seizures
- Review history of bone pain/fractures; stones; hyperparathyroidism; excessive intake of alkali, vitamin D, milk; premature birth

PHYSICAL EXAM

- >50% of patients will have a normal exam.
- Symptomatic patients will present with findings based on the etiology (eg, CVA tenderness, if obstructing stone).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Test to identify causative disorder, since nephrocalcinosis is a radiographic diagnosis.
- Blood/serum:
  - Electrolytes, BUN and creatinine to asses renal function
  - Serum calcium, phosphate, albumin: To establish presence of hypercalcemia
  - If serum calcium is high, it should be followed by a PTH level to identify hyperparathyroidism
  - TSH level, if suspecting thyroid disorder
  - Serum oxalate level
  - Uric acid, to assess for other gouty diseases.
- Urine:
  - Routine urinalysis with culture, if indicated (especially if signs of infection).
  - Urine PH with Nitrazine paper (must record over 48 hr) for RTA.
  - 24-hr urinary excretion of calcium, oxalate, citrate, and protein: Assessment of hypercalciuria and possible nephrotic syndrome
  - Urinary magnesium: Magnesium-losing nephropathy
- Other: TB skin test if patient is suspected to have TB and comes from TB-endemic areas.

Imaging

- Abdominal x-rays: Detection of nephrocalcinosis, urinary stones
- US: More sensitive than conventional radiography
- CT is more effective in detecting calcification and can be used to differentiate medullary and cortical deposition.

DIFFERENTIAL DIAGNOSIS

- Hyperparathyroidism
- Medullary sponge kidney
- Renal tubular acidosis
- Hypercalcemia
- Renal TB: Dystrophic calcifications of TB may be seen in renal pyramids;
- Renal artery calcifications (aneurysms)

- Milk of calcium
- Multiple diffuse recumbent calculi associated with spinal injury
- Renal calcifications:
  - Calcified rim as seen in chronic UPJ or ureterocele with hydronephrotic changes
  - Calcifications of renal infarction
  - Calcifications associated with renal masses (hypernephroma)

TREATMENT

- Early recognition is important, especially if it is secondary to iatrogenic causes (ie, excessive diuretics). A misdiagnosis of nephrocalcinosis may lead to irreversible renal injury. Differentiating between nephrolithiasis and nephrocalcinosis is important because, although they may coexist, they are managed differently.
- Treatment must be tailored to the specific etiology of nephrocalcinosis.

MEDICATION

- Cortical nephrocalcinosis:
  - Correct condition producing shock, fever, dehydration
  - IV fluid hydration
  - Broad-spectrum antibiotics
- Chronic glomerulonephritis:
  - Long-term support for renal insufficiency
  - Dialysis for renal failure
  - Low-protein diet
  - Treat HTN to slow vascular disease
  - Steroids to decrease proteinuria in nephrotic syndrome
- Alport syndrome:
  - Supportive measures to stabilize and reduce uremia
  - Monitor and treat UTI/HTN
- Medullary nephrocalcinosis:
  - Hyperparathyroidism: Best treated with surgery to remove adenoma
  - Thiazide diuretics if patient cannot undergo parathyroidectomy
  - Monitor calcium levels.
- RTA:
  - High fluid intake to produce >2 L urine
  - Potassium citrate 20 mEq b.i.d.
- Medullary sponge kidney:
  - High fluid intake to produce >2 L urine

  - Monitor urine cultures to rule out UTI
  - Rule out possible hypercalciuria/hypercalcemia.
- Hypervitaminosis D: Alter diet.
- Sarcoidosis: Reduce dietary calcium.

SURGERY/OTHER PROCEDURES

- Surgical intervention may be required for significant stone formation in urinary tract (pyelocaliceal system, ureter), especially if causing obstruction or infection.
- Choice of endourologic intervention (ureteroscopy/percutaneous) depends on the location and size of the stone.
- Lithotripsy may be used if able to locate stones within the pyelocaliceal system.

ALERT

Be careful when opting for shockwave therapy in nephrocalcinosis, since stones are intraparenchymal and may lead to more renal damage. Ensure that stones are in pyelocalyceal system, and focus the shock accordingly.

ONGOING CARE

PROGNOSIS

The prognosis depends mainly on the etiology of the nephrocalcinosis.

COMPLICATIONS

- Acute renal failure
- Chronic renal failure
- Kidney stones (stones within the pyelocaliceal system)
- Obstructive uropathy (acute or chronic, unilateral or bilateral):
  - May lead to sepsis
  - Intractable pain
  - Renal failure as above
- May also lead to uncontrolled HTN, renal infection, scarring, renal colic, defects of renal tubular function, and renal failure

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow-up with:

- Periodic renal function tests, urine cultures, calcium level and controlled of metabolic conditions (hypercalcemia, HTN).
- In-office US if flank/abdominal pain

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Calcifications, Renal
- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General

CODES

ICD9

275.49 Other disorders of calcium metabolism

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CT: Computed tomography
- CVA: Costovertebral angle
- ESWL: Extracorporeal shock wave lithotripsy
- HTN: Hypertension
- HUS: Hemolytic uremic syndrome
- IV: Intravenous
- PTH: Parathyroid hormone
- RTA: Renal tubular acidosis
- TB: Tuberculosis
- TSH: Thyroid-stimulating hormone
- UPJ: Ureteropelvic junction

- US: Ultrasound
- UTI: Urinary tract infection

NEPHROTIC SYNDROME

Gaurav Bandi, MD

BASICS

DESCRIPTION

- Involves the tetrad of proteinuria (>3 g/d/1.73 m2), hypoproteinemia, edema, and hyperlipidemia.
- Can be primary (idiopathic) or secondary (associated with systemic disease):
  - 80% in children are primary NS, usually minimal change disease
  - Only 25% of adult patients have primary NS.
  - Presentation of nephrotic syndrome in adults may signal a serious underlying disease.

EPIDEMIOLOGY

- Uncommon disease:
  - Children: 2/100,000 new cases/yr
  - Adults: 3/100,000 new cases/yr
- Incidence varies, depending on age, race, prevalence of infections (malaria, hepatitis B, schistosomiasis)
- Predominant age:
  - Children: 1.5–6 yr
  - Adults: All ages

RISK FACTORS

See “Commonly Associated Conditions.”

Genetics

- 2–8% cases are familial
- Finnish type congenital nephrotic syndrome inherited in an autosomal recessive fashion (associated with NPHS1 and NPHS2 genes)

GENERAL PREVENTION

- Primary NS: None
- Secondary NS: Treatment or prevention of systemic disease (eg, tight control of diabetes, prevention of STDs)

PATHOPHYSIOLOGY

- GBM normally restricts passage of proteins >70 kd.
- All forms of NS feature severe proteinuria due to abnormal leakage of proteins across GBM:
  - Signs/symptoms of NS worsen 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.

• Hyperlipidemia 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.

COMMONLY ASSOCIATED CONDITIONS

• Primary renal disease:
  - Primary fibrillary glomerulopathy
  - Focal glomerulonephritis
  - Focal segmental glomerulosclerosis
  - IgA nephropathy
  - Membranous glomerulopathy
  - Membranoproliferative glomerulonephritis
  - Mesangial proliferative glomerulonephritis
  - Minimal change disease
  - Rapidly progressive glomerulonephritis
  - Congenital nephrotic syndrome
• Secondary renal disease:
  - Medications: NSAIDs, captopril, gold, penicillamine, heroin
  - Toxins and allergens: Insect stings, pollens, mercury, snake venoms, poison ivy
  - Infections:
    Bacterial: Syphilis, endocarditis, PSGN, TB, leprosy
    Viral: HIV, hepatitis B, hepatitis C
    Protozoal: Malaria
    Helminthic: Schistosomiasis, trypanosomiasis, filariasis
  - Malignancy:
    Solid tumors: Lung, colon, stomach, breast
    Hematologic: Leukemia, lymphoma, multiple myeloma
  - Systemic disease: Amyloidosis, SLE, sarcoid, amyloidosis, erythema multiforme, Henoch-Schönlein purpura, polyarteritis nodosa, Sjögren syndrome, rheumatoid arthritis
  - Metabolic diseases: Diabetes mellitus, myxedema
  - Heredofamilial disease: Sickle cell anemia, Alport syndrome, Fabry disease
  - Miscellaneous: Preeclampsia, renal artery stenosis, reflux nephropathy, malignant HTN

DIAGNOSIS

HISTORY

- Symptoms of fluid/sodium retention:
  - Periorbital edema, especially on awakening
  - Peripheral edema, especially at end of day
  - Dyspnea/orthopnea secondary to pleural effusion
  - Ascites, HTN, scrotal swelling
- Other symptoms: Anorexia, HTN, oliguria, orthostatic hypotension, retinal sheen, skin striae, foamy urine
- History of systemic disease causing NS:
  - See “Commonly Associated Conditions.”
  - History of infection: HIV disease, hepatitis B or C
  - Medication or illicit drug use
  - History of cancer or signs of malignancy (weight loss, bowel changes, bleeding)
  - Travel history (especially to endemic areas for malaria)
  - Evidence of other systemic disease: Rash, arthralgias, night sweats
  - Other medical illnesses: Diabetes, HTN
  - Family history: Deafness, renal disease, sickle cell anemia

PHYSICAL EXAM

- Along with signs of fluid retention, patients may have signs of systemic disease causing NS
- Vital signs: BP, temperature, weight
- Skin exam: Rash (eg, butterfly rash of SLE), pallor, edema, lymphadenopathy
- Ophthalmic exam: Uveitis in sarcoid, diabetic retinopathy
- Heart/lung exam: Endocarditis, pleural effusion
- Abdominal exam: Masses, ascites
- Neurologic exam: Diabetic neuropathy, CNS lesion, mononeuritis multiplex

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - Marked proteinuria causes urine to foam.
  - Albuminuria detected by dipstick; all proteinuria detected by SSA
  - Positive SSA and negative dipstick: Non-albumin 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)
  - Lipiduria: Maltese crosses
  - Microscopic: Oval fat bodies, fatty casts, hyaline casts, cellular casts
- 24-hr urine protein:
  - NS characterized by massive proteinuria (mostly albumin)
- CBC:
  - Cause of anemia should be evaluated.
  - Leukocytosis suggests infection or leukemia.
  - Leukopenia or thrombocytopenia may be seen in SLE, lymphoma, etc.
- Renal function/electrolytes:
  - Abnormal renal function suggests longstanding NS or a nephritic syndrome.
- Serology:
  - Serum albumin
  - Liver function enzymes
  - VDRL test, HIV, hepatitis panel may be appropriate.
  - Other screening tests: Antinuclear antibody, complements, rheumatoid factor
- Urine and serum protein electrophoresis if multiple myeloma suspected
- Coagulation profile
- Lipid profile: Cholesterol, triglycerides

Imaging

- Renal US:
  - Increased echogenicity of renal parenchyma suggests advanced glomerular disease
  - A solitary kidney (unilateral renal agenesis, previous nephrectomy) can result in FSGS
  - Doppler US for renal artery stenosis
- CXR, CT, and endoscopy: To rule out malignancy or sarcoidosis if suspected.

Diagnostic Procedures/Surgery

Renal biopsy:

- In children, due to high prevalence of minimal change disease, biopsy not necessary and treatment usually empiric
- If cause of NS not identified in an adult, kidney biopsy indicated
- Contraindications to biopsy: Coagulopathy, uncooperative patient, uncontrolled HTN, pyelonephritis, severe anemia
- Relative contraindication: Solitary kidney

Pathological Findings

Various pathologic patterns can be differentiated on kidney biopsy:

- Minimal change glomerulopathy
- Membranous glomerulopathy
- Focal segmental glomerulosclerosis
- Mesangioproliferative glomerulonephritis
- Membranoproliferative glomerulonephritis
- Diabetic glomerulosclerosis
- Fibrillary glomerulonephritis
- Light-chain deposition disease
- Other rare lesions

DIFFERENTIAL DIAGNOSIS

Any edema-forming state (congestive heart failure, cirrhosis, malnutrition, protein-losing enteropathy); however, these conditions usually do not cause heavy proteinuria

TREATMENT

- Sodium restriction (2–3 g/d)
- Low-protein, low-lipid/cholesterol diet
- Strict input/output, daily weights
- Vigorous treatment of infections
- Avoid excessive sunlight.
- Avoid nephrotoxic drugs.
- Vaccines: Pneumococcal, influenza, and Haemophilus influenzae

MEDICATION

First Line

- Secondary NS: Treat the underlying cause.

)[A]

- Steroids and/or immunosuppression: Frequently relapsing MCD, RPGN, MGN, SLE
- Diuretics: Thiazide and loop diuretics to treat edema

)[A]

)[B]

  - Reduce proteinuria, hyperlipidemia, thrombotic tendency, progression of renal failure
  - Control HTN if present, indicated even in normotensive patients
  - Side effects include hyperkalemia and potential worsening of renal function.

- Prophylactic anticoagulation therapy in high-risk patients (serum albumin <2.5 g/dL, proteinuria >10 g/d):

  - Low-dose aspirin may be of benefit.
  - Chronic anticoagulation: Indicated if a thromboembolic complication has occurred

Second Line

)[A]

- Vitamin D for hypocalcemia

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

- Sodium retention: Ascites, pleural effusion
- Hyperlipidemia, cardiovascular disease
- Thromboembolism:
  - Renal vein thrombosis in 20–30% of patients with membranous glomerulopathy
  - Risk of DVT and PE
- Infections: Increased susceptibility due to low levels of both IgG and components of alternative complement pathway
- Renal failure
- Protein malnutrition

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Most patients can be managed as outpatient; inpatient admission for complications
- 24-hr urine for protein to judge response to therapy
- Monitor for treatment toxicity:
  - Leukopenia: Alkylating agents
  - Infections: Steroids, alkylating agents, cyclosporine
  - Steroid-induced hyperglycemia, osteoporosis
- Attention to sodium retention, hyperlipidemia, thromboembolic complications

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ADDITIONAL READING

- www.kidney.niddk.nih.gov

See Also (Topic, Algorithm, Electronic Media Element)

- Glomerulonephritis, Acute
- Nephropathy, Membranous
- Nephropathy, Minimal Change
- Proteinuria

CODES

ICD9

- 581.9 Nephrotic syndrome with unspecified pathological lesion in kidney
- 581.89 Other nephrotic syndrome with specified pathological lesion in kidney

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- BP: Blood pressure
- CBC: Complete blood count
- CNS: Central nervous system
- CXR: Chest x-ray
- DVT: Deep venous thrombosis
- FSGS: Focal segmental glomerulosclerosis
- GBM: Glomerular basement membrane
- HIV: Human immunodeficiency virus
- MCD: Minimal change disease
- MGN: Membranous glomerulonephropathy
- NS: Nephrotic syndrome
- NSAID: Nonsteroidal anti-inflammatory drug
- PE: Pulmonary embolism
- PSGN: Post-streptococcal glomerulonephritis
- RPGN: Rapidly proliferative glomerulonephritis
- SLE: Systemic lupus erythematosus
- SSA: Sulfosalicylic acid
- STD: Sexually transmitted disease

- US: Ultrasound

NEUROBLASTOMA

Paul F. Austin, MD

BASICS

DESCRIPTION

- A heterogeneous malignancy arising from cells of neural crest that form the sympathetic nervous system.
- Staging:
  - TNM classification based on anatomic location of tumor determined by surgery, adopted by the POG
  - Worldwide consensus on staging (INSS):

    Stage 1: Localized tumor with complete excision; ipsilateral nodes negative

    Stage 2A: Localized tumor with incomplete excision; ipsilateral nodes negative

    Stage 2B: Localized tumor with or without complete excision; ipsilateral nodes positive; enlarged contralateral nodes negative

    Stage 3: Unresectable unilateral tumor infiltrating across the midline, or localized unilateral tumor with contralateral nodes positive

    Stage 4: Any primary tumor with metastasis to distant nodes, bone, bone marrow, liver, skin

    Stage 4S: Localized primary (1, 2A, 2B) age <1 yr, with metastasis limited to skin, liver, or bone marrow
- Synonym(s): Small blue round cell neoplasm of childhood

EPIDEMIOLOGY

- 1 in 100,000 live births
- 10.5 per million children <15 yr of age
- Peak age: 0–4 yr of age
  - Median age of 18–24 mo
- Incidental autopsy 400 times greater clinical incidence
- 7–8% of all childhood malignancies
- Most common solid tumor of infancy
- 2nd most common extracranial malignant tumor of childhood
- 50% in children <2 yr of age
- 15% of cancer deaths in children

RISK FACTORS

- The risk of NB in a sibling or offspring is <6%.
- Environmental factors are implicated in the development of NB:

- Paternal exposure to electromagnetic fields
- Prenatal exposure to alcohol, pesticides, or phenobarbital
- Potential relationship with assisted pregnancies

Genetics

- 20% MYCN oncogene amplification in primary:
  - Most common genetic aberration associated with poor outcome
- Chromosome 1p deletion:
  - 25–35% of NB
  - 70–80% of the near-diploid tumors
- Allelic loss of 11q:
  - Present in 35–45% of primary tumors
- Familial forms of NB are rare, accounting for about 1% of all cases:
  - 20% familial are autosomal dominant

GENERAL PREVENTION

- Genetic counseling as indicated
- Screening initiatives (Japan and Quebec) using urinary catecholamines are not effective.

PATHOPHYSIOLOGY

- Depends on site of tumor origin, disease extent, and the presence of paraneoplastic syndromes
- Spinal cord and sympathetic ganglia involvement:
  - Urinary retention, constipation, extremity paresis, Horner syndrome
- Presence of metastasis:
  - Fever, lethargy, weight loss, bony pain, pallor
- Bone metastasis: More common in older children
- Metastasis to liver: More common in younger children
- Active biochemical products:
  - 90% of tumors produce catecholamines:
    Paroxysmal HTN, palpitation, flushing, and headache
  - HVA is the primary by-product in less differentiated tumors.
  - VMA is the primary by-product in more differentiated tumors.
  - VIP: Diarrhea

COMMONLY ASSOCIATED CONDITIONS

Other neural crest disorders or malignancies:

- Hirschsprung disease

- Neurofibromatosis type 1 (von Recklinghausen disease)
- Congenital central hypoventilation syndrome

DIAGNOSIS

HISTORY

- Early satiety, poor appetite, vomiting:
  - A large intra-abdominal mass may cause partial intestinal tract obstruction.
- Unexplained fever, weight loss, anorexia, pallor, irritability suggests metastatic disease.
- Urinary frequency, urinary retention, or constipation:
  - Presacral mass may cause extrinsic compression of pelvic organs and/or nerves
- Poor truncal balance, jerky muscle movements, or uncontrolled eye movement:
  - Acute myoclonic encephalopathy ~2%:
    Toxic byproducts/autoimmune phenomenon
- Pain in skull and long bones:
  - Metastasis to the bones
- Pallor and anemia:
  - Suggests bone marrow involvement:
    Present in 50% of children with NB
- Bleeding diathesis, easy bruising:
  - Liver metastasis may cause coagulopathy.
- Lower or upper extremity weakness, sensory symptoms:
  - Paravertebral sympathetic ganglia NB may compress the spinal cord.
- Paroxysmal HTN, sweating, headaches, palpitations:
  - Not common (5%) because catecholamines are sequestered within intracellular vacuoles
- Watery diarrhea secondary to VIP secretion
- Family history of NB

PHYSICAL EXAM

- HTN:
  - Rare; may be due to catecholamine release
- Abdominal mass:
  - 55% NB within the abdomen; adrenal gland most common site
- Bluish/erythematous subcutaneous nodules:
  - Metastatic spread is to the skin; origin of misnomer blueberry-muffin baby
  - NB has an eruption that resembles a blueberry muffin appearance that is more often due to rubella

- Ataxia, myoclonus, multidirectional eye movement:
  - Toxic effects of catecholamine by-products or autoimmune phenomenon
- Ptosis, loss of pupillary dilation, unilateral anhydrosis:
  - Unilateral Horner syndrome: Tumor compressing sympathetic ganglia or cord
- Ocular proptosis and upper eyelid ecchymosis:
  - Periorbital metastasis
- Extremity paresis, sensory deficits:
  - Paravertebral lesion growing into and compressing spinal cord

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Anemia suggests bone marrow replacement.
- PT/PTT: Elevation suggests liver involvement
- 24-hr urine for VMA and HVA:
  - Elevated in 95% of patients with NB
- Serum ferritin in 40–50% with advanced disease. Must be elevated >3 standard deviations

Imaging

- US is often 1st test of choice in children with an abdominal mass. Can be usually performed without the need for sedation
- Full body CT or MRI:
  - Often requires sedation in a younger child
  - Most useful to evaluate primary tumor and regional extent:

    Paravertebral tumors may grow through the intervertebral foramen into the spinal canal, producing a dumbbell-shaped tumor.
  - Assess for distant spread
- Site of primary tumor in decreasing order: Abdomen (adrenal the most common), chest, neck, pelvis, and neck
- Skeletal survey/bone scan:
  - Evaluate for skeletal metastasis
- MRI brain imaging:
  - Recommended only if clinically indicated by exam or neurologic symptoms
- Incidental KUB: Speckled calcification in 50%
- MIBG scan images primary as well as metastatic sites; useful for both bone and soft-tissue metastasis

Diagnostic Procedures/Surgery

- Pathologic confirmation from tumor tissue or by tumor cells in a bone marrow sample
- Bone marrow biopsy:
  - Bilateral posterior iliac crest marrow aspirates and core biopsies are required to exclude marrow involvement.

Pathological Findings

- Gross: Vascular, purple mass usually solid but may be cystic, hemorrhagic, poorly encapsulated
- Histology: Classified as small round cell tumor of childhood, with lobular growth, and cells forming pseudorosettes
- Common histopathology markers:
  - MYCN
  - DNA ploidy
  - Shimada classification
  - TrkA neurotrophin receptors
  - MRP
- NSE staining is specific for NB.
- PAS staining can distinguish sarcomas.

DIFFERENTIAL DIAGNOSIS

- Ganglioneuroma:
  - Benign counterpart of NB
- Ganglioneuroblastoma:
  - Intermediate differentiation between NB and ganglioneuroma
- Intra-abdominal mass in childhood:
  - Wilms tumor
  - Teratomas
  - Rare primary neoplasms of liver and pancreas
  - Lymphoma
  - Rhabdomyosarcoma
  - Ewing sarcoma

TREATMENT

- Multidisciplinary approach:
  - Common modalities: Surgery, chemotherapy, and bone or stem cell transplantation
- Generally, the more advanced the disease, the more complex and radical the protocol needed to induce remission.

- Treatment schema based on INSS stage, age, MYCN amplification, DNA ploidy, and Shimada histopathology.
- Observation of stage 4S patients:
  - Nearly all spontaneously regress

MEDICATION

- Low risk (none unless surgery fails):
  - Low-dose cycles of cyclophosphamide, Adriamycin, and cisplatin/VM-26
- Intermediate risk: Induction with cyclophosphamide and Adriamycin cycles with or without radiotherapy. Maintenance with cisplatin/VM-26 or others
- High risk: Cyclophosphamide, Adriamycin, VM-26, doxorubicin, cisplatin, etoposide in various combinations

SURGERY/OTHER PROCEDURES

- Low risk (stages 1, 2A, 2B, 4S with age <1 yr, or age >1 yr with favorable pathology):
  - Surgical resection of tumor
- Intermediate risk (stage 3 with age <1 yr, or >1 yr with favorable pathology, or stages 4, 4S with age <1 yr):
  - Surgery and multiagent chemotherapy
- High risk (stages 2A, 2B with age >1 yr with unfavorable histopathology, or stages 3, 4, 4S with amplification of MYCN regardless of age):
  - Intensive chemotherapy with or without bone marrow ablation and repeated surgery

ADDITIONAL TREATMENT

RADIOTHERAPY

- Cytoreduction in anticipation of 2nd-look surgical excision
- Adjunct to chemotherapy
- Palliation/treatment of pain
- Part of bone marrow transplant protocol

Additional Therapies

Bone marrow transplantation

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Targeted delivery with radionuclides:

- Iodine131 MIBG for refractory NB

ONGOING CARE

PROGNOSIS

- Prognosis ranges from near uniform survival to fatal demise:

- 5-yr survival:
  - Low risk: 85–98%
  - Intermediate risk: 55–90%
  - High risk: 10–30%
- Favorable prognostic factors include:
  - Nonadrenal primary
  - Stages I, II, IV–S
  - Age at diagnosis <1 yr of age
  - Serum ferritin <150 ng/mL
  - High expression of TrkA
- Poor prognostic factors include:
  - Adrenal origin
  - Age >1 yr of age
  - Stages III and IV
  - MYCN amplification
  - NSE >100 ng/mL
  - Chromosome 1p deletion
  - Increased vascularity.
- DNA index is a prognostic marker:
  - Diploid, less favorable
  - Hyperdiploid, more favorable
- Shimada classification:
  - Favorable tumors:

    Mature and stroma-rich histology (Schwannian stroma content)

    Low mitosis-to-karyorrhexis index (MKI)

    Young age

COMPLICATIONS

- Dumbbell NB with spinal cord compression:
  - Best treated with chemotherapy
  - Neurosurgical intervention is reserved for emergent decompression.
- Associated with tumor presentation and with treatment modalities

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- 1st yr: Exam every month, with imaging and bone marrow biopsy every 3 mo
- 2nd yr: Exam every 2 mo, with imaging and bone marrow biopsy every 6 mo

- 3rd yr: Exam every 3 mo, with imaging and bone marrow biopsy if indicated
- HVA or VMA may be followed if the pretreatment workup showed elevated levels.

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See Also (Topic, Algorithm, Electronic Media Element)

- Abdominal Mass, Newborn/Child, Urologic Considerations
- Renal Mass

CODES

ICD9

194.0 Malignant neoplasm of adrenal gland

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- HVA: Homovanillic acid
- INSS: International Neuroblastoma Staging System
- KUB: Kidneys, ureters, bladder
- MIBG: Metaiodobenzylguanidine
- MKI: Mitosis-to-karyorrhexis index
- MRI: Magnetic resonance imaging
- MRP: Multidrug resistance protein
- MYCN: Myelocytomatosis viral related oncogene, neuroblastoma derived
- NB: Neuroblastoma
- NSE: Neuron-specific enolase
- PAS: Periodic-acid Schiff
- POG: Pediatric Oncology Group
- TrkA: Tyrosine kinase receptor A
- VMA: Vanillylmandelic acid
- VIP: Vasoactive intestinal peptide
- VM-26: Teniposide

NEUROGENIC BLADDER, GENERAL

Patrick J. Shenot, MD

BASICS

DESCRIPTION

Dysfunction of the urinary bladder due to disease of the central nervous system or peripheral nerves involved in the control of micturition

EPIDEMIOLOGY

Prevalence of voiding dysfunction is reported for specific conditions:

- Cerebrovascular accident: 20–50%
- Parkinson disease: 35–70%
- Multiple sclerosis: 50–90%
- Diabetes mellitus: 5–59%

RISK FACTORS

- Neurologic disease, injury, or congenital malformation
- Diabetes mellitus
- Radical pelvic surgery

Genetics

Genetic diseases that may be associated with neurogenic bladder include muscular dystrophy, hereditary spastic paraplegia, neurofibromatosis, and familial dysautonomia.

GENERAL PREVENTION

- Prevention aimed at preventing secondary complications
- Infections
- Incontinence
- Skin breakdown
- Urolithiasis

PATHOPHYSIOLOGY

- Voiding center include:
  - Higher centers (suprapontine):

    Function: Inhibits sacral micturition center

    Predicted type of voiding dysfunction with suprapontine lesion would be detrusor overactivity due to loss of inhibition on sacral micturition center
  - Pontine micturition center:

    Function: Coordinates sphincter relaxation during bladder contraction

    Predicted type of dysfunction with lesion between pontine and sacral micturition centers is detrusor overactivity with sphincter dyssynergia

- Sacral micturition center:

  Function: Mediates reflex and voluntary bladder contraction

  Predicted type of dysfunction with lesion of sacral micturition centers is detrusor underactivity or areflexia

- Peripheral lesions: Voiding dysfunction is variable including:
  - Detrusor underactivity
  - Impaired bladder sensation
  - Impaired sphincteric function

COMMONLY ASSOCIATED CONDITIONS

- CNS diseases:
  - Cerebrovascular accident
  - Spinal cord injury
  - Transverse myelitis
  - Multiple sclerosis
  - Parkinson disease
  - Normal-pressure hydrocephalus
- Peripheral nerve disease:
  - Following radical pelvic surgery:

    Abdominoperineal resection

    Radical hysterectomy
  - Diabetes mellitus
  - Intervertebral disk disease
  - Spinal stenosis
  - Guillain-Barré syndrome
- Neural tube defects
- Static disorders of development such as cerebral palsy

DIAGNOSIS

HISTORY

- Neurologic disease: Onset, duration
- Diabetes
- Congenital disorders:
  - Neural tube defects
  - Cerebral palsy
- History of radical pelvic surgery
- Voiding symptoms:

  - Irritative or obstructive
  - Incontinence: Urge, stress
- Method of urinary management:
  - Volitional or reflex voiding
  - Condom catheter urinary collection
  - Intermittent self-catheterization
  - Indwelling urethral or suprapubic catheter
  - Credé, Valsalva voiding
- UTI:
  - Severity of infection: Febrile, hospitalization, IV antibiotics required
  - Frequency of recurrence
- Urolithiasis episodes, surgical intervention, calculus composition
- AD: Associated with urination in spinal cord disease at or above T6

PHYSICAL EXAM

- HTN:
  - Often noted with renal dysfunction
  - Autonomic dysreflexia with lesions between T6 and pontine micturition center with manipulation of the GI/GU systems
- Generalized edema: Severe renal insufficiency
- Palpable flank mass: Hydronephrosis
- Flank tenderness: Ureteral obstruction, pyelonephritis
- Abdominal mass: Distended bladder, urinary retention
- Incontinence of urine:
  - Stress maneuvers: Marshall test
- Testicular mass:
  - Epididymo-orchitis/epididymitis; secondary abscess
- Prostate:
  - Size: BPH may coexist with neurogenic bladder dysfunction
- Evaluate for sacral abnormalities:
  - Sacral dimple or tuft of hair
  - Sacral agenesis
- Neurologic:
  - Sacral root
  - Perianal sensation
  - Anal tone, sphincter control

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood studies:
  - Serum chemistry: Renal function, creatinine
  - CBC: Elevated WBC, secondary anemia due to decreased renal function or chronic infection
- Urinalysis:
  - Proteinuria: Renal dysfunction
  - Pyuria, nitrite, leukocyte esterase: Acute or chronic infection
  - Hematuria: Infection or lithiasis

Imaging

- Imaging is most important in patients with risk factors for upper-tract compromise:
  - Detrusor sphincter dyssynergia, particularly males who void reflexively
  - Impaired bladder compliance
- Renal US: To screen for calculus, hydronephrosis, or mass
- Excretory urography:
  - Delayed excretion of contrast with high urinary-storage pressures
  - Hydroureteronephrosis:
    Marked elevation of intravesical pressure (ie, NDO/DSD) or calculi
- Nuclear medicine renal scan:
  - Sequential studies detect deterioration of renal function.

Diagnostic Procedures/Surgery

Urodynamics: Necessary to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction

Pathological Findings

Bladder wall thickening and fibrosis common

DIFFERENTIAL DIAGNOSIS

- Classification of neurogenic bladder most often done using urodynamic classification scheme
- NDO (uncontrolled reflex bladder contraction):
  - Collateral sprouting of new neural pathways
  - Loss of inhibitory impulses from cortical centers; primitive reflex pathways
- DSD (abnormal reflexive sphincter contraction during involuntary detrusor contraction):
  - Functional bladder outflow obstruction, elevated intravesical pressure
  - Secondary damage: Pressure, infection, urolithiasis

– Detrusor overactivity must be present for DSD. NDO may occur without DSD.

– 10–20% of patients have internal (bladder neck) sphincter dyssynergia with external sphincter dyssynergia.

– Elevated intravesical pressure >40 cm H2O responsible for sequelae of NDO-DSD

- Detrusor underactivity or areflexia:
  - Interruption of sacral reflex arc; no detrusor contraction
  - Typically low-pressure storage (volumes up to 500 mL)
  - Adrenergic overgrowth: May result in decreased bladder compliance, elevated storage pressure

TREATMENT

- Urodynamics are essential to determine lower urinary tract function/dysfunction and to plan urologic management.
- Control intravesical pressure; protects upper tracts
- Spontaneous voiding with continence is possible with NDO controlled medically.
- Urinary drainage: Intermittent catheterization or external collection appliance
- Indwelling catheterization: Avoid due to complications (UTI, erosion, calculi, etc.).
- Intermittent self-catheterization: Most effective treatment; requires low storage pressure

MEDICATION

First Line

- Anticholinergics to improve urinary storage pressure/decrease involuntary contraction:
  - Oxybutynin 5 mg PO t.i.d.–q.i.d.
  - Hyoscyamine 0.125 mg PO q.i.d.
  - Tolterodine LA 4 mg/d PO
- 1-Adrenergic blockers: Decrease internal sphincter resistance, lower voiding pressure; ineffective for DSD. May help control symptoms of autonomic dysreflexia:
  - Doxazosin 2–8 mg/d PO
  - Terazosin 2–5 mg PO q.d.–b.i.d.
  - Tamsulosin 0.4 mg/d PO

Second Line

)[C]

- Botulinum toxin injection into the detrusor for detrusor overactivity:
  - Duration of action is 3–9 mo
  - Requires repeated injections

SURGERY/OTHER PROCEDURES

- Endoscopic sphincter ablation or stenting:

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- Augmentation cystoplasty using an intestinal segment to enlarge the bladder, increasing bladder volume and decreased pressure:
  - Intermittent catheterization for urinary drainage
  - Limited dexterity mandates construction of a continent catheterizable stoma for the urinary reservoir, especially in females.
- Ileovesicostomy (bladder chimney):
  - Useful for those unable to perform self-catheterization (ie, quadriplegia)
- Cystectomy with continent urinary reservoir
- Ileal or colon pouch; continent catheterizable stoma (appendix or tapered ileum) on abdomen
- Cystectomy with ileal conduit

ADDITIONAL TREATMENT

- Vanilloid agents such as capsaicin and resiniferatoxin: Suppress uninhibited involuntary detrusor contraction
- Sacral neuromodulation in selected cases

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Acupuncture has been reported to improve symptoms of neurogenic bladder.

ONGOING CARE

PROGNOSIS

Proper urologic management greatly improves quality of life in patients with neurogenic bladder dysfunction.

COMPLICATIONS

- Recurrent UTI
- Urinary retention
- Hydroureteronephrosis
- Neoplastic transformation: Associated with chronic catheter
- Urethral erosion

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

):

- Urodynamics
- Imaging: Typically renal US
- Serum creatinine

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Areflexia (Detrusor Areflexia)
- Detrusor Overactivity
- Detrusor-Sphincter Dyssynergia (DSD)
- Incontinence, Urinary, Adult Male
- Incontinence, Urinary, Adult Female
- Incontinence, Urinary, Pediatric
- Overactive Bladder
- Spinal Cord Injury, Urologic Considerations
- Stroke (CVA), Urologic Considerations

CODES

ICD9

596.54 Neurogenic bladder nos

ABBREVIATIONS

- AD: Autonomic dysreflexia
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- DSD: Detrusor sphincter dyssynergia
- NDO: Neurogenic detrusor overactivity
- SCI: Spinal cord injury
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

NOCTURIA

Doron S. Stember, MD
Neil H. Grafstein, MD

BASICS

DESCRIPTION

- Nocturia, or waking at night to void, is a common cause of sleep disturbance.
- It is differentiated from enuresis (bedwetting) in that the person does not wake and the bladder empties regardless.
- Nocturia negatively impacts quality of life, and is associated with depression, daytime fatigue, and increased orthopedic morbidity among the elderly.
- The underlying etiologies of nocturia, either in isolation or in combination, are:
  - Nocturnal polyuria: The rate of urine output is excessive only at night and total 24-hr output is within normal limits.
  - Reduced voided volumes
  - 24-hr polyuria
- Differentiating between these causes enables the physician to direct a rational, targeted treatment plan.
- Voiding diary: Analysis of a patient-generated frequency-volume chart is crucial to this differential diagnosis.
- Sleep disorders: Must distinguish between the urge to void as the primary factor in awakening vs. a primary sleep disorder such as insomnia or restless leg syndrome:

)[A]

EPIDEMIOLOGY

- The incidence of nocturia and total number of voiding episodes increases with age.
- Overall: 28%
- Age >60: 41%
- Body mass index >29: 36%

)[A]

RISK FACTORS

- Advanced age
- Diuretic usage
- Lower urinary tract dysfunction
- Cardiac disease
- Obesity, sleep apnea

GENERAL PREVENTION

• Avoid excessive evening fluid intake, alcohol, and caffeine, all of which can exacerbate nocturia irrespective of the etiology.

• Closely monitor and control of the underlying conditions that cause nocturia

• Maintain bowel regularity and avoid constipation.

PATHOPHYSIOLOGY

• 24-hr polyuria: Excessive total urine production due to either pathologic (eg, diabetes insipidus) or physiologic (polydipsia) increased excretion:

– Diabetes mellitus: Secondary to polydipsia and osmotic diuresis from hyperglycemia

– Diabetes insipidus: Under-secretion (central) or impaired response (nephrogenic) to ADH

– Medications: Lithium (mechanism similar to nephrogenic diabetes insipidus), diuretics, caffeine, nephrotoxic medications (eg, NSAIDs, aminoglycosides)

– Hypercalcemia: Can cause osmotic diuresis

– Hyperaldosteronism:

Psychogenic polydipsia

• Nocturnal polyuria refers to a relative increased production of urine at night that is often offset by lowered daytime urine production resulting in normal 24-hr urine volume. Causes include:

– Age-related loss of the normal diurnal secretion of vasopressin, resulting in increased nocturnal urine output

– Peripheral edema: Fluid that accumulates in the lower extremities when upright during the day is mobilized when supine at night, causing an increase in GFR and excretion. Conditions: CHF, liver disease, nephrotic syndrome, hypoalbuminemia, venous insufficiency, lymphedema

– Sleep apnea: Transient periods of hypoxemia lead to increased pulmonary vascular resistance and secretion of atrial natriuretic peptide, a potent diuretic.

– Medications: Poorly timed/dosed diuretics that exert maximal effect during sleeping hours

– Excessive fluid intake prior to bedtime, resulting in a physiologic large volume excretion.

• Reduced bladder capacity implies intrinsic lower urinary tract dysfunction and results in reduced voided volumes. The nocturia is a manifestation of any pathologic process that leads to reduced bladder capacity, poor compliance, or detrusor overactivity:

– Idiopathic, nonneurogenic OAB

– Neurogenic OAB: Multiple sclerosis, stroke, Parkinson disease, spina bifida, diabetic cystopathy, herniated disk, spinal stenosis

– Inflammatory: UTI (prostatitis, cystitis, urethritis), radiation cystitis, bladder calculi, interstitial cystitis

– Neoplastic: BPH and bladder outlet obstruction, bladder cancer and CIS, locally advanced prostate cancer

– Traumatic: Spinal cord injury, neurogenic bladder, urethral stricture, iatrogenic injury to pelvic nerves or bladder, foreign body within bladder (ureteral stent, eroded synthetic sling)

– Mixed: Noctural polyuria in a patient with low bladder capacity can be nocturnal or global (over 24 hr)

COMMONLY ASSOCIATED CONDITIONS

- Bladder outlet obstruction
- OAB: Idiopathic and neurogenic
- Detrusor hyperactivity with impaired contractility
- Radiation cystitis
- Diabetes mellitus
- Psychogenic polydipsia
- Depression
- Obesity
- See also “Pathophysiology.”

DIAGNOSIS

HISTORY

- Over the past month, how often did patient most typically get up at night to urinate from time of going to bed until time of waking in the morning (AUA symptom index)
- Assess daytime lower urinary tract symptoms: Storage and voiding symptoms.
- Degree of bother assessment may be more valuable than quantification of nocturia episodes.
- Sleeping habits: Differentiate between awakening due to the urge to void or due to other sleep disturbance (restless leg syndrome, anxiety, etc.)
- Fluid intake habits including timing, volume; caffeine and alcohol consumption
- Previous pelvic surgery or radiation
- Indirect symptoms of nocturia: Daytime fatigue and depression
- Review of medications known to contribute to nocturia: Diuretics, cardiac glycosides, lithium, and phenytoin

- Swelling of lower extremities

PHYSICAL EXAM

- Global or focal neurologic deficits
- Digital rectal: Fecal impaction and 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 increases possibility of sleep apnea

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: Low specific gravity (polyuria), RBCs (rule out stones, bladder cancer, foreign body, etc.), proteinuria (nephrotic syndrome), glucosuria (diabetes mellitus), pyuria (UTI)
- Urine culture: UTI
- Urine osmolality: Dilute low values suggest inappropriate excretion or excess intake of water
- PSA if indicated
- Serum electrolytes: Hypokalemia with diuretic use, CHF, or hyperaldosteronemia

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; routinely ordered in cases of neurogenic bladder.

Diagnostic Procedures/Surgery

- Voiding diaries are essential for elucidating the underlying etiology of nocturia:
  - All voiding episodes and volumes should be recorded for a 24-hr period; the time the patient actually goes to sleep and awakens for the day should also be noted.
  - 24-hr urine volume is the total volume voided in 24 hr.
  - Nocturnal urine volume is the total volume of urine voided during the night (the 1st morning void is included in this sum since it represents urine excreted during sleep hours).
  - The NPi is calculated by dividing nocturnal urine volume by the total volume voided over the 24-hr period:

    NPi >35% = nocturnal polyuria
- Urodynamic studies can be helpful when nocturia is associated with reduced voided volumes, particularly when empiric treatment for OAB or bladder outlet obstruction has failed

to improve nocturia.

- Polysomnographic sleep studies: Differentiate between sleep disorder and true nocturia

DIFFERENTIAL DIAGNOSIS

Nocturia is a simple term defined as waking at night to urinate; the use of voiding diary data narrows the diagnosis category to nocturnal polyuria, reduced voided volumes, or mixed nocturia.

- Sleep disorders: Most patients awaken due to the sleep disturbance, but recall this as an awakening to void. Difficult to distinguish by history alone; may need polysomnography
- Urologic: Benign prostatic obstruction, OAB, incomplete bladder emptying.
- Nonurologic: Renal failure, idiopathic nocturnal polyuria, diabetes mellitus, central diabetes insipidus, nephrogenic diabetes insipidus, primary polydipsia, hypercalcemia, drugs, autonomic failure, obstructive sleep apnea.

TREATMENT

- Bedside commode or urinal to obviate repeated trips to restroom, particularly in elderly or neurogenics at high risk for falls
- Behavioral modification, including limiting evening oral fluid intake, especially of caffeine and alcohol
- When nocturnal polyuria is secondary to peripheral edema, use compressive stockings and leg elevation during the daytime hours to prevent sequestration of fluid in the lower extremities.
- Timed voiding: Empty bladder prior to bedtime

MEDICATION

First Line

- Nocturnal polyuria secondary to furosemide: Change to afternoon dosing to induce an early evening diuresis rather than a nocturnal diuresis.

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- Treatment of underlying condition associated with nocturia (ie, antiglycemics and diet control) to reduce the osmotic effect of glycosuria in patients with diabetes mellitus

Second Line

)[B]:

  - Dosing: 0.1 mg PO titrate up to 0.4 mg

Geriatric Considerations

- DDAVP has high risk of hyponatremia.

- CPAP for obstructive sleep apnea

SURGERY/OTHER PROCEDURES

)[B]

ADDITIONAL TREATMENT

)[A]

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, from rising from sleep to urinate
- DDAVP can lead to hyponatremia.
- Urinary retention secondary to antimuscarinics

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Bladder sonography with PVR as needed, particularly when treating men with antimuscarinics
- Repeat 24-hr voiding diaries
- Regular monitoring of serum electrolytes with DDAVP use

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Outlet Obstruction
- Diabetes Mellitus
- Incontinence, Adult Female
- Incontinence, Adult Male
- Neurogenic Bladder
- Nocturia Algorithm
- Overactive Bladder
- Urgency, Urinary (Frequency and Urgency)
- Urodynamics
- Voiding Diory

CODES

ICD9

788.43 Nocturia

ABBREVIATIONS

- ADH: Antidiuretic hormone
- AUA: American Urological Association
- BPH: Benign prostatic hypertrophy
- CHF: Congestive heart failure
- CIS: Carcinoma in situ
- CPAP: Continuous positive airway pressure
- DDAVP: Desmopressin
- GFR: Glomerular filtration rate
- NPi: Nocturnal polyuria index

- NSAID: Nonsteroidal anti-inflammatory drug
- OAB: Overactive bladder
- PSA: Prostate-specific antigen
- PVR: Post void residual
- RBC: Red blood cells
- US: Ultrasound
- UTI: Urinary tract infection

ORCHITIS, GENERAL

Jeremy A. Davis, MD

J. Brantley Thrasher, MD

BASICS

DESCRIPTION

- An inflammatory reaction of the testes secondary to an infectious or noninfectious etiology
- Can be acute or chronic if present for >6 wk
- Untreated, epididymitis can progress to epididymo-orchitis.

EPIDEMIOLOGY

- Has declined dramatically since the development of a mumps vaccination
- 4 out of 5 cases occur in prepubertal males (<10 years old)
- ~20% of prepubertal males with mumps develop orchitis
- Rarely occurs in postpubertal males with mumps
- Bacterial orchitis is even more rare and is usually associated with concurrent epididymitis.

RISK FACTORS

- Not being vaccinated against mumps virus
- STD that can lead to epididymo-orchitis (ie, Neisseria, Chlamydia, Treponema)
- Epididymitis or BPH (ie, Escherichia, Klebsiella, Pseudomonas, Staphylococcus, and Streptococcus spp.)
- Fungal infections occasionally (ie, candidiasis, aspergillosis, histoplasmosis, coccidioidomycosis, blastomycosis, actinomycosis)
- Few case reports of mumps orchitis after immunization with MMR vaccine
- Immunocompromised patients (ie, Mycobacterium, Tuberculosis, Cryptococcus, Toxoplasma, Haemophilus, and Candida)
- History of intravesical BCG for bladder cancer

GENERAL PREVENTION

- Vaccination against mumps virus
- Protection from STD

PATHOPHYSIOLOGY

- Most commonly caused by the mumps virus by direct attack of testicular tissue forming parenchymal edema, congestion of seminiferous tubules, and perivascular infiltration of lymphocytes
- Rare case reports of other viruses causing orchitis (mononucleosis, coxsackie virus, others)

- Onset of scrotal pain and edema is acute.
- Unilateral in 70% of cases
- Contralateral testis involvement usually follows by 1–9 days
- Seminiferous tubules can experience necrosis from increased pressure and edema.
- Cases of bacterial orchitis usually result from local spread of an ipsilateral epididymitis.
- Truly noninfectious orchitis is usually idiopathic, trauma-related, or possibly autoimmune in etiology.

COMMONLY ASSOCIATED CONDITIONS

- Bladder cancer and history of intravesical BCG
- BPH particularly in men >50
- Epididymitis
- Immunocompromised states
- Mumps or other viral infections
- STDs in sexually active men
- UTI in boys or elderly men

DIAGNOSIS

HISTORY

- Testicular pain and swelling:
  - Mild discomfort to severe pain
- History of recent scrotal trauma
- Systemic symptoms:
  - Fatigue
  - Malaise
  - Myalgias
  - Fever and chills
  - Nausea
  - Headache
- Mumps orchitis follows development of parotitis by 4–7 days
- Obtain sexual history, when appropriate
- Evidence of immunocompromise
- Vaccination history
- History of BPH
- Recent instrumentation (ie, catheterization, prostate biopsy, cystoscopy) increases likelihood of epididymo-orchitis.
- BCG therapy may cause granulomatous orchitis.

PHYSICAL EXAM

- Testicular exam:
  - Unilateral or bilateral involvement
  - Enlargement, induration, tenderness common
  - Determine if masses are present
  - Erythema and edema of overlying scrotal skin
  - An enlarged epididymis is associated with epididymitis, typically unilateral
- Rectal exam:
  - A soft, boggy prostate, which signifies prostatitis, can be associated with epididymitis.
- Other:
  - Fever and or chills
  - Urethral discharge
  - Abdominal masses or tenderness
  - Parotitis
  - Urethritis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture
- Urethral cultures, if concerned for urethritis
- Mumps: Serum immunofluorescence antibody assay

Imaging

Trans-scrotal color Doppler US is considered required by many clinicians:

- Can rule out testicular torsion or malignancy

Diagnostic Procedures/Surgery

Usually not necessary

Pathological 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
- Hernia
- Granulomatous orchitis, infectious and non-infectious

- Reactive hydrocele
- Scrotal pyocele
- Testicular malakoplakia
- Testicular torsion
- Testicular tumor
- Torsion of testicular appendage

TREATMENT

- Supportive care
- Bed rest
- Hot or cold packs for analgesia:
  - Applied for 10–15 min q.i.d. or until pain subsides
- Scrotal elevation and support
- Counsel patient on safe sex practices if STD suspected.

MEDICATION

First Line

- No medications are indicated in the treatment of viral orchitis
- Bacterial orchitis requires coverage with an appropriate antibiotic for suspected infectious agents:
  - <35 yr and sexually active: Coverage for sexually transmitted pathogens is indicated with ceftriaxone 125–250 mg IM once and either doxycycline 100 mg PO b.i.d. for 7 days or azithromycin 1–2 g PO once
  - >35: Require additional gram-negative coverage with a fluoroquinolone or TMP-SMX

Second Line

- Analgesics
- NSAIDs
- Antiemetics

SURGERY/OTHER PROCEDURES

- Surgical procedures are generally not indicated in the treatment of orchitis.
- An associated hydrocele or pyocele may require surgery.

ADDITIONAL TREATMENT

Interferon-2B has been used in bilateral mumps orchitis, given that the mumps virus replicates with a virion-associated transcriptase.

ONGOING CARE

PROGNOSIS

- Most cases of mumps orchitis are self-limited and resolve within 3–10 days.
- With appropriate bacterial coverage, most cases of bacterial orchitis resolve without complication.

COMPLICATIONS

- No definitive evidence for increased risk of testicular tumor with a history of orchitis
- Unilateral testicular atrophy in up to 60%
- Sterility is rarely a sequela of unilateral orchitis.
- Impaired fertility is reported at a rate of 7–13%.

FOLLOW-UP RECOMMENDATIONS

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 HIV.

ADDITIONAL READING

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- Erpenach K. Systemic treatment with interferon-2B: An effective method to prevent sterility after bilateral mumps orchitis. J Urol 1999;146:54–56.
- Lane TM, Hines J. The management of mumps orchitis. BJU Int 2006;97(1):1–2.

See Also (Topic, Algorithm, Electronic Media Element)

- Acute Scrotum
- Mumps Orchitis
- Orchitis, Granulomatous
- Scrotum and Testicle, Mass
- Testis, Pain (Orchalgia)
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General

CODES

ICD9

- 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

ABBREVIATIONS

- BCG: Bacillus Calmette Guérin
- BPH: Benign prostatic hypertrophy

- HIV: Human immunodeficiency virus
- MMR: Measles, mumps, and rubella
- NSAID: Nonsteroidal anti-inflammatory drug
- STD: Sexually transmitted disease
- TMP-SMX: Trimethoprim sulfamethoxazole
- US: Ultrasound
- UTI: Urinary tract infection

OVERACTIVE BLADDER (OAB)

Debra L. Fromer, MD

Daniel I. Brison, MD

BASICS

DESCRIPTION

A disorder during which patients experience urgency ± urge incontinence, usually accompanied by frequency and/or nocturia in the absence of causative infection or identified pathologic conditions

EPIDEMIOLOGY

- ~16% of men and women over 40 suffer from OAB
- In patients >75 yr, the prevalence increases to 31% of women and 42% of men.

RISK FACTORS

- Caucasian
- Insulin-dependent diabetes mellitus
- Depression
- Age >75
- Arthritis
- Increased BMI

GENERAL PREVENTION

- High-fiber diet
- Limited consumption of caffeine and alcohol

PATHOPHYSIOLOGY

Overactivity of detrusor muscle:

- Neurogenic (eg, MS, Parkinson disease, stroke, spinal cord lesions, trauma)
- Myogenic (eg, aging, chronic bladder outlet obstruction, diabetes)
- Idiopathic
- Transient causes (DIAPPERS acronym):
  - Delirium
  - Infection
  - Atrophic urethritis/vaginitis
  - Pharmaceutical
  - Psychological
  - Excessive urine output
  - Restricted mobility
  - Stool impaction

DIAGNOSIS

HISTORY

- Factors associated with the onset of symptoms (eg, position, physical activity)
- Medical/surgical/ob-gyn history associated with the initial symptom presentation:
  - Possible nerve injury
  - Overcorrection of problem (cystocele repair/midurethral sling)
- Medications being used (prescription, OTC)
- Excessive/routine use of tobacco, alcohol, fluid intake
- Childbirth (NSVD, C-sections)
- Recent UTIs/Infections
- Postmenopausal:
  - Contributes to atrophic vaginitis/urethritis
- Neurologic history or events (eg, CVA/TIA, MS, Parkinson disease, trauma)

PHYSICAL EXAM

- Condition of vaginal mucosa: Atrophy
- Urethral mobility
- Pelvic organ prolapse
- Pelvic floor strength
- Bimanual exam
- Cough test: Stress incontinence
- Rectal exam: Constipation
- Mental status
- Bulbocavernosus reflex/anal wink: Nerve injury
- Knee/ankle deep tendon reflexes: Sacral nerve compromise/injury

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urinalysis, urine cultures:

- Infection
- Glycosuria: Possible diabetes
- Hematuria: Possible kidney/bladder pathology
- Proteinuria: Kidney/chronic disease
- Dysuria: Infection
- Cytology: Atypia, urothelial carcinoma

Imaging

- Cystography/video urodynamics

- Renal/bladder US

Diagnostic Procedures/Surgery

- Urodynamics:
  - Anatomic/functional information about bladder and urethra
  - True detrusor pressure
  - Involuntary contractions
  - Outlet obstruction
- Uroflowmetry: Abnormal voiding patterns
- Urethral pressure profilometry: Resting/dynamic urethral pressures
- Endoscopy/cystoscopy: Identifies lesions and foreign bodies
- Voiding/intake diary
- Pad test
- ICIQ
- PVR (catheterized or US)

DIFFERENTIAL DIAGNOSIS

- Bladder calculi
- Bladder neoplasms
- CIS
- IC
- Pelvic prolapse
- Polyuria
- Urethral diverticula
- UTIs

TREATMENT

MEDICATION

First Line

Antimuscarinics:

- Oxybutynin 5 mg b.i.d.–t.i.d.
- Oxybutynin XL 10–15 mg/d
- Tolterodine 2–4 mg/d
- Trospium XR 60 mg/d
- Solifenacin 5–10 mg/d
- Hyoscyamine extended-release 0.375 mg b.i.d.
- Transdermal oxybutynin patch 3.9 mg/d
- Fesoterodine 4–8 mg/d

Second Line

BOTOX injection: Pending FDA approval:

- Addresses both motor efferent innervation and sensory afferent nerves that contribute to refractory OAB
- Office procedure
- Transient effect

SURGERY/OTHER PROCEDURES

- Sacral nerve stimulation/InterStim®: Implanted neurostimulation of sacral nerves:
  - Modulates bladder, sphincter, and pelvic floor muscles
- Augmentation:
  - Reserved for people who failed other treatment modalities with severe symptomatology
  - Diversion

ADDITIONAL TREATMENT

- Behavioral therapy:
  - Bladder retraining (education, diaries, self-monitoring)
  - Dietary and lifestyle modification (reduce caffeine intake)
  - Pelvic floor exercises (Kegel)
  - Pelvic floor biofeedback
  - Transvaginal/transrectal electrical stimulation
- Estrogens (topical or oral):
  - Increase growth of vaginal epithelium
  - Increase volume of submucosal plexus
  - Strengthen pelvic floor musculature
- Intravesical therapies (capsaicin, resinofentoxin)

ONGOING CARE

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

Higher rates of hip fractures and institutionalizations have been reported.

ADDITIONAL READING

- Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the US. World J Urol 2003;20:327–336.

• Voelzke BB. Overactive bladder; prevalence, pathophysiology, and pharmacotherapy. Urol Rep 2007;1:16–22.
• Wein AJ, Rackley RR. Overactive bladder: A better understanding of pathophysiology, diagnosis, and management. J Urol 2006;175:S5–S10.

See Also (Topic, Algorithm, Electronic Media Element)

- Incontinence, Urinary, Adult Female
- Incontinence, Urinary, Adult Male
- Nocturia
- Urgency, Urinary (Frequency and Urgency)

CODES

ICD9

596.51 Overactive Bladder

ABBREVIATIONS

- BMI: Body mass index
- CIS: Carcinoma in situ
- CVA: Cerebrovascular accident
- DIAPPERS: Delirium, infection, atrophic urethritis/vaginitis, pharmaceutical, psychological, excessive urine output, restricted mobility, stool impaction
- IC: Interstitial cystitis
- ICIQ: International Consultation on Incontinence Questionnaire
- MS: Multiple sclerosis
- NSVD: Normal spontaneous vaginal delivery
- OAB: Overactive bladder
- OTC: Over the counter
- PVR: Post void residual
- TIA: Transient ischemic attack
- US: Ultrasound
- UTI: Urinary tract infection

PAPILLARY NECROSIS, RENAL

Stanley Zaslau, MD, MBA
Justin Gyorfi, MD
Rocco A. Morabito, MD

BASICS

DESCRIPTION

- Coagulative necrosis of the renal medullary pyramids and papilla due to ischemia:
  - Ischemia results from medullary vasculature impairment caused by other associated diseases, most commonly diabetes mellitus, urinary tract obstruction, and analgesic nephropathy.
- Most cases are bilateral.
- The clinical course can range from chronic and protracted to acute and rapidly progressive:
  - Typically chronic forms are asymptomatic and are discovered incidentally by radiographic studies.
  - Acute forms of renal papillary necrosis are symptomatic and often present with pyelonephritis and hydronephrosis.
- Presenting symptoms include fever and chills, flank or abdominal pain, and hematuria.
- Symptoms similar to that of renal colic.

EPIDEMIOLOGY

- Most cases occur during or after 6th decade of life; renal papillary necrosis is uncommon in patients <40.

)[B]

- True incidence is unknown.

RISK FACTORS

- In general, any condition causing ischemia can predispose an individual to develop renal papillary necrosis; many individuals with renal papillary necrosis have 2 risk factors
- Diabetes mellitus
- Analgesic abuse:
  - Most commonly Phenacetin and NSAIDs
- Antiretroviral treatment:
  - Most commonly with Indinavir use
- Urinary tract obstruction
- Sickle cell trait or disease
- Pyelonephritis

- Systemic vasculitis
- Global ischemia:
  - Shock, hypoxia, dehydration
- Lupus nephritis
- Wegener granulomatosis
- Renal artery stenosis
- Systemic vasculitis

)[B]

GENERAL PREVENTION

No specific prevention measures other than treatment of underlying ischemic causes

PATHOPHYSIOLOGY

- The renal medulla and papilla are vulnerable to ischemic necrosis due to the arrangement of their blood supply and the hypertonic environment.
- At baseline, the renal medulla and papilla exist in a state of relative hypoxia because of the slow rate of blood flow in the vasa recta; conditions that further reduce blood flow may produce ischemic necrosis:
  - Perfusion compromise as a consequence of vasculitis in diabetes mellitus
  - Infection that causes inflammation of the interstitium and leads to compression of the medullary vasculature
  - Curtailment of flow due to sickling of blood cells (sickle cell disease)
- Analgesic use causes COX inhibition and decreased prostaglandin production. This leads to decreased vascular perfusion, vasoconstriction, and eventually causes ischemic necrosis.
- Other medications can cause direct interstitial cell necrosis and consequential decrease in prostaglandin production.

)[B]

COMMONLY ASSOCIATED CONDITIONS

- Analgesic abuse
- Diabetes mellitus
- Hematuria
- Pyelonephritis
- Sickle cell disease
- Urinary tract obstruction

DIAGNOSIS

HISTORY

- May present with symptoms of pyelonephritis and/or hydronephrosis:
  - Fever or chills, episodic hematuria, dysuria, frequency, urgency, flank pain, and renal colic
- Rarely, renal papillary necrosis can present as acute oliguric renal failure.
- Ask about personal or family history of diabetes or sickle cell disease, previous UTIs, and drug use.

PHYSICAL EXAM

- Costovertebral angle tenderness
- Gross hematuria
- Fever

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine cultures:
  - Typical findings include proteinuria, pyuria, bacteriuria, and low urine-specific gravity.
  - Epithelial cells and casts may be present.
- CBC: Often have leukocytosis
- Metabolic panel: Can have azotemia and elevated creatinine.

Imaging

- IVP:
  - Gold standard to diagnose renal papillary necrosis. Findings include shrinkage and irregularity of papilla demarcated by contrast material as a ring shadow often in a triangular shape
  - A calix without a papilla
  - A filling defect in the renal pelvis (sloughed papilla)
  - Contrast-containing rice-grain–sized cavities in the papilla (medullary form)
- CT:
  - Imaging modality of choice in a clinical scenario of acute obstruction.
  - Findings with contrast include:
    Ring shadows in the medullae
    Contrast-filled clefts in the renal parenchyma
    Renal pelvic filling defects
- Retrograde pyelogram:
  - Can be useful in patients with azotemia, contrast sensitivity, or other situations where IVP is contraindicated.

– Findings may reveal a club-shaped calyx or a filling defect in the ureter.

Diagnostic Procedures/Surgery

Individuals who present with hematuria require a full urologic workup, even if renal papillary necrosis is confirmed. A concomitant bladder tumor must be excluded.

Pathological Findings

• Grossly, the cortex features depressed areas of cortical atrophy overlying raised necrotic papilla. The papilla within the kidney shows various stages of necrosis, desquamation, and sloughing.

• Microscopically, papillary changes range from a patchy appearance to complete coagulative necrosis. Glomeruli are typically unchanged.

DIFFERENTIAL DIAGNOSIS

• Acute tubular necrosis
• Carcinoma of ureter or bladder
• Nephrolithiasis
• NSAID abuse and/or overuse
• Pyelonephritis
• Renal trauma
• TB
• Ureteral stricture disease

TREATMENT

• Oral or IV hydration
• Glycemic control if diabetic

MEDICATION

• Broad-spectrum IV antibiotics if associated with pyelonephritis.
• Urinary alkalinization if urinary obstruction is present.
• Cessation of analgesic abuse
• Treatment of underlying cause of ischemia

SURGERY/OTHER PROCEDURES

• If patient presents with acute urinary obstruction, immediate percutaneous nephrostomy, ureteral stent placement, or endoscopic/ureteroscopic removal of obstructing sloughed papilla is necessary.

• Elective evaluation of renal pelvic or ureteral filling defect with ureteroscopy for non-acute

• In the situation of overwhelming infection, nephrectomy may be warranted.

ONGOING CARE

PROGNOSIS

- Depends on the etiology of the ischemic insult, number of compounding factors, and amount of necrosis
- In general, elderly patients with multiple medical problems have a worse prognosis.

COMPLICATIONS

- Renal papillary necrosis can lead to secondary infection of desquamated necrotic papilla, deposition of calculi, and separation and sloughing of papilla.
- Multiple sloughed papilla can obstruct the urinary tract locally at the calyces or at more distal sites such as the ureteropelvic junction, ureter, or ureterovesical junction.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patient monitoring should be based on underlying causes of ischemia.

REFERENCES

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2. Jung DC, et al. Renal papillary necrosis: Review and comparison of findings at multi-detector row CT and intravenous urography. RadioGraphics 2006;26:1827–1836.

3. Brix AE. Renal papillary necrosis. Toxicol Pathol 2002;30(6):672–674.

4. Dieleman JP, et al. Papillary necrosis associated with the HIV protease inhibitor indinavir. Infection 2001;29(4):232–233.

ADDITIONAL READING

Refer to urinary tract obstruction and hematuria for further information on these topics.

See Also (Topic, Algorithm, Electronic Media Element)

- Diabetes Mellitus, Urologic Considerations
- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Hematuria, Gross and Microscopic, Adult
- Nephropathy, Analgesic
- Sickle Cell Disease, Urologic Considerations

CODES

ICD9

- 583.7 Nephritis and nephropathy, not specified as acute or chronic, with lesion of renal medullary necrosis
- 584.7 Acute renal failure with lesion of renal medullary (papillary) necrosis
- 590.80 Pyelonephritis, unspecified

ABBREVIATIONS

- CBC: Complete blood count
- COX: Cyclooxygenase
- CT: Computed tomography
- IV: Intravenous
- IVP: Intravenous pyelogram
- NSAID: Nonsteroidal anti-inflammatory drug
- RPN: Renal papillary necrosis
- TB: Tuberculosis
- UTI: Urinary tract infection

PARATESTICULAR TUMORS, GENERAL

Danielle A. Stackhouse, MD
Judd W. Moul, MD

BASICS

DESCRIPTION

- Intrascrotal tumors involving the testicular tunic, epididymis, or cord structures. Can be benign or malignant.
- 90% of extratesticular tumors are found within the spermatic cord:
  - Of these, 30% 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 tumors in this region and are benign:
  - Typically seen in the 3rd or 4th decade of life
- Leiomyosarcoma is the most common type of paratesticular sarcoma in adults:
  - Incidence peaks in the 6th and 7th decades.
- Cystadenoma is a benign tumor that involves the epididymis in young adults:
  - Strongly associated with Von Hippel-Lindau disease
- Malignant mesothelioma presents in older patients (55–75 yr) and usually presents in association with a hydrocele
- Malignant lymphoma: Cord structures are frequently invaded by testicular lymphoma, but primary lymphomas do occur rarely.

EPIDEMIOLOGY

- 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 > Black (3:1)
- Leiomyosarcoma: Exceedingly rare, ~110 reported cases in the literature

RISK FACTORS

- Marijuana and cocaine use in the parents is associated with rhabdomyosarcoma.
- von Hippel-Lindau syndrome is associated with epididymal cystadenomas.

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 widely and have a tendency for local recurrence.

• Rhabdomyosarcoma:

– 97% belong to the favorable histology group of embryonal cell tumors.

COMMONLY ASSOCIATED CONDITIONS

Renal cell carcinoma with Von Hippel Lindau

DIAGNOSIS

ALERT

It is impossible to distinguish a benign from a malignant tumor based on physical exam.

HISTORY

• Patient complains of mass within his scrotum, distinct from the testicle.

• Typically not painful

PHYSICAL EXAM

• Palpation of the testes, epididymis, and cord structures bilaterally:

– Rhabdomyosarcoma reveals a firm mass that is usually distinct from the testis.

– Adenomatoid tumor appears clinically as small solid lumps and are 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-appearing mass.

– Lymphoma presents as a hard, non-tender mass, separate from the testis; seen in young adults. Transillumination suggests a fluid-filled lesion such as a hydrocele.

• Careful exam of the groin is necessary to rule out hernia and to evaluate for lymphadenopathy.

• Masses are occasionally accompanied by hydrocele.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and culture if epididymitis is suspected.
- Tumor markers to include -hCG, AFP, or LDH should be sent if the origin of the tumor is in question.

Imaging

- 1st step: Scrotal US to evaluate location and characteristics of the lesion within the scrotum: Testicular vs. paratesticular, solid vs. cystic:
  - Solid lesions almost always require exploration.
  - Simple cystic lesions are almost always benign.
- CT of the abdomen with and without contrast for staging: Paratesticular tumors may spread to retroperitoneal lymph nodes or hematogenously depending on the histology of the primary tumor.
- Clinical staging of retroperitoneal lymph nodes
- Radioisotope bone scan:
  - Especially for elevated alkaline phosphatase or symptoms with rhabdomyosarcoma

Diagnostic Procedures/Surgery

- Percutaneous biopsies are contraindicated.
- Bone marrow aspirate:
  - Routine part of staging at time of diagnosis for rhabdomyosarcoma

Pathological Findings

- Electron microscopy can help differentiate between the different types of sarcoma; these differences can be quite subtle
- Leiomyosarcoma spreads 1st by lymphatics, then hematogenously and last, by local extension.

DIFFERENTIAL DIAGNOSIS

- Adenomatoid tumors: The most common benign paratesticular tumor
- Angiomyofibroblastoma
- Cystadenoma of the epididymis
- Epididymal cyst
- Epididymitis
- Fibrous pseudotumor of testicular tunic
- Fibrosarcoma
- Hydrocele
- Hydrocoele of the spermatic cord
- Inguinal hernia

- Leiomyosarcoma
- Lipoma of the spermatic cord
- Liposarcoma
- Malignant fibrous histiocytoma
- Mesothelioma, benign, testicular tunic
- Mesothelioma, malignant, of the tunica vaginalis: Associated with asbestos exposure
- Postoperative changes (sperm granuloma after vasectomy)
- Spermatocele
- Testicular torsion
- Traumatic injury
- Tunica albuginea lesions (cysts, fibrous pseudotumor)
- Varicocele

TREATMENT

- US suggests initial management.
- Lesions suggestive of a benign process can be observed with serial examinations.
- If there is any concern about the malignant potential, the scrotum should be explored through a high inguinal incision.
- Transscrotal manipulation or biopsy is contraindicated.
- Rhabdomyosarcoma always requires primary surgical excision via inguinal orchiectomy.
- Leiomyosarcoma should also be treated with radical orchiectomy to be followed with adjuvant radiation therapy to reduce local recurrence:
  - No survival benefit has been demonstrated from the addition of RPLND to radical orchiectomy.

MEDICATION

Chemotherapy for malignant rhabdomyosarcoma:

- Vincristine, cyclophosphamide, and dactinomycin, and actinomycin D-based chemotherapy in patients with gross or microscopic residual disease

SURGERY/OTHER PROCEDURES

- Testicular or paratesticular lesions suspected to be malignant should be removed by radical inguinal orchiectomy with high ligation of the spermatic cord.
- Early clamping of the cord can prevent hematogenous spread in the case of leiomyosarcoma.
- For rhabdomyosarcoma:
  - Consider hemiscrotectomy for any degree of scrotal wall involvement.

– The IRS V-recommended radical inguinal orchiectomy and routine RPLND in all males >10 yr old and in boys <10 with metastasis noted on imaging.

- Complete surgical excision with a negative margin has a significant impact on local recurrence and overall survival in soft tissue sarcomas.

ADDITIONAL TREATMENT

Radiotherapy

For rhabdomyosarcoma:

- 4,000–6,000 cGy over 5 to weeks
- Dose and port size are determined by the tumor's primary site, age of the patient and tumor burden.

Additional Therapies

The role of adjuvant chemotherapy in adult paratesticular sarcomas is not fully established.

ONGOING CARE

PROGNOSIS

- Rhabdomyosarcoma: 75% 5-yr survival when multimodal therapy is administered:
  - Tumor stage and site are important prognostic indicators.
  - Survival by stage: Stage 1 (91%), stage II (86%), stage III (35%), and stage IV (5.2%)
- Leiomyosarcoma: Reported survival rate is 50–80%, with microscopic residual disease present in 27% of cases:
  - Adjuvant treatment via radiation warranted
- Malignant mesothelioma is an aggressive tumor with a high recurrence and mortality rate.
- Larger tumor size, metastasis, higher-grade tumor, and incomplete primary resection all lead to a poorer overall prognosis.
- Adenomatoid tumor is considered benign and are amenable to conservative local resection.

COMPLICATIONS

- Disease-associated complications include death in ~10% with malignancy.
- Treatment-associated complications:
  - Retrograde ejaculation and intestinal obstruction secondary to retroperitoneal surgery if RPLND is performed
  - Growth abnormalities secondary to radiation therapy (spinal and renal in children)
  - Hypogonadism of contralateral testis and hemorrhagic cystitis secondary to chemotherapy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Serial US for equivocal lesions, especially in the epididymis
- For benign lesions, have patient perform testicular self-exam monthly.
- Routine guidelines are not established for rhabdomyosarcoma:
  - A suggested schedule is a physical exam, CXR, and CT every 2–3 mo for the 1st yr and every 3–4 mo the next:

    In subsequent years, the examinations can be spread out to every 6 mo and then annually.

    Patients who present with metastases require much closer monitoring.

    Recurrence after 2 yr is unusual.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Adenomatoid Tumors (Testis/Tunic/Epididymis)
- Epididymis, Mass (Epididymal Tumor and Cysts)
- Epididymis, Cystadenoma
- Fibrous Pseudotumor of Testicular Tunic
- Hydrocele of the Spermatic Cord
- Scrotum and Testicle, Mass
- Mesothelioma, Benign, Testicular Tunic
- Mesothelioma, Malignant, Testicular Tunic
- Spermatic Cord Mass and Tumors

CODES

ICD9

- 187.5 Malignant neoplasm of epididymis
- 187.8 Malignant neoplasm of other specified sites of male genital organs

– 222.8 Benign neoplasm of other specified sites of male genital organs

ABBREVIATIONS

- AFP: -Fetoprotein
- -hCG: -Human chorionic gonadotropin
- CGY: Centigray units of radiation
- CT: Computed tomography
- CXR: Chest x-ray
- IRS V: Intergroup Rhabdomyosarcoma Study
- LDH: Lactate dehydrogenase
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound

PARKINSON DISEASE, UROLOGIC CONSIDERATIONS

Patrick J. Shenot, MD

BASICS

DESCRIPTION

- PD is a progressive neurodegenerative movement disorder.
- Any combination of tremor, rigidity, bradykinesia, progressive postural instability
- Mild intellectual deterioration may occur.
- Often associated with voiding dysfunction and incontinence

EPIDEMIOLOGY

- Incidence has been estimated at 4.5–21 cases per 100,000 population per year
- Most studies reveal a prevalence of ~120 per 100,000.
- Voiding dysfunction occurs in 35–70% of PD patients

RISK FACTORS

- PD is about 1.5 times more common in men than in women.
- The incidence and prevalence of PD increases with age:
  - The average age of onset is ~60 yr.
  - Onset in persons <40 yr is relatively uncommon.

Genetics

- Genetic component long hypothesized; probably accounts for small proportion of cases
- Evidence for linkage to polymorphic markers on chromosome 4
- All currently known genetic causes of PD probably account for <5% of cases.

PATHOPHYSIOLOGY

- Loss of pigmented dopaminergic neurons in the substantia nigra, a subdivision of the basal ganglia, results in dopamine deficiency in the nigrostriatal pathways accounting for the classic clinical motor features of PD.
- The basal ganglia normally have an inhibitory effect on the micturition reflex.
- Inhibitory effect may be abolished by cell loss in the substantia nigra, leading to detrusor overactivity.
- Sphincter function is synergic but a delay in striated sphincter relaxation (sphincter bradykinesia) is common.
- Increased urinary incontinence may be directly related to progressive neurodegeneration.

COMMONLY ASSOCIATED CONDITIONS

- Sleep disturbance
- Dementia

- Depression
- Difficulty swallowing and chewing
- Impotence
- Autonomic dysfunction:
  - Sweating
  - Constipation

DIAGNOSIS

HISTORY

- Assess for concurrent urologic conditions:
  - BPH in men and SUI in women
- Careful review of medications:
  - Anticholinergics listed with typical doses below provide good tremor relief but may be associated with incomplete bladder emptying and urinary retention, especially in men with BPH.
  - Benztropine mesylate (Cogentin) 1–6 mg, biperiden (Akineton) 2–12 mg, orphenadrine (Disipal, Norflex) 150–400 mg, procyclidine (Kemadrin) 7.5–30 mg, trihexyphenidyl (Artane) 6–20 mg

PHYSICAL EXAM

- Observation of mental status, coordination, and motor movements is important, as many patients are best managed by intermittent self-catheterization.
- Resting tremor, bradykinesia, and rigidity are hallmarks.
- Tremor 4–6 cycles/sec:
  - Most conspicuous at rest
  - Enhanced by stress
  - Often less severe during voluntary activity
- Infrequent blinking and fixity of facial expression
- Small shuffling steps and a loss of the normal automatic arm swing
- A neurourologic exam permits direct assessment of sacral spinal cord segments:
  - Should focus on perianal sensation, anal tone and control, and bulbocavernosus reflex
- Abdomen: Palpable bladder
- Prostate size

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No laboratory biomarkers exist for PD

- Serum creatinine optional; consider if significant urinary retention is present

Imaging

- Neuroimaging is not necessary for routine clinical diagnosis in patients with typical presentation.
- Renal US (hydronephrosis) generally not indicated unless urinary retention or secondary complications occur.

Diagnostic Procedures/Surgery

- PD is primarily a clinical diagnosis.
- Urodynamic investigation with close attention to sphincter EMG forms the basis for rational treatment:
  - Detrusor overactivity is present in the majority of PD patients with urologic complaints.
  - Sphincter bradykinesia, or delayed relaxation of the external sphincter at the onset of voluntary micturition, is common.
  - Impaired contractility less common; may coexist with detrusor overactivity
- Detrusor areflexia is uncommon
- Urodynamics is invaluable in diagnosing BPH associated outlet obstruction in males with PD.

Pathological Findings

- Abnormal accumulation of the protein -synuclein bound to ubiquitin in the damaged cells in the substantia nigra
- This protein accumulation forms proteinaceous cytoplasmic inclusions called Lewy bodies.

DIFFERENTIAL DIAGNOSIS

- Multiple system atrophy
- Shy-Drager syndrome
- Multi-infarct states
- Non-neurogenic causes of voiding dysfunction such as BPH associated outlet obstruction
- Stress incontinence in women

TREATMENT

- PD is progressive with or without medications.
- Sinemet (carbidopa/levodopa) is the 1st drug of choice in older patients to control symptoms.
- Many PD patients have coexisting detrusor overactivity with impaired bladder contractility; consider combining intermittent catheterization with antimuscarinic drugs.

MEDICATION

First Line

Anticholinergics/antimuscarinics:

- Oxybutynin 5 mg PO t.i.d.
- Tolterodine LA 4 mg/d PO
- Others (trospium, solifenacin, fesoterodine)

Second Line

TCAs: Imipramine 10–25 mg PO b.i.d.–t.i.d.

SURGERY/OTHER PROCEDURES

Consider prostate surgery only if coexisting bladder outlet obstruction is confirmed.

ADDITIONAL TREATMENT

Deep brain stimulation may improve voiding symptoms.

ONGOING CARE

PROGNOSIS

- PD is characterized by progressive neurologic deterioration.
- Course of disease may be variable, but prognosis is generally poor.

COMPLICATIONS

- Urinary retention
- Urinary incontinence
- Skin breakdown due to incontinence

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Monitor for increasing PVR, especially if taking antimuscarinic medications

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Incontinence, Adult Female
- Incontinence, Adult Male
- Neurogenic Bladder, General

CODES

ICD9

- 332.0 Paralysis agitans
- 596.59 Other functional disorder of bladder
- 788.30 Urinary incontinence, unspecified

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- EMG: Electromyography
- PD: Parkinson disease
- PVR: Post void residual
- SUI: Stress urinary incontinence
- TCA: Tricyclic antidepressant
- US: Ultrasound

PELVIC PAIN, FEMALE

Debra L. Fromer, MD

Daniel I. Brison, MD

BASICS

DESCRIPTION

- Chronic pelvic pain is defined as discomfort lasting 6 mo.
- Usually of unknown clear etiology or with pain out of proportion for possible etiology
- Accompanied by significantly altered physical activity, including work, recreation, sexual life, as well as disturbance of mood

EPIDEMIOLOGY

- Affects ~1 in 7 women
- Rates of up to 39% have been quoted in several studies.

RISK FACTORS

- Anxiety
- Depression
- Drug addiction
- 1st-degree relative with similar diagnosis
- Previous STDs or PID
- Prior sexual or physical abuse
- Reproductive age

GENERAL PREVENTION

- Early detection, diagnosis and treatment
- Practice safe sex
- Abstinence

PATHOPHYSIOLOGY

- Complex and multifactorial
- Unclear etiology in the absence of a defined pathologic process

COMMONLY ASSOCIATED CONDITIONS

- Ectopic pregnancy
- Ovarian cysts
- STDs
- UTIs
- PID
- Nephrolithiasis

DIAGNOSIS

HISTORY

- Complete history
- Description of pain (location, precipitators, duration, severity, radiating):
  - Pain that get worse throughout menses suggests endometriosis.
  - Pain better while supine, worse while upright suggests pelvic prolapse or pelvic congestion syndrome.
  - Pain with bladder filling, with frequency and urgency: Interstitial cystitis or other bladder pathology
  - Radiation from pelvis to lower extremities suggests spinal or sciatic irritation.
  - Crampy pain with diarrhea/constipation suggests diverticulitis or IBS.
- Deep dyspareunia: PID, interstitial cystitis, endometriosis, pelvic floor spasm
- Superficial or entry dyspareunia: Atrophic vaginitis, vulvodynia, urethral diverticulum
- Comestibles (food items) that exacerbate the pain
- Childhood or adult sexual and/or physical abuse
- History or family history of psychological disorders
- Previous trauma
- Previous abdominal or pelvic surgeries
- Gynecologic history

PHYSICAL EXAM

- Abdominal exam:
  - Locate trigger points that may suggest a hernia or tenderness associated with urolithiasis.
  - Back and musculoskeletal system exam:

    Gait

    Scoliosis

    Betty maneuver: Abduction of the thigh against resistance causing pain (piriformis syndrome)

    Obturator sign: Disfunction of the obturator muscles or fascia

    Straight-leg raising test: Possible herniated disc, radiculopathy

    Psoas sign: Flexion of hip against resistance causing pain suggests inflammation along the course of the iliopsoas muscle
- Gynecologic exam:
  - Pelvic exam (external internal inspection):

    Inspect vulva for lesions, irritation, trauma, or significant pelvic relaxation

    Discharge suggests PID or urethral diverticulum.

Sims retractor or single-blade speculum exam of the vagina and pelvic muscles

– Evaluation for trigger points:

A cotton-tipped swab

Single-digit examinations of the vulva, pubic arch, levator ani coccyx, introitus, urethral, trigonal, cervix, paracervical areas, vaginal fornices, uterus, and adnexa

Anterior vaginal wall tenderness with urethral diverticulum: Interstitial cystitis or urethritis

– Bimanual exam:

Assess shape, direction, and mobility of uterus and adnexa, as well as any masses or tenderness elicited with uterine motion

– Rectovaginal exam for nodularity or masses

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Elevated white counts with shift suggest infection
- ESR: Elevated in subacute or chronic inflammation
- CA-125 level: Elevated in endometriosis, PID, and malignancies
- Urine analysis: Evaluate for blood, WBC and nitrite (infection, neoplasm)
- Urine cytology: Test for urothelial malignancy
- Cervical and urine cultures: UTI, STD, or PID
- PAP smear
- Serum drug screen

Imaging

- US:
  - Transvaginal: Evaluation of the uterus and adnexa
  - Renal/pelvic: Pyeloureteral diseases and Müllerian anomalies
- Plain x-ray:
  - KUB: Urolithiasis, dermoid cysts
  - Spine: Osteoarticular disease
  - Hysterosalpingography: Infiltrative endometriosis of the uterosacral ligaments or obstructive anomalies in adolescents
  - MRI: Evaluation of infection, inflammation and malignancy
  - CT: Evaluation of pelvic masses

Diagnostic Procedures/Surgery

- Laparoscopy:
  - Up to 66% negative rate with CPP

  - Endometriosis and pelvic adhesions most common findings
- Barium enema/colonoscopy: Evaluate for GI etiology
- Urodynamics: Evaluate for chronic urethral syndrome and interstitial cystitis
- Hydrodistention/bladder biopsy: Evaluate for interstitial cystitis or other bladder pathology

DIFFERENTIAL DIAGNOSIS

- Urologic:
  - Bladder cancer/carcinoma in situ
  - Chronic and recurrent UTIs
  - Chronic urethral syndrome
  - Interstitial cystitis
  - Pelvic floor dysfunction
  - Urethral diverticula
  - Urethritis
  - Urinary retention
  - Urolithiasis
- OB-Gyn:
  - Adhesions
  - Adnexal tumors
  - Cervical stenosis
  - Endocervical and endometrial polyps
  - Endometriosis and endosalpingiosis
  - Lichen sclerosis
  - Ovarian remnant syndrome
  - Ovarian retention syndrome
  - Pelvic congestion syndrome
  - Pelvic floor relaxation disorders
  - Uterine leiomyomas
  - Vulvodynia/vaginitis
- GI:
  - Appendicitis (chronic)
  - Chronic constipation
  - Chronic intermittent bowel obstruction
  - Colitis
  - Diverticular disease

- Inflammatory bowel disease
- IBS
- Peritoneal abscess

- Other:
  - Depression
  - Hernias (eg, obturator, sciatic, inguinal, femoral, perineal, spigelian, umbilical, ventral)
  - Mononeuropathy and nerve entrapment
  - Neoplasia of the spinal cord or sacral nerves
  - Pelvic floor pain syndrome
  - Piriformis syndrome
  - Rectus abdominis pain
  - Spinal malformation
  - Spinal tumors
  - Substance abuse

TREATMENT

- Treatment is directed at correction of identifiable cause.
- Chronic pelvic pain is best treated with individualized therapy, with best results achieved with multimodal therapy (diet and behavior modification, biofeedback, physical therapy, pharmacotherapy, and selective surgical interventions).
- Use of a syndrome-specific validated questionnaire such as the PUF (Pelvic Pain and Urgency/Frequency Patient Symptom Scale) may help monitor progress
- Voiding diary may help with further assessment.
- Physical therapy:
  - Pelvic floor training/biofeedback
  - Massage/manipulations
  - US therapy
  - TENS
  - Neuromodulation (ie, InterStim)
  - Intravesical instillations based on diagnosis (DMSO, heparin)
  - Intravesical injection of botulinum toxin type A

MEDICATION

First Line

- NSAIDs (acetaminophen, ibuprofen, naproxen, aspirin)
- Opiate agonists (oxycodone, OxyContin, fentanyl, morphine, etc.):

– Discourage long-term use and overuse due to risk of dependence and abuse.

- TCAs (amitriptyline, nortriptyline)

Second Line

- SSRIs (fluoxetine, paroxetine, sertraline)
- Neurontin (gabapentin)
- Tizanidine (muscle relaxant):
  – May improve the inhibitory function in the CNS thus providing relief

SURGERY/OTHER PROCEDURES

- Trigger point injections and peripheral nerve blocks
- Neuroablation: Thermocoagulation (radiofrequency ablation), cryoablation, or injection of chemical agents (alcohol, hypertonic saline, phenol)
- Various neurectomies

ADDITIONAL TREATMENT

Psychological therapy:

- Avoidance of dietary comestibles that may exacerbate pelvic pain symptoms (ie, spicy foods, coffee, tea, alcoholic beverages, vegetables, chocolate, specific dairy products, etc.)

ONGOING CARE

PROGNOSIS

Variable, depending on cause of pain and therapeutic progress

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Dyspareunia
- Interstitial Cystitis (IC)
- Pelvic Prolapse (Cystocele and Enterocoele)
- Vaginal Atrophy, Urologic Considerations
- Vaginal Discharge, Urologic Considerations

- Voiding Diary
- Vulvodynia

CODES

ICD9

625.9 Unspecified symptom associated with female genital organs

ABBREVIATIONS

- CBC: Complete blood count
- CNS: Central nervous system
- CPP: Chronic pelvic pain
- DMSO: Dimethylsulfoxide
- ESR: Erythrocyte sedimentation rate
- GI: Gastrointestinal
- IBS: Irritable bowel syndrome
- KUB: Kidneys, ureters, bladder
- MRI: Magnetic resonance imaging
- NSAID: Nonsteroidal anti-inflammatory drug
- PID: Pelvic inflammatory disease
- SSRI: Selective serotonin reuptake inhibitor
- STD: Sexually transmitted disease
- TCA: Tricyclic antidepressant
- TENS: Transcutaneous electrical nerve stimulation
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

PELVIC PAIN, MALE (NIH III B. NON-INFLAMMATORY CHRONIC PELVIC PAIN SYNDROME)

Aisha K. Taylor, MD

Anthony J. Schaeffer, MD

BASICS

DESCRIPTION

- CPPS or NIH type III B is unexplained pelvic pain involving the groin, genitalia, or perineum, and may be associated with voiding symptoms occurring in the absence of pyuria or bacteruria.
- This was previously described by some as prostatodynia, but the use of this term is currently discouraged.
- Many believe that the symptoms of CPPS in men closely relate to the similar symptom complex in women with interstitial cystitis.
- NIH classification and current definitions of prostatitis:
  - Type I: Acute bacterial prostatitis
  - Type II: Chronic bacterial prostatitis: Recurrent infection
  - Type III: Chronic abacterial prostatitis/chronic pelvic pain syndrome; no demonstrable infection:

    IIIA: Inflammatory chronic pelvic pain syndrome; WBCs present in semen/expressed prostatic secretions or voided bladder urine (VB3)

    IIIB: Noninflammatory chronic pelvic pain syndrome; WBCs not present in semen/expressed prostatic secretions or voided bladder urine (VB3)
  - Type IV: Asymptomatic inflammatory prostatitis; detected by prostate bx or presence of WBCs in prostatic secretions during evaluation for other disorders

EPIDEMIOLOGY

- ~1 in 5 men with lower urinary tract symptoms typical of BPH likely have CPPS at the same time
- The annual prevalence in the general population of chronic pelvic pain syndrome is 0.5%.
- CPPS is most prevalent in men 36–50 years old, shows no apparent racial predisposition

RISK FACTORS

- Psychologic stress and depression associated with flare-ups of CPPS
- Suggestion that inadequately treated episodes of acute prostatitis may increase risk for developing chronic prostatitis syndromes

PATHOPHYSIOLOGY

- Exact etiology is not determined.
- It has been postulated that dysregulation of pro- and anti-inflammatory cytokines lead to inflammation from otherwise normal prostate bacteria.
- Probable dysfunction of the perineal afferent nerves, which result in heightened pain responses to otherwise normal stimuli in this region
- Other theories suggest fastidious organisms that cannot be easily cultured, autoimmune factors, or neuropathy.

COMMONLY ASSOCIATED CONDITIONS

- Anxiety, depression
- Chronic fatigue syndrome
- Chronic pain syndromes
- Functional somatic syndromes
- Myofascial pain syndrome
- Sexual dysfunction

DIAGNOSIS

HISTORY

Severe pain characterized by:

- Pelvic pain
- Lower back pain
- Perineal pain
- Penile/scrotal pain
- Pelvic floor muscle spasms
- Decreased libido
- Sexual dysfunction
- Painful ejaculation
- Irritative and obstructive voiding symptoms
- Impact of symptoms on quality of life
- Identify specific triggers of symptoms: Foods, beverages, activities (physical, sexual)

PHYSICAL EXAM

- No uniformly distinguishing physical exam characteristics
- Exam of the genitalia may reveal vague widespread pelvic discomfort.
- DRE may reveal high anal sphincter tone.
- DRE revealing a severely tender prostate or bogginess may suggest acute bacterial prostatitis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Negative urethral, prostatic, and bladder cultures (VB1, VP2, EPS, and VB3 negative)
- Normal prostatic secretions with no evidence of excess WBCs
- Hematuria should prompt workup for other causes such as carcinoma in situ.
- PSA may not be useful for CPSS but should be considered as part of prostate cancer screening.

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
- Transrectal US performed in patients with pain on ejaculation may reveal enlargement of seminal vesicle caused by obstruction of ejaculatory duct as source of chronic pain.

Diagnostic Procedures/Surgery

- Mears Stamey 4-glass test
- Videourodynamic evaluation sometimes reveals spastic dysfunction of the bladder neck or prostatic urethra, and can rule out underlying neurologic dysfunction.
- Cystoscopy can rule out interstitial cystitis as source of pain.
- Anal sphincter electromyography and or sphincter function profiles can help diagnosis hypertonicity and failure of the pelvic floor musculature to relax.
- Uroflowmetry may demonstrate diminished flow with intermittency.

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis
- Anal fistula
- Bladder cancer or carcinoma in situ
- Bladder outlet obstruction/BPH
- Chronic bacterial prostatitis
- Chronic nonbacterial prostatitis
- Coccydynia
- Epididymo-orchitis
- Hernia
- Interstitial cystitis
- Myofascial pain syndrome
- Pelvic joint dysfunction
- Prostatic abscess
- Prostatic cyst

- Seminal vesiculitis
- STD
- Tuberculous prostatitis
- Urethritis or urethral pathology

TREATMENT

- CPPS is generally considered a diagnosis of exclusion.
- Good physician–patient relationship is essential, as many patients with CPPS have difficult-to-manage symptoms.
  - Patient should understand that this is not a traditionally treatable disease but rather a chronic condition that can often be controlled.
  - Use of a tool such as the NIH chronic prostatitis symptom index or voiding diaries can be useful in monitoring progress.
  - Medical therapy is directed toward symptomatic relief.
  - Empiric antibiotic therapy has a role in selected patients.
  - -Blockers have become a primary therapy in the treatment of CPPS.

MEDICATION

First Line

- -Blockers
- Doxazosin 1–4 mg, then effective dose daily for 12 wk (can cause decrease in BP, headache)
- Tamsulosin 0.4 mg/d for 12 wk (can cause decreased ejaculate volume, headache; rarely, absent ejaculate, decrease in BP)
- Alfuzosin 10 mg b.i.d. for 12 wk (can rarely cause decrease in BP, headache; contraindication is moderate hepatic insufficiency, or with cytochrome P-450 3A4 inhibitors)
- Antimicrobial therapy:
  - Fluoroquinolones

    Ciprofloxacin, levofloxacin 500 mg/d for 4 wk

    Common adverse events include dizziness, restlessness, headache, diarrhea, nausea, rash; rarely, convulsion, psychosis, severe hypersensitivity, tendon rupture
  - Trimethoprim/sulfamethoxazole:

    160/80 mg b.i.d. for 4 wk

    Common adverse events: Anorexia, nausea, vomiting, rash, urticaria

    Rarely: Blood dyscrasias, hypersensitivity, or photosensitivity, hepatic necrosis
- 5-Reductase inhibitors:
  - Finasteride 5 mg/d PO

– Dutasteride 0.5 mg/d PO:

Common adverse events: Decreased libido

Second Line

- Geared at treating neuropathic-like pain
- TCAs:

– Nortriptyline 10 mg PO at bedtime, titrating up to a maximum of 75–100 mg PO mouth at bedtime

- Gabapentin
- Pregabalin

– Opioids; should not be widely used

SURGERY/OTHER PROCEDURES

Not generally recommended:

- Transurethral microwave thermotherapy as a last option

ADDITIONAL TREATMENT

- Biofeedback
- Acupuncture
- Frequent ejaculation (in patients with enlarged, symptomatically congested glands)
- Prostatic massage; not currently popular
- Physical therapy
- Myofascial or trigger point release
- Acupuncture
- Physiologic counseling in cases with severe debilitating pain, stress, or tension with impact on overall psychologic functioning
- Low-dose diazepam (muscle spasm relief and anxiolytic) may help relieve myalgia in the pelvic floor muscles.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Quercetin:

- A bioflavonoid with antioxidant properties that was reported to produce significantly greater improvement than placebo according to scores on the NIH Chronic Prostatitis Symptom Index.

ONGOING CARE

PROGNOSIS

Variable course with remissions and flare-ups

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Following prostate cancer screening guidelines is recommended

ADDITIONAL READING

- Dimitrakov JD, Kaplan SA, Kroenke K. Management of chronic prostatitis/chronic pelvic pain syndrome: An evidence-based approach. Urology 2006;67(5): 881–888.
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See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatis Algorithm
- Prostatitis, Asymptomatic Inflammatory (NIH IV)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory/Noninflammatory (NIH III A)
- Stamey Test (Meares-Stamey Test)

CODES

ICD9

- 601.1 Chronic prostatitis
- 789.09 Abdominal pain, other specified site

ABBREVIATIONS

- BP: Blood pressure
- BPH: Benign prostatic hypertrophy
- CPPS: Chronic pelvic pain syndrome
- DRE: Digital rectal exam
- EPS: Expressed prostatic secretion
- NIH: National Institutes of Health
- PSA: Prostate-specific antigen
- RBC: Red blood cells
- STD: Sexually transmitted disease

- TCA: Tricyclic antidepressant
- US: Ultrasound
- VB1: Voided bladder 1
- VB2: Voided bladder 2
- VB3: Voided bladder 3
- WBC: White blood cell

PELVIC PROLAPSE (CYSTOCELE AND ENTEROCELE)

Chad P. Huckabay, MD

Robert M. Moldwin, MD

BASICS

DESCRIPTION

- From Latin prolapsus, a slipping forth
- Pelvic organs slipping, falling, or herniating into the vagina (also called vaginal hernia)
- May involve anterior compartment, posterior compartment, or apical compartment with site-specific organs prolapsing behind their respective vaginal wall compartments. Most occur in combinations.
- Cystocele (bladder), rectocele (anterior rectal wall), and enterocoele (small intestine) most common pelvic organ prolapse

EPIDEMIOLOGY

- >200,000 women each year in US have surgery for pelvic organ prolapse
- 1 in 3 women undergoing surgery for prolapse or urinary incontinence may require a repeat operation.
- Lifetime risk that a woman in the US will require therapy for prolapse or incontinence is 11%.

RISK FACTORS

- Pregnancy, childbirth
- Congenital or acquired connective tissue abnormalities
- Denervation (spinal dysraphism) or weakness of the pelvic floor
- Aging, menopause
- Hysterectomy or other radical pelvic surgery
- Colposuspension or retropubic urethropexy predisposes to de novo enterocele formation
- Factors associated with chronically raised intra-abdominal pressure (constipation, BOO, COPD, obesity, ascites, pelvic mass)

PATHOPHYSIOLOGY

- The bony pelvis, pelvic diaphragmatic muscles consisting primarily of the components of the levator ani (pubococcygeus, iliococcygeus, and ischiococcygeus), and fascial connective tissue support and provide fixation to hold pelvic viscera in place and prevent herniation, which when occurs vaginally is termed prolapse.
- Pathophysiology is likely multifaceted involving injury to ligaments, metabolic and genetic connective tissue abnormalities, abnormal intra-abdominal pressures, and denervation of the levator ani.

COMMONLY ASSOCIATED CONDITIONS

- Urinary incontinence, voiding dysfunction, or difficulty possibly related to bladder outlet obstruction
- Rarely, hydronephrosis or bladder stones with high-grade prolapse
- Defecatory dysfunction

DIAGNOSIS

HISTORY

- Symptoms: May be asymptomatic; bowel, bladder, and sexual complaints including but not limited to urinary and fecal incontinence, defecatory dysfunction and dyspareunia, lower abdominal or vaginal pain/pressure/bulge
- Previous pelvic surgeries or procedures for incontinence
- Hormonal status: Vaginal epithelial atrophy
- Obstetric history
- Conditions/lifestyles with increased abdominal pressure such as constipation, straining at stool, chronic cough, heavy lifting

PHYSICAL EXAM

- Presence of SUI with degree of urethral mobility with cough/Valsalva
- Vaginal epithelial atrophy and introital size
- Examine in lithotomy and standing position to assess size of prolapse (may be worse at end of day)
- Reduction of prolapse to test for presence of occult or potential SUI
- Use half speculum to depress posterior vaginal wall to examine descent of anterior vaginal wall with rest/straining (cystocele).
- Similarly use half speculum to reduce anterior vaginal wall to examine for presence of posterior wall descent (rectocele/enterocele).
- To better assess descent of vaginal apex (enterocele) or cervix, may examine standing with digital exam or use calibrated instrument to assess vaginal length at rest and with straining.
- Look for loss of vaginal rugation in anterior midline (central defect) or at lateral anterior vaginal wall (paravaginal defects).
- Thin instruments or tongue depressor placed under anterior midline or bilaterally supporting these areas with straining may help differentiate midline central cystocele defect vs. lateral paravaginal defects.
- Rectovaginal exam may aid in differentiating rectocele from enterocele; finger in rectum may tent up rectocele but not enterocele:

– Simultaneous rectovaginal exam for enterocele (enterocele impulse on straining upon the anterior tip of index finger in rectum while thumb in vagina)

- Grade prolapse with descriptors and either Baden-Walker system or more detailed with POP-Q grading system.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis with culture
- Creatinine if clinically indicated

Imaging

- Renal/bladder US: Presence of incomplete bladder emptying or high-grade prolapse may be associated with ureteral obstruction/hydronephrosis, or rarely bladder stones.
- Defecography: Rectocele, defecatory dysfunction
- VCUG: Resting and straining may assess urethral hypermobility, stress incontinence, central or lateral cystocele, PVR
- Pelvic MRI: May supplement exam in complex cases

Diagnostic Procedures/Surgery

- PVR
- Urodynamics studies assist in identifying causes of voiding dysfunction:
  - Should be done with and without prolapse reduced
  - Filling and voiding phases with pressure/flow studies and simultaneous
  - Fluoroscopy may increase diagnostic yield.
- Cystoscopy if hematuria, recurrent UTI, persistently abnormal urinalysis

DIFFERENTIAL DIAGNOSIS

Determination of specific prolapsed organ is difficult:

- Distal anterior vaginal wall under urethra: diverticulum, Skene cyst
- Cystocele
- Urethrocele
- Rectocele
- Enterocele
- Uterine prolapse
- Soft-tissue tumors

TREATMENT

- Only definitive therapy is surgical.
- Weight loss, stool softeners with high-fiber diet, limiting heavy lifting may decrease some symptoms.

- Pessaries in those who are not surgical candidates.

MEDICATION

- Stool softeners to minimize constipation
- Topical vaginal estrogen to restore epithelial integrity in women with atrophy or ulceration of vaginal wall; may be used prior to surgery, with pessaries, or for local symptoms and recurrent UTI

SURGERY/OTHER PROCEDURES

- General measures:
  - Preoperative topical estrogen if significant atrophic vaginitis
  - Preoperative: Bowel prep, DVT prophylaxis
  - Preoperative antibiotic at time of surgery
  - Negative urine culture
  - Postop vaginal packing with impregnated antibiotics, Foley catheter for 24–48 hr
  - Temporary urinary retention postoperatively may be managed with indwelling Foley for usually <7–10 days or CIC.
- Cystocele:
  - Transvaginal repairs of combined lateral and central defects
  - Graft materials: Porcine and human dermal grafts (biologics), allografts with cadaveric fascia, and synthetic grafts (macroporous soft polypropylene mesh)
  - These are introduced via vaginal incisions and anchored to the ATFP usually at the level of the pubic bone and the ATFP toward the ischial spine.
  - These are secured with sutures passed traditionally or with the use of specialized needle drives or trocar systems passed transcutaneously.
  - These have come about because of higher failure rates seen with traditional anterior colporrhaphy alone.
  - High failure rates of only midline placation or lateral paravaginal repairs likely result from not correcting a transverse defect toward apex or not addressing apical defects in support.
- Lateral paravaginal defect:
  - May be repaired transabdominally.
  - Plication of anterior vaginal wall and pubocervical fascia to the lateral ATFP and internal obturator muscle with interrupted permanent sutures extending from the ischial spine to the bladder neck (paravaginal repair)
- Transvaginal paravaginal repair
- Central cystocele:

– Anterior colporrhaphy:

Suture plication of the pubocervical fascia in the midline extending from the apex of the cardinal ligaments or cervix to the level of the bladder neck or mid-urethra (this method has higher failure rate).

May combine with graft/mesh

Should not be used as a treatment for stress incontinence, as failure rate is 50%

- Enterocele and vault prolapse:

– Abdominal sacrocolpopexy: Considered gold standard. Can be performed by open techniques, laparoscopically, or robotically. Lower rate of recurrent vault prolapse and dyspareunia compared to sacrospinous colpopexy. Vaginal apex is connected via graft (usually synthetic; autologous fascia or cadaveric fascia can also be used) to the presacral fascia at S3–S4.

– Transvaginal repair: Must mobilize enterocele sac, perform high purse-string ligation of enterocele sac to circumferentially incorporate bilateral uterosacral-cardinal ligament complexes, the presacral fascia, and the peritoneum overlying the base of the bladder. Then the sac is excised.

– Transvaginal colpopexy component:

Uterosacral ligament suspension: Interrupted sutures placed into the uterosacral ligaments bilaterally then brought through the apical pubocervical and rectovaginal fascia after they have been plicated.

Sacrospinous ligament fixation: Sutures placed uni- or bilaterally into the sacrospinous ligament, then into the vaginal cuff. High recurrence rate of cystocele if combined with simple anterior colporrhaphy alone. Technique now commonly performed with graft augmentation using synthetic or other graft materials attached to the sacrospinous ligament and to the ATFP for level II support of the bladder as well.

Iliococcygeus suspension: Bilateral suspension of the vaginal apex to the iliococcygeus fascia just anterior to the ischial spine. May cause vaginal shortening.

ADDITIONAL TREATMENT

- Pessary:

– Mechanical support devices in different configurations, more commonly used as a ring with support for anterior prolapse

– Not as effective for posterior compartment (rectocele)

– Requires regular care by patient and physician, as may be associated with epithelial ulceration, rarely erosive events such as vesicovaginal or rectovaginal fistula

– May be used in poor surgical candidates, pregnancy, or temporarily for diagnostic purposes as it may unmask stress incontinence (occult or potential stress incontinence)

- Colpocleisis (closure or removal of vagina):
  - Advantage: Elderly patients or poor surgical candidates, quicker operation with less morbidity, highly successful with minimal risk of recurrent prolapse
  - Disadvantage: No functional vagina, higher rate of stress incontinence

ONGOING CARE

PROGNOSIS

- Increasing BMI and increasing parity increase risk for progression.
- 29% risk repeat procedure.
- Regression may occur with small grade I cystoceles.
- Progression more common
- Cohort followed over 3 yr:
  - Progression with further descent of >2 cm: 11%
  - Regression descent decrease <2 cm: 2.7%

COMPLICATIONS

- Intraoperative: Bleeding, cystotomy, nerve injury, rarely enterotomy or rectotomy, transvisceral passage of graft materials
- Postoperative: Pain, UTI, de novo urgency or stress incontinence, urinary retention (usually temporary), fistula (unrecognized bladder/bowel injury), ureteral obstruction (can be recognized intraoperatively by IV indigo carmine and visualizing ureteral efflux)
- Postoperative late: Vaginal shortening, dyspareunia, vaginal extrusion of graft (poor wound healing), erosion of graft into viscera (bladder more common), permanent suture extrusion or erosion into vaginal epithelium or urothelium, recurrent vaginal prolapse

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Periodic follow-up to assess bladder emptying, incontinence, extrusion of suture or graft material, UTI, or recurrent prolapse

ADDITIONAL READING

- Chen CC, et al. Biologic grafts and synthetic meshes in pelvic reconstructive surgery. Clin Obstet Gynecol 2007;50:383–411.
- Marinkovic SP, Stanton SL. Incontinence and voiding difficulties associated with prolapse. J Urol 2004;171:1021–1028.

See Also (Topic, Algorithm, Electronic Media Element)

- Cystocele
- Pelvic Organ Prolapse Quantification System (POPQ)
- Rectocele

- Urethrocele
- Vaginal Prolapse

CODES

ICD9

- 618.01 Cystocele, midline
- 618.02 Cystocele, lateral
- 618.03 Urethrocele

ABBREVIATIONS

- ATFP: Arcus tendineus fascia pelvis
- BMI: Body mass index
- BOO: Bladder outlet obstruction
- CIC: Clean intermittent catheterization
- COPD: Chronic obstructive pulmonary disease
- DVT: Deep venous thrombosis
- MRI: Magnetic resonance imaging
- POP-Q: Pelvic organ prolapse quantification
- PVR: Post void residual
- SUI: Stress urinary incontinence
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

PENILE PROSTHESIS PROBLEMS (INFECTION/EXTRUSION/MALFUNCTION)

Irvin H. Hirsch, MD

BASICS

DESCRIPTION

- Penile prosthesis available in the US include malleable semirigid rods; positionable, 2-piece (cylinder with pump); and 3-piece (cylinders, pump, and reservoir) inflatable prosthesis.
- Prosthetic infections require removal of all components since the device harbors micro-organisms within its biofilm.
- Prosthetic infections are most commonly Staphylococcus epidermidis or S. aureus; fungal and gonococcal infections have also been reported.
- Prosthetic components may extrude (erode) out of the urinary meatus, scrotum, or into adjacent bowel or bladder.
- Device malfunction may consist of erectile deformity, failure to inflate/deflate, or pump malposition.

EPIDEMIOLOGY

- Recent studies report an overall infection rate of 4%. Can occur immediately or several months after the implantation.
- Historically, rates up to 20% have been reported.
- The 5-yr mechanical failure rate of the 3-piece inflatable prosthesis ranges from 7–16%.
- In some studies diabetic patients have twice the incidence of infection compared to nondiabetic patients.
- Initial implantation carries a 1–3% risk of infection.
- Revision implantation carries a 7–18% risk of infection.
- Extrusion complications are most rare.
- Over a 5-yr interval, prosthesis malfunction may be as high as 16% for 3-piece and 4% for 2-piece inflatable penile prostheses.

RISK FACTORS

- The following are associated with an increased risk of penile prosthesis infection:
  - Diabetes
  - Spinal cord injury
  - Prior implant
- Intraoperative or delayed visceral organ perforation may occur in the setting of prior pelvic surgery or radiation.

- No difference in incision site (penoscrotal vs. infrapubic) with respect to infections

GENERAL PREVENTION

- Infection:
  - Prior to implantation, assure the absence of urinary tract and cutaneous infections.
  - Perioperative broad-spectrum IV antibiotics (gentamicin and vancomycin)
  - 10-minute antiseptic skin preparation
  - Minimize OR traffic.
  - Meticulous surgical scrub by OR staff
  - Irrigation of wound and component compartments with bacitracin 50,000 U/L.
  - Immerse prosthesis in antibiotic solution prior to implantation.
  - Continue antibiotics postoperatively.
  - Assure desirable glycemic control and HgbA1C preoperatively.
  - Use of cephalosporins for 1–2 wk following implantation.
- Extrusion/erosion:
  - Careful placement of components without overzealous dilatation
  - Proper sizing of corporal cylinders
- Malfunction:
  - Complete dilation of corporal compartments, perivesical space, and Dartos pouch
  - Detect malfunction by intraoperative inflate and deflate tests.
  - Prevent device perforation by closure sutures by preplacing sutures in the corporal bodies before positioning the cylinders.

PATHOPHYSIOLOGY

- Early infections are associated with gram-negative bacteria.
- Late infections are associated with gram-positive (S. epidermidis).
- Infections thought to be due to bacterial adherence to the prosthetic's biofilm. Can occur at initial implantation or by hematogenous spread.
- Most component erosions are also associated with infection.
- Oversized cylinder can cause pressure necrosis of the glans with subsequent ischemia:
  - With inflatable prosthesis this problem is not as common as when rigid noninflatable prosthesis were commonly used.
- Mechanical failures are usually due to device failure, with loss of fluid due to breakage of a component (tubing, pump, reservoir, or cylinder). Aneurysmal dilation of a component can cause breakage or failure to pressurize the system.
- Reservoir complications can include migration of the reservoirs (too large a space) and rarely fibrous pseudocapsule that prevents filling of the reservoir.

- Rarely autoinflation can occur. This is when the prosthesis activates with physical activity.

COMMONLY ASSOCIATED CONDITIONS

Conditions associated with erectile dysfunction:

- Acromegaly
- Addison disease
- Atherosclerosis
- Cushing syndrome
- Diabetes
- Hyperprolactinemia
- Hyperthyroidism
- Hypogonadism
- Pelvic trauma or surgery
- Penile trauma
- Peyronie disease
- Priapism
- Medication-related: (partial listing) alcohol, -blockers, antiandrogens, antihistamines, clonidine, LHRH analogues, recreational drugs, SSRIs, spironolactone, thiazide diuretics, tri-cyclic antidepressants
- Multiple sclerosis
- Psychogenic erectile dysfunction
- Spinal cord trauma
- Spinal cord tumor
- Stroke

DIAGNOSIS

HISTORY

- Pain, swelling, local erythema, or inability to operate the device.
- Infection can be difficult to diagnose in the perioperative period due to the absence of typical symptoms.
- Constant penile pain since insertion may suggest too large a prosthesis or infection.
- Spraying of the urinary stream, urethral discharge, or dysuria may indicate cylinder erosion.

PHYSICAL EXAM

- Fever may occur occasionally.
- Prosthetic infection presents with focal swelling, erythema, tenderness, pump adher-ence, or purulent wound drainage.

- Extrusion of the cylinder or pump demonstrates obvious appearance of the silicone component at the skin or meatus.
- Improperly undersized prosthesis may present with a SST or Concorde deformity with excess downward mobility of the glans penis.
- Oversized cylinder can cause an S-shaped or sigmoid deformity of the penis with buckling.
- Malfunction will present by the patient's inability to operate the prosthesis or his cosmetic complaint.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC with differential
- Complete metabolic profile
- Urine culture

Imaging

- Usually not necessary
- Pelvic x-ray or CT scan may reveal leak, component migration, or viscus erosion.
- MRI may have a limited role in determining the nature of the problem.
- Scrotal US may identify abscess in indeterminate cases.

Diagnostic Procedures/Surgery

Urethroscopy may confirm urethral erosion of cylinder.

Pathological Findings

- Staph epidermitis most commonly found in infected prosthesis
- Other Staph species, Gram negatives, fungi, and gonococcus also reported

DIFFERENTIAL DIAGNOSIS

- Patient's inadequate understanding of inflation or deflation of device
- Hematoma
- Seroma

TREATMENT

IV antibiotics should be started (vancomycin or cefazolin), but explant of all prosthetic components is mandatory in cases of prosthesis infection.

MEDICATION

IV antibiotics should be started, but explant of all prosthetic components is mandatory in cases of prosthesis infection.

SURGERY/OTHER PROCEDURES

- Infection:

– Prior to prosthesis revision, a review of the prior operative report and accounting for all previously implanted components is required. This included accounting for rear tip sizing extenders.

– In the absence of contraindications, immediate prosthesis salvage may be attempted to avoid the corporal fibrosis complicating delayed implantation.

– Relative contraindication to salvage and immediate reimplantation include an frank pus especially in a diabetic, eroded device, sepsis, the presence of necrotic tissue, and the rapid development of a severe infection within 2 wk of initial implantation.

– Mulcahy protocol for immediate prosthesis salvage. Sequential irrigation after explantation:

Gentamicin 80 mg/L + bacitracin 1 g/L
Half-strength hydrogen peroxide.
Pressure irrigation with 5 L saline containing 1 g vancomycin + 80 mg gentamicin
Half-strength povidone iodine
Half-strength hydrogen peroxide
Kanamycin 80 mg/L + bacitracin 1 g/L
Change all gowns, gloves before reinsertion of prosthesis
Do not use drain.
Oral antibiotics for at least 1 mo

• Prosthesis explantation and delayed reimplantation if contraindications to immediate reimplantation after Mulcahy protocol.

• Extrusion:

– Proximal corporal (crural) perforation by secure fixation of the properly sized cylinder during corporal closure or by fashioning a Dacron sleeve windsock and securing it at the crus limit.

– Distal corporal (urethral) perforation usually requires abandoning the procedure and prolonged Foley catheter drainage. If 1 cylinder has previously been placed, completion of the procedure with 1 cylinder remains optional, with subsequent placement of the remaining cylinder.

• Types of malfunction and treatment:

– Glans bowing: Treat by dorsal subglandular corporoplasty (Ball procedure) or redilation and reimplantation with appropriate sized cylinders

– Pump migration: Treat with expansion of Dartos pouch and repositioning of pump.

– Leak: Treated by explantation and reimplantation of all components.

– Improper cylinder size selection may lead to pain, insufficient shaft support, or corporal bulge: Treat with accurate corporal measurement and cylinder selection.

– Autoinflation: Treat with repositioning or re-dilation of the encapsulated reservoir.

ADDITIONAL TREATMENT

• Infection rates have decreased with the introduction of antibiotic-coated prosthetics: InhibiZone (rifampin and minocycline) (AMS) or Titan (polyvinylpyrrolidone hydrophilic coating + antibiotic immersion) (Mentor).

• Verify that patient understands warning signs of possible complications and understands proper technique for inflation and deflation.

ONGOING CARE

PROGNOSIS

• Revision surgery typically results in a satisfactory outcome.

• Up to 85% success with Mulcahy salvage protocol and immediate reimplantation with infection

COMPLICATIONS

• Infection, extrusion, and malfunction may occur during revision surgery.

• With device removal and delayed reimplantation, the corporal bodies may undergo extensive fibrosis.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Frequent follow-up postoperatively to assure proper appearance, patient operation, and function of the prosthesis.

ADDITIONAL READING

• LaRochelle JC, Levine, LA. Complications of benign adult penile and scrotal surgery. In: Loughlin KR, ed., Complications of Urologic Surgery and Practice: Diagnosis, Prevention, and Management. Boca Raton: CRC Press, 2007.

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See Also (Topic, Algorithm, Electronic Media Element)

Erectile Dysfunction/Impotence (ED)

CODES

ICD9

– 996.39 Other mechanical complication of genitourinary device, implant, and graft

– 996.65 Infection and inflammatory reaction due to other genitourinary device, implant, and graft

– 996.76 Other complications due to genitourinary device, implant, and graft

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- IV: Intravenous
- MRI: Magnetic resonance imaging
- SSRI: Selective serotonin reuptake inhibitor
- US: Ultrasound

PENIS, CANCER, GENERAL

Gerald L. Andriole, MD

BASICS

DESCRIPTION

- The overwhelming majority of penile carcinomas are squamous cell
- Can be SCC in situ (erythroplasia of Queyrat, Bowen disease of the penis, bowenoid papulosis), low-grade noninvasive (eg, verrucous carcinoma), or invasive carcinoma
- Other rare types of penile cancer include adeno- 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.

ALERT

Patient denial may cause delay in presentation to the physician, resulting in poor outcomes.

EPIDEMIOLOGY

- Rare in developed countries. Only about 1,500 new cases annually in US
- Blacks are more commonly affected than whites.
- Circumcision is protective.
- Accounts for up to 10% of cancers in men in South America.

RISK FACTORS

- Presence of foreskin and/or phimosis and poor hygiene
- HPV types 16, 18, and 33
- HIV infection
- Multiple sex partners
- Smoking

OTHER

- TNM staging: See “Appendix”
- Jackson system:
  - Stage I: Tumor confined to glans or prepuce
  - Stage II: Invasion into shaft of corpora; no nodal or regional metastases
  - Stage III: Tumor confined to penis; operable inguinal nodal metastases
  - Stage IV: Tumor involves adjacent structures; inoperable inguinal nodes and/or distant metastases

GENERAL PREVENTION

- Good penile hygiene
- Newborn circumcision more protective than circumcision later in life
- Smegma that forms from desquamated epithelial cells is thought to be a primary instigating factor in penile cancer; good hygiene and circumcision limit smegma accumulation.

PATHOPHYSIOLOGY

- Invasive SCC is thought to be preceded by superficial CIS (Bowen disease or erythroplasia of Queyrat). Invasive SCC grows into the skin locally before invading the corporal bodies and extending locally.
- Penile SCC cancer spreads by a relatively reliable pattern: Form superficial pelvic lymph nodes to deep pelvic lymph nodes
- SCC is found on the glans in 48%, prepuce in 21%, glans and prepuce in 9%, coronal sulcus in 6%, and shaft <2%.

COMMONLY ASSOCIATED CONDITIONS

- Phimosis
- Irritation of glans penis
- STDs
- Premalignant lesions that predispose to the development of invasive SCC of the penis and penile cancer:
  - Leukoplakia
  - BXO
  - Bowen disease
  - Erythroplasia of Queyrat
  - Giant condylomata

DIAGNOSIS

HISTORY

- Induration, erythema, nodularity of prepuce and/or glans
- Bleeding ulcer on glans
- Inguinal adenopathy
- Penile pain if lesion infected
- Patients often deny or ignore symptoms, resulting in presentation at advanced stage:
  - New onset priapism with a mass suggests a metastatic corporal body lesion.

PHYSICAL EXAM

- Induration, erythema, nodularity of prepuce and/or glans
- Bleeding ulcer on glans
- Inguinal adenopathy

- Occasional purulence

DIAGNOSTIC TESTS & INTERPRETATION

Lab

CBC, urinalysis, urine culture

Imaging

- CT of pelvis and inguinal nodes
- Penile US may help local staging.

Diagnostic Procedures/Surgery

Biopsy, preferably excisional or deep rather than a shave of the superficial lesion

Pathological Findings

- Most malignancies involve the epithelial surface of the penis.
- CIS (erythroplasia of Queyrat, Bowen disease of the penis, bowenoid papulosis)
- Verrucous carcinoma, warty carcinoma, Buschke-Lowenstein 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.
- Invasive cancer:
  - 95% are SCC
  - Tongues of invasive atypical keratinocytes with multiple mitosis invade the lamina propria or deeper. Sites contain foci of aberrant and ectopic keratinization known as squamous pearls.
  - SCC are graded using Broders classification system:

    Grade I: Well-differentiated, keratinization, prominent intercellular bridges, keratin pearls.

    Grade II–III: Greater nuclear atypia, increased mitotic activity, decreased keratin pearls.

    Grade IV: Cells deeply invasive, marked nuclear pleomorphism, nuclear mitoses, necrosis, lymphatic and perineural invasion, no keratin pearls.

DIFFERENTIAL DIAGNOSIS

- BXO
- Bowen disease (red, scaly patches on the keratinized skin of the penis (typically penile shaft)
- Bowenoid papulosis (multiple flat, warty lesions, sometimes pigmented)
- Condyloma acuminatum
- Condyloma lata

- Erythroplasia of Queyrat; shiny red patches on mucosal surfaces (glans and prepuce if uncircumcised)
- Extramammary Paget disease
- Giant condylomata
- Kaposi sarcoma
- Lichen sclerosis
- Psoriasis
- Seborrheic keratosis
- Ulcer from STD
- Zoon balanitis

TREATMENT

- 1st-line is surgical excision of lesion on penis
- Wound care issues are paramount after excision of the primary and after inguinal node dissections.
- Surgical care should be taken to minimize the complications of penile deformity and/or meatal stenosis after excising 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. For other tumor types, see specific chapters.

MEDICATION

- For invasive SCC of the penis, after resection of the primary tumor, inguinal adenopathy should be treated with 6 wk of broad-spectrum antibiotics (Augmentin or cephalosporin)
- Topical 5-fluorouracil for cases of CIS
- There is no established chemotherapeutic regimen for metastatic disease.
- Potential active agents include 5-FU, bleomycin, methotrexate, and cisplatin.

SURGERY/OTHER PROCEDURES

- Initial dorsal slit may be necessary to assess the lesion in phimosis.
- Circumcision, if preputial and noninvasive
- Laser ablation, if small and noninvasive
- Mohs micrographic surgery, if small and noninvasive or minimally invasive
- Wide local excision for small lesions. A 2-cm margin considered necessary.
- Partial penectomy, if invasive into distal penis
- Total penectomy with perineal urethrostomy, if proximal and invasive
- Inguinal lymphadenectomy is mandatory for persistent lymphadenopathy after antibiotics and control of the primary lesion.

- Inguinal lymphadenectomy is controversial if inguinal nodes are palpably normal before and after eradication of the primary.
- Lymph node sampling (either sentinel node biopsy or modified inguinal dissection) may be offered for patients with palpable normal inguinal nodes and T2 or above lesion:
  - Usually, bilateral dissections are recommended.
  - A total inguinal and pelvic lymphadenectomy is necessary if metastases are noted on sentinel or modified dissection.

ADDITIONAL TREATMENT

Radiotherapy

- External radiation to primary lesion if patient refuses surgical excision
- Some advocate this as primary therapy with salvage surgery with recurrences.
- Typical doses are 50–60 Gy over 4–6 wk.
- Some limited experience with interstitial brachytherapy

Additional Therapies

Investigational chemotherapy may be considered for men with advanced disease that is not surgically resected or as an adjuvant.

ONGOING CARE

PROGNOSIS

- Depends on T-stage and nodal status
- Overall survival for men with node-negative disease is 80–90%.
- Men with nodal metastases have a 30–40% 5-yr survival.
- 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

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Close inspection for local recurrence usually every 3 mo for 5 yr
- Consider imaging for ambiguous findings on physical exam

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Balanitis Xerotica Obliterans (BXO)
- Bowen Disease and Erythroplasia of Queyrat
- Genital Ulcer Algorithm
- Penis, Bowenoid Papulosis
- Penis, Lesion, General
- Penis, Leukoplakia
- Penis, Mass (Corporal Body Mass)
- Penis, Squamous Cell Carcinoma
- Penis, Squamous Cell Carcinoma Algorithm

CODES

ICD9

- 187.1 Malignant neoplasm of prepuce
- 187.2 Malignant neoplasm of glans penis
- 187.3 Malignant neoplasm of body of penis

ABBREVIATIONS

- BXO: Balanitis xerotica obliterans
- CBC: Complete blood count
- CIS: Carcinoma in situ
- CT: Computed tomography
- HPV: Human papilloma virus
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- US: Ultrasound

PENIS, CURVATURE AND/OR PAIN

Irvin H. Hirsch, MD

BASICS

DESCRIPTION

- Curvature and pain with erection often coexist, but can occur independently.
- Acquired penile curvature in men, known as Peyronie disease, is an inflammatory condition of the tunica albuginea and is usually associated with painful erection with 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.

EPIDEMIOLOGY

- Present in up to 10% of men 40–70.
- Increased since the availability of PDE5 inhibitors as more men seek treatment for ED.

RISK FACTORS

- Buckling erectile trauma
- Fracture of the tunica albuginea during sexual activity
- Intracavernous injection of vasoactive agents
- Priapism
- Urethroplasty
- See also “Commonly Associated Conditions.”

Genetics

- Associated with HLA (histocompatability B7) cross reactive antigens
- Peyronie disease less frequent in patients with Asian or African ancestry

GENERAL PREVENTION

Avoidance of penile trauma during intercourse

PATHOPHYSIOLOGY

- Mechanical tunical stress forces causing microvascular hemorrhage inflammation in the tunical wall or septum. The result is hypertrophic scar formation (plaque).
- Autoimmune components have been demonstrated in 38–75% of men with Peyronie disease.
- Altered cell-mediated immunity and antielastin antibodies support an immunologic component.
- In the setting of erectile trauma, an altered immunologic response to wound healing may predispose a subpopulation to Peyronie disease.

COMMONLY ASSOCIATED CONDITIONS

- Chronic intracavernous injection therapy
- Dupuytren contracture
- ED (veno-occlusive dysfunction)
- Ledderhose disease (Plantar fasciitis)
- Paget disease
- Tympanic sclerosis
- Urethral stricture

DIAGNOSIS

HISTORY

- Obtain a thorough medical, surgical, and sexual history.
- It is critical to differentiate penile pain from urethral pain.
- Establish duration, degree and location of curvature and pain.
- Dyspareunia
- Painful erection (suggests Peyronie disease)
- Nature of deformity: Curvature, indentation or instability (hinge-effect)
- Condition causes distress to patient or partner
- Coexisting ED
- Palpable nodule
- History of penile prosthesis
- History of penile surgery as a child
- Sickle cell disease suggests predisposition to priapism.

PHYSICAL EXAM

- Circumcised/uncircumcised; retractable foreskin
- Measurement of stretched penile length
- Palpation of stretched shaft to amplify plaque and determine its location and size
- Plaque tenderness
- Location of meatus for evidence of hypospadias
- Evidence of hematoma that suggests acute trauma
- Solitary or multiple plaques
- Erythema and crepitus with Fournier gangrene

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Usually not useful unless for workup of infections
- Urinalysis with or without culture in cases of referred pain from other GU cause

- Serum free testosterone (morning) and prolactin levels if erectile dysfunction coexists

Imaging

- Radiograph of penile shaft if calcification is suspected
- Duplex Doppler US with intracavernous pharmacologic injection to assess cavernous arterial function, presence of veno-occlusive dysfunction, and degree of erectile curvature, lateral indentation or circumferential wasting.
- Private self-photography of erect penis using instant (Polaroid) or digital film imaging is useful to classify the extent of the curvature.

Diagnostic Procedures/Surgery

- Uroflowmetry to rule out associated urethral stricture
- Bladder US for residual
- Urethroscopy for urethral pathology

Pathological Findings

- Peyronie disease is characterized by a fibrous noncompliant plaque within the tunica albuginea preventing uniform expansion of the corpora cavernosa during erection.
- Plaques may calcify.
- Microscopy: Affected tunica albuginea demonstrates nonpolarized arrangement of collagen fibers and disordered arrangement of elastin fibers in Peyronie disease.

DIFFERENTIAL DIAGNOSIS

- Balanitis, balanoposthitis, paraphimosis
- Chordee
- Congenital penile curvature
- Epispadius
- Erectile dysfunction
- Fournier gangrene
- Hypospadias
- Idiopathic urethralgia
- Insect bite
- Leukemic infiltration of the penile shaft
- Penile fracture or trauma
- Penile pain syndrome
- Penile prosthesis problem: S-shaped or sigmoid curvature with buckling with prosthesis cylinders; pain suggests infected prosthesis components
- Priapism is usually an obvious cause of penile pain.
- Psychiatric causes of pain

- Pudendal neuralgia
- Referred pain, GI (rectum, hemorrhoids, fistula, fissures)
- Referred pain, GU (cystitis, urethritis, prostatitis, retention, urolithiasis, urethral calculus)
- Reiter disease
- STD (herpes, chancroid)
- Torn frenulum
- Urethral foreign bodies
- Urethral shortening following urethroplasty
- Urethral stricture

TREATMENT

- Identification of the specific cause of the penile pain or curvature
- For Peyronie disease, watchful observation, as up to 15% may resolve spontaneously
- Steroids (anti-inflammatory) are ineffective in Peyronie disease.
- Discussion below refers primarily to the most common cause of penile curvature and pain, Peyronie disease

MEDICATION

- Peyronie disease oral therapy includes antioxidants and collagen synthesis inhibitors (antifibrotic agents).
- All oral agents yield insignificant therapeutic benefit:
  - Vitamin E (antioxidant), -tocopherol 1,200–1,600 IU divided b.i.d. for 3–6 mo. Limited by anticoagulation properties.
  - Potaba, potassium aminobenzoate (antifibrotic), 3 mg q.i.d.; limited by GI side effects.
  - Colchicine (antifibrotic), 0.6 mg t.i.d.; limited by diarrhea.
  - Tamoxifen (antifibrotic), 20 mg b.i.d.; limited by endocrine changes.
  - L-carnitine (antioxidant), 1 mg b.i.d. may relieve pain in Peyronie disease.
- Peyronie disease 2nd-line intralesional therapy:
  - Verapamil (antifibrotic), 84% resolution of pain and 62% improvement in curvature.
  - Collagenase (antifibrotic), limited improvement in curvature.
  - Interferon- (antifibrotic), subjective improvement in plaque size and curvature; limited by fever and myalgia.

SURGERY/OTHER PROCEDURES

- Peyronie disease:
  - Clinicians should assure that plaque is stable (ie, has not progressed in terms of pain and deformity) prior to embarking on surgical repair.

– Circumcision is recommended with surgical treatment of uncircumcised men.
– General surgical approaches depend on the severity and type of deformity:
Plication
Plaque incision with graft
Penile prosthesis
– Severe curvature (>45 degrees), multiplanar deformity, and indentation deformity may preclude plication techniques. Plication techniques may be performed with or without tunical incision (Nesbit, Yachia, Essed-Schroeder, and Lue 16-dot).
– Plaque incision with graft interposition may be done with the following graft materials:
Synthetic (Dacron)
Autologous (buccal mucosa, dermis, tunica albuginea, tunica vaginalis)
Prepackaged biologic (porcine small intestine submucosa)
– Penile prosthesis implantation with manual molding, if necessary.

- Chordee and epispadius:
  – See specific topic for surgical correction

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Vitamin E (-tocopherol)
- Potaba (potassium aminobenzoate)
- L-carnitine

ONGOING CARE

PROGNOSIS

- Surgical straightening of erection is predictably successful (>85%).
- Shortened penile length and sensory loss may be noted postoperatively.

COMPLICATIONS

- ED
- Loss of penile length due to disease itself or due to surgical repair

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Periodic monitoring of erectile function, penile length, and sensory function.

ADDITIONAL READING

- Gholami SS, Lue TF. Correction of penile curvature using a 16-dot placation technique: A review of 132 patients. J Urol 2002;167:2066–2068.
- Leffell MS. Is there an immunogenetic basis for Peyronie's disease? J Urol 1997;157:295–297.

• Levine LA, Goldman KE, Greenfield JM. Experience with intraplaque injection of verapamil for Peyronie's disease. J Urol 2002;168:621–625.

• Schwarzer U, Sommer F, Klotz T, et al. The prevalence of Peyronie's disease: Results of a large survey. BJU Int 2001;88:727–301.

See Also (Topic, Algorithm, Electronic Media Element)

- Chordee
- Epispadias
- Penis and Corporal Body Mass
- Peyronie Disease
- Priapism, General

CODES

ICD9

- 607.85 Peyronie's disease
- 752.63 Congenital chordee
- 752.69 Other penile anomalies

ABBREVIATIONS

- ED: Erectile dysfunction
- GI: Gastrointestinal
- GU: Genitourinary
- PD: Peyronie's disease
- PDE5: Phosphodiesterase type-5
- STD: Sexually transmitted disease
- US: Ultrasound

PENIS, LESION, GENERAL

Stephen E. Strup, MD

Bradley W. Warner, MD

BASICS

DESCRIPTION

- Occurs in either adult or pediatric population
- Often occurs in conjunction with cutaneous lesions elsewhere
- May be a manifestation of systemic, sexually transmitted, or metastatic disease

EPIDEMIOLOGY

In adults, can occur in either circumcised or uncircumcised males. In children, the vast majority of penile lesions are found in uncircumcised males.

RISK FACTORS

Recent trauma, sexual contact (heterosexual and homosexual), change in laundry/bath soaps or lotions, recurrent infections, use of medications, contact with animal or plant life, family history, degree of personal hygiene and others

Genetics

- Reiter syndrome: Strong association with HLA-B27 haplotype
- Hailey-Hailey disease: Autosomal dominant

GENERAL PREVENTION

Safe sex practices can reduce STD risk.

PATHOPHYSIOLOGY

- Many lesions resemble each other.
- Correct diagnosis may require biopsy and/or laboratory evaluations.
- Descriptive terms for the lesions include erythema, patch, nodule, papule, bulla, erosion, vesicle, scale, crust, and others.

COMMONLY ASSOCIATED CONDITIONS

- Celiac disease: Dermatitis herpetiformis
- Diabetes-phimosis
- HIV: Kaposi sarcoma, seborrheic dermatitis

DIAGNOSIS

HISTORY

- Age of the patient:
  - Children most commonly will have balanoposthitis or phimosis.
- Trauma
- Sexual practices:

  - Homosexual, heterosexual, promiscuity, lesions in sexual partner
- Family history of dermatologic disorders
- Previous history of similar lesions
- History of systemic illness
- History of change in laundry/bath soaps or lotion
- History of sharing of clothing with another who demonstrates symptoms consistent with dermatologic disease
- Any social contacts with similar symptoms
- History of contact with strange plants, strange animals or insects
- Association with a urethral discharge
- Association with pruritus
- Association with pain
- Length of time of symptoms
- History of blood transfusion
- Types of self-treatments attempted
- History of cancer
- History of medication use
- Occupational risk factors: Chemical/industrial exposure
- Recent travel

PHYSICAL EXAM

- Thorough dermatologic exam of the entire body:
  - Similar to lesions elsewhere on the body (eczema, seborrheic dermatitis)
  - Skin folds/pubic region involved (fungal infection, infestation)
- Circumcised/uncircumcised
- Foreskin retraction
- Foreskin fixed to the glans
- Urethral discharge
- Character of the lesion:
  - Smooth, raised
  - Painful, nonpainful
  - Erythematous, patchy, scaly, weepy, bullous
  - Nodular, plaque, vesicle, pustule, ulcerative
  - Color of lesion(s)
- Adenopathy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis
- Urethral swab for Gram stain and culture
- Serum chemistry profile:
  - Diabetes is occasionally diagnosed in phimosis.
- HIV screening:
  - Kaposi sarcoma

Imaging

If clinically indicated (eg, malignancy)

Diagnostic Procedures/Surgery

- Aspiration:
  - Pap smears can identify intranuclear inclusions
  - Cytologic exam
- Incisional/excisional biopsy (to include punch biopsy):
  - Viral culture (HSV, etc.)
  - Special stains (IgG, IgA, immunofluorescent, etc.)
  - Depth of lesion
  - Tzanck preps (Molluscum contagiosum, herpes, varicella)
- Immunofluorescence
- Potassium hydroxide preps
- Antibody stains

Pathological Findings

See “Differential Diagnosis.”

DIFFERENTIAL DIAGNOSIS

- Allergic dermatitis, usually involving the outer layer of skin, appearing red and weepy, with or without crusting:
  - Atopic dermatitis (eczema): Red and scaly with excoriations. Intensely pruritic. The cause is unknown although some may have trigger factors (dust mites, chemicals, detergents, etc.).
  - Contact dermatitis: Scaly with crust formation; response by the skin to an externally applied substance. Due to direct cytotoxic effect of substance or type IV hypersensitivity reaction to allergen. Most common allergen is nickel (jewelry, belt buckle, etc.).
  - Erythema multiforme: Can be minor or major variants. Major variant is Stevens-Johnson syndrome, and is manifested by targetoid lesions, blisters, and mucosal membrane involvement.

- Papulosquamous disorders; a scaly lesion on an erythematous base:
  - Psoriasis: Affects about 2% of the population; a hyperproliferation of the epidermis with silvery scales; begins generally in the 3rd decade and can be life-long. Genital involvement rarely occurs without nongenital disease.
  - Seborrheic dermatitis: Most often found on hair-bearing regions; can cause a lifetime of exacerbations and remissions. Extensive cases may be associated with HIV.
  - Lichen planus: A pruritic inflammatory disease. When present on the genitalia, it most often affects the glans penis.
  - Lichen nitidus: Very small, flat-topped papules. They can be flesh-colored, pink, or yellow-red. Cause is unknown.
  - Reiter syndrome: Urethritis, arthritis, ocular findings, oral ulcers, and skin lesions. Most commonly affecting immunocompromised individuals. A systemic illness as a result of Gonococcus, Chlamydia, Yersinia, Shigella, Salmonella, Campylobacter, Neisseria, or Ureaplasma.
  - Lichen sclerosis: In later stages, becomes balanitis xerotica obliterans. Patients with this tend to have a high prevalence of autoimmune diseases. Has been associated with SCC of penis.
  - Fixed drug eruption: A reaction to oral medication (1–2 wks after treatment started). Lesion tends to occur in the same location with each challenge.
- Vesicobullous disorders:
  - Bullous pemphigoid: An IgG mediated blistering, most commonly found in the elderly.
  - Pemphigus vulgaris: Autoimmune mediated blistering of the skin, directed at keratinocytes. Associated with painful oral lesions. Severe cases may be fatal.
  - Dermatitis herpetiformis: An IgA-mediated blistering of the skin. Associated with celiac disease.
  - Hailey-Hailey disease: Autosomal dominant blistering; develops in 2nd–3rd decade. In axilla, inguinal, and perianal areas.
- Ulcers: Lesions that extend into the dermis; most commonly related to STDs.
  - Pyoderma gangrenosum: A chronic, painful ulcer associated with the cutaneous manifestations of Crohn disease, ulcerative colitis, or collagen vascular disease.
  - Traumatic ulcers: May be secondary to sexual activity, body ornamentation, or cleansing techniques.
  - STDs: Includes herpes simplex, primary syphilis, chancroid, lymphogranuloma venereum, and granuloma inguinale. Diagnosis based on diagnostic tests.

– Behçet disease: Syndrome of oral and genital ulcers, and uveitis. Lesions are painful; must rule out STDs.

- Neoplastic lesions:

– SCC in situ (Bowen disease/erythroplasia of Queyrat): Sharply demarcated erythematous plaques. Rarely may progress to invasive disease.

– SCC: Can be a fungating lesion, most often seen in uncircumcised individuals. Poor hygiene and recurrent infections may be predisposing factors.

– Bowenoid papulosis: Resemble SCC in situ, occurring usually in the 3rd and 4th decades of life and associated with HPV infections. Female partners at risk for cervical cancer.

– Kaposi sarcoma: Associated with herpes virus and AIDS (3% of males with HIV present with this lesion).

– Melanoma: Commonly found on the glans penis; lesions may be blue, red, black, brown, or nonpigmented and with an irregular border.

– Basal cell carcinoma: The most common cutaneous malignancy, but penis is an uncommon location.

– Verrucous carcinoma: Also known as Buschke-Lowenstein tumor; a variant of SCC. Low malignant potential. 20–25% of all penile tumors.

– Extramammary Paget disease: If on the genitalia, can be associated with malignancies of the urethra, bladder, rectum, and sweat glands.

- Infections/Infestations:

– Erythrasma: May appear like tinea cruris (jock itch), but is due to a member of the Corynebacteriaceae.

– Balanoposthitis: Inflammation of the glans and foreskin, occurring exclusively in uncircumcised males of any age. Recurrent episodes may lead to phimosis.

– Folliculitis: An infection of the follicles in hair-bearing areas.

– Furunculosis: Otherwise known as a boil, is a red, tender, fluctuant pustule or abscess.

– Genital warts: Commonly associated with HPV types 6 and 11. Passage of this lesion to a female may lead to cervical carcinoma.

– Pediculosis pubis: Infestation with the crab louse.

– Scabies: Infestation with the mite Sarcoptes Scabiei. The pruritus resulting from this infestation is so severe that excoriation may initially be identified on exam. Burrows are pathognomonic.

– Molluscum contagiosum: Results from a virus related to the pox family. Requires skin to skin contact.

- Common benign lesions:
  - Pearly penile papules: Commonly seen in uncircumcised males; small, raised, dome-shaped papules that encircle the corona.
  - Angiokeratoma of Fordyce: Small ectasias of the dermal blood vessels. May cause concern due to periodic bleeding.
  - Cysts: Most commonly are epidermal inclusion cysts, and can be postsurgical in nature, following circumcision or hypospadias repair.
  - Phimosis: The inability to retract the foreskin. May be a manifestation of a systemic illness, such as diabetes.
  - Sclerosing lymphangitis: Commonly associated with vigorous sexual activity and is a translucent cordlike lesion involving the coronal sulcus.
  - Zoon's balanitis: A patch-like lesion seen only in uncircumcised men; must be differentiated from SCC in situ.
  - Vitiligo: Sharp depigmentation of the skin that results in varying sized patches.

TREATMENT

- Most lesions can be diagnosed by characteristic gross appearance.
- Ulcers that do not respond to therapy should be biopsied to exclude malignancy.
- Further investigation including biopsy based on suspicion of malignancy

MEDICATION

Corticosteroids for simple dermatitis:

- In general, when applied to genital skin, only low-potency topical corticosteroids should be used for short treatment courses.
- Specific antibiotics and antivirals based on pathogen

SURGERY/OTHER PROCEDURES

- Ranges from excisional biopsy to total penectomy
- Less invasive procedures include laser therapy, photodynamic therapy, ultraviolet radiation, and cryotherapy for malignancy.

ADDITIONAL TREATMENT

Limited role in SCC

ONGOING CARE

PROGNOSIS

Based on disease

COMPLICATIONS

Consequences of untreated primary lesion may include advanced malignancy or progression of localized infection.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Should be monitored for resolution/changes
- If oncologic, based upon diagnosis
- If associated with HIV, follow-up should also be based upon level of disease

ADDITIONAL READING

- Buechner SA. Common skin disorders of the penis. BJU Int 2002;90:498–506.
- Gerber GS. Carcinoma in situ of the penis. Urol 1994;151:829–833.

See Also (Topic, Algorithm, Electronic Media Element)

- Genital Ulcer Algorithm
- Sexually Transmitted Diseases (STD), General
- Penis, Cancer, General

CODES

ICD9

- 099.8 Other specified venereal diseases
- 607.1 Balanoposthitis
- 607.89 Other specified disorders of penis

ABBREVIATIONS

- AIDS: Acquired immunodeficiency syndrome
- HIV: Human immunodeficiency virus
- HPV: Human papilloma virus
- HSV: Herpes simplex virus
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease

PENIS, SQUAMOUS CELL CARCINOMA

Michael S. Cookson, MD
Benjamin M. Whittam, MD

BASICS

DESCRIPTION

- Penile cancer is almost always a squamous carcinoma of the penile skin, which may involve the prepuce, glans, shaft, or base of the penis.
- While in its early stage and confined to the penis, there is a tendency for delay in diagnosis. Accordingly, it may first metastasize to inguinal and pelvic lymph nodes, and then to other organs.

EPIDEMIOLOGY

- 1,250 cases annually in the US
- The lifetime risk of a man developing IPC in the US is 1 in 600 if he is uncircumcised, and >3 times lower if he was circumcised neonatally.
- Rare <40; peak incidence around age 75; mean age: 58
- Racial factors: Blacks are affected about twice as often as whites.
- Rare in the US (0.2/100,000)
  - May constitute 10–20% of male cancer in parts of South America and Africa

RISK FACTORS

- Uncircumcised males: Circumcision at birth reduces the incidence.
- A history of condyloma acuminata, balanitis xerotica obliterans, and leukoplakia may predispose.
- Poor hygiene: The chronic irritative effect of smegma may be a factor.
- Phimosis
- History of condyloma acuminata, balanitis xerotica obliterans, and leukoplakia may predispose
- HPV-16 and HPV-18 strains identified in >50% of squamous carcinomas of the penis
- Having unprotected sex with multiple partners (increasing the likelihood of HPV infection)
- Cigarette smoking
- AIDS/HIV

GENERAL PREVENTION

- Circumcision at birth appears to protect against development; disease is rare where infant circumcision is widely practiced.
- Good hygiene

PATHOPHYSIOLOGY

- Most (95%) of penile cancers are SCC. Less common are sarcoma (including Kaposi sarcoma), melanoma, basal cell carcinomas, and lymphomas.
- Buschke-Lowenstein tumor (giant condyloma, verrucous carcinoma) is a histologically benign tumor that is characterized by aggressive local extension, which may destroy the penis if not treated but does not metastasize.
- SCCs that metastasize usually spread 1st to superficial inguinal nodes, then deep inguinal nodes, then pelvic nodes. Both groins may be involved.

COMMONLY ASSOCIATED CONDITIONS

- Condyloma or other inflammatory conditions
- Balanitis
- STD

DIAGNOSIS

HISTORY

- Uncircumcised state is the norm for most men with penile cancer.
- May present as itching or burning under foreskin, which may progress to ulceration.
- Usually long history of inability to retract foreskin (phimosis); tumor may be concealed by prepuce
- Usually not painful; often secondarily infected
- History of condyloma or other inflammatory conditions may be present.

PHYSICAL EXAM

- The presenting lesion may range from patchy erythema, induration, or verrucous growth to extensive destruction of penile tissue.
- The lesion may be flat or papillary.
- In the presence of unretractable foreskin (phimosis); the primary lesion may be palpable but not visible until the preputial skin is retracted or until a dorsal slit is performed.
- Lesion on penis: Glans most common (50%), prepuce (21%), both prepuce and glans (9%), coronal sulcus (6%), shaft (2%)
- Palpate shaft to assess for corporal involvement; rectal exam for urethral/prostatic involvement
- Palpate groins for lymphadenopathy
- Exam repeated after 4–8 wk of antibiotic therapy to rule out lymphatic enlargement from infection
- Persistently enlarged nodes require lymphadenectomy.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Biopsy of lesion to include some normal adjacent penile skin
- Serology, cultures, and skin tests may be required.
- Rarely, hypercalcemia (without evidence of bone metastases) may occur.

Imaging

- CT of the abdomen, pelvis, and groin may be helpful in staging or identifying inguinal nodal involvement in some patients.
- CT-guided biopsy of abnormal inguinal or pelvic nodes may guide the planning of surgical therapy or chemotherapy.
- MRI and/or US may be helpful in delineating corporal and adjacent tissue involvement. Very useful if the physical exam findings are not clear
- Lymphangiography and cavernosography may be helpful in selected cases

Diagnostic Procedures/Surgery

- Biopsy of lesion to include some normal adjacent penile skin
- For smaller lesions, may be diagnostic and therapeutic
- Inguinal and deep pelvic lymphadenectomy (see below)

Pathological Findings

- Most (95%) of penile cancers are squamous cell carcinomas. Less common are sarcoma (including Kaposi sarcoma), melanoma, basal cell carcinomas, and lymphomas.
- The Buschke-Lowenstein tumor (giant condyloma, verrucous carcinoma) is a histologically benign tumor characterized by aggressive local extension, which may destroy the penis if not treated.
- Tumors with vascular invasion, corporal body invasion increases risk for lymph node involvement.
- Tumors are graded as well-differentiated (grade I), moderately well-differentiated (grade II–III), and poorly differentiated (grade IV) (Bruder classification system).

DIFFERENTIAL DIAGNOSIS

- Erythroplasia of Queyrat (Bowen disease of penis)
- Mycotic skin infections
- Balanitis xerotica obliterans
- Sarcoma

TREATMENT

- Many patients with penile cancer delay treatment.
- Biopsy confirmation and depth of invasion of the lesion is necessary before starting any treatment.

• Patients with low-grade, favorable histologies or with low risk of metastasis (CIS) are considered for organ preserving therapies.

• Early lymphadenectomy is preferable to delayed salvage intervention.

MEDICATION

• Treatment of the primary tumor followed by 4–8 wk of therapy with broad-spectrum antibiotics (cephalosporin, Augmentin) to reduce inguinal nodal infection and inflammation, is recommended before proceeding with inguinal lymphadenectomy.

• Up to 50% of enlarged nodes will regress.

• Additional surgical therapy of the groin and pelvic nodes is required where nodal enlargement persists.

• In patients with surgically resectable recurrences, salvage surgery may be considered.

• Radiation therapy and chemotherapy may be used for palliative treatment and in those patients with metastatic disease, respectively.

• There is no uniformly accepted chemotherapy regimen for advanced penile cancer. Common regimens use combination therapy with agents such as cisplatin, methotrexate, and bleomycin. Results are generally poor, with median survival of <1 yr with metastatic cancer.

SURGERY/OTHER PROCEDURES

• Primary excision: Depending on the size and location of the lesion, this may involve wide local excision, circumcision, partial penectomy, total penectomy.

• A 2-cm margin is classically considered optimal, but a negative margin is essential.

• Total penectomy is limited to larger tumors (>4 cm) or those with high-grade, invasive histology into the gland, corpora, or urethra

• In patients in whom partial penectomy does not leave sufficient penile length to allow voiding while standing (usually 2–3 cm minimum), total penectomy with perineal urethrostomy may be preferable.

• For persistent lymphadenopathy or suspected groin node metastases, inguinal node dissection is indicated. 2 inguinal dissections have been described:

  – Modified superficial inguinal lymphadenectomy may result in reduced morbidity including less lower extremity lymphedema.

  – Classical superficial and deep lymphadenectomy

• Pelvic lymphadenectomy (unilateral or bilateral) remains controversial. Proponents argue for improved staging and local control. On the balance, there is an increase risk of lymphedema, and long-term cancer-free survival is rare in the setting of positive pelvic nodes

• With palpably negative nodes and stage To, Ta, grade I–II tumor, careful follow-up may be used. Similar strategy may be used for T1 although controversial with micrometastases in the inguinal nodes in 15–20%.

• With palpably negative nodes and tumor T2, or any grade III–IV histology, bilateral modified superficial lymphadenectomy is performed, proceeding to complete lymphadenectomy and pelvic lymphadenectomy if positive nodes are found.

• Because of lymphatic crossover at the base of the penis, bilateral superficial inguinal lymphadenectomies are performed, with deep inguinal and pelvic dissections done on the involved side if nodal metastases are confirmed.

• In patients who develop unilateral palpable or enlarged inguinal nodes in subsequent follow-up (late), a unilateral superficial and deep inguinal lymphadenectomy is performed on the involved side only.

ADDITIONAL TREATMENT

Radiotherapy

• Radiation therapy may be an effective treatment in small primary lesions, but can be complicated by severe edema and skin problems:

– May be a useful palliative measure in poor surgical candidates or in unresectable disease, including inguinal and pelvic lymph nodes

• Selective interstitial brachytherapy is practiced at some centers.

Additional Therapies

• Alternative approaches to formal lymph node dissection are being investigated including sentinel lymph node biopsy, fine needle aspiration, and lymphatic mapping at the time of surgery using dyes and radio tracers.

• Laser surgery of the primary lesion may be effective in small tumors, but does not provide tissue for histologic evaluation and staging. Circumcision is recommended at the time of procedure.

• Mohs micrographic surgery is a technique allowing removal of penile cancer by excision of tissue in thin layers. Mohs micrographic surgery allows excellent local control rates while maximizing organ preservation. Mohs reported a cure rate of 81% for tumors on the glans or prepuce.

• Combination chemotherapy has demonstrated effectiveness in selected cases and is being further evaluated.

ONGOING CARE

PROGNOSIS

• Outcomes are directly correlated with stage of disease and treatment rendered.

• The 5-yr survival is 95% for CIS. The 5-yr survival is 80% for T1/T2NOMO. If lymph node spread, the 5-yr survival drops to 50%. The 5-yr survival is 18% once the cancer spreads beyond the inguinal lymph nodes.

• More recent National Cancer Database figures for all patients diagnosed from 1995–2000 show a 5-yr relative survival of 75%.

COMPLICATIONS

• Urethral stenosis may occur as a result of the partial or total penectomy.

• Lower extremity lymphedema, lymphocele, flap necrosis, wound infection, and cellulitis may occur following the lymphadenectomy.

• Major complications, such as debilitating lymphedema, flap necrosis, and lymphocele requiring intervention, occur in 5–21% of cases

• Local recurrence and development of metastases may occur. The reported local recurrence rate after partial or total penectomy has ranged from 0–8%.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• In patients being followed expectantly, groin examinations should be conducted at least every 2 mo for the 1st 2 yr after diagnosis, then every 6 mo for 2 yr, then annually.

• A periodic groin US, CT, or MRI may be indicated.

• Poorly compliant patients may be better managed with inguinal lymphadenectomy.

• Patients who have undergone lymphadenectomy should be followed every 3 mo for 2 yr, then every 6 mo for 2 yr, then annually.

ADDITIONAL READING

• Catalona WJ. Modified inguinal lymphadenectomy for carcinoma of the penis with preservation of the saphenous vein: Technique and preliminary results. J Urol 1988;140:306.

• Tabatabaei S, MDougal WS. Invasive carcinoma of the penis: Management and prognosis. In Richie JP, D'Amico AV, eds., Urologic Oncology. Philadelphia: Saunders Elsevier, 2005:770–722.

See Also (Topic, Algorithm, Electronic Media Element)

• Genital Ulcer Algorithm

• Penis, Cancer, General

• Penis, Lesion, General

• Penis, Squamous Cell Carcinoma Algorithm

CODES

ICD9

• 187.1 Malignant neoplasm of prepuce

• 187.2 Malignant neoplasm of glans penis

• 187.3 Malignant neoplasm of body of penis

ABBREVIATIONS

- CIS: Carcinoma in situ
- CT: Computed tomography
- HPV: Human papilloma virus
- IPC: Invasive penile cancer
- MRI: Magnetic resonance imaging
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- US: Ultrasound

PENIS, TRAUMA (FRACTURE, STRANGULATION, AMPUTATION)

Scott G. Hubosky, MD

BASICS

DESCRIPTION

General classification of penile trauma:

- Blunt trauma:
  - Penile fracture (rupture of tunica albuginea)
  - Penile strangulation (foreign body acts as constricting device causing reduced blood flow, increasing edema and ischemia)
- Penetrating trauma:
  - Amputation
  - Gunshot wound
  - Laceration
- Avulsions:
  - Degloving injuries (penile tissues deep to dartos fascia get trapped and stripped)
- Burns
- Radiation changes

EPIDEMIOLOGY

- Penile fracture infrequently seen in US, with incidence of 1 in 175,000 hospital admissions
- Penetrating trauma to genitals is relatively rare in civilian setting.
- Gunshot wounds and penetrating injuries make up 40–60% of battlefield urologic injuries during times of war; likely due to lack of protection to external genitalia.
- Penile fractures are common in Iran where it is an actual social practice (Taghaandan).

RISK FACTORS

- Penile fracture occurs during rigorous intercourse in woman-on-top position.
- Penetrating injury may be secondary to occupational hazard (soldiers, heavy equipment operators, farmers).

GENERAL PREVENTION

Cautious sexual practices

PATHOPHYSIOLOGY

- Penile fracture:
  - Rupture of tunica albuginea secondary to misguided erect penis striking partner's pubic symphysis or perineum

- Penile strangulation (foreign body constricts blood flow, induces edema/ischemia, constricts micturition:
  - Pediatric patients:
    Hair or string causes constriction
  - Adult patients:
    Penile constricting devices designed for sexual enhancement
- Degloving injuries:
  - Penile tissues deep to dartos fascia get trapped and stripped off

COMMONLY ASSOCIATED CONDITIONS

- Penile fracture is associated with urethral injury in up to 38% of cases.
- Penile amputation is most commonly result of self-mutilation during active psychotic episode.

DIAGNOSIS

HISTORY

Mechanism and timing of injury:

- Penile fracture:
  - Recent vigorous sexual activity
  - Patient hears or feels a pop during intercourse followed by detumescence, swelling, ecchymosis, and pain
  - Blood at urethral meatus or inability to urinate may signal urethral injury.
- Penile amputation:
  - Timing since amputation is critical; amputated penis usually won't survive >24 hours of cold ischemia or 6 hours of warm ischemia
  - Status of amputated segment (discarded or preserved)

PHYSICAL EXAM

- Penile fracture:
  - Penile swelling, ecchymosis with possible palpable defect in corpora cavernosa
  - If bleeding is confined by Buck fascia, may see sleeve of penis or eggplant sign with normal scrotum
  - If bleeding is through Buck fascia, then may be contained by Colles fascia and get classic butterfly ecchymosis in the perineum
- Penile strangulation:
  - Penile edema, ischemic changes, gangrene
  - Suprapubic fullness secondary to urethral constriction
- Gunshot wounds:

– Search for associated injuries especially injured femoral vessels, urethral injury, or rectal injury.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

CBC and electrolytes as needed in the given trauma situation (mostly needed if large blood loss or associated injuries)

Imaging

Penile fracture:

- Cavernosography can be performed to detect cavernosal injury if diagnosis in doubt (seldom).
- MRI and US are described, and in some cases can pinpoint exact location of the tunical disruption (seldom indicated).
- RUG if blood at meatus or suspect urethral injury

Diagnostic Procedures/Surgery

Good physical exam and imaging as above

TREATMENT

- Resuscitation as needed. Bleeding with penile amputation can cause hypovolemic shock.
- Search for urethral injury with retrograde urethrogram in any situation where there is blood at urethral meatus or high index of suspicion for injury exists.
- Penile amputation:
  – Amputated portion must be wrapped in sterile gauze wet with saline, then placed in plastic bag to be placed in container of ice water.

MEDICATION

None specific; supportive medications such as pain medications and prophylactic antibiotics

SURGERY/OTHER PROCEDURES

- Penile fracture:
  – Circumcising incision via subcoronal approach:
    Evacuation of hematoma
    Close cavernosal injuries with absorbable suture.
    Explore for urethral injuries and, if present, repair in spatulated watertight fashion.
- Penile strangulation:
  – Incision of offending agent if possible (hair, string, rubber bands, soft rings can be cut with scissors)

– Solid constricting devices may require attempts at removal with lubrication; distal penile compression with manual pressure may decrease tissue edema long enough to remove foreign body.

– Some solid constricting devices may require ring cutters, operative drills, industrial drills, various saws; every attempt should be made to protect phallus with tongue depressors, malleable retractors, etc.

– Suprapubic tube may be needed for bladder decompression.

- Penile amputation:

– If amputated segment is available and has been adequately preserved (see below), then replantation performed:

2-layer urethral repair over catheter done 1st to stabilize penis.

Identify vessels and nerves dorsally in neurovascular bundle.

Close tunica albuginea with 4-0 absorbable suture.

Microscopic anastomotic repair of dorsal penile artery with 11-0 nylon

Dorsal vein repair with 9-0 nylon

Neural repair of dorsal nerve with 10-0 nylon

Divert with suprapubic tube

Microvascular repair of cavernosal arteries generally not done; revascularization of dorsal arteries alone preserves erectile function and blood supply

– If amputated segment not able to be reattached:

Close remaining corporal bodies with 4-0 PDS

Spatulate urethral meatus to tunica.

Can gain penile length later by cutting suspensory ligament, defatting pubis, or considering reconstruction with free flap

- Avulsions (degloving injury):

– Exposed surface should be immediately covered with sterile saline-soaked gauze and area re-examined in 24 hr to assess extent of injury.

– Penile shaft can be covered with split-thickness skin graft.

– Scrotum can be covered with meshed split-thickness skin graft.

- Gunshot wounds:

– If wound contaminated, then conservatively débride and allow healing by secondary intention.

– If wound clean, tunical margins can be reapproximated with absorbable suture; urethral injuries should be sought and repaired as needed.

ADDITIONAL TREATMENT

Penile fracture:

- Nonoperative conservative treatment with ice packs, sedatives, and pressure bandages no longer recommended due to complications:
  - 10% with significant penile deformity
  - Prolonged penile pain
  - Pulsatile cavernosal diverticulum
  - Large residual penile mass/expanding hematoma

ONGOING CARE

PROGNOSIS

- Penile fracture:
  - Generally good outcomes for those undergoing surgery; <5% get mild penile curvature
- Penile amputation:
  - Microsurgical reattachment gives best results, with some patients able to achieve penetration; some develop urethral stricture or fistula.
  - Macroscopic repair without microvascular reanastomoses usually results in partial skin necrosis.

COMPLICATIONS

- Penile fracture:
  - Impotence:
    Traumatic corporeal veno-occlusive dysfunction
    Persistent venous leakage
    Arterial insufficiency
    Significant angulation in unrepaired cases may cause functional inability for intercourse.
  - Urethral stricture if urethral injury unrecognized
- Penile amputation:
  - Impotence
  - Urethral stricture
  - Urethral fistula
  - Skin necrosis
  - Decreased sensation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Follow-up for development of long-term complications

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bites to Penis (Animal and Human)
- Penis, Trauma Algorithm
- Scrotum and Testicle, Trauma
- Taghaandan
- Urethra, Trauma (Anterior and Posterior)

CODES

ICD9

- 607.89 Other specified disorders of penis
- 959.13 Fracture of corpus cavernosum penis
- 959.14 Other injury of external genitals

ABBREVIATIONS

- CBC: Complete blood count
- MRI: Magnetic resonance imaging
- PDS: Polydioxanone suture
- RUG: Retrograde urethrogram
- US: Ultrasound

PEYRONIE DISEASE

Anthony John Schaeffer, MD
Trinity J. Bivalacqua, MD, PhD

BASICS

DESCRIPTION

)[C]

)[C]:

- Most commonly dorsal plaque on side of penis to which curvature directed

- Penile angulation may preclude sexual intercourse.
- Synonym(s): Acquired penile curvature, penile induration

EPIDEMIOLOGY

)[C]

)[C]

- Mean age: 53

)[C]

RISK FACTORS

- Inherent tendency to produce abnormal fibrous tissue
- Trauma or injury to penis; may incite fibrotic reaction

)[C]

Genetics

)[C]

PATHOPHYSIOLOGY

)[C]

- Origin of initial inflammatory process that leads to fibrosis, calcification, elastic fiber alterations, and plaque formation in tunica albuginea unknown, but likely predisposing genetic alteration with inciting trauma
- Acute phase:
  - Occurs in 1st 6–18 mo
  - Pain with erections, slight penile curvature, and nodule formation
  - Medical therapy most effective in acute phase
- Chronic phase:
  - 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

COMMONLY ASSOCIATED CONDITIONS

)[C]

- PD is found in 10% men with ED

DIAGNOSIS

HISTORY

Inquire about:

  - Duration and onset of symptoms
  - Pain: With or without erection; during intercourse
  - Penis: Induration; degree of penile angulation; hourglass deformity; shortening
  - Erections: Quality; sufficient for intercourse

PHYSICAL EXAM

- Penile exam noting plaque size and location
- Photograph helpful in assessing degree of angulation (See figure)
  - Hand exam for associated Dupuytren contracture

DIAGNOSTIC TESTS & INTERPRETATION

Imaging

- No imaging necessary for diagnosis/medical therapy
- Preoperative color Doppler US with CIS: Assess penile deformity and vascular status of penis

Diagnostic Procedures/Surgery

Preoperative CIS: Intracavernous injection of vasodilator and genital/audiovisual sexual stimulation with measurement of erection and curvature

Pathological Findings

Excess collagen deposition and inflammatory infiltrate is found in the tunica albuginea

DIFFERENTIAL DIAGNOSIS

- Cancer
- Kelami syndrome: Fibrosis of the corpus spongiosum that limits expansion of the ventral corpora cavernosa
- Penile fracture (hematoma)

TREATMENT

- A small percent of men will undergo spontaneous remission.
- Surgery is not a common 1st-line option and is ultimately offered to a minority of patients.
- The lack of randomized, placebo-controlled trials makes evaluation of efficacy and comparison between any medical therapies for PD difficult.

)[C]

- All medical therapies provide varying decrease in pain, curvature, or plaque size.

MEDICATION

- Oral therapy:
  - No therapy has proven more or less effective than another
  - Vitamin E (tocopherol):
    800–1,000 U/d PO in divided doses
    Antioxidant effects
    May cause bleeding
  - Potassium aminobenzoate (Potaba):
    3 g PO q6h
    May increase monoamine oxidase, decrease serotonin, or increase utilization of oxygen by tissues
    Expensive, GI side effects
  - Colchicine:
    0.6 mg PO q8h
    May decrease collagen synthesis and increase collagenase activity
  - Other reported oral therapy: Tamoxifen, acetyl-L-carnitine, propylaeum
- Intralesional therapy:
  - No therapy has proven more or less effective than another

)[C]:

12 injections (10 mg/10mL) given once every 2–4 wk
Calcium blockage inhibits extracellular transport of collagen; increases collagenase activity in vitro
Must commit to full course
Good agent for young patients in acute phase

)[C]:

10,000 U in 0.25 cm3 per injection
3 injections over 7–10 days, repeated in 3 mo
Breaks down collagen, promotes remodeling

)[C]:

5 for 106U biweekly for 3–6 mo
Inhibits fibroblast proliferation, diminishes collagen production, increases collagenase activity
Good agent for young patients in acute phase
Flu-like side effects

– Intralesional corticosteroids no longer recommended due to local side effects

SURGERY/OTHER PROCEDURES

)[C]

- Patient must be in chronic phase with stable plaques.
- Preoperative US and CIS useful to evaluate vasculature and anatomy of penis, as described above
- Plication procedures:
  – Candidates: Longer penis, mild, distal curvature, good erectile function
  – Relative to corporal plaque, plication of opposite aspect of corpora cavernosa with hidden knots, with or without loosening incision of plaque
  – Complications/side effects: Hematoma, stitch erosion/granuloma, penile shortening
- Plaque excision with grafting:
  – Candidates: Shorter penis, proximal plaque, severe curvature, hourglass deformity, good erectile function
  – Plaque excised and corporotomy defects grafted with autogenous (dermis, saphenous vein, tunica vaginalis, temporalis fascia, cadaveric pericardium) or synthetic (Dacron, Gore-Tex, or silastic) material
  – Complications: Loss of sensitivity, infection, hematoma, emergence of venoocclusive erectile dysfunction
- Inflatable penile prosthesis placement:
  – Candidates: Significant erectile dysfunction, severe curvature
  – Modeling:

    When prosthesis placement alone fails to straighten penis, manual modeling is recommended, with good outcomes

    Forcible manual manipulation of penis over inflated prosthesis
  – Complications: Infection (1–3%), erosion (<5%), mechanical malfunction (5–10%), urethral injury

ADDITIONAL TREATMENT

Extracorporal shockwave therapy: No good placebo-controlled studies to document efficacy; studies report decreased pain after ESWL therapy.

ONGOING CARE

PROGNOSIS

See “Pathophysiology–Natural History”

COMPLICATIONS

See specific therapies

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Patients should be reexamined frequently to assess disease status and response to therapy

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7. Hellstrom WJ, Kendirci M, Matern R, et al. Single-blind, multicenter, placebo controlled, parallel study to assess the safety and efficacy of intralesional interferon -2b for minimally invasive treatment for Peyronie’s disease. J Urol 2006;176:394–398.

See Also (Topic, Algorithm, Electronic Media Element)

- Erectile Dysfunction/Impotence (ED)
- Penis, Curvature and/or Pain
- Penis and Corporal Body Mass

CODES

ICD9

607.85 Peyronie’s disease

ABBREVIATIONS

- CIS: Combined intracavernous injection and stimulation
- ED: Erectile dysfunction
- ESWL: Extracorporeal shockwave lithotripsy
- GI: Gastrointestinal
- PD: Peyronie disease
- US: Ultrasound

PHEOCHROMOCYTOMA

Joseph C. Klink, MD

Judd W. Moul, MD

BASICS

DESCRIPTION

- Tumor arising from catecholamine-producing chromaffin cells in the adrenal medulla
- Paraganglioma of adrenal origin

ALERT

Hypertensive crisis and life-threatening complications can be seen with pheochromocytoma.

EPIDEMIOLOGY

- 1–2 per 100,000 adults per year
- No gender predilection
- Average age in sporadic cases: 40–50
- Hereditary cases often <40 yr old
- In all hypertensive patients, prevalence of pheo is 0.1–0.6%.
- Prevalence in autopsy series is 0.05%.
- >50% of catecholamine-producing tumors are undiagnosed until death.

RISK FACTORS

- Familial tumors associated with MEN syndrome:
  - MEN IIA (Sipple syndrome): Pheochromocytoma (<50%), medullary carcinoma of the thyroid (50%), and parathyroid adenoma (25%):
    Autosomal dominant, chromosome 10, secrete mostly EPI, with paroxysmal HTN
  - MEN IIB (MEN III): Pheochromocytoma, medullary carcinoma of the thyroid, ganglioneuromatosis, multiple mucosal neuromas of eyelids, lips, tongue
- Von Recklinghausen syndrome: 1% have pheochromocytoma; 5% of patients with pheochromocytoma have neurofibromatosis.
- Von Hippel-Lindau disease (retinal cerebellar hemangioblastomatosis): 10% with pheochromocytoma

Genetics

- Hereditary predisposition in 20–30%
- Germ-line mutations in 1 of these 5 genes can cause pheo:
  - RET proto-oncogene (MEN2)
  - Von Hippel-Lindau gene
  - Neurofibromatosis type I gene (von Recklinghausen disease)

- Succinate dehydrogenase subunit B gene
- Succinate dehydrogenase subunit D gene (familial nonsyndromic paragangliomas)

- Not cost-effective to test all 5 genes in every patient
- Hereditary tumors usually present at a younger age than sporadic tumors.

PATHOPHYSIOLOGY

- Tumors arise form 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, 50% of familial tumors bilateral
  - Extra-adrenal up to 20%
  - Hereditary 20–30%
  - Malignant up to 5% in adrenal pheo, 33% for extra-adrenal pheo
- 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
- Bladder pheochromocytomas account for <1% of bladder tumors and <1% of pheochromocytomas:
  - Can present with micturition syncope
  - Partial cystectomy is the treatment of choice. Transurethral excision is contraindicated because it may precipitate a hypertensive crisis.

COMMONLY ASSOCIATED CONDITIONS

- MEN IIa, IIb
- Von Recklinghausen syndrome
- Von Hippel-Lindau disease

DIAGNOSIS

HISTORY

- Most patients are symptomatic, presenting with paroxysms of HTN with severe headache, drenching perspiration, and palpitations.
- Other symptoms include nervousness, panic, tremor, pallor, pain in the chest and abdomen, nausea, fever, and flushing.
- Hypertension: Most common sign, 3 patterns, only 10% normotensive:
  - Sustained HTN: Most common in children (90%), and MEN2 syndrome
  - Paroxysmal HTN: Dramatic attacks of HTN, females > males, occur 3–4 times a week

– Sustained HTN with superimposed paroxysms: 50% incidence

- Hypertensive attacks may be initiated by a variety of stimuli:

– Compression of tumor: Physical activity, trauma, increase abdominal pressure with Valsalva, micturition, etc.

– Foods rich in tyramine: Beer, wine, cheese, etc.

– Drugs: Tyramine, histamine, nicotine, glucagon, etc.

PHYSICAL EXAM

- Can be unremarkable if patient not symptomatic at time of exam
- Hypertensive most often, but may also be normotensive or hypotensive
- Fine tremors, pallor, and perspiration
- Rarely have palpable tumor
- Accelerated hypertensive retinopathy: Papilledema, exudate, A-V knicking
- Raynaud phenomenon or livedo reticularis
- Hyperhidrosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Plasma or urinary fractionated metanephrines are the best screening tests:

– Chromaffin cells metabolize NE to NMN and EPI to MN

– Fractionated metanephrines refers to MN and NMN

– Both the plasma metanephrines test and the urine metanephrines test are acceptable options, and current recommendations do not recommend either test over the other.

- All metanephrine values are on a spectrum with no absolute cut-off for normal values.
- Urine test: 24-hr urine for NE, EPI, MN, NMN, and VMA:

– VMA highly specific (95%) but not sensitive (64%)

– Normal values: NE <100 g/24 h; EPI <25 /24 hr; VMA <6.5 mg/24 h; NMN + MN <1.3 mg/24 hr

– 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 pharmacologic testing.

- Plasma free metanephrine and NE/EPI testing:

– Measure NMN, MN with the patient fasting and supine, with the needle in place in the vein for at least 20 min prior to drawing the sample.

– Plasma catecholamine test positive if plasma NE + EPI >950 pg/mL (sensitivity: 88–100%)

– Plasma NMN <112 pg/mL and MN <61 pg/mL normal. Plasma NMN >400 pg/mL and MN >236 pg/mL virtually diagnostic. In the gray zone between these numbers, more test-

ing is needed.

- Pharmacologic testing:
  - Stimulation and suppression tests are generally not utilized.
  - Useful in patients with essential HTN but borderline elevated catecholamines
  - Provocative tests dangerous, with several reported deaths
- Clonidine suppression test:
  - Most often used suppression test
  - Centrally acting 2-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/70 kg)
  - Plasma catecholamines remain the same or elevated in patients with pheochromocytoma.

Imaging

- Localization studies should be started only if clinical evidence for the tumor's existence is strong (hereditary predisposition or signs and symptoms with very high MN/NMN).
- CT or MRI for initial localization:
  - Neither CT nor MRI is recommended above the other.
  - 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
- Iodine123-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.

Pathological Findings

- Sporadic tumors are solitary, well-circumscribed, and encapsulated.
- Malignant pheo cannot be differentiated from benign pheo by exam of primary tumor. Malignant pheo is defined by metastases.

DIFFERENTIAL DIAGNOSIS

- Essential HTN

- Renovascular disease
- Anxiety, tension states, psychoneurosis
- Hyperthyroidism
- Paroxysmal tachycardia
- Menopause
- Vasodilating headaches (migraine and cluster)
- Acute hypertensive encephalopathy
- Nephrologic diseases
- Cocaine, amphetamines

TREATMENT

Surgical removal of the tumor is the only definitive method of treatment.

MEDICATION

First Line

- Appropriate antihypertensive drugs to manage HTN, control symptoms, and prepare for surgery
- -Adrenergic blocking agents essential before surgery:
  - Phenoxybenzamine 0–40 mg b.i.d. or t.i.d.
  - Prazosin 1–10 mg b.i.d.
- -Blocking agents contraindicated in the absence of established -blockade:
  - Use only for concomitant cardiac arrhythmias or persistent tachycardia

Second Line

See “Additional Therapies.”

SURGERY/OTHER PROCEDURES

- Preoperative adrenergic blockade is mandatory!
- Close hemodynamic monitoring and anesthetic management are essential.
- Laparoscopic surgical removal of the tumor is the preferred treatment for tumors <10 cm:
  - Initial dissection aimed toward early control and division of the main adrenal vein
- Malignant pheochromocytoma:
  - Usually slow growing; attempt complete resection
  - Large masses can be debulked surgically to relieve symptoms.

Pregnancy Considerations

Simultaneous cesarean section and removal of tumor is indicated if fetal maturity is compatible with extrauterine survival at the time of diagnosis; if not, treat with -blockers.

ADDITIONAL TREATMENT

Radiotherapy

An option for malignant pheochromocytoma, see “Additional Therapies.”

Additional Therapies

Malignant pheochromocytoma:

- Iodine131-MIBG radiation is the most effective treatment after surgery.
- Combination chemotherapy with cyclophosphamide, vincristine, and dacarbazine: 50–60% partial response
- Local radiation or chronic blockade with metyrosine for symptomatic disease

ONGOING CARE

PROGNOSIS

- 10-yr survival for nonmalignant tumors: >80%
- 5-yr survival for malignant pheo: 34–60%:
  - Currently no cure for malignant pheo

COMPLICATIONS

- Persistent HTN can result in retinopathy and nephropathy.
- Catecholamine-induced cardiomyopathy:
  - Can see hypotension and shock
  - Cardiomyopathy reversible with -blockade and -methylparatyrosine
  - All patients should have cardiac evaluation, including echocardiogram
- Cerebral vascular accident
- Hypertensive encephalopathy
- Renal insufficiency
- Hemorrhagic necrosis of pheochromocytoma
- Dissecting aneurysm
- Ischemic enterocolitis
- Neurogenic pulmonary edema

FOLLOW-UP RECOMMENDATIONS

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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Adrenal Mass, Solid Algorithm
- Multiple Endocrine Neoplasia (MEN I and II)
- Urine Studies, Section IV

CODES

ICD9

- 194.0 Malignant neoplasm of adrenal gland
- 227.0 Benign neoplasm of adrenal gland

ABBREVIATIONS

- BP: Blood pressure
- CT: Computed tomography
- EPI: Epinephrine
- HTN: Hypertension
- MEN: Multiple endocrine neoplasia
- MIBG: Meta-iodobenzylguanidine
- MN: Metanephrine
- MRI: Magnetic resonance imaging
- NE: Norepinephrine
- NMN: Normetanephrine
- Pheo: Pheochromocytoma
- VMA: Vanillylmandelic acid

PHIMOSIS AND PARAPHIMOSIS

Douglas E. Coplen, MD

BASICS

DESCRIPTION

- Phimosis (preputial stenosis) is the inability to retract the foreskin.
- Physiologic (congenital) phimosis:
  - Foreskin is usually not retractile in a newborn. The majority can be retracted by 4–5 yr of age
- Pathologic (acquired) phimosis:
  - The foreskin cannot be retracted when previously possible or it has never been retractile and is associated with symptoms
  - Can be seen in children and adults
- Paraphimosis:
  - The foreskin is retracted and cannot be reduced into its natural position because it was left in position and is now edematous.

ALERT

Failure to reduce a paraphimosis can result in progressive edema of the glans with the possibility of vascular compromise and necrosis of the glans penis.

ALERT

There is an increased risk of penile cancer in males with poor hygiene and phimosis.

EPIDEMIOLOGY

- 10% nonretractile at age 3–5
- 1% nonretractile at puberty

RISK FACTORS

- Forced or traumatic retraction of foreskin
- Indwelling catheter
- Chronic balanitis
- Genital piercings

GENERAL PREVENTION

- Good hygiene
- Don’t prematurely manipulate the foreskin

PATHOPHYSIOLOGY

- Physiologic phimosis:
  - The foreskin is naturally adherent to the glans in infants.
  - Glandular secretions and keratin debris (smegma) facilitates separation.

– This is best observed only; the newborn foreskin does not require manipulation or retraction.

- Pathologic phimosis:
  – Chronic irritation, often due to poor hygiene, leads to sclerosis of the preputial opening.
  – Premature manipulation and trauma leads to scarring of the delicate prepuce.
  – Inadequate circumcision or post-circumcision care allows constriction of the circumcision line.

COMMONLY ASSOCIATED CONDITIONS

Diabetes mellitus

DIAGNOSIS

HISTORY

- Foreskin previously retractile
- Circumcision
- Local irritation and redness
- Dysuria or other voiding symptoms
- Discharge
- Cracking or bleeding from the foreskin
- Ballooning of the foreskin with voiding
- Post-void dribbling
- History of UTI
- Prior course of topical or oral antibiotics for irritation

PHYSICAL EXAM

- Evaluate for penile abnormalities such as hypospadias, chordee, webbed penis
- Appearance of foreskin:
  – Normal skin color
  – Erythema and inguinal adenopathy
  – Discharge
  – Circumferential white discoloration
  – Meatus can be visualized
  – Crack in skin with attempted retraction
  – Severe scarring or BXO
  – Smegma (normal finding)
- Paraphimosis:
  – Marked edema of inner prepuce distal to the constricting band

- Ulcerations if chronic
- Evaluate glans for ischemia
- Rule out hair or foreign body in a circumcised male

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Usually not necessary unless symptoms of UTI 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 pre-pubic or scrotal skin after neonatal circumcision.
  - BXO
- Paraphimosis:
  - Penile edema
  - Post-circumcision cicatrix
  - Hair/thread tourniquet:

    Hair or thread wraps around a child's penis and causes penile edema or strangulation

Geriatric Considerations

In the elderly male undergoing bladder catheterization, failure to replace the foreskin to its normal reduced position may result in paraphimosis.

TREATMENT

- Physiologic phimosis:
  - Observation and reassurance
  - Topical steroids (0.05% betamethasone) may allow atraumatic retraction
  - Parents should be taught to never force back the foreskin but gradually retract it over time.
- Phimosis:
  - Urgent manual reduction should be attempted
  - Pain medication (eg, morphine, Demerol) or local anesthesia (lidocaine without epinephrine, infiltration or penile block) may be necessary
  - 1st attempt manual compression for 5 min to reduce edema and reposition foreskin

– Manual reduction technique:

Place thumbs on the glans while stabilizing the foreskin in between the 2nd and 3rd fingers.

Apply pressure on the thumbs while attempting to pull the foreskin over the glans

– If above maneuver fails, try a dorsal slit or incision of constricting band if manual reduction is not feasible.

– Recurrent paraphimosis may need definitive circumcision to prevent recurrence.

MEDICATION

- Pathologic phimosis:
  – 0.05% betamethasone diprionate cream b.i.d. for 3 wk facilitates retraction in up to 80%
- Balanitis: Oral cephalosporin for acute cellulitis
- Culture specific antibiotics for UTI

SURGERY/OTHER PROCEDURES

- Phimosis:
  – 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
- Dorsal or ventral slit urgently treats narrowing and preserves the foreskin
- Postcircumcision cicatrix requires excision of scar and perhaps fixation of the shaft in an extruded position to prevent recurrence
- Paraphimosis: Emergency circumcision rarely necessary

ADDITIONAL TREATMENT

- Some advocate stretching or balloon dilation under anesthesia for phimosis rather than circumcision.
- Puncture technique for paraphimosis, whereby a 21-gauge needle is used to create openings in the edematous tissue to allow fluid to be compressed more easily

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Reports of application of finely ground sugar to reduce edema in paraphimosis reported

ONGOING CARE

PROGNOSIS

- 95% of physiologic phimosis resolves by puberty with the majority retractile by age 5
- Circumcision is curative.

COMPLICATIONS

- Complications of phimosis:
  - UTI
  - Post-void dribbling
  - Chronic inflammation with recurrent balanitis or balanoposthitis
  - Calculi or pearls from smegma
  - Penile carcinoma (rarely)
- Complications of circumcision:
  - Hemorrhage
  - Persistent adhesions
  - Skin bridges
  - Inadequate skin removal
  - Insufficient skin removal
  - Inclusion cyst
  - Cicatrix/concealed penis
  - Meatal stenosis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Proper hygiene of uncircumcised males

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Balanitis Xerotica Obliterans (BXO)
- Balanoposthitis
- Circumcision, Adult Considerations
- Circumcision, Pediatric Considerations

CODES

ICD9

605 Redundant prepuce and phimosis

ABBREVIATIONS

- BXO: Balanitis xerotica obliterans
- UTI: Urinary tract infection

PNEUMATURIA (GAS IN URINE)

Paul R. Young, MD

BASICS

DESCRIPTION

Passage of gas in the urine:

- Usually caused by enterovesical fistula (CVF most common cause)
- Can be secondary to gas forming UTI or recent instrumentation, but spontaneous pneumaturia should be considered secondary to CVF until proven otherwise.

EPIDEMIOLOGY

)[B]

)[B]

RISK FACTORS

- Diverticulitis (sigmoid to bladder fistula)
- Colorectal cancer (fistula to bladder)
- Crohn disease (terminal ileum to bladder fistula)
- Less common causes of fistulae: Radiation including brachytherapy, trauma (penetrating or iatrogenic surgical trauma)
- DM: CO2 formation due to fermentation of sugar in urine by bacteria

PATHOPHYSIOLOGY

- Pneumaturia is usually a sign of underlying pathology.
- Occasionally secondary to instrumentation: Recent Foley placement most common or following cystoscopy
- Fistula most likely cause:

)[B]

)[B]

  – Most common malignancy associated with vesicoenteric fistula is colorectal; occasionally bladder, cervix, ovary

- Radiation induced (prostate, bladder, cervical)
- Infection with gas-forming organisms less likely cause:
  – Almost exclusively in diabetics (sugar in urine fermented by bacteria, forming CO2)

)[B]

)(A)

  – Candida-associated UTI has been reported.

COMMONLY ASSOCIATED CONDITIONS

- Diverticulitis

- Fecaluria
- Colorectal cancer
- Crohn disease
- DM
- UTI

DIAGNOSIS

HISTORY

- Symptoms of fistula usually present as urinary tract symptoms secondary to UTI (suprapubic pain, UTI symptoms)
- Associated fecaluria is highly suggestive of enterovesical fistula
- History of diverticulitis, Crohn, DM
- Symptoms of colorectal cancer
- History of radiation or surgical trauma

PHYSICAL EXAM

- Abdominal tenderness with Crohn, diverticular disease
- Flank tenderness with pyelonephritis
- Acutely ill with high fevers suggests diverticular abscess, emphysematous pyelo, or urinary obstruction

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urine culture:

- Usually positive if fistula (can be multiple organisms, but can show 1 organism (E. coli is most common).

)[B]

Imaging

)[B]:

  - Air in bladder on uninstrumented CT
  - Diverticulitis/pericolonic inflammation
  - Mass around bladder
  - Oral contrast in bladder
  - Air in bladder/renal parenchyma and/or collecting system (emphysematous cystitis or pyelonephritis)

- Role of MRI unclear:
  - May be useful to delineate fistula
  - IVP, cystogram, barium enema less useful

Diagnostic Procedures/Surgery

)[B]:

– Discrete area (edematous dimple, erythema, papillary changes) with or without fecal matter/mucous

- Colonoscopy: Useful to rule out colorectal cancer; may occasionally identify site of fistula or identify diverticular disease
- Other diagnostic tests if diagnosis of fistula elusive and suspicion high:

– Charcoal test: Look for orally ingested charcoal particles in urine 12–48 hr after ingestion; passing urine through a white stone filter is helpful

)[B]

DIFFERENTIAL DIAGNOSIS

- Emphysematous cystitis
- Emphysematous pyelonephritis
- Renoalimentary fistula
- UTI with gas-forming organism
- Urinary tract instrumentation
- Urethrorectal fistula
- Vesicoenteric fistula
- Vesicovaginal fistula

TREATMENT

- Culture of the urine
- Identification of the source is essential 1st step.

MEDICATION

Antibiotics guided by culture results

SURGERY/OTHER PROCEDURES

- Iatrogenic due to instrumentation will clear spontaneously
- Fistula:

– Delayed surgery is mainstay of treatment (mostly elective), but initial nonoperative approach in nontoxic patient may be considered

)[B]

- Emphysematous cystitis: Surgery rarely necessary

)[B]

)[C]

ONGOING CARE

PROGNOSIS

Depends on underlying disease process:

- Significant mortality rate with emphysematous pyelo
- Chronic problems with Crohn

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Manage underlying disease processes.

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Cystitis, Emphysematous
- Fecaluria
- Fistula, Enterovesical
- Fistula, Urethrorectal
- Fistula, Vesicouterine
- Fistula, Vesicovaginal, Ureterovaginal
- Pyelonephritis, Emphysematous
- Reno-alimentary Fistula

CODES

ICD9

599.84 Other specified disorders of urethra

ABBREVIATIONS

- CT: Computed tomography
- CVF: Colovesical fistula
- DM: Diabetes mellitus
- IVP: Intravenous pressure
- MRI: Magnetic resonance imaging
- UTI: Urinary tract infection

POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL DOMINANT (ADPKD)

Costas D. Lallas

BASICS

DESCRIPTION

- Characterized by renal and extrarenal cysts with HTN and variable progression to ESRD, requiring either dialysis or transplantation
- Autosomal dominant disease; usually presents in adulthood although it has been recognized in newborns.

EPIDEMIOLOGY

- Most frequent autosomal dominant fatal disease (1:500–1:1,000 incidence):
  - 10 times more prevalent than Huntington disease; 2 times more prevalent than cystic fibrosis
- >500,000 persons in US; >5 million at risk worldwide
- Multisystem disease; can lead to ESRD
- Contributes 10% of all patients on chronic hemodialysis

RISK FACTORS

- Etiology theories:
  - Epithelial hyperplasia: Epidermal growth factor and receptor found in cyst fluid and wall. Hyperplasia causes tubular obstruction with weakening and outpouching.
  - Defect in extracellular connective tissue matrix: Similar manifestations with other multiorgan diseases (Ehlers-Danlos and Marfan syndromes)
  - Abnormal cell polarity: Na+-K+ ATPase and epidermal growth factor receptor found apically, as well as its normal basolateral position; may reverse sodium transport and allow fluid accumulation within cysts
- Risk factors: Parents or close relatives with the disease
- Progression of symptoms:
  - Increased severity of manifestations in males, patients with PKD1, age of diagnosis <30, age of HTN diagnosis <35, gross hematuria <30, and 3 pregnancies.
  - Severity of manifestations may be directly related to maternal imprinting (receiving the defective gene from the mother) and anticipation (disease more severe and earlier onset in the next generation).
  - Diet is not shown to affect progression to ESRD.

Genetics

- Autosomal dominant inheritance with 100% penetrance
- At least 3 genes are responsible:
  - PKD1 (chromosome 16p13.3) (85–90%) encodes polycystin. Expression regulated during renal development. May regulate cell-to-cell and/or cell-to-extracellular matrix interaction in the maintenance of renal epithelial differentiation and organization
  - PKD2 on chromosome 4q.21–23 encodes a 968-amino acid protein. Both PKD1- and PKD2-encoded proteins are postulated to function as a voltage-gated ionic channel.
  - No assignment of genomic locus for the 3rd gene, PKD3

GENERAL PREVENTION

Genetic counseling; in utero US and genetic testing, with termination of pregnancy if disease is found

PATHOPHYSIOLOGY

- Renal manifestations:
  - Usually bilateral renal cysts in an enlarged kidney
  - ESRD
  - The rate of renal deterioration correlates with the rate of cyst growth
  - ADPKD will cause ESRD in 2% at age 40, 23% at age 50, and 48% at age 73.
  - 4–5 times the risk of renal adenomas, but RCC risk is not elevated.
  - If RCC is present, it is more often bilateral, multicentric, and sarcomatoid.
  - Can have decreased urinary concentrating ability, decreased citrate excretion, increased renin production
  - 20–30% of patients develop stones
- Extrarenal manifestations:
  - Hepatic and pancreatic cysts, colonic diverticula, cardiac valvular abnormalities (mitral valve prolapse, aortic incompetence, and tricuspid prolapse), intracranial aneurysms, and rare miscellaneous cysts (arachnoid, pineal, splenic, testicular, seminal vesicle, and ovarian)
- Usual presentation: 30–50 yr with HTN (60–80%), flank pain (50–70%), microscopic or gross hematuria (50%) without anemia, GI symptoms, and intracerebral (from HTN) or subarachnoid bleeding (from associated berry aneurysms)
- HTN most common symptom; renin-mediated through ischemia caused by the stretching of intrarenal vessels around the cyst. Patients are not anemic due to adequate erythropoietin production
- Anemia may be present in ESRD due to cystic hemorrhage and/or uremic hematopoietic depression.

- 70% of intracranial bleeds are intracerebral due to HTN; 10–40% have berry aneurysms, but only 10% die of subarachnoid hemorrhage.
- Renal cysts are found in utero in 2% of ADPKD patients, with a high recurrence (45%) of early polycystic kidney presentation in subsequent siblings.
- Neonates present with renomegaly and respiratory distress. Children (<1 yr old) typically present with HTN and renomegaly.
- Men tend to develop HTN and renal insufficiency earlier, whereas women have a high incidence of liver cysts, UTIs, and flank pain.

COMMONLY ASSOCIATED CONDITIONS

TSC2/PKD1 contiguous gene syndrome; characteristics of both ADPKD and TSC, but ESRD earlier (2nd decade)

DIAGNOSIS

HISTORY

- Family: At least 3 generations of renal disease, HTN, and strokes
- Patient history of renal disease, HTN, stroke, hematuria, stones, UTIs

PHYSICAL EXAM

- BP, hypertensive changes of the retina
- Heart murmur, signs of uremia, cysts within the seminal vesicles
- Enlarged kidneys on abdominal palpation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Electrolytes, BUN, serum creatinine, urine analysis

Imaging

- US of abdomen, CT of abdomen or head, MRI of head. Bilateral renal cysts and 2 of the following: Bilateral renal enlargement; >3 hepatic cysts; cysts of spleen, pancreas, or pineal gland; cerebral artery aneurysm
- IVP: Bilateral renal enlargement with calyceal distortion and the bubble/Swiss cheese nephrogram. This reflects the nonfunctional cysts within the normal renal tissue.

Diagnostic Procedures/Surgery

Cytogenetics: Due to genetic heterogeneity of ADPKD mutations, linkage analysis is still needed to confirm diagnosis at the molecular level:

- Phenotypic heterogeneity between family members with the same genomic genetic mutation may be explained by somatic 2nd-hit loss of heterozygosity.

Pathological Findings

- Gross pathology:

– Enlarged kidneys with renal cysts ranging from millimeters to centimeters in diameter, creating a cobblestone-like surface with either a normal or distorted kidney morphology. Cyst fluid can be straw-yellow, hemorrhagic, or gelatinous.

- Histopathology:

– Cysts can involve all portions of the nephron (both in the cortex and medulla), and the wall epithelium can resemble the nephron segment from which it arose. Still, only 1% of nephrons develop cysts in ADPKD. Also, epithelial hyperplasia, arteriosclerosis, and interstitial fibrosis are present.

DIFFERENTIAL DIAGNOSIS

- Autosomal recessive PKD (autosomal recessive disease that presents in childhood with hepatic fibrosis), medullary dysplastic kidney (dysplastic renal parenchyma without a reniform configuration, and increased risk of contralateral UPJ obstruction [3–12%] or VUR [18–43%])
- Simple renal cysts
- Von Hippel-Lindau syndrome: Autosomal dominant disease with cerebellar hemangioblastomas, retinal angiomatosis, pheochromocytoma, pancreatic and epididymal cysts, with 35–38% incidence of RCC
- Tuberous sclerosis: Hamartomas in brain, skin, and kidneys; CNS abnormalities such as mental retardation and seizure activity; renal angiomyolipomas; <5% also present with polycystic kidneys; 2% incidence of RCC; and associated PKD contiguous gene syndrome (see “Commonly Associated Conditions”)
- Sporadic glomerulocystic kidney disease: Nonheritable condition diagnosed in neonates with bilateral enlarged kidneys, glomerular cysts, and no extrarenal abnormalities
- In neonates and children, juvenile nephronophthisis (autosomal recessive) and medullary cystic disease (autosomal dominant but typically medullary cysts alone)
- Contrast nephropathy and renal vein thrombosis must be considered in a neonate with bilateral renomegaly and homogenous hyperechogenic kidneys.

TREATMENT

- Coordinated care with nephrology recommended; neurosurgical consultation for CNS aneurysms
- Control BP and monitor renal function.
- Extreme physical activity and contact sports are to be avoided.
- Low-salt diet if hypertensive; low-protein diet is of questionable value.
- If not in renal failure, encourage fluid intake with adequate hydration.
- Hematuria/cyst hemorrhage usually resolves spontaneously. Treat conservatively, but uncontrolled bleeding may need embolization.

MEDICATION

- HTN: ACE inhibitors in patients with early disease
- Pain: Caution in using NSAIDs because of their nephrotoxic potential; can be caused by intracystic hemorrhage, cyst pressure, obstruction by blood clot or stone, and infection.
- Infections: Most commonly in females and occurs in cysts (87%) and in parenchyma (91%). Treat cystic infection with lipid-soluble antibiotics (trimethoprim-sulfamethoxazole, chloramphenicol, ciprofloxacin, vancomycin, clindamycin, and erythromycin).
- Stones: With normal renal function, treat stones with same standard of care as given to non-ADPKD patients

SURGERY/OTHER PROCEDURES

- Cyst pressure relief: Aspirate percutaneously or perform Rovsing procedure (unroofing cyst) via the open or laparoscopic method:
  - 2 approaches: Treat as many cysts as possible or treat only the largest cyst(s).
  - Results: 90% pain-free 6 mo after procedure; 77% pain-free at 5 yr
- Transplantation: Success rate is same between ADPKD and non-ADPKD recipients
- Removal of native kidney(s) indicated only if:
  - Recurrent pyelonephritis poorly controlled by medical therapy
  - Hematuria requiring transfusion
  - Bulky kidneys that pose an obstacle to caval flow or to transplanted kidney

ONGOING CARE

PROGNOSIS

- Life expectancy is 4–13 yr after clinical presentation. Death is usually due to uremia, heart failure, or cerebral hemorrhage.
- ADPKD diagnosed in utero has a poor prognosis; 43% died before the age of 1 yr, and 67% of survivors developed HTN.

COMPLICATIONS

- HTN
- Death from ESRD, intracerebral or subarachnoid hemorrhage
- Chronic pain, nephrolithiasis, renal cyst hemorrhage, and pyelonephritis are common.
- Liver cysts rarely lead to portal HTN, while congenital hepatic fibrosis and cholangiocarcinoma are also rare.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Presymptomatic patients: Follow BP and creatinine.
- For marriage, prenatal diagnosis and the search for potential kidney donors in the family

- US screening of children of patients with ADPKD has become commonplace.
- Issue of early diagnosis of disease:
  – In favor: Early diagnosis allows early medical management and a chance to rule out the disease early.
  – Against: Emotions of anxiety, grief, and fear of being a burden with early diagnosis. Also, exclusion from career opportunities and health/life insurance

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Acquired Renal Cystic Disease
- Polycystic Kidney Disease, Autosomal Dominant
- Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)
- Renal Mass
- Retroperitoneal Mass and Cysts

CODES

ICD9

753.13 Polycystic kidney, autosomal dominant

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ADPKD: Autosomal dominant polycystic kidney disease
- BP: Blood pressure
- BUN: Blood urea nitrogen
- CNS: Central nervous system
- CT: Computed tomography
- ESRD: End-stage renal disease

- HTN: Hypertension
- IVP: Intravenous pressure
- MRI: Magnetic resonance imaging
- NSAID: Nonsteroidal anti-inflammatory drug
- PKD: Polycystic kidney disease
- RCC: Renal cell carcinoma
- TSC: Tuberous sclerosis
- UPJ: Ureteropelvic junction
- US: Ultrasound
- VUR: Vesicoureteral reflux

POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL RECESSIVE (ARPKD)

Costas D. Lallas, MD

BASICS

DESCRIPTION

- A group of inherited disorders involving cystic dilatation of the renal collecting ducts and varying degrees of biliary dysgenesis and periportal fibrosis
- An overlap in the spectrum of renal and liver involvement precludes use of the Blyth and Orkenden 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

- Most common inherited cystic renal disease in infancy and childhood
- Incidence: 1–2 in 10,000 live births
- Commonly discovered in perinatal period; can present early in childhood or adolescence
- Males = Females
- Severely affected neonates usually die hours after birth; overall survival is much improved if they live beyond the neonatal period.
- Survival: For patients living to 1 mo: 86% alive at 1 yr, 67% alive at 15 yr

RISK FACTORS

- The cause of ARPKD remains poorly understood.
- Genetic and/or epigenetic factors may promote aberrant epithelial hyperplasia that causes cystic expansion of the collecting ducts and fluid accumulation. Less is known about hepatobiliary changes; however, epithelial hyperplasia may have role.
- Definite risk factors: Heterozygous parents

Genetics

- Autosomal recessive, heterozygotes unaffected, gene locus at chromosome 6p21
- Multiple allelism is likely responsible for variable phenotypic presentation; produces a protein called fibrocystin
- Offspring of heterozygotes: 25% risk of disease, 50% carriers

GENERAL PREVENTION

Genetic counseling for families with proven ARPKD (linkage studies with polymorphic DNA markers)

PATHOPHYSIOLOGY

- Clinical course (renal):
  - Severely affected neonates commonly die of pulmonary complications hours after birth.
  - Patients surviving the neonatal period have a better prognosis; they can have some renal maturation.
  - Progressive renal cyst enlargement, fibrosis, and renal insufficiency
  - Eventually, most develop renal failure.
  - Later presentation: Less severe renal component
- Clinical course (hepatobiliary):
  - Development of hepatosplenomegaly, portal HTN, extrahepatic bile duct dilation, gall bladder enlargement, occasional choledochal cyst formation, and hepatic dysfunction
  - Liver failure ultimately develops later in childhood.

COMMONLY ASSOCIATED CONDITIONS

Ehlers-Danlos syndrome

DIAGNOSIS

HISTORY

- Age of the patient:
  - Other cystic renal disorders rarely present in the pediatric population: Younger, more respiratory and renal issues; older, more hepatobiliary issues.
- Prenatal care:
  - Characteristic changes on prenatal US after week 30, abnormal uterine growth measurements, maternal -fetoprotein levels, amniocentesis results, history of stillbirth
- Birth history:
  - Difficult delivery suggests possible flank or abdominal mass.
- Family history:
  - Normal parents with a normal renal US suggests recessive disease.
- Medical history:
  - For older patient, may suggest evolution of disease
- Present illness: Polydipsia, polyuria, fatigue, unexplained fever, hematuria, pyuria, edema, difficult feeding, recent GI bleed or vague GI symptoms

PHYSICAL EXAM

- HTN, respiratory rate, temperature
- General appearance:
  - Potter phenotype, pallor

- Palpable kidneys: Hepatosplenomegaly
- Extremities: Joint contractures, edema

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Electrolytes, blood chemistry, urine analysis, urine culture
- CBC (exclude anemia, hypersplenism)
- Coagulation profile (access liver disease)
- Liver function tests (usually normal)
- High maternal -fetoprotein (associated with ARPKD), high amniotic fluid release (possible correlation)

Imaging

- US (best test): Prenatal-enlarged kidneys, oligohydramnios, normal liver, no bladder filling (more reliable after 30 wks' gestation); infancy-enlarged reniform kidneys, cortical echogenicity, hypoechoic subcapsular rim; older macrocysts (<2 cm diameter), decreased size, medullary echogenicity, hepatosplenomegaly:
  - Loss of corticomedullary differentiation: The pyramids in ARPKD are hyperechogenic and blend in with the rest of the kidney, so that the kidneys typically have a homogeneous appearance.
- CT may be used in confusing cases: More sensitive to inhomogeneity of cysts

Diagnostic Procedures/Surgery

- Renal biopsy
- Liver biopsy

Pathological Findings

- Renal:
  - Bilateral enlarged kidneys with reniform shape
  - Pinpoint opalescent dots on capsule (cortical collecting duct cysts)
  - Cut surface with sponge-like quality due to linear distention of nephrons in radial pattern
  - Normal pelvicaliceal system and renal vessels
  - In neonates, kidneys at least 10% of body weight
  - Older children: Macrocyst development can give the appearance of ADPKD.
  - Microscopic pathology: Fusiform cysts (<2 mm + diameter) lined by low columnar or cuboid epithelium
  - Decreased number of glomeruli secondary to collecting duct ectasia and interstitial edema

  - No obstruction shown by microdissection studies or electron microscopy
  - No normal parenchyma
- Hepatobiliary:
  - All children with ARPKD have lesions in the periportal areas of the liver
  - Can have hepatosplenomegaly at presentation; frequently normal
  - Elongated, hyperplastic biliary ducts with ectasia
  - Periportal fibrosis with normal hepatocellular histology

DIFFERENTIAL DIAGNOSIS

- ADPKD
- Bardet-Biedl syndrome
- Caroli disease
- Chondrodysplasia syndrome
- Congenital hypernephronic nephromegaly with tubular dysgenesis
- Glutaric aciduria type II
- Ivemark syndrome
- Jeune syndrome
- Juvenile nephronophthisis
- Meckel-Gruber syndrome
- Renal dysplasia
- Trisomy 9 and 13
- Zellweger syndrome

TREATMENT

- 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
- Social support and respite care

MEDICATION

- Thiazides to help urine-concentrating defect
- Treatment of renal osteodystrophy with vitamin D phosphate binders
- Recombinant human erythropoietin
- Growth hormone treatment

SURGERY/OTHER PROCEDURES

- Preemptive bilateral nephrectomy and peritoneal dialysis catheter (significant pulmonary distress)
- Unilateral nephrectomy (improve feedings, help with breathing)

- Gastrostomy tube placement (improve feedings)
- Splenorenal shunt or portocaval shunt procedures (portal HTN)
- Renal transplantation (ESRD)
- Liver transplantation (hepatic failure)

ADDITIONAL TREATMENT

- Adequate hydration
- Correct acid-base and electrolyte abnormalities
- Aggressive HTN control
- Peritoneal dialysis
- Enteral feedings
- Advanced pulmonary support as required

ONGOING CARE

PROGNOSIS

- Prenatal: Abnormal prenatal US (oligohydramnios, enlarged reniform kidneys, absent urine in bladder, seen after 30 wks' gestation)
- Neonates:
  - Palpable flank masses that cannot be transilluminated, difficult vaginal delivery, respiratory distress (most common cause of death in neonates), poor urine output, edema, feeding intolerance
  - Potter phenotype (oligohydramnios): Deep-set eyes, beaked nose, micrognathia, low-set ears, extremity contractures.
  - If present at birth, the usual clinical course is death.
- Infants: Palpable flank masses, abdominal mass, respiratory distress, HTN, polydipsia, polyuria, edema, feeding intolerance, Potter phenotype, nonspecific GI complaints, failure to thrive, growth retardation, infection
- Older children: Palpable flank mass, abdominal mass, Potter phenotype, GI bleed, hematuria, pyuria, 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 milder ARPKD. Also, the younger the patient presents with a disorder, the milder they will develop the other condition.

COMPLICATIONS

- Renal: Renal failure (concentrating defect with polydipsia and polyuria), HTN, anemia, occasional metabolic acidosis, hyponatremia, osteodystrophy, growth failure

- Hepatobiliary: Hepatosplenomegaly, bleeding esophageal varices, portal thrombosis, hypersplenism, choledochal cysts, bacterial cholangitis
- Pulmonary: Respiratory failure, pulmonary hypoplasia, pneumothorax, atelectasis, poor diaphragmatic excursion
- GI: Feeding intolerance, failure to thrive

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Close monitoring of renal and liver function; prevent associated complications of renal and hepatobiliary disease.
- Genetic counseling:
  - Thorough understanding of the pathogenesis and progression of disease
  - Emphasis on team approach; pediatric sub-specialists and support staff

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Aquired Renal Cystic Disease
- Meckel-Gruber Syndrome (Meckel Syndrome)
- Nephronophthisis (Juvenile, Infantile, and Adolescent)
- Polycystic Kidney Disease, Autosomal Dominant
- Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)
- Renal Dysplasia, Hypodysplasia and Hypoplasia
- Renal Mass

CODES

ICD9

753.14 Polycystic kidney, autosomal recessive

ABBREVIATIONS

- ADPKD: Autosomal dominant polycystic kidney disease

- ARPKD: Autosomal recessive polycystic kidney disease
- CBC: Complete blood count
- CT: Computed tomography
- ESRD: End-stage renal disease
- GI: Gastrointestinal
- HTN: Hypertension
- US: Ultrasound

POLYHYDRAMNIOS/OLIGOHYDRAMNIOS

Peter D. Metcalfe, MD

BASICS

DESCRIPTION

- Oligohydramnios is defined as an abnormally low amniotic fluid volume:
  - Associated with increased fetal morbidity and mortality
- Polyhydramnios is defined as an abnormally high amniotic fluid volume:
  - Up to 20% of neonates will have a congenital anomaly.
  - Associated with increase in aneuploidy, congenital malformations, preterm delivery, and perinatal death
- These conditions are diagnosed using prenatal US with strict criterion described below.

EPIDEMIOLOGY

- Oligohydramnios in 0.5–5.5% of pregnancies.
- Polyhydramnios in ~0.4% of pregnancies
- Usually discovered in 2nd trimester with 40% normal by term

RISK FACTORS

Oligohydramnios:

- Rupture of membranes

Genetics

See “Pathophysiology.”

PATHOPHYSIOLOGY

- Amniotic fluid is primarily fetal urine in the latter half of the pregnancy.
- Absence of fetal urine production or urinary tract blockage may cause oligohydramnios.
- Fetal swallowing normally reduces the amount of fluid.
- With absent swallowing or a fetal GI blockage, polyhydramnios can result
- Total amniotic fluid is ~800–100 mL at 36 wks’ gestation
- Amniotic fluid allows for fetal movement and musculoskeletal development and prevents somatic compression.
- Polyhydramnios can be rapid (acute) or chronic:
  - 67% idiopathic
  - 15% maternal cause: Glucose intolerance, teratogenic infections (syphilis, rubella, CMV, toxoplasmosis, parvovirus), isoimmunization, hemorrhage
  - 13% fetal causes; persistence associated with CNS, GI, and karyotype malformations

- Oligohydramnios:
  - Decreased amniotic fluid (<300 mL) after 16 wk associated with poor renal function
  - Etiology can be secondary to obstructive and nonobstructive etiologies.
  - Nonobstructive can be prerenal or renal:

    Prerenal: Placental insufficiency, fetal demise, maternal hypotension, autoimmune disorders, drugs (NSAIDs, ACE inhibitors)
  - Severe obstructive uropathy associated with hydronephrosis:

    Both, or solitary, renal units must be affected.

    Posterior valves and prune-belly syndrome associated with dilated bladder
  - Decreased amniotic fluid associated with pulmonary hypoplasia:

    45% mortality with posterior valves secondary to pulmonary insufficiency.

COMMONLY ASSOCIATED CONDITIONS

- Oligohydramnios:
  - Rupture of membranes
  - Placental insufficiency
  - Chronic maternal HTN
  - Post-date gestation
  - Multicystic dysplastic kidney, or prune-belly syndrome.
  - Severe cardiac disease
  - Pulmonary hypoplasia, limb abnormalities
  - Potter syndrome:

    Characteristic appearance usually due to bilateral renal agenesis, obstructive uropathy, renal hypoplasia, autosomal recessive polycystic kidney disease

    Less severe form referred to as Potter sequence
- Polyhydramnios:
  - Anencephaly
  - Neural tube defects
  - GI obstruction (esophageal atresia, duodenal atresia)
  - Multiple gestation
  - Nonimmune hydrops fetalis
  - Maternal diabetes

DIAGNOSIS

HISTORY

- Polyhydramnios:
  - Increased maternal weight

- Maternal drug use
- Maternal infectious exposure

- Oligohydramnios:
  - Poor weight gain

PHYSICAL EXAM

- Polyhydramnios: Increased maternal fundal height
- Oligohydramnios: Decreased maternal fundal height:
  - Enlarged newborn urinary bladder due to obstruction
  - Potters facies:
    Characteristic of bilateral renal agenesis and other severe renal malformations
    Ocular hypertelorism, low-set ears, receding chin, flattening of the nose

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Polyhydramnios:
  - Maternal testing for glucose, auto-antibodies, TORCH screen, parvovirus, fetal karyotype.
- Oligohydramnios:
  - General: Fetal karyotype, pulmonary maturity, maternal antibodies (lupus, anticardiolipin, antinuclear)
  - Renal: Urinary electrolytes
  - Better outcome associated with Na <100 mmol/L, Cl <90 mmol/L, and osm <210 mmol/L.
  - Serial measurements may have better prognostic value.
  - May also measure -2 microglobulin, -microglobulin, and retinal binding protein

Imaging

- US measurements of amniotic fluid volumes are very operator-dependent and very variable.
- No perfect means to determine actual volume, but several surrogate markers are used:
  - Maximum vertical pocket: Polyhydramnios >8 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

- Oligohydramnios:
  - Fetal causes:

Abnormal placenta
Obstructive uropathy (posterior urethral valves)
Prolonged pregnancy
Renal agenesis

– Maternal conditions:
Antiphospholipid syndrome
Dehydration-hypovolemia
Hypertensive diseases
Idiopathic
Spontaneous or premature rupture of the membranes
Uteroplacental insufficiency

- Polyhydramnios:
  – Fetal causes:
  Anencephaly
  Beckwith-Wiedemann syndrome
  Chromosomal abnormalities (eg, trisomy 21)
  Diaphragmatic hernia
  Duodenal atresia/stenosis
  Esophageal atresia
  Gastroschisis
  Hydrops fetalis
  Muscular dystrophy syndromes
  Sacrococcygeal teratoma
  Severe fetal anemia
  Skeletal dysplasias
  Thoracic/mediastinal masses
  Twin-to-twin transfusion
  – Maternal causes:
  Idiopathic
  Poorly controlled diabetes
  Substance abuse
  Placental chorioangioma or arteriovenous fistula

TREATMENT

- Polyhydramnios:
  – US every 3–4 wk

- Follow pregnancy to 38 wk.
- Monitor for uterine hemorrhage.

- Oligohydramnios:
  - US every 3–4 wk for fetal viability and BPP
  - Consider early delivery with steroids for pulmonary development.
  - Newborn needs intensive care and urologic assessment.

MEDICATION

- Maternal indomethacin has been used in cases of polyhydramnios.
- Surfactant for the neonate with severe oligohydramnios and pulmonary hypoplasia

SURGERY/OTHER PROCEDURES

Posterior urethral valves: Postnatal ablation or vesicostomy

ADDITIONAL TREATMENT

- Instillation of isotonic sodium chloride solution in the 2nd trimester may benefit some patients.
- In utero vesicoamniotic shunts for bladder outlet obstructions

ONGOING CARE

PROGNOSIS

- Polyhydramnios:
  - If not associated with any other findings, the prognosis is usually good.
- Oligohydramnios:
  - With renal agenesis, mortality rate is 100%
  - Mild forms of obstructive uropathy may cause renal insufficiency.

COMPLICATIONS

- Polyhydramnios can cause increased preterm labor.
- Oligohydramnios can cause fetal distress before or during labor and severe respiratory distress and pneumothorax due to pulmonary hypoplasia.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Posterior Urethral Valves
- Potter Syndrome/Potter Facies

CODES

ICD9

- 657.00 Polyhydramnios, unspecified as to episode of care
- 658.00 Oligohydramnios, unspecified as to episode of care

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- AFI: Amniotic fluid index
- BPP: Biophysical profile
- CMV: Cytomegalovirus
- CNS: Central nervous system
- GI: Gastrointestinal
- HTN: Hypertension
- NSAID: Nonsteroidal anti-inflammatory drug
- TORCH: Toxoplasmosis, other infections, rubella, cytomegalovirus, and herpes simplex
- US: Ultrasound

POSTERIOR URETHRAL VALVES

Steve J. Hodges, MD
Anthony Atala, MD

BASICS

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 kidney:

- Functional bladder changes include increased bladder wall thickness, increased collagen deposition, poor emptying.
- Bladder changes may affect upper tract by transmitting high pressure to renal parenchyma.
- Patients may have congenital renal dysplasia.

EPIDEMIOLOGY

- Congenital disorder
- 1 in 4,000–75,000 male births
- No racial predilection
- Most common cause of lower urinary tract obstruction in males:
  - Accounts for 16.8% of children with ESRD
- The prevalence is 1:2,400 to 1:8,000

RISK FACTORS

- No racial predilection
- Affects only males

Genetics

- This disorder is usually sporadic.
- Cases have been seen in twins and siblings, suggesting a poorly understood genetic component.

PATHOPHYSIOLOGY

- Congenital mucosal membrane (fold/valve) 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 walls: Most common type (95%)
  - Type II: Mucosal folds extending from the verumontanum to the bladder neck, superiorly; not clinically obstructed, only historical significance
  - Type III: Transverse membrane in the posterior urethra; has a central aperture; no attachment to the verumontanum and located distal to the verumontanum; uncommon (5%)

COMMONLY ASSOCIATED CONDITIONS

- Renal dysplasia
- Bladder diverticula
- Ascites
- Urine extravasation
- Vesicoureteral reflux
- Azotemia
- Hydroureteronephrosis
- VURD

DIAGNOSIS

HISTORY

- Antenatally:
  - No specific questions in the maternal or family history aid in the diagnosis.
  - Prenatal US usually demonstrates bilateral hydroureteronephrosis and thick-walled bladder in males, ± low amniotic fluid levels
- Postnatally:
  - Nature of the urinary stream is unreliable predictor of valves.
  - Failure to thrive
  - Symptoms indicative of sepsis in a neonate/infant
  - Delayed presentation considered in any male with a chronic history of day and night urinary incontinence; UTI; chronic polydipsia/polyuria

PHYSICAL EXAM

Common neonatal presentation:

- General: Palpably enlarged bladder, possible abdominal distention secondary to ascites
- Pulmonary: Respiratory distress syndrome, pulmonary hypoplasia
- Potter facies, limb deformities (rare; in patients with severe obstruction and oligohydramnios)
- Genitalia: Bulge in the penoscrotal junction during urination is indicative of an anterior urethral valve.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis and urine culture
- Serum electrolytes, BUN, and creatinine:
  - Creatinine has early prognostic value.

– Elevated Cr after 1st few days of life indicates renal dysfunction and unfavorable prognosis

- CBC: Check for signs of sepsis, anemia:
  - Blood culture/spinal tap if signs of sepsis present

Imaging

- Renal and bladder US to assess for degree of hydroureteronephrosis, quality of renal parenchyma (corticomedullary differentiation, echogenicity feature of renal dysplasia, thickness of renal parenchyma, thickness of the bladder wall)
- Contrast (fluoroscopic) VCUG: Only study that can diagnose the urethral valve accurately. Check for vesicoureteral reflux.
- A radionuclide renal scan (DMSA) is usually delayed until the neonate is a few weeks old, so that better imaging can be obtained of the differential function of the kidneys.

Diagnostic Procedures/Surgery

- Antenatal:
  - Antenatal US: Bilateral hydroureteronephrosis, ± oligohydramnios
  - Earlier the diagnosis, the poorer the prognosis
- Postnatal:
  - US, VCUG, laboratory tests

Pathological Findings

Radiographic imaging:

- Dilated posterior urethra, hydroureteronephrosis, trabeculated bladder, vesicoureteral reflux, less commonly urinary ascites
- Azotemia, sepsis, electrolyte disturbances, or acidosis
- Pulmonary hypoplasia, Potter facies, limb abnormalities

DIFFERENTIAL DIAGNOSIS

- Anterior urethral valves
- Bilateral UPJ obstruction
- Congenital urethral polyp
- Congenital urethral stricture (Cobb collar)
- Megacystis-megaureter
- Megalourethra
- Multicystic dysplastic kidneys
- Neuropathic bladder
- Nonneurogenic neurogenic bladder (Hinman syndrome)
- Plicae colliculi (normal anatomic structure, thin fins of mucosa that extend from the bottom of the seminal colliculus (verumontanum)

- Prune-belly syndrome (Eagle-Barrett syndrome or triad syndrome)
- Urethral atresia

TREATMENT

- Insertion of a 5F–8F feeding tube into the bladder and leave indwelling. Passage of the catheter into the bladder is not difficult, as a rule.
- Daily weights
- Accurate input and output fluid-balance record
- Routine vital signs
- Establish an IV line to give fluids and electrolytes, and antibiotics

MEDICATION

- Antibiotic prophylaxis (typically amoxicillin)
- In setting of sepsis, use broad-spectrum antibiotics with close monitoring of drug levels and renal function
- Anticholinergics for bladder dysfunction

SURGERY/OTHER PROCEDURES

- Transurethral incision/destruction of the valve possible in >80% of neonates. Miniaturization of cystoscopes/resectoscopes has made this possible.
- Cutaneous vesicostomy in patients whose urethra is too small to accept the urethral instruments:
  - Transurethral destruction of the valve and closure of the vesicostomy is done, simultaneously, at a later age (2–4 mo).
- Bilateral cutaneous ureterostomies as immediate treatment; rare today, but popular 20 yr ago

ADDITIONAL TREATMENT

- In children with ureterovesical junction obstruction (demonstrated by persistent urine extravasation, renal insufficiency, UTI, and severe hydronephrosis following ablation):
  - May require high urinary diversion
- Persistent vesicoureteral reflux following valve ablation:
  - May require ureteral reimplantation
- Low compliance bladder (valve bladder) may require augmentation cystoplasty, clean intermittent catheterization
- Nephroureterectomy of a nonfunctional upper tract is done at a later stage.

ONGOING CARE

PROGNOSIS

Depends on the amount of congenital renal dysplasia, vesicoureteral reflux, bladder function:

- Incontinence and later ESRD correlated

COMPLICATIONS

A proportion of these children develop ESRD and require transplantation:

- Growth problems, renal insufficiency, ESRD all can develop.
- Voiding dysfunction, incontinence, late toilet training

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Requires long-term follow-up:

- Serial creatinine, routine US, repeat VCUG to evaluate valve ablation, bladder emptying
- UDS for bladder dysfunction
- Monitor renal function with scintigraphy
- Long-term prophylactic antibiotics

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Anterior Urethral Valves
- Bladder Outlet Obstruction (BOO)
- Bladder Wall Thickening, Differential Diagnosis
- Bladder, Trabeculation
- Hydronephrosis/Hydroureteronephrosis, (Dilated Ureter/Pelvic), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal
- Incontinence (Urinary Incontinence), Pediatric
- Polyhydramnios/Oligohydramnios
- Urethra, Obstruction
- VURD Syndrome

CODES

ICD9

753.6 Congenital atresia and stenosis of urethra and bladder neck

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CBC: Complete blood count
- DMSA: Dimercaptosuccinic acid
- ESRD: End-stage renal disease
- IV: Intravenous
- PUV: Posterior urethral valves
- UPJ: Ureteropelvic junction
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VURD: Vesicoureteral reflux and renal dysplasia

POSTOBSTRUCTIVE DIURESIS (POD)

Jason C. Hedges, MD, PhD
Michael J. Conlin, MD

BASICS

DESCRIPTION

- Polyuria resulting from the relief of bilateral ureteral obstruction or obstruction of a solitary kidney
- More likely with chronic rather than acute obstruction
- After relief of obstruction, >3 L over 24 hr or >200 mL/hr over each of 2 consecutive hours is diagnostic of polyuria found with POD.

EPIDEMIOLOGY

- Peak incidence in men 70–90, due to increased obstruction from BPH and prostatic cancer
- Peak incidence in women 40–60, due to obstruction from pregnancy and carcinoma of the cervix and uterus

RISK FACTORS

- Urinary tract obstruction is caused by a number of processes, grouped into extrinsic and intrinsic causes:
  - Intrinsic: Nephrolithiasis, blood clot, ureteral strictures, urethral strictures, neurogenic bladder, anticholinergic agents, levodopa
  - Extrinsic: BPH, prostate cancer, tubo-ovarian abscess, ovarian tumor or cyst, endometriosis, arterial aneurysms, tumors of the kidney, ureter, bladder, and urethra and their corresponding lymphatic and metastatic spread
- Obstructed patients most likely to have POD are those with chronic obstruction, edema, congestive heart failure, HTN, weight gain, azotemia, and uremic encephalopathy.

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.

)[B]

DIAGNOSIS

HISTORY

- Obstruction:
  - Asymptomatic but often associated with flank pain radiating to groin and/or ipsilateral thigh, nausea, vomiting, fevers, chills

)[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
- Acute obstruction:
  - Flank pain associated with forced diuresis (consumption of coffee, tea, or alcohol), nausea, vomiting, hematuria, anuria

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.
- 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:

- Avoid risk of contrast agents
- Without hydronephrosis, diagnosis of POD should be questioned.

Diagnostic Procedures/Surgery

Monitor urine output

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

TREATMENT

- After the obstruction is relieved, admit the patient to the hospital to closely monitor hemodynamic status and electrolytes.
- Monitor urine output q2h and replace with IV fluids (0.5–1.0 mL of 1/2 NS/cm3 of urine output) in addition to PO fluids.
- Check serum sodium and potassium q6–12h and replace as needed.
- Follow BUN and creatinine values to normal:
  - If they remain elevated, obtain a follow-up renal US to rule out hydronephrosis.

)[A]

MEDICATION

None usually necessary beyond IV fluid replacement

ADDITIONAL TREATMENT

Management of any renal insufficiency

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 RECOMMENDATIONS

Patient Monitoring

Serial (weekly to monthly) renal function testing (creatinine, BUN), renal US imaging if lab values do not return to normal range

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See Also (Topic, Algorithm, Electronic Media Element)

Urinary Retention, General

CODES

ICD9

788.42 Polyuria

ABBREVIATIONS

- ANP: Atrial natriuretic peptide
- ATN: Acute tubular necrosis
- BPH: Benign prostatic hyperplasia
- CBC: Complete blood count
- HTN: Hypertension
- POD: Postobstructive diuresis
- US: Ultrasound

PREGNANCY, UROLITHIASIS

David M. Albala, MD
Emily Bratt, BA

BASICS

DESCRIPTION

Formation of stones in the urinary tract during pregnancy. Urolithiasis is the most common cause of nonobstetric abdominal pain that requires hospitalization among pregnant patients.

Pregnancy Considerations

Urolithiasis can result in premature labor and fetal loss. It may also lead to urosepsis, which requires the appropriate antibiotics to avoid complications in both the mother and fetus.

EPIDEMIOLOGY

- Calculi in pregnant women occur at a rate of 1/1500 pregnant patients; this is similar to that of nonpregnant patients (0.03–0.53%)
- Ureteral stones occur twice as often as kidney stones in pregnant patients.
- Usually presents in 2nd or 3rd trimester
- Incidence of symptomatic stones equal, right side vs. left side
- Hispanics and whites are more likely than blacks to develop stones during pregnancy.
- Multiparous women are more commonly affected than are primiparous women:
  - May be due to increasing incidence of stones with aging overall

RISK FACTORS

- Dehydration
- Genetic predisposition (heredity)
- Immobility (relative)
- Voluntary dietary modification (increased calcium)
- Occupation

Genetics

A increased risk of stone formation is possible with a positive family history.

GENERAL PREVENTION

- Consider prophylactic measures to prevent the difficult course of treating urolithiasis in pregnancy.
- Metabolic evaluation is recommended for known stone formers, as well as prophylactic treatment of asymptomatic stones prior to pregnancy.
- Women with known cystinuria should obtain genetic counseling and management of their disease prior to becoming pregnant.

PATHOPHYSIOLOGY

- Pregnancy factors that may enhance the formation of stones:
  - Pregnancy-induced urinary stasis
  - Hypercalcemia
  - Decreased ureteral peristalsis
  - Physiologic hydronephrosis
  - Infection
  - Increased urinary calcium excretion
- Associated with a higher incidence of maternal UTI (10–20%)
- Stone passage can precipitate premature labor and/or interfere with normal labor.
- May cause a higher rate of spontaneous abortions (controversial)
- Physiologic dilation of calyces, ureters, and renal pelves begins in the 1st trimester and persists into the postpartum period.
- Dilation is greater on the right side than on the left because of pressure due to physiologic engorgement of the right ovarian vein and dextrorotation of the uterus
- Decreased ureteral peristaltic activity due to hormonal and mechanical factors
- Dilation and decreased peristalsis allow urinary stasis and infection.
- Increased urinary calcium excretion in pregnancy:
  - Increases 2–3 times
  - Increased levels of 1,25-dihydroxy vitamin D
  - Increase in calcium salt excretion
  - GFR increases 25–50% in pregnancy.
- Urine is more alkaline in pregnancy:
  - Protective against uric acid stones
- Increase in excretion of stone inhibitors: Citrate and magnesium
- Overall, with all factors considered, pregnancy has no adverse affect on stone disease.

COMMONLY ASSOCIATED CONDITIONS

Hydroureteronephrosis is the most significant renal alteration during pregnancy. Physiologic dilatation of the collecting system begins in the 1st trimester at 6–10 wks' gestation and persists until 4–6 wk following delivery

DIAGNOSIS

HISTORY

- Pregnancy history
- History of previous stones
- Medications
- Dietary modifications

- Urgency and frequency with urination

PHYSICAL EXAM

- CVA tenderness (flank pain)
- Abdominal tenderness
- Fever/chills
- Vomiting/nausea

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum creatinine:
  - Adjust for lower values, given the increased GFR (25–50%) in pregnancy
- BUN:
  - 25% lower for pregnant patients
- CBC
- Urinalysis:
  - Accept some degree of microscopic hematuria secondary to the gravid state.
- Urine culture:
  - UTIs are more common in pregnancy associated with stone disease (10–20%).
  - A UTI can induce premature labor.

Imaging

- Standard IVP and CT are discouraged during the 1st and 2nd trimesters
- KUB, 1-shot IVP:
  - Timing of IVP (30, 60, 120 min) not standardized
  - No adverse effect of contrast material on the fetus has been reported.
  - A greater concern is radiation exposure to the fetus:

    A typical urogram gives <1.5 rads of exposure.

    5–15 rads to the maternal pelvis in the 1st trimester increases the risk of congenital anomalies by 1–3%.

    However, fetal exposure to as little as 0.4–1.0 rads can increase the risk of childhood malignancy 2.4 times.
- Renal US (standard initial imaging study in evaluation of pregnant patient):
  - Hydronephrosis
  - Renal stones/proximal ureteral stones
  - Extravasation/perirenal urinoma
  - Resistive index >0.70 in intrarenal arteries supportive of acute obstruction
  - Abscess

  - Poor assessment of pyelonephritis
  - No radiation exposure to fetus
- Transvaginal US:
  - Useful for visualizing distal ureteral stones
  - May visualize ureteral jets, verifying lack of a complete obstruction
  - Document the diameters of distal ureters.
- Noncontrast helical/spiral CT:
  - Increasing utilization in nonpregnant patients
  - Unlikely to be utilized much, due to relatively high radiation exposure
  - CT imaging should be avoided during pregnancy because the radiation dose is high.
- MRI urography:
  - Effect on fetal development unknown
  - Unlikely to prove useful in this setting
- Percutaneous nephrostogram:
  - Presumably can be performed at time of placement of percutaneous nephrostomy tube
  - Radiation exposure with fluoroscopy is time dependent.
  - Unlikely to be used as a diagnostic tool until obstruction is proven by another modality

DIFFERENTIAL DIAGNOSIS

- Hydronephrosis of pregnancy
- Acute pyelonephritis
- Renal vein thrombosis
- Gastroenteritis
- Appendicitis
- Cholecystitis
- Neurologic/musculoskeletal pathology
- Obstetric etiology of pain
- Other intra-abdominal conditions

TREATMENT

- Conservative measures should be undertaken as the initial management of urolithiasis in pregnancy.
- Hydration and analgesia along with bed rest, antiemetics, and antibiotics as needed
- ~64–84% of renal calculi pass spontaneously with conservative management, especially if <4 mm. Stones >7 mm are much less likely to pass without intervention

• Urolithiasis associated with ureteral obstruction and upper tract infection mandates immediate treatment; this is a true urologic emergency that can potentially lead to urosepsis.

MEDICATION

• Morphine, hydromorphone, butorphanol, meperidine, and acetaminophen provide short term pain relief without fetal harm. Avoid long-term use.

• Avoid codeine during pregnancy because of its association with fetal defects.

• NSAIDs are contraindicated (increased risk of miscarriage in 1st trimester. Fetal renal anomalies, fetal pulmonary HTN, and premature closure of the ductus arteriosus are risks when used near term.

• In calcium stone disease, medical management for reduction of calcium stone disease is contraindicated.

SURGERY/OTHER PROCEDURES

• Surgical intervention is required in 20–30% cases

• Cystoscopy/stent placement:
  – With or without US guidance
  – With or without ureteroscopy
  – Stents should be changed every 6–8 wk.

• Percutaneous nephrostomy tube:
  – US can be used for guidance to minimize radiation exposure.
  – The stone/obstruction can then be addressed postpartum.
  – Tube should be changed every 6–8 wk

• Ureteroscopic technology and intracorporeal lithotriptors have made it possible to access and treat any stone in the upper urinary tract successfully, even in the pregnant patient.

• Nephrolithotomy/ureterolithotomy is extremely rare during gestation, given the other temporizing options available.

• ESWL:
  – Not enough data to prove safety during pregnancy

COMPLEMENTARY AND ALTERNATIVE MEDICINE

• Limit high-oxalate foods and purines.

• Increase in fluid intake.

• Limit salt and sodium intake.

• Low-calcium diets may cause a paradoxical rise in calcium stone formation.

ONGOING CARE

PROGNOSIS

Pregnancy outcome is not appreciably worsened because of symptomatic urolithiasis.

COMPLICATIONS

- Premature labor, fetal loss
- Urosepsis, renal insufficiency

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- During gestation:
  - Conservative management with hydration
  - Indications for intervention:
    Worsening renal function associated with persistent obstruction
    Intractable pain
    Obstruction of a solitary kidney
    Persistent infection associated with an obstruction
    Renal colic, precipitating premature labor that is refractory to tocolysis
  - Preventive medications have unacceptable side effects during pregnancy:
    Thiazides: Can cause fetal thrombocytopenia, hypoglycemia, and hyponatremia
    Xanthine oxidase inhibitors: No adverse effects on fetal animals; effects on human fetus unknown
    Penicillamine: Teratogenic in rats; fetal defects have been found in infants of mothers who took this during gestation.
- Postpartum:
  - Metabolic screening should be delayed until post-delivery and lactation:
    Calcium and urate metabolism is not at baseline during these times.

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See Also (Topic, Algorithm, Electronic Media Element)

- Pregnancy, Urologic Considerations
- Urolithiasis, Adult General
- Urolithiasis, Ureteral Calculi Algorithm

CODES

ICD9

- 592.0 Calculus of kidney
- 592.1 Calculus of ureter
- 646.80 Other specified complications of pregnancy, unspecified as to episode of care

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CBC: Complete blood count
- CT: Computed tomography
- CVA: Costovertebral angle
- ESWL: Extracorporeal shock wave lithotripsy
- GFR: Glomerular filtration rate
- HTN: Hypertension
- IVP: Intravenous pyelogram
- KUB: Kidneys, ureters, bladder
- MRI: Magnetic resonance imaging
- NSAID: Nonsteroidal anti-inflammatory drug
- US: Ultrasound
- UTI: Urinary tract infection

PRIAPISM, GENERAL

Irvin H. Hirsch, MD

BASICS

DESCRIPTION

- Persistent erection lasting hours beyond the original stimulus:
  - Results from dysregulation of mechanisms governing penile tumescence and flaccidity
  - Occurs spontaneously; not associated with sexual arousal
  - Not relieved by ejaculation/orgasm
- Ischemic priapism (low-flow): Corpora are painful and rigid (most common type).
- Nonischemic priapism (high-flow): Corpora are usually not painful nor fully rigid.
  - Characterized by a permanent partial erection and frequently a normal erection with sexual activity.
- Recurrent (Stuttering) priapism: Episodes are recurrent but of limited duration.
- Refractory priapism: Persistent after surgical therapy.
- Clitoral priapism: Has been described in case reports and usually presents as severe vulvar pain; associated with the use of antipsychotics:
  - Management is conservative with removal of the inciting agent.

ALERT

A low-flow ischemic priapism is considered an emergency since early intervention improves the chances for proper erectile function after.

EPIDEMIOLOGY

- 1/100,000 in studies including subjects using intracavernous therapy.
- The lifetime probability of priapism is 30% in men with sickle cell anemia.
- Up to 60% of pediatric cases of sickle cell anemia

RISK FACTORS

- Erythropoietin therapy
- Drug-induced (hydralazine, guanethidine, -adrenergics [eg tamsulosin], psychotropics, trazodone, SSRIs), PDE5 inhibitors (eg, tadalafil)
- Fracture of long bone with fat embolism
- Hemodialysis
- Hemoglobinopathies (sickle cell anemia, thalassemia)
- Heparin withdrawal
- Intracavernous injection of vasoactive agents (papaverine, phentolamine, prostaglandin E1)

- Leukemia (chronic granulocytic)
- Metastatic urologic cancers (GU tumors are most common), melanoma
- Penile or perineal trauma
- Polycythemia (neonate)
- Psychiatric history
- Thrombotic predilections (asplenism)
- Total parenteral nutrition

Genetics

Associated with genetic blood dyscrasias (sickle cell anemia, sickle cell trait, thalassemia) and Fabry disease

GENERAL PREVENTION

Oral pseudoephedrine (60 mg) in high-risk patients for prevention of recurrence

PATHOPHYSIOLOGY

- Dysregulation of corporal smooth muscle tone and altered corporal hemodynamics
- Low-flow priapism:
  - Related to medications, sickle cell disease
  - Very rarely caused by spinal cord injury, fat embolus, leukemic infiltration, or metastatic cancer to the corpora (eg, prostate and bladder cancer most frequent)
  - Veno-occlusive mechanism in corpora is disrupted with apparent prolonged relaxation of corpora cavernosa smooth muscles.
  - High intracorporal pressures (80–120 mm Hg) causing further ischemia
  - Associated with ischemia, stasis of blood, corporal hypoxia and acidosis
  - May lead to liquefactive necrosis of corporal smooth muscle and ultimately corporal fibrosis, loss of compliance and elasticity of erectile tissue, and ensuing ED.
- High-flow priapism:
  - Usually traumatic injury-related (blunt straddle injury or penetrating); rarely injury to cavernosal artery by intracavernosal therapy
  - Unregulated arterial flow due to arterial lacunar fistula formation
  - Penis is not fully rigid and usually not painful since there is no ischemia.

COMMONLY ASSOCIATED CONDITIONS

- Alcohol abuse
- Blood dyscrasias
- Cocaine abuse
- Epidural anesthesia and analgesia
- Hemoglobinopathies

- Hypercoagulable state
- Intracavernous or intraurethral ED therapy
- Oral PDE5 inhibitors (sildenafil, etc)
- Prostate or bladder cancer
- Renal failure and dialysis

DIAGNOSIS

HISTORY

- Elicit a history of pain, duration of priapism, precipitating factors and prior episodes.
- Obtain a comprehensive medical, drug, and social history. Include intracorporal injection of PDE5 inhibitors.
- Determine current level of sexual function.
- Establish prior episodes and any successful treatment measures.
- History of intracavernous injection or perineal straddle injury

PHYSICAL EXAM

- Palpation of penis will demonstrate nontender tumescence (nonischemic priapism) or tender rigidity (ischemic priapism).
- The hallmark of a priapism is that the corpora are involved but the glans penis and corpora spongiosum are flaccid and soft.
- Abdominal, perineal, and digital rectal exam to search for traumatic or malignant etiology

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC with differential and platelet count
- Sickle cell prep
- Hemoglobin electrophoresis
- Urine toxicology for prohibited drugs
- Psychoactive drug screen
- PSA to evaluate for prostate cancer as a rare cause

Imaging

- Color Doppler US imaging of the cavernous arteries can distinguish ischemic priapism (minimal arterial flow) from nonischemic priapism (high peak systolic arterial flow velocity).
- Color Doppler imaging may reveal cavernous arterial fistula or perineal arterial extravasation.
- Pudendal arteriography (with therapeutic super-selective embolization) if nonischemic priapism is suspected.

Diagnostic Procedures/Surgery

- Corporal blood gas and intracavernosal pressure reading. Blood gas determinations have been more convenient and practical than pressure readings:
  - Ischemic priapism (pO2 <30 mmHg, pCO2 >60 mm Hg, pH <7.25)
  - Nonischemic priapism (pO2 >90 mm Hg, pCO2 <40 mm Hg, pH >7.4).
- Ischemic corpora as indicated by dark blood upon corporeal aspiration

Pathological Findings

- Liquefactive necrosis of the corporal tissue
- Corporal smooth muscle fibrosis

DIFFERENTIAL DIAGNOSIS

- Distinguish between ischemic vs. nonischemic priapism.
- Pseudo priapism in men with penile prosthesis

TREATMENT

- 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; considered the 1st step:
  - Use local anesthesia (lidocaine without epinephrine) and choose technique (local injection site, dorsal nerve block, etc.). Systemic analgesia may also be used.-Agonist injection may be attempted and is most useful in cases of intracorporal therapy–related priapism or in priapism of short duration (<6 hr):

Cardiac monitoring should be used when any -agonist is employed.

1 mL (1 mg) of phenylephrine (Neo-Synephrine) is mixed with 9 mL of injectable normal saline. A 27–29 gauge needle is used to inject about 0.5 mL directly into the corpora every 15 min until a response. Can be repeated to a max of 1.5 mg phenylephrine has been administered or a total of 1 hr. Corporal compression helps facilitate the process.

- If -agonist injection is not successful, begin corporal aspiration and irrigation. This technique has best results for priapism <24 hr in duration:

Aspirate with a large needle (16–18 gauge) connected to a 50-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 a 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 refilling of corpora.

- Nonischemic priapism is not an emergency and may be treated expectantly:
  - Super-selective arteriography and embolization of fistula for unresolved nonischemic priapism.
  - Can use absorbable gel or autologous clot

MEDICATION

- Injection of epinephrine (1 mg in 1,000 mL saline) has been used in place of phenylephrine; however, phenylephrine is more of a pure -agonist with a lower systemic side-effect profile.
- Maximum dose of phenylephrine is 1,500 g (1.5 mg)

SURGERY/OTHER PROCEDURES

- Considered 2nd line after all of the corporal injection and aspiration attempts fail.
- Corpora-glandular (distal) shunts. These rely on creating a fistula between the corpora cavernosa and the glans. Unilateral procedure is usually sufficient; if not immediately successful a bilateral procedure can be performed:
  - Winter shunt: 16-G core biopsy needle (eg, Tru-Cut) passes from glans into 1 or both of the corporal bodies. The biopsy needle ensures that a core of tissue is removed.
  - Ebbehoj procedure using a pointed scalpel blade
  - El-Ghorab shunt is an open excision of tunical tip and usually next if Winter shunt fails.
- Proximal shunts are used if distal shunts are not successful and are associated with a higher complication rate:
  - Quackles (caverno-spongiosal) shunt
  - Grayhack (caverno-Saphenous vein) shunt
- Penile prosthesis:
  - Immediate placement of penile prosthesis if priapism is of significantly prolonged duration and ED is highly likely is advocated by some.

ADDITIONAL TREATMENT

- In addition to the techniques described above, priapism of sickle cell disease should be managed systemically by hypertransfusion, alkalinization, oxygenation, and hydration.
- Treat underlying blood dyscrasia or malignancy.
- Oral pseudoephedrine or subcutaneous terbutaline for prolonged erection due to intracavernous injection therapy (PGE-1, papaverine, or phentolamine) is reported.
- LHRH agonist (eg, leuprolide) or antiandrogens may be used to manage recurrent episodes of priapism but should not be used if the patient is not fully mature.

ONGOING CARE

PROGNOSIS

- Priapism associated with sickle cell disease may resolve in 35% of patients treated systemically.
- ED is not uncommon despite active intervention. The duration of the priapism is most predictive. In men treated for a priapism that was of <24 hr duration, over 90% will have return of erectile function. Longer duration of priapism will adversely affect return, with about 20% having return of function with a priapism of >7 days duration:
  - High-flow priapism has better prognosis, with 20% rate of ED

COMPLICATIONS

- Corporal fibrosis
- ED
- Penile deformity
- Recurrent episodes of priapism can result in enlarged penis.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Resolution of ischemic priapism may be confirmed by repeat corporal blood gas and color Doppler US
- Follow erectile function.
- Inquire about recurrence or stuttering priapism.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Priapism Algorithm
- Priapism, Ischemic (Low-flow, Veno-occlusive Priapism)
- Priapism, Nonischemic (High-flow, Arterial Priapism)
- Priapism, Stuttering (Intermittent Priapism)
- Sickle Cell Disease, Urologic Considerations

CODES

ICD9

607.3 Priapism

ABBREVIATIONS

- CBC: complete blood count
- ED: Erectile dysfunction
- GU: Genitourinary
- LHRH: Luteinizing hormone releasing hormone
- PDE5: Phosphodiesterase type 5
- PSA: Prostate-specific antigen
- SSRI: Selective serotonin reuptake inhibitor
- US: Ultrasound

PROSTATE CANCER, GENERAL

Christopher L. Amling, MD

Sean J. Clark, MD

BASICS

DESCRIPTION

Prostate cancer usually refers to CaP as other types are rare

EPIDEMIOLOGY

- Most common solid tumor in US males
- American Cancer Society projects 192,280 new cases and 27,360 deaths in 2009
- Advent of PSA blood test led to a sharp increase of CaP incidence from 1989–1992
- In 1994, incidence declined 27% for Whites and 11% for African Americans and has now reached a new plateau
- Highest worldwide incidence is in African Americans, with a relative incidence of 1.6 compared to US Whites
- Lowest worldwide incidence is in Asian men (1.9/100,000/yr in China); however, Asians who immigrate to US and adopt a Western diet increase their risk to approach that of US men.
- Mortality rate decreased sharply since 1991; now lower than before PSA era
- As of January 1, 2005, about 2.1 million men were living with a diagnosis of CaP.

Geriatric Considerations

Peak incidence is 70–74, but many cancers in men >70 are clinically insignificant.

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 and inflammation: Positive association between CaP, prostatitis, and STD
- Oxidant stress: Several genetic determinant of CaP code for proteins that repair oxidant stress
- Western diet (high levels of meat, dairy, and saturated fat); folate supplements
- Molecular factors:
  - Androgens:

    Essential for development and maturation of prostate gland

    Lack of androgen associated with decreased risk of CaP, although no dose-dependent relationship has been established

    Shortened CAG repeat length in the AR gene associated with increased risk

– Estrogen: Mixed effects on CaP
– IGF-1
– Vitamin D may protect against CaP:

Japanese diet high in vitamin D; increased CaP mortality in groups with vitamin D deficiency (northern latitudes, African Americans)

Genetics

• HPC-1 gene on chromosome 1 associated with familial CaP; HPC-1 mutation leads to defective RNase L, accumulation of genetic defects, and eventually cancer

• Identified cancer susceptibility genes: Include P53 tumor suppressor gene, ELAC2/HPC2, SR-A/MSR1, CHEK2, BRCA2, PON1, OGG1, and MIC1. Multifocal and heterogenous nature of CaP makes clinical genetic studies difficult.

• Familial CaP tends to follow a similar clinical course to sporadic CaP.

GENERAL PREVENTION

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• SELECT examined antioxidants in CaP prevention; terminated in 2008 due to lack of benefit; ? increased risk of CaP and diabetes

• REDUCE Trial (Dutasteride vs. placebo) in high risk demonstrated 23% reduced CAP risk

PATHOPHYSIOLOGY

• Normal adult prostate is 20–25 g; gland secretes fluid comprising about 30% of ejaculate

• Majority of prostate cancer (>95%) is adenocarcinoma, the remainder TCC or rare cancer types

• HGPIN thought to be a premalignant lesion:

– Risk of cancer on subsequent biopsy ranges from 16–44%; repeat biopsy within a year not necessary unless other signs of cancer

• ASAP considered premalignant; 42–49% risk of cancer, biopsy should be repeated

COMMONLY ASSOCIATED CONDITIONS

ED and urinary incontinence are associated with all local CaP therapies.

DIAGNOSIS

HISTORY

• Rarely presents with symptoms; most cases are detected by PSA screening and/or DRE.

• Occasionally presents with symptoms of local tumor growth: Urinary obstruction, irritative voiding symptoms, rarely impotence, hematuria, hematospermia

• Metastatic symptoms include bone pain, weight loss, malaise; spinal cord compression can lead to paralysis

PHYSICAL EXAM

DRE may reveal induration, nodularity, or asymmetry in the gland.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• PSA, a serine protease involved in liquefaction of semen, is typically elevated in serum of patients with CaP (See Section I: PSA Elevation, General).

• PSA is the most widely used screening test, although sensitivity and specificity are suboptimal.

)[B]

• Free PSA: The proportion of PSA not bound to serum proteins (lower % free PSA indicates higher risk of CaP)

• Prostatic acid phosphatase

• Alkaline phosphatase: Elevated with bony metastases

Imaging

• TRUS of the prostate used to guide biopsies:

  – Classically a hypoechoic nodule on TRUS, but can be iso- and hyperechoic

• MRI with or without endorectal coil can be used to assess local extent of disease, but clinical use is limited at present.

• Bone scan: Increased radiotracer uptake is suspicious for blastic bone lesions.

• CT abdomen/pelvis: Used to assess for visceral or lymph node metastasis; indicated for high-risk patients (PSA 10, Gleason 7)

• ProstaScint: Nuclear scan which uses a PSMA monoclonal antibody to detect occult metastases. FDA approved, but use not widespread

Diagnostic Procedures/Surgery

• TRUS-guided needle biopsy:

  – Extended biopsy template now standard (10–12 cores)

  – Effort should be made to sample all hypoechoic lesions and palpable nodules

Pathological Findings

• >95% of prostate cancers are adenocarcinoma, with <5% transitional cell (next most common), small cell carcinoma, and sarcoma

• Grade (1–5) is determined by architectural features observed at low magnification.

• The 2 most prominent grades are added together to arrive at the Gleason score (2–10):

– Main criterion of CaP: Loss of basal cell layer
– Small, crowded acini with irregular contours, nuclear and nucleolar enlargement
– Hormonal treatment may artifactually increase grade.

- Staging:
  – TNM staging, see Section VII
  – 75% of newly diagnosed cases are T1c
  – PSA >20, Gleason score >7, or T3 disease should undergo CT imaging and bone scan
  – CaP spreads from the prostate directly to adjacent tissues, usually via the perineural and lymphovascular spaces.
  – Can also directly invade the seminal vesicle
  – Early metastasis to the pelvic lymph nodes
  – Distant metastasis: To bone, less common lung, and in advanced stages, the liver and CNS

DIFFERENTIAL DIAGNOSIS

- BPH
- Prostatitis

TREATMENT

- Optimum treatment of localized disease is controversial and must be individualized; includes active surveillance, radical prostatectomy, XRT, cryotherapy.
- Metastatic disease less controversial and relies primarily on reduction of testosterone
- Active surveillance is an option for many patients due to the slow progression of prostate cancer, especially in men >70 who may be likely to die of other causes.
- Ideal patient: PSA <10, low-stage (T1 or T2), low-grade (Gleason <7), low-volume disease

MEDICATION

First Line

- Hormonal therapy (androgen deprivation):
  – LHRH agonists: Leuprolide, goserelin, triptorelin; suppress LH and FSH release by the pituitary
  – Antiandrogens: Flutamide, bicalutamide, nilutamide, directly block the activity of androgens on the androgen receptor
  – LHRH agonists can be used alone or in combination with oral antiandrogens
  – When LHRH agonist therapy is initiated, a release of testosterone is induced (androgen flare) that may exacerbate symptoms from metastatic lesions. In particular, patients with spinal metastasis may be in jeopardy of cord compression. Flare avoided by initiat-

ing antiandrogen therapy 2 wk prior to 1st LHRH agonist injection

- Chemotherapy:

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Second Line

Ketoconazole: Inhibits adrenal and gonadal androgen synthesis, castration hormone levels in <8 hr, indicated with spinal compression and impending paralysis

SURGERY/OTHER PROCEDURES

- For low-risk (T1 and T2a) cancer, 5-yr biochemical disease-free rates are equivalent for prostatectomy, radiation therapy, and brachytherapy. Thus, therapy should be driven by the preferences of the well-informed patient.
- Radical prostatectomy:
  - Resection of prostate and seminal vesicles and reanastomosis of bladder to urethra
  - Nerve-sparing technique if possible
  - Surgical approaches include open, laparoscopic, or robot-assisted laparoscopic
  - Laparoscopic approaches may offer quicker recovery, lower blood loss, equivalent functional results; long-term data lacking
- Bilateral orchiectomy provides permanent androgen ablation in men with advanced disease.
- Cryotherapy uses multiple probes to ablate prostate tissue by freezing and thawing, using TRUS to monitor the extent of the ice ball.

ADDITIONAL TREATMENT

Radiotherapy

- XRT:
  - IMRT: Provides high doses of radiation to prostate, minimal dose to surrounding tissues
  - Wide-field pelvic XRT with neoadjuvant androgen deprivation may be considered in men at high risk for nodal metastases
  - Proton beam gaining support; hypofractionation (eg, CyberKnife) controversial
- Brachytherapy radiation is delivered locally by permanent radioactive (low dose rate I125 or Pd103) seeds or temporary (high dose rate with Ir192) placed percutaneously through the perineum:
  - Low-dose monotherapy appropriate for low-risk disease and gland <60 g
  - Gleason 7, PSA 10, and T2b use XRT in lieu of or in addition to seeds

)[A]

Additional Therapies

HIFU: Focal ablative therapy in use outside of the US; investigational

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Consider dietary changes: Reduced meat and saturated fat; increased vitamin D (see “Risk Factors”); increased lycopenes (in cooked tomato products, red fruits and vegetables); increased fiber; exercise

ONGOING CARE

PROGNOSIS

- Determining prognosis is multimodal.
- Increased recurrence risk with:
  - High PSA (10), high Gleason score (7), advanced clinical stage (T3)
  - Pathologic features: Positive surgical margins, seminal vesicle invasion, capsular penetration, lymph node involvement

COMPLICATIONS

- Of disease:
  - Bladder outlet obstruction, bone pain, pathologic fractures, spinal cord compression, ureteral obstruction usually due to metastasis
- Of treatment:
  - Local therapy (surgery, radiation): Impotence, incontinence, rectal injury
  - Androgen deprivation: Hot flashes, loss of libido, impotence, fatigue, osteoporosis
  - Chemotherapy: Neutropenia, sepsis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- PSA every 3–6 mo for the 1st yr and every 6–12 mo thereafter:
  - Should be undetectable (<0.2) after prostatectomy
  - Should drop to <0.5 after radiation for best prognosis
- Bone scan if patient has new bone pain, rapid PSA rise, short doubling time

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate Cancer, Hormone Refractory/Androgen Independent/Castration resistant
- Prostate Cancer, Localized (T1, T2)
- Prostate Cancer, Locally Advanced (T3, T4)
- Prostate Cancer, Metastatic (N+, M+)
- PSA Elevation, General

CODES

ICD9

185 Malignant neoplasm of prostate

ABBREVIATIONS

- AR: Androgen receptor
- ASAP: Atypical small acinar proliferation
- BPH: Benign prostatic hypertrophy
- CaP: Adenocarcinoma of the prostate
- CNS: Central nervous system
- CT: Computed tomography
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- HGPIN: High-grade prostatic intraepithelial neoplasia
- HIFU: High intensity focal ultrasound
- IGF-1: Insulin growth factor
- IMRT: Intensity modulated radiation therapy
- LH: Luteinizing hormone
- LHRH: Luteinizing hormone releasing hormone
- MRI: Magnetic resonance imaging

- PCPT: Prostate Cancer Prevention Trial
- PSA: Prostate-specific antigen
- SELECT: Selenium and Vitamin E Cancer Prevention Trial
- STD: Sexually transmitted disease
- TCC: Transitional cell carcinoma
- TRUS: Transrectal ultrasound
- XRT: External beam radiation

PROSTATE CANCER, HORMONE-REFRACTORY/ANDROGEN INDEPENDENT/CASTRATION RESISTANT

Matthew D. Katz, MD

Gerald L. Andriole, MD

BASICS

DESCRIPTION

- HRPC is clinical or biochemical disease progression of CaP while on hormone ablation (castrate testosterone level <50 ng/mL)
- Tx Nx M1 in TNM system
- “D3” in ABCD system (unofficial designation)
- Androgen-independent, but hormone-sensitive CaP, is sometimes differentiated from true HRPC:
  - The 1st group still responds to secondary hormonal manipulations, such as anti-androgen withdrawal,
  - HRPC is resistant to all hormonal measures.
- Synonym(s): Hormone resistant CaP; Androgen-independent CaP; Castration-resistant CaP becoming preferred term

EPIDEMIOLOGY

- 192,280 new cases of prostate cancer in 2009

)[B]

- Presumed that all men who die of CaP have HRPC
- Once HRPC develops, median survival historically has been 12–18 mo, although recently survival has been lengthened
- Lifetime risk of CaP among American men is 17%
- CaP estimated to cause 2–3% of all deaths among American men

RISK FACTORS

Genetics

Clonal expansion of androgen-independent cancer cells is 1 hypothesis, although temporal changes in the androgen receptor and androgen-dependent genes over the long natural history of hormone-deprived CaP is also possible.

PATHOPHYSIOLOGY

- Anemia secondary to hematuria
- Bone fractures caused by metastases and/or treatment-induced osteopenia

- ARF, uremia secondary to malignant bilateral ureteral obstruction
- Cord compression syndrome secondary to collapse of spinal column
- Visual impairment, mental status changes secondary to brain metastases
- Bone pain secondary to metastases
- Rectal obstruction secondary to local malignant growth

COMMONLY ASSOCIATED CONDITIONS

Metastasis related: Bone pain/fractures, hematuria, urinary retention, ARF secondary to bilateral ureteral obstruction, impotence, altered mental status, visual impairment

DIAGNOSIS

HISTORY

- Age, initial PSA, and tumor parameters such as Gleason score and TNM stage
- 1st-line previous treatment and its response (eg, PSA nadir)
- When PSA rises, PSA dynamics (velocity, doubling time)
- Voiding function and history of hematuria
- Recent onset of bone pain, impotence, weight loss, or night sweats
- Change in stool caliber
- Mental status change or visual impairment
- New-onset severe back pain, extremity weakness, or neurologic deficit
- Evaluate for possible depression

PHYSICAL EXAM

- Chest exam to evaluate for gynecomastia
- GU exam
- Neurologic exam to rule out signs of cord impingement

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Testosterone to confirm androgen ablation status (<0.5 ng/mL or 50 ng/dL)
- PSA every 3–4 mo
- Electrolytes, BUN/Cr every 6 mo

Imaging

- Bone scan every 6–12 mo
- Renal US to evaluate for hydronephrosis
- MRI to evaluate for impending cord compression if suspected

Diagnostic Procedures/Surgery

- PVR to evaluate for urinary retention
- Cystoscopy and other tests if indicated

DIFFERENTIAL DIAGNOSIS

- Bone pain may be due to degenerative joint disease, osteoarthritis, or Paget disease.
- Weight loss due to other malignancies, failure to thrive, depression

TREATMENT

- Verify castrate level of testosterone (<50 ng/mL)
- No uniformly effective treatment
- Continuation of androgen suppression recommended
- Treatment choices include: Observation, secondary hormonal therapy, chemotherapy, investigational therapy
- Most patients with death due to CaP.
- Palliative treatment for bone pain

MEDICATION

- Secondary hormonal therapy manipulations include: Withdrawal or addition of antiandrogens, estrogenic compounds, adrenal androgen suppression
- Addition of one of the following to LHRH:
  - Steroidal antiandrogens: CPA OR
  - Nonsteroidal antiandrogens: Flutamide (Eulexin), bicalutamide (Casodex), or nilutamide (Nilandron) to LHRH analogue
- AAWD if patient on CAB: Biochemical response in 15–30% of patients with stopping antiandrogen. Usually not durable:

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  - Duration of response only 3–5 mo

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  - PSA response still not proven to translate to prolonged survival
- Adrenal androgen suppression:
  - ~10% of circulating androgens are secreted by adrenals
  - Ketoconazole 200 or 400 mg t.i.d. and hydrocortisone 20 mg b.i.d.:

    Ketoconazole is an antifungal that interferes with cytochrome 3A4 and inhibits steroid production from adrenals and testes
  - Aminoglutethimide 250 mg t.i.d. and hydrocortisone 20 mg b.i.d.:

    Aminoglutethimide is an adrenal steroid synthesis inhibitor blocking conversion of cholesterol to pregnenolone
  - Corticosteroid monotherapy (hydrocortisone 50 mg/d or dexamethasone 0.75 mg b.i.d.)—suppresses pituitary production of ACTH
  - Arbitratione acetate: New oral 17-hydroxylase inhibitor that appears to selectively inhibit adrenal androgens and decreases serum and possibly intraprostatic testosterone to su-

per castrate levels (investigational)

- DES: Synthetic estrogen that decreases testosterone by decreasing LHRH secretion and inhibiting LH secretion by pituitary
- Progestins: 3 main agents used are CPA, megestrol, and medroxyprogesterone:
  - CPA not approved in US, widely used in Canada
  - Megestrol useful for appetite stimulant
  - Medroxyprogesterone limited use other than relief of bone pain
- Chemotherapy:
  - Docetaxel is now considered standard chemotherapy choice for HRPC
  - 2 important recent large multi-institutional phase III trials, SWOG 99–16 and TAX327:

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SURGERY/OTHER PROCEDURES

Surgical castration is an option if not already done.

ADDITIONAL TREATMENT

Radiotherapy

Directed XRT for palliation of severe pain secondary to bony metastases

Additional Therapies

- For the management of severe bone pain, -emitting radioisotopes such as strontium89 and samarium153, can decrease bone pain in up to 70% of patients. However, use can make subsequent administration of chemotherapy more difficult (myelosuppression).

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- Some evidence of a palliative benefit from mitoxantrone in the setting of progression after docetaxel

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Consider enrolling in a clinical trial; current options may include calcitriol, liarozole, GnRH antagonists, vaccines.

ONGOING CARE

PROGNOSIS

Most patients will die of their disease within 12–18 mo.

COMPLICATIONS

- Anemia
- Hematuria
- Pathologic fractures

- ARF
- Paralysis secondary to cord compression
- Visual impairment, altered mental status, impaired balance secondary to brain metastases
- Urinary retention
- Rectal obstruction
- Priapism secondary to corporeal invasion

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- History/physical exam, PSA, PVR, electrolytes, and urine analysis every 3 mo
- Bone scans and renal US every 3–6 mo or as indicated by history

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See Also (Topic, Algorithm, Electronic Media Element)

- Antiandrogen Withdrawal Syndrome (Flutamide Withdrawal Syndrome)
- Prostate Cancer, General
- Prostate Cancer, metastatic (N+, M+)

CODES

ICD9

185 Malignant neoplasm of prostate

ABBREVIATIONS

- AAWD: Antiandrogen withdrawal
- ACTH: Adrenocorticotropic hormone
- AIPC: Androgen independent prostate cancer
- ARF: Acute renal failure
- BUN: Blood urea nitrogen
- CAB: Combined androgen blockade
- CaP: Adenocarcinoma of the prostate
- CPA: Cyproterone
- Cr: Creatine
- DES: Diethylstilbestrol
- GU: Genitourinary
- HRPC: Hormone refractory prostate cancer
- LHRH agonist: Luteinizing hormone-releasing hormone agonist
- MRI: Magnetic resonance imaging
- PFS: Progression-free survival

- PSA: Prostate-specific antigen
- PVR: Post void residual
- US: Ultrasound
- XRT: External-beam radiation therapy

PROSTATE CANCER, LOCALIZED (T1, T2)

Herbert Lepor, MD

Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Localized prostate cancer (PCa) is biopsy-proven adenocarcinoma of the prostate with no extraprostatic disease on DRE or imaging.
- Using the TNM classification, localized PCa includes T1 and T2 disease without evidence of nodal (N0) or systemic (M0) metastasis.
- T1: Tumor is not palpable:
- T1a: 5% of tissue resected by TURP
- T1b: >5% of tissue resected by TURP
- T1c: Tumor identified by needle biopsy
- T2: Tumor is palpable confined to prostate
- T2a: Tumor involves 50% of 1 lobe
- T2b: Tumor involves >50% of 1 lobe
- T2c: Tumor involves both lobes
- T1/T2 CaP with high Gleason scores and/or markedly elevated PSA levels have a high risk of extraprostatic disease, but are categorized as localized disease since there is no clinical or radiographic evidence of extraprostatic disease.

EPIDEMIOLOGY

- PCa is the most common newly diagnosed cancer in men, with 192,280 new cases and 27,360 deaths in 2009 in the US.
- 1 in 6 men in the US will be diagnosed with CaP during their lifetime.
- Worldwide, it is the 3rd most commonly diagnosed cancer in men.
- In the modern era, ~90% of newly diagnosed PCa cases will be localized.
- CaP incidence is age- and race-dependent.
- 75% of cases occur at 65.
- African American men have a 40% increased risk of disease and 2.4 times the risk of mortality.
- The prevalence of PCa by autopsy study ranges from 20–35% worldwide.
- The prevalence of PCa is age-dependent.
- The cumulative prevalence of PCa in US men aged 50–60 vs. 70–80 in autopsy series was 44% and 83%, respectively.
- Autopsy CaPs are considered latent cancers (too small to detect and of no clinical relevance).

RISK FACTORS

- Age, family history
- Race (African Americans have highest risk)
- Evidence of HGPIN
- Western diet; ? folate supplementation

Genetics

- The genetics of PCa has not been stratified according to localized vs. nonlocalized disease
- Alterations associated with PCa: RNaseL/HPC1 on 1q24–25; HPC2/ELAC2 on 17p11; MSR1 on 8p22; CHEK2 on 22q12; BRCA2 on 13q12
- Polymorphisms of the androgen receptor gene (X chromosome), 5-reductase gene (chromosome 2), and the vitamin D receptor gene (chromosome 12) are also associated with PCa.

GENERAL PREVENTION

- Level 1 evidence: 5-reductase inhibitors (finasteride) reduce the risk of PCa by ~25%.
- Dutasteride (REDUCE trial) risk reduction 23% in high-risk men
- Recent SELECT (vitamin E and selenium) trial did not reduce risk.
- Weak evidence that lycopenes, low-fat diet, soy products, and green tea lower the risk of PCa.

PATHOPHYSIOLOGY

- Genetic predisposition, inflammatory states, and oxidative stress may be involved in the earliest steps of PCa.
- Epigenetic events such as telomere shortening and abnormal methylation further contribute to PCa development.
- Additional genetic events such as LOH of tumor suppressor genes likely are responsible for androgen independence and progression to metastasis.

COMMONLY ASSOCIATED CONDITIONS

While BPH is commonly associated with PCa, there is no evidence that the 2 conditions are causally related.

DIAGNOSIS

HISTORY

- Localized PCa is rarely associated with disease related symptoms.
- The development of LUTS arising from CaP suggests bulky localized disease.
- In most men with LUTS and localized CaP the LUTS are attributed to BPH and not the malignancy.

• Evidence of unintentional weight loss or new-onset of skeletal pain suggests disease is no longer localized, especially in men with high-risk features.

PHYSICAL EXAM

There may be induration or nodularity on DRE but in localized disease, cT1: Not palpable; cT2 nodule cannot extend beyond the prostate.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• PSA is a serine protease produced by prostatic epithelium that has a half-life of 2–3 days; the single test with the highest predictive value for PCa (see also “PSA Elevation, General”).

• The suspicion of CaP is based on an abnormal DRE and/or elevated PSA but can only be confirmed by biopsy.

• A rapid change in PSA level over time (PSA velocity, PSADT) is an indicator of CaP.

• Assaying % free PSA or CPSA or calculating the PSA density by dividing by the volume of the prostate can improve the specificity of PSA testing.

• A PSA of 4 ng/mL traditionally used to recommend biopsy but lower levels (eg, PSA 2.5) age-specific cutoff values have been shown to have increased sensitivity, although exact values remain controversial.

• Although there is no absolute cutoff, higher PSA at diagnosis is more likely to be associated with advanced disease (ie, >10–20 ng/mL).

Imaging

• The objective of imaging is to identify local, regional, or systemic extraprostatic disease; there are recommendations but no consensus regarding the role of imaging for localized CaP.

• General agreement that the risk of nodal or systemic metastasis is low in low/intermediate risk localized CaP and routine imaging is not justified.

• Bone scan and imaging lymph nodes with CT or MRI for high-risk localized disease

• There is no evidence that ProstaScint imaging has any role in localized disease.

• There is no definitive evidence that MRI reliably identifies extraprostatic diseases to influence decisions regarding nerve preservation.

• Early studies suggest lymphotropic nanoparticle-enhanced MRI may identify occult lymph nodes metastases (but not FDA approved).

Pathological Findings

• Increasing tumor size, Gleason score, tumor volume and the presence of PNI increase the likelihood of extraprostatic disease. No parameters alone or in combination exclude the diagnosis of localized CaP.

- Upstaging or upgrading seen in 20–30% following RP.

DIFFERENTIAL DIAGNOSIS

- Abnormal DRE: Granulomatous prostatitis prostatic cyst, calcifications
- Elevated PSA: UTI, enlarged prostate acute or chronic prostatitis, recent prostatic instrumentation or vigorous prostate exam

TREATMENT

- Review risk and benefits of all treatments and provide recommendations based on biology of CaP, patient overall health, life expectancy, and patient preferences.
- Assess guidelines for risk groups:
  - Low risk: PSA 10, Gleason <7, and clinical stage T1c or T2a
  - Intermediate risk: PSA 10–20, Gleason 7, or clinical stage T2b
  - High risk: PSA >20, Gleason 8–12, or clinical stage T2c

MEDICATION

LHRH agonists:

- Offered to some men who are not deemed candidates for definitive treatment, but no data that this increases survival in localized disease

SURGERY/OTHER PROCEDURES

- RP may be performed open (perineal vs. retropubic) or laparoscopically (with or without robotic assistance).
  - Lymphadenotomy excluded by some if nodal risk low (<7%).
  - Bilateral nerve sparing standard with early stage disease.
- Appropriate for man with >10-yr life expectancy, no major comorbidities, and a high likelihood of complete resection
- Level 1 evidence that RP is associated with increased survival in localized disease over watchful waiting
- No definitive evidence suggests that the laparoscopic/robotic approach offers more rapid recovery or superior quality of life outcomes.
- Studies suggest laparoscopic/robotic approach may be associated with higher treatment failure rate (increase in secondary hormonal or RT) but does result in decreased blood loss and often shorter hospital stay.

ADDITIONAL TREATMENT

Radiotherapy

- Delivered via interstitial seeds (brachytherapy), temporary radioactive implantation (HDR) or external beam with or without IMRT, or via combinations.
- EBRT: Total 70–78 Gy over 6 wk for low risk.

• Neoadjuvant/concomitant/adjuvant hormonal therapy (LHRH agonist) can increase CaP-specific survival for intermediate- (4–6 mo) and high-risk 2–3 yr) disease when combined with EBRT, but exact duration of treatment is debated.

• Brachytherapy: Delivered locally by permanent (low-dose rate I125 or Pd103) seeds or temporary (high-dose rate Ir192) implant placed percutaneously through the perineum

• Seeds alone only for low-risk disease (doses for monotherapy I125145 Gy and Pd103126 Gy).

• Seeds combined with EBRT (40–50 Gy) for intermediate-risk, but higher risk of side effects.

• Note: Avoid seeds with previous TURP, very large >60–80 g) or small (<20 g) gland due to increased side effects. Use of LHRH to reduce size for seeds is controversial.

• SBRT using IGRT typically involves 5 fractions of radiation (hypofractionation) using commercial devices (CyberKnife, Tomotherapy):

– ASTRO does not endorse for CaP as it is not proven to be equivalent to standard radiation.

• Proton therapy has limited data at present.

Additional Therapies

• Cryosurgery and HIFU are being offered for localized disease:

– There is inadequate long-term data to determine the impact of these options on survival.

– The appeal is possible reduction of erectile dysfunction, incontinence and, focal ablation in selected cases and the retreatment option.

• See also “Prostate Cancer, Active Surveillance, Section II”:

– Many men with low-risk CaP would suffer no consequences from CaP if untreated. Increasing interest in following elderly men with low-risk localized CaP with PSA and surveillance biopsies to minimize unnecessary intervention.

– Life expectancy nomograms can aid in the decision to treatment or do surveillance:

Challenge is to identify those men who truly have low-risk disease and are not compromised by deferring treatment.

– 40% of men on active surveillance ultimately pursue treatment within 5 yr due to progression or uncertainty with the surveillance.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

• Vitamin supplements, dietary modification, and lifestyle modifications are appealing to some physicians and patients, but evidence is lacking.

- Use of nerve grafting with RP is investigational.
- Penile rehabilitation to encourage return of erections commonly used; limited data (see Section II: Penile Rehabilitation)

ONGOING CARE

PROGNOSIS

- Biochemical recurrence is defined differently for RP and RT; biochemical recurrence rates reported in the literature should not be directly compared between these different treatments.
- Biochemical recurrence following RP is defined as a PSA >0.2 ng/dL and rising and usually indicates residual disease. Adjuvant or salvage RT should be used based on adverse pathology or rising PSA (Level 1)
- Most recent Phoenix definition for recurrence after RT is PSA >2.0 ng/dL above nadir, which indicates poor prognosis.
- Probability of recurrence following RP and RT depends on the pretreatment risk group.

COMPLICATIONS

- RP most common:
  - Intraoperative: Rectal injury, massive bleeding
  - Postoperative: Deep vein thrombosis, pulmonary embolus, lymphocele
  - Long-term complications: Incontinence, anastomotic stricture, ED (Note: May take 18–24 mo for some men to recover erectile function after RP).
- RT most common:
  - Short-term: Bowel symptoms (bleeding, diarrhea, fecal incontinence), LUTS
  - Long-term: Rectal urinary fistulae, erectile dysfunction, urethral strictures, intractable hematuria, persistent bowel symptoms, resistant LUTS, contracted bladder, slightly elevated risk of secondary cancers of the bladder/colon/rectum

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- 1st evidence of treatment failure is a rising PSA level. It is rare to identify imagable metastases without a rising PSA level.
- There is no consensus for follow-up after definitive treatment of localized disease.
- The author recommends PSA level 3, 6, 12, 18, 24, 30, and 36 mo following definitive treatment and annually thereafter.
- PSA is obtained at shortened intervals if increasing levels are observed.
- Imaging studies should be obtained after the PSA reaches a threshold level, or if there is clinical suspicion for metastases.

- There is no consensus as to this threshold level; the author recommends obtaining PSA levels and imaging studies when the PSA exceeds 10.
- Post implant dosimetry for brachytherapy

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate Cancer, General
- Prostate Cancer, Locally Advanced (T3,T4)
- Prostate Cancer, Metastatic (N+,M+)

CODES

ICD9

185 Malignant neoplasm of prostate

ABBREVIATIONS

- ASTRO: American Society for Therapeutic Radiology and Oncology
- BPH: Benign prostatic hyperplasia
- CaP: Adenocarcinoma of the prostate
- CPSA: Complexed PSA
- CT: Computed tomography
- DRE: Digital rectal exam
- EBRT: External beam radiotherapy
- ED: Erectile dysfunction
- HGPIN: High-grade prostatic intraepithelial neoplasia
- HIFU: High-intensity focal ultrasound
- IGRT: Image-guided radiotherapy
- IMRT: Intensity-modulated radiotherapy
- LHRH: Luteinizing hormone-releasing hormone
- LOH: Loss of heterozygosity

- LUTS: Lower urinary tract symptoms
- MRI: Magnetic resonance imaging
- PCa: Prostate cancer
- PNI: Perineural invasion
- PSA: Prostate-specific antigen
- PSADT: PSA doubling time
- RP: Radical prostatectomy
- RT: Radiation therapy
- SBRT: Stereotactic body radiotherapy
- TURP: Transurethral resection of prostate
- UTI: Urinary tract infection

PROSTATE CANCER, LOCALLY ADVANCED (T3–T4)

Michael O. Koch, MD
Helen J. Kuo, MD

BASICS

DESCRIPTION

- Clinical stage T3 CaP (cT3) refers to disease that has penetrated the prostatic capsule to extend into the peri-prostatic fat or extends into the seminal vesicles.
- Pathologic stage T3 CaP refers to disease that extends beyond the prostatic capsule into the periprostatic fat (pT3a) or extends into the seminal vesicles (pT3b)
- Pathologic T4 disease has direct tumor extension into the bladder neck, external sphincter, rectum, levator, or into pelvic sidewall
- Clinical stage is most commonly determined by the suggestion of disease extension outside of the prostate on DRE, but clinical staging may be supplemented by findings from TRUS or endorectal MRI.
- Overstaging of cT3 CaP occurs in 13–27% of cases.

EPIDEMIOLOGY

cT3: Accounts for 18–20% of newly diagnosed CaPs (SEER, 2000–2005)

RISK FACTORS

- Likelihood of pT3 disease increases with increased PSA, Gleason grade, clinical stage, and tumor volume on biopsy.
- African American males have a higher likelihood of more locally advanced disease and do less well with curative therapy.

Genetics

See Section I: “Prostate Cancer, General.”

GENERAL PREVENTION

- Level 1 evidence that 5-reductase inhibitors (finasteride) reduce the risk of CaP by ~25%. Dutasteride (REDUCE trial) reduces risk by 23% in men with increased risk of prostate cancer
- Weak evidence that lycopenes, selenium, vitamin E, low-fat diet, soy products, and green tea lower the risk of CaP.

PATHOPHYSIOLOGY

- Extension beyond the prostatic capsule occurs when a tumor develops the biologic ability to degrade physical barriers to cancer cell movement, such as the prostatic capsule or the fascial investments of the prostate and seminal vesicles.
- Low-grade CaPs (Gleason 6 and below) uncommonly extend through the capsule or into the seminal vesicles until they reach a large tumor size.

- Intermediate-grade CaPs (Gleason 7) and high-grade CaPs (Gleason 8, 9, and 10) extend outside the prostate much more commonly, especially when they reach larger sizes.
- Even when intermediate- and high-grade CaPs are fully resected surgically, they are frequently associated with either local or systemic disease recurrence.

COMMONLY ASSOCIATED CONDITIONS

While BPH is commonly associated with CaP, there is no evidence that the 2 conditions are causally related.

DIAGNOSIS

HISTORY

- Family history of CaP
- Voiding symptoms (obstructive or irritative voiding symptoms or gross hematuria)

PHYSICAL EXAM

- cT3a: Palpable induration may extend into the lateral sulcus on DRE (unilateral or bilateral)
- cT3b: Palpable induration extending above the prostate into the seminal vesicles on DRE

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PSA: High sensitivity for detecting cancer, but little predictive value alone in determining stage. A linear correlation exists between tumor volume and PSA levels, but an inverse relationship between PSA and Gleason score has been suggested.
- The contribution of BPH to the PSA elevation must be considered eg very large prostates can be associated with high PSA levels (>10 ng/ml)
  - PSAD is a volume-based quotient that accounts for PSA per gram of prostate and can nullify any contribution of BPH to elevated PSA levels. In 1 study, a PSAD cutoff value >0.35 was associated with 66% extra-prostatic extension.

Imaging

- TRUS and TRUS-guided biopsy have consistently proven effective at diagnosing disease but are unreliable at cancer staging.
- The TRUS-guided biopsy together with preoperative PSA and biopsy Gleason score can establish probabilities of extraprostatic disease, but stage T3 disease is only confirmed by pathologic sampling.
- Most patients with extraprostatic extension are still cured by surgical resection of the prostate. In those cases where the choice of treatment approach demands the most accurate diagnostic modality, endorectal MRI offers the highest accuracy rate. It is not available in all centers, and its accuracy is subject to the experience of the radiologist interpreting the study.

• Other diagnostic imaging modalities currently available are not reliable in detecting extracapsular involvement.

• AUA guidelines: Bone scans should only be done with PSA >10 ng/mL, whereas a CT scan or MRI should only be ordered with PSA levels >20 ng/mL.

• ProstaScint or CT/PET imaging with FDG cannot distinguish T3 from T2 disease but may exclude metastatic disease in patients with clinical stage T3 disease.

Pathological Findings

Disease extension into the periprostatic tissues or seminal vesicles seen on final pathologic analysis after prostatectomy or occasionally seen on needle biopsy

DIFFERENTIAL DIAGNOSIS

• No single diagnostic modality can diagnose, confirm, or rule out cancer extension outside the prostate except biopsy evidence.

• DREs have been the traditional method of staging CaP, although the poor sensitivity characteristically understages the extent of disease:

– Of clinically staged T1/T2 tumors, only 50–60% are organ-confined.

– Of clinically staged T3 tumors, 40–50% are actually organ-confined on final pathologic analysis.

– If judged to be T2/T3, it is more likely to be T3.

– Partin et al. devised nomograms that combine PSA, Gleason grading, and DRE to predict the pathologic stage in men with localized CaP (see Section VII, “Partin Tables”)

TREATMENT

• Management of CaP is controversial; depends on many factors (age, life expectancy, comorbidities, extent of disease, quality-of-life issues, preferences of patient and family)

• Variety of treatment options: Watchful waiting, surgery, external radiation, and hormonal therapy. However, cT3 disease has a high likelihood of progression to symptomatic disease if not treated.

• Bulky T3/T4 disease is not as prevalent as it was a decade ago. Historically, TURP or hormonal therapy was used to relieve obstructive symptoms, with RT or hormones for palliation.

MEDICATION

• Androgen ablation is appropriate in patients where curative therapy not an option.

• Androgen ablation is effective in conjunction with radiation-based modalities (see below).

SURGERY/OTHER PROCEDURES

• Radical prostatectomy for cT3 disease is controversial. Some centers have advocated prostatectomy for cT3 disease based upon their findings that many of these patients actually

have pT2 disease.

- Extended lymph node dissection should be performed in these patients (obturator, external iliac, internal iliac, and presacral nodes)
- Neoadjuvant hormonal therapy has not been shown to consistently improve surgical outcomes for cT3 disease.

RADIOTHERAPY

- EBRT at >65 GY with 1–3 yr of neoadjuvant and concomitant androgen ablation therapy:
  - Level 1 evidence suggests this is a mainstay for cT3 disease. Overall survivals of 50–70% with this approach at 10 yr
  - Largest randomized clinical trials use 2–3 yr of total androgen blockade, but other smaller trials suggest shorter courses of hormonal therapy may be sufficient
- Recent advances with techniques and equipment 3D conformal, IMRT, and IGRT are designed to deliver a higher dosage and limit the side effects associated with radiation.
- No sufficient body of evidence for the use of proton therapy in the postop setting.

ADDITIONAL TREATMENT

- Extracapsular invasion (pT3) has an increased risk of local recurrence (up to 30%).
- Adjuvant RT has been shown to minimize the risk of biochemical recurrence and appears to improve cancer-specific survival in patients with pT3 disease:
  - EORTC trial 2911 compared immediate postoperative radiotherapy (60 Gy) to radiotherapy delayed until local recurrence (70 Gy).
  - Found improved 5-yr clinical or biochemical survival: 72.2% vs. 51.8%, but no effect on overall survival yet.
- Best to wait for recovery of urinary function before starting radiation.
- Radiation is best delivered postop or before PSA reaches 1.0 ng/mL for best long-term disease control.

ONGOING CARE

PROGNOSIS

10-yr biologic disease-free survival is ~50%.

COMPLICATIONS

Complications with therapy are similar to other treatments for localized CaP.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients should be monitored with periodic DRE and PSA.
- When PSA >10 ng/mL after therapy, consideration should be given to obtaining periodic bone and abdominal imaging.

ADDITIONAL READING

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CODES

ICD9

185 Malignant neoplasm of prostate

ABBREVIATIONS

- AUA: American Urology Association
- BPH: Benign prostatic hypertrophy
- CaP: Adenocarcinoma of the prostate
- CT: Computed tomography
- DRE: Digital rectal exam
- EBRT: External beam radiation therapy
- FDG: Fluorodeoxyglucose
- IGRT: Image-guided radiation therapy
- IMRT: Intensity-modulated radiation therapy
- MRI: Magnetic resonance imaging
- PET: Positron emission tomography

- PSA: Prostate-specific antigen
- PSAD: PSA density
- RT: Radiation therapy
- TRUS: Transrectal ultrasound

PROSTATE CANCER, METASTATIC (N+, M+)

Daniel P. Petrylak, MD

Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Metastatic 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, bone, and less often lung, liver, brain, and skin.
- Can be the initial presentation or develop after previous local therapy for CaP, such as radiation therapy or RP

EPIDEMIOLOGY

Nearly 28,800 men die annually (US) from metastatic disease. With PSA screening, the number of men with metastatic disease at 1st presentation has declined over the last 20 yr.

RISK FACTORS

African American ancestry, high fat consumption in diet, family history

Genetics

No specific genetic signature can be ascribed to metastatic CaP.

GENERAL PREVENTION

Early androgen blockade for high-risk patients with localized cancer can delay the development of metastatic disease. The impact of early androgen blockade is best seen in patients post prostatectomy who already have established metastases.

PATHOPHYSIOLOGY

- CaP arises in the glandular epithelium of the prostate and can spread through the lymphatics as well as hematogenously.
- Batson plexus are paravertebral veins that extend up from the pelvis to the dural sinuses. This plexus is likely responsible for the high rate of spread of CaP to the vertebral column.
- Testosterone and its most active metabolite, dihydroxytestosterone, are the primary regulators of normal and cancerous prostate growth. These steroid molecules stimulate CaP cells by the binding to the androgen receptor in the nucleus.
- 2 sources of androgens in men; testes (95% of total androgens); adrenal glands (remaining 5%).

COMMONLY ASSOCIATED CONDITIONS

Osteoporosis secondary to hormonal therapy

DIAGNOSIS

HISTORY

- Prior history of CaP or other malignancy
- 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 vertebrae, pelvis, or ribs.

PHYSICAL EXAM

- DRE may reveal a nodular or enlarged prostate, but the exam may be unremarkable.
- After RP the fossa may be empty or contain palpable recurrent cancer.
- Adenopathy may be detected in the supraclavicular and inguinal lymph nodes.
- Point tenderness elicited on vertebral bodies may be indicative of spinal or epidural metastasis.
- CaP metastatic to the spine may result in neurologic symptoms, either from vertebral instability or epidural extension of tumor. Note any leg weakness or urinary and fecal incontinence.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum PSA should be obtained on all patients prior to the start of therapy and is a useful although controversial marker of response to therapy.
- Creatinine, liver functions, CBC are useful parameters to monitor
- Prostatic acid phosphatase, elevated in up to 67% with metastatic disease

Imaging

- 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.

Diagnostic Procedures/Surgery

Biopsy of prostate or metastatic lesions is required to establish a diagnosis. Identification of visceral metastasis with neuroendocrine features may alter initial management to include initial chemotherapy.

Pathological Findings

The most commonly identified histology is adenocarcinoma. Neuroendocrine carcinoma of the prostate is associated with high Gleason score (9–10), low or undetectable PSA levels, visceral sites of metastasis, and lytic bone metastasis.

DIFFERENTIAL DIAGNOSIS

• Bony metastasis can be confused with Paget disease. Kidney, lung, and other tumors may metastasize to bone.

• Adenopathy can be due to lymphoma or other metastatic cancer.

TREATMENT

• Treatment initially consists of the androgen blockade for metastatic disease, which is usually considered noncurative.

• Chemotherapy is reserved for patients who have failed androgen blockade or present with neuroendocrine disease.

MEDICATION

First Line

• Hormonal therapy:

– 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 LHRH.

– LHRH agonists (leuprolide, goserelin, triptorelin) interfere with this pulsatile secretion, and after initial flare (testosterone increase) at 7–10 days, achieve medical castration at about 30 days. Must be continued to maintain suppression.

– LHRH antagonists (degarelix) rapidly decrease testosterone levels with 44% testosterone castration (<50 ng/dL) at Day 1, 96% by Day 3. Lack of flare like the LHRH agonists makes this agent particularly useful in situations such as spinal cord compression.

– Surgical castration by bilateral orchiectomy is infrequently performed today.

– Antiandrogens (flutamide, bicalutamide, nilutamide) block the LHRH flare reaction initially caused by LHRH agonists and should be used for 7–10 days. Long-term use of antiandrogens past the flare period (CAB) is controversial.

Studies suggested a small (4%) improvement in survival in favor of CAB blockade; other studies have detected no difference.

• ADT using high-dose bicalutamide (150 mg/d), called antiandrogen monotherapy, is associated with less side effects but may also be a less effective form of ADT and should not be routinely used.

• ADT can be administered continuously as well as intermittently (IHT); studies suggest similar survivals when continuous CAB is compared to intermittent CAB, with improved quality of life in favor of intermittent therapy, but there is no universal protocol for this.

• Median time to progression in metastatic patients on combined blockade is 18–24 mo.

Second Line

Secondary hormone therapy:

- Castration-resistant CaP: Progression on primary hormonal with a testosterone level of <50 ng/mL, a rising PSA, or worsening of bone or CT scan of the abdomen and pelvis. (See also “Prostate Cancer, Hormone Refractory”).
- No secondary manipulation has been shown to extend survival in any trial to date.
- If on antiandrogen, the antiandrogen should be discontinued; this will result in a PSA decline in 5–20% of patients.
- Addition of an antiandrogen will result in PSA declines of 50% in 15–54% of patients, with median duration of response 4–6 mo.
- Ketoconazole inhibits cytochrome P-450 and blocks testicular and adrenal androgenesis:
  - At doses of 200–400 mg PO t.i.d., with or without hydrocortisone 10–20 mg PO b.i.d., ketoconazole results in PSA decline of >50% in 50–70%. Duration of response is similar to other secondary hormonal manipulations. Also useful for rapid reduction in testosterone with epidural metastasis.
- Estrogens may also be considered
- The number of secondary hormonal manipulations is controversial, with some patients responding to multiple agents.
- ADT therapy should be maintained while patients are on chemotherapy or on 2nd-line hormonal therapy.

COMPLEMENTARY

- Generally reserved for symptomatic patients; however, can be considered in asymptomatic rapidly progressive patients; LHRH agonists are continued during therapy to prevent escape from androgen blockade.
- FDA-approved agents: Docetaxel, mitoxantrone, and estramustine
- Mitoxantrone 12 mg/m2 with prednisone 5 mg PO b.i.d. every 3 wk palliates bone pain in 30%. Improved survival not seen when mitoxantrone with prednisone compared to prednisone alone.
- 2 trials (TAX 327/SWOG 99–16) compared docetaxel 60–70 mg/m2 every 3 wks with estramustine 280 mg PO t.i.d. for 5 days or docetaxel 75 mg/m2 every 3 wk with prednisone had a 20–24% improvement in survival compared to mitoxantrone 12–14 mg/m2 and prednisone.
- Palliation of bone pain was superior in those treated with docetaxel compared to those treated with mitoxantrone (TAX 327 study).
- Clinical trials under way to evaluate docetaxel combined with agents targeting angiogenesis (thalidomide, bevacizumab, aflibercept) and bone-targeted agents (atrasentan).

• No standard therapy for patients who fail docetaxel; mitoxantrone in this setting has PSA decline rates in 50% of 10–20%

• Clinical trials are evaluating novel immunotherapeutic, cytotoxic, and antiangiogenic agents in this setting and should be encouraged.

• In patients with neuroendocrine features, androgen blockade should be initiated along with immediate chemotherapy using agents such as cisplatin/etoposide or carboplatin/etoposide or a docetaxel-based regimen.

SURGERY/OTHER PROCEDURES

• Resection of solitary metastases is not generally performed with curative intent.

• Decompression of epidural metastatic CaP can result in stabilization of the spinal cord and neurologic symptoms. Best results obtained if the procedure is performed within 24 hr 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.

ADDITIONAL TREATMENT

Radiotherapy

• Radiation can be used to palliate painful bony metastases rather than for curative intent. (Typical treatment 300 cGy in 10 divided doses).

• Strontium89 and samarium153 can palliate bone pain and are most useful for diffuse metastasis.

Additional Therapies

• At present, no defined role for so-called triple therapy LHRH/antiandrogen/5-reductase inhibitor.

• Bisphosphonates inhibit osteoclast bone resorption:

– Patients should receive calcium (1200 mg/d) and vitamin D (800–1000 IU/d) supplements.

– With ADT, consider zoledronic acid 4 mg IV yearly or alendronate 70 mg PO week.

– Castration-resistant CaP: Zoledronic acid 4 mg (most widely studied agent) adjusted to renal function every 3–4 wk IV to prevent skeletal related events.

– Skeletal-related events: Defined by pathologic fracture, spinal compression/vertebral body collapse, radiation or surgery to bone, or change in antineoplastic therapy. Androgen blockade can cause osteopenia/osteoporosis; bisphosphonate therapy can limit reductions in bone mineral density.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

• Several herbal remedies have been evaluated in metastatic CaP; however none has been shown to improve survival.

• Soy products and acupuncture may reduce the rate of hot flashes from androgen blockade.

• Weight-bearing exercise and stopping smoking benefits osteoporosis.

ONGOING CARE

PROGNOSIS

• For patients with lymph node–positive disease post RP, adjuvant hormone ablation following RP increases overall survival by 2.6 yr vs. RP alone (13.9 yr vs 11.3 yr) and reduces the risk of dying by ~46%.

• With metastatic CaP starting androgen blockade, the median time to progression is 18–24 mo. The median survival once patients progress on androgen blockade is 12–19 mo.

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.

• Chemotherapy: Monitor for fevers. Neutropenia typically 7–14 days after dose. Colony-stimulating factors such as G- or GM-CSF can improve white cell counts:

– Docetaxel: Peripheral neuropathy, fluid retention, fatigue, alopecia

– Mitoxantrone: Decreased cardiac function

– Zoledronic acid: Renal insufficiency, adjust based on creatinine. Osteonecrosis of the jaw can result from bisphosphonates; avoid major dental work (extractions) while on treatment

• Antiandrogens: Increased liver function test

• Strontium or samarium: Associated with neutropenia, and thrombocytopenia

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Monitoring patients is controversial. With start of androgen blockade: Check PSA every 3 mo. Confirm castrate testosterone.

• At PSA progression, antiandrogen should be withdrawn, and if the patient continues to progress, a CT scan of the abdomen and pelvis should be obtained.

• Timing of PSA testing during chemotherapy is controversial; usually every 3 wk.

• Most clinical trials obtain repeat imaging while on chemotherapy every 3 mo, or at the time of PSA progression.

• Serum creatinine should be monitored for patients on bisphosphonates. Zoledronic acid should not be given with a creatinine level of >2.0 mg/dL.

• Monitoring for osteoporosis, obesity, insulin resistance, lipid alteration, and the concern of increased risk of diabetes and cardiovascular diseases in men on ADT should be con-

sidered.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Antiandrogen Withdrawal Syndrome (Flutamide Withdrawal Syndrome)
- Prostate Cancer, General
- Prostate Cancer, Hormone Refractory/Androgen Independent/Castration Resistant
- TNM Staging

CODES

ICD9

- 185 Malignant neoplasm of prostate
- 196.9 Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified
- 198.5 Secondary malignant neoplasm of bone and bone marrow

ABBREVIATIONS

- ADT: Androgen deprivation therapy
- BPH: Benign prostatic hypertrophy
- CAB: Combined androgen blockade
- CaP: Adenocarcinoma of the prostate
- CT: Computed tomography
- DRE: Digital rectal exam
- IHT: Intermittent hormonal therapy
- LHRH: Leuteinizing hormone releasing hormone
- PSA: Prostate-specific antigen
- RP: Radical prostatectomy

PROSTATE CANCER, UROTHELIAL

Herbert Lepor, MD
Tracy P. Marien, MD
William C. Huang, MD

BASICS

DESCRIPTION

- Urothelial carcinoma of the prostate can occur:
  - Without bladder involvement
  - From nondirect tumor implantation with concurrent bladder TCC
  - From direct extension of bladder TCC
- TNM classification of bladder cancer (1997/2002) defines prostatic invasion as T4a disease in the setting of direct extension.
- Primary urothelial carcinoma of the prostate has a separate TNM classification (1997) system:
  - TIS/pu: CIS involving prostatic urethra
  - TIS/pd: CIS involving the prostatic ducts
  - T1: Invades subepithelial connective tissue
  - T2: Invades prostatic stroma, spongiosum, periurethral tissue
  - T3: Invades cavernous body, prostatic capsule, bladder neck
  - T4: Invades surrounding organs
- However, this TNM staging system has not necessarily been able to predict outcomes.
- Some have advocated different staging for contiguous and noncontiguous prostatic invasion given variable prognosis depending on method of invasion.
- Synonym(s): TCC

EPIDEMIOLOGY

- 12–48% of patients with primary bladder TCC will have prostatic involvement.
- Most reports of TCC prostatic involvement are retrospective and likely underestimate the true incidence of prostatic TCC.
- 7–17% of patients with primary bladder TCC will have stromal invasion of the prostate.
- 1–4% of patients have primary prostatic urothelial carcinoma.
- CIS of the prostatic urethra is almost always associated with CIS of the bladder.
- Prostatic involvement in TCC results in a 4-fold increased risk of urethral recurrence.

RISK FACTORS

Risk factors for prostatic involvement:

- CIS of the bladder

- Multifocal disease
- High-stage bladder cancer
- Previous involvement of the prostate
- Bladder tumors in the trigone or bladder neck
- Intravesical chemotherapy
- Ureteral carcinoma

Genetics

- No known specific genes associated with prostatic TCC
- Genes associated with TCC of the urinary tract include HRAS/FGFR3 (low-grade TCC), p53/RB (high-grade TCC), NAT2, and GSTM1.

GENERAL PREVENTION

Follows similar preventive guidelines as bladder cancer

PATHOPHYSIOLOGY

- Prostatic urothelial carcinoma may involve:
  - Prostatic urethra as CIS
  - Mucosa of the transitional urothelium
  - Prostatic ducts (CIS)
  - Prostatic acini
  - Prostatic stroma
  - Seminal vesicle invasion
- Occurs from either nondirect extension or direct extension with or without bladder involvement
- Most common sites of metastases are bone, lung, and liver.

COMMONLY ASSOCIATED CONDITIONS

Most (96–99%) are associated with bladder TCC.

DIAGNOSIS

HISTORY

- History of risk factors for TCC (ie, tobacco smoking, exposure to aniline dyes, etc.)
- Hematuria and obstructive voiding symptoms
- Bone pain, anorexia, weight loss, or fatigue

PHYSICAL EXAM

- Bloody urethral discharge, periurethral mass, lymphadenopathy
- Fixation and/or nodularity on DRE

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis for microhematuria
- Urine cytology for abnormal cells
- PSA of little value

Imaging

- Abdominal and chest CT/MRI to evaluate for regional extension and lung and liver metastases
- Bone scan to evaluate for metastases:
  - Bone metastases are osteolytic, in contrast to ADC of the prostate

Diagnostic Procedures/Surgery

- Cystoscopy to evaluate for macroscopic prostatic urethral lesions and concurrent intravesical lesions:

)[C]
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- No consensus exists on the best method to evaluate the prostatic urethra prior to cystectomy:

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Pathological Findings

- Significant difficulty in accurately identifying T1 vs. T2 lesions of the prostate
- Immunohistochemical stains for PSA and prostate-specific acid phosphatase are negative.
- 57–70% of TCC cases are positive for high-molecular-weight CK (34E12).
- CK7 and CK20 are positive in TCC in 57–100% and 15–71% respectively; however these are not specific for TCC and maybe positive in ADC of the prostate.

DIFFERENTIAL DIAGNOSIS

Prostatic ADC or non-ADC prostatic tumors (may occur concurrently with TCC of prostate)

TREATMENT

- Increase fluid intake.
- Stop tobacco smoking.
- Differentiate between ductal and stromal invasion.
- Ductal most commonly treated with resection and intravesical BCG, whereas stromal invasion carries a higher risk of spread and is more commonly treated by cystoprostatectomy

MEDICATION

Intravesical BCG for noninvasive TCC of the prostate:

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- To decrease the risk of systemic infection with BCG, BCG should not be administered to anyone with traumatic catheterization, cystitis, or persistent gross hematuria after TURBT.

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- Statins may interfere with the efficacy of BCG.
- Adverse reactions from BCG include frequency, cystitis, fever, and hematuria.
- Dosing: BCG is instilled into the bladder weekly for 6 wk as reconstituted TheraCys® (81 mg) or 2-mL ampule of TICE® BCG (50 mg) plus 50 mL of sterile saline through catheter and retained for 2 hr.

SURGERY/OTHER PROCEDURES

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ADDITIONAL TREATMENT

Radiotherapy

Inadequate data exist regarding treatment of prostatic TCC with radiation therapy.

Additional Therapies

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ONGOING CARE

PROGNOSIS

- 5-yr survival rate with urethral mucosal involvement is 100%, with ductal/acinar involvement is 50%, and with stromal involvement is 40%.
- For stromal invasion, 5-yr survival for node-negative disease is 44–61% vs. node-positive disease, which is 13–34%.
- 5-yr survival rate with contiguous malignant involvement is 7%, and with noncontiguous malignant involvement is 46%.
- Seminal vesicle invasion prognosis is worse than prostatic involvement alone.

- Risk factors for urethral recurrence following radical cystoprostatectomy may include prostatic involvement and form of urinary diversion used (less likely with orthotopic diversions).

COMPLICATIONS

- Hematuria, obstructive voiding, or signs and symptoms of metastatic disease
- Patients with fever >103°F following BCG treatment should be hospitalized and treated with INH, rifampin with or without a fluoroquinolone
- BCG sepsis following treatment with BCG is rare and is treated with INH, rifampin, ethambutol, a fluoroquinolone with or without steroids
- Impotence following cystoprostatectomy
- Complications of conduits, cutaneous continent diversion, and orthotopic neobladders: Electrolyte abnormalities, vitamin B12 deficiencies (with use terminal ileum), hematuria-dysuria syndrome, and ureteral stenosis
- Complications of urethrectomy: Local abscesses, perineural sinuses, rectoperineal fistulas

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- If undergo cutaneous urinary diversion, stoma care training
- Urine cytologies and cystoscopy
- Vigilant urethral washing followed by cystoscopy for treatment without en bloc urethrectomy
- TURP biopsy in presence of positive cytology in absence of recurrent bladder tumor and in those with previous history of superficial prostate TCC treated with BCG
- Some recommend frequent random biopsies of the prostatic urethra during repeat cystoscopy exams following treatment of CIS of the prostatic urethra.

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3. Liedberg F, Chebil G, Månsson W. Urothelial carcinoma in the prostatic urethra and prostate: Current controversies. Expert Rev Anticancer Ther 2007;7(3):383–390.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Cancer, General
- Bladder Cancer, Urothelial, Invasive (T2/T3/T4)
- Bladder Cancer, Urothelial, Superficial (CIS,Ta,T1)
- Prostate Cancer, General

CODES

ICD9

185 Malignant neoplasm of prostate

ABBREVIATIONS

- ADC: Adenocarcinoma
- BCG: Bacille Calmette-Guérin
- CIS: Carcinoma in situ
- CK: Cytokeratin
- CT: Computed tomography
- DRE: Digital rectal exam
- INH: Isoniazid
- MRI: Magnetic resonance imaging
- PSA: Prostate-specific antigen
- TCC: Transitional cell carcinoma
- TIS/pd: Tumor in situ/prostatic ducts
- TIS/pu: Tumor in situ/prostatic urethra
- TURP: Transurethral resection of prostate
- TURBT: Transurethral resection of bladder tumor

PROSTATE NODULE

Marc C. Smaldone, MD
Joel B. Nelson, MD

BASICS

DESCRIPTION

- Abnormal prostate findings by physician on DRE; most often raises concern for CaP.
- Can be subjectively described as soft, rubbery, firm, hard, or stony hard.
- Nodule consistency can range from well circumscribed to irregular and diffuse.
- A normal prostate is about the size of a chestnut and has a consistency similar to that of the contracted thenar eminence 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.

EPIDEMIOLOGY

Prostate nodule as an isolated finding with normal PSA is found in <10% of cases of CaP in the US.

RISK FACTORS

- CaP:
  - Nodule that changes in consistency and size over time
  - Serum PSA level >2.5–4.0 ng/mL
  - Positive family history
  - Prior external beam radiation or prostate brachytherapy
- Benign nodule:
  - No significant change over time, softer consistency
  - Prior episodes of prostatitis
  - Prior therapy with intravesical BCG
  - Prior prostate surgery (ie, TURP) or biopsy
  - Granulomatous nodules due to:

    Infectious: Bacterial, viral, fungal, parasitic, including Mycobacterium

    Systemic granulomatous diseases: Wegener granulomatosis, Churg-Strauss syndrome, sarcoidosis, rheumatoid arthritis, polyarteritis nodosa, malakoplakia, STD

Genetics

See “Prostate Cancer, General” for genetics of CaP

PATHOPHYSIOLOGY

- Normal prostate has soft, uniform consistency.
- Prostate enlarges with age.
- Microscopically, nodular prostatic 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 0.2 mL or larger to be detected by DRE.

COMMONLY ASSOCIATED CONDITIONS

- Prostatic adenocarcinoma
- BPH
- History of intravesical BCG for urothelial carcinoma of the bladder

DIAGNOSIS

HISTORY

History of LUTS:

- Irritative voiding symptoms
- Obstructive voiding symptoms
- Fever
- Previous prostate biopsy or surgery
- Previous pelvic external beam radiation or prostate brachytherapy
- History of prostatitis, abscess, or exposure to TB
- Systemic granulomatous disease (Wegner, etc.)
- Family history of genitourinary malignancies

ALERT

Where prostate abscess or acute prostatitis is suspected, rectal exam may be contraindicated.

PHYSICAL EXAM

- DRE:
  - Carcinoma (prostatic adenocarcinoma and transitional cell):

Palpable as firm, indurated nodules or regions within the prostate gland often characterized by having a woody consistency.

CaP most commonly arises in the posterior peripheral region of the prostate.

As the prostatic carcinomas progress, the entire gland can become firm. The medial and lateral sulci of the prostate may become obliterated.

Eventually, these tumors may progress beyond the capsule of the prostate, extending cephalad into the seminal vesicles and laterally toward the pelvic side wall causing fixation of the gland.

Following radiation therapy, the entire gland may be very firm

Lymphoma: Diffusely firm gland

- BPH:
  - Typically generalized variable enlargement with rubber consistency
  - Findings usually limited to the prostate
  - There is only a general correlation between prostatic size and degree of symptoms.
- Infectious lesions:
  - Prostatitis: Warm, tender prostate that can be fluctuant or boggy in consistency. The prostate should never be massaged for secretions in men with acute prostatitis.
  - Prostatic abscess: Localized fluctuant, tender region within the prostate
- Calculus:
  - Hard, firm, small nodule

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PSA:
  - May be within normal age-specific range in up to 30% of men with CaP
  - Age-adjusted PSA increase
  - PSA >2.5–4.0 ng/mL is a relative strong indication for prostate biopsy in patients with an abnormal DRE, a family history positive for CaP, or an abnormal DRE
  - Free PSA <25% has been recommended to maximize cancer detection in younger men while avoiding unnecessary biopsies in older men.
  - PSA velocity >0.75 ng/mL in an optimal patient with a PSA of 4.0ng/mL
  - BPH and prostatitis can have significantly elevated serum PSA levels, confounding the utility of PSA as a CaP screening tool.
- Urine analysis:
  - Variable findings in men with an abnormal DRE; serial pyuria with granulomatous prostatitis
  - Most commonly normal in a patient with an abnormal DRE due to CaP in the absence of infection
  - Urine culture: Usually positive for gram-negative organisms in acute and chronic bacterial prostatitis
  - Urine cytology: Commonly positive in high-grade TCC, very rarely positive in advanced adenocarcinoma

Imaging

- TRUS:
  - Prostatic adenocarcinoma:

Classic appearance of prostatic adenocarcinoma is a round or oval hypoechoic lesion located in the peripheral zone.

~1/3 of prostate tumors are isoechoic with peripheral zone tissue.

1% of prostate tumors are hyperechoic; can be related to associated calcifications.

Only 20% of lesions <10 mm are detectable with US.

Hypoechoic lesions are nonspecific in nature and can be confused with benign lesions such as granulomas. Must differentiate with biopsy.

  - TCC: Often a centrally located lesion, can invade the base of the bladder
  - BPH:

Variable findings ranging from diffuse enlargement of lateral lobes and central zone to isolated hypoechoic or hyperechoic adenomatous nodules

Cannot be differentiated from adenocarcinoma without a biopsy

  - Prostatitis: Hyperechoic, asymmetric enlargement
- Excretory urography:
  - >90% of urograms in patients with prostatic disease will be normal studies.
  - Advanced lesions (CaP, TCC, lymphoma, BPH): Lesion extending into bladder, bladder wall thickening, and large PVR volumes, lateral displacement of ureters, hydroureteronephrosis
- Abdominal CT or MRI:
  - Both abdominal CT and body and endorectal surface coil MRI can be used to detect CaP, but are primarily reserved for staging purposes.
  - Body coil MRI has not been proven to surpass TRUS for the diagnosis of CaP, but MRI performed with an endorectal surface coil increases the accuracy of detection and staging (local extension, pelvic lymph node involvement).

Diagnostic Procedures/Surgery

- TRUS-guided biopsy:
  - The major role of TRUS is to ensure accurate wide-area sampling of prostate tissue in men at higher risk for harboring CaP on the basis of positive DRE and elevated PSA.
  - The original sextant biopsy scheme (1 core from the base, mid, and apex bilaterally) significantly improved cancer detection over digitally directed biopsy of palpable nodules and US-guided biopsy of specific hypoechoic lesions.
  - Modifications to the standard sextant biopsy scheme have focused on the importance of laterally directed cores.

– This is best accomplished by targeted biopsy of TRUS-suspicious lesions and systematic biopsy of areas without hypoechoic lesions (8–13 biopsies).

– Cystoscopy: Identifies bladder outlet obstruction and used to evaluate bladder when hematuria is present

Pathological Findings

See specific chapters on disease entities

DIFFERENTIAL DIAGNOSIS

- Neoplasm, malignant:
  - Lymphoma: Primary and secondary
  - Prostatic adenocarcinoma
  - Sarcoma, small-cell carcinoma, and other rare tumors and metastases
  - TCC
- Benign:
  - BPH
  - Calculus/calcification
  - Ejaculatory duct cyst
  - Granulomatous prostatitis
  - Prostatic intraepithelial neoplasia
  - Scarring from previous surgery or infection
  - Rectal wall lesions (thrombosed hemorrhoid, carcinoma, etc.)

TREATMENT

- Abnormal DRE is an absolute indication for TRUS prostate biopsy.
- Standard work-up includes measurement of serum PSA followed by prostate biopsy.
- Cystoscopy is only necessary if obstructive symptoms or hematuria is present.
- CT, bone scan, and/or MRI is reserved for cases suspicious for local extension or metastatic disease (PSA >10 ng/mL)

MEDICATION

May be needed for infectious causes of nodules such as TB

SURGERY/OTHER PROCEDURES

Based on diagnosis of nodule

ADDITIONAL TREATMENT

May be option if nodule proves to be cancer-related.

ONGOING CARE

PROGNOSIS

Based on diagnosis

COMPLICATIONS

Based on diagnosis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Negative biopsy in a patient with an abnormal DRE or elevated PSA requires rigorous follow-up with serial DRE and PSA documentation.
- Repeat abnormal DRE/PSA findings may warrant repeat TRUS biopsies.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate, Abscess
- Prostate Cancer, General
- Prostate Cancer, Urothelial
- Prostate Infarction
- Prostate, Benign Hyperplasia/Hypertrophy (BPH)
- Prostatic Intraepithelial Neoplasia (PIN)
- Prostatitis, General
- PSA Elevation, General

CODES

ICD9

- 600.10 Nodular prostate without urinary obstruction
- 600.11 Nodular prostate with urinary obstruction

ABBREVIATIONS

- BCG: Bacillus Calmette Guérin
- BPH: Benign prostatic hypertrophy

- CaP: Adenocarcinoma of the prostate
- CT: Computed tomography
- DRE: Digital rectal exam
- LUTS: Lower urinary tract symptoms
- MRI: Magnetic resonance imaging
- PSA: Prostate-specific antigen
- PVR: Post void residual
- STD: Sexually transmitted disease
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- TRUS: Transrectal ultrasound
- TURP: Transurethral resection of prostate
- US: Ultrasound

PROSTATE, ABSCESS

Daniel J. Canter, MD

S. Bruce Malkowicz, MD

BASICS

DESCRIPTION

- Infection of the prostate usually as a result of ineffective antibiotic therapy for acute prostatitis
- Rare in nonhospitalized patients

Pediatric Considerations

Exceedingly rare event in the newborn, with only 13 cases reported; however, can be an unrecognized source of urosepsis in newborns with devastating outcomes if not recognized

EPIDEMIOLOGY

- Difficult to determine because of the widespread use of antibiotics for prostate problems
- Acute prostatitis estimated to be 1/1,000, thus incidence of abscess formation would be far less

RISK FACTORS

- Indwelling catheters
- Lower urinary tract instrumentation
- Bladder outlet obstruction, history of prostatitis
- Compromised immune system (eg, AIDS, diabetes, etc.)

GENERAL PREVENTION

- Aimed at preventing/treating STDs (eg, gonorrhea)
- Relieving/improving signs/symptoms of bladder outlet obstruction
- Diabetic glycemic control

PATHOPHYSIOLOGY

- Usually an ascending infection in association with poor bladder emptying
- Urethral infection combined with intraprostatic reflux of infected urine causes acute prostatitis.
- Acute prostatitis can, in patients with immunosuppression or other risk factors, progress to abscess.
- Can be hematogenous route especially with Staphylococcus sp. in immunocompromised patients/IV drug users
- Most common etiologic agent is E. coli with occasional S. aureus
- With the advent of antibiotics, the incidence of Neisseria gonorrhea as causative agent has decreased significantly.

- With severe immunocompromise, such as HIV; more unusual organisms such as TB, Cryptococcus, histoplasmosis, and Candida should be considered
  - Melioidosis is an infection (usually abscesses in many sites including the prostate) caused by the gram-negative Burkholderia pseudomallei. Usually associated with diabetes; very high prevalence in East Asia and Northern Australia

COMMONLY ASSOCIATED CONDITIONS

Any disease process that causes immunocompromise:

- HIV/AIDS
- Cancer
- Diabetes
- Chronic renal failure, hemodialysis
- Cirrhosis

DIAGNOSIS

HISTORY

- Fevers, chills, urinary symptoms with attention paid to voiding patterns prior to acute presentation
- Acute urinary retention
- Sexual history/social history (IV drug use, etc.)
- Associated medical comorbidities

PHYSICAL EXAM

ALERT

Where prostate abscess or acute prostatitis is suspected, rectal exam may be contraindicated:

- Perineal pain, tenderness
- Urethral discharge
- DRE can reveal exquisitely tender prostate with fluctuance or simply an enlarged prostate
- Signs of other medical comorbidities (ie, new cardiac murmur, ascites, cough, track marks, etc.)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC with differential
- PSA
- Urinalysis, urine/blood cultures
- Gram stain/culture of prostatic fluid once drained

- AFB or mycobacterium specific PCR if TB suspected

Imaging

TRUS, CT scan, and MRI:

- TRUS will reveal hypoechoic zones with irregular internal echoes, septations, and indirect borders with the surrounding prostate

Diagnostic Procedures/Surgery

TRUS, CT scan, MRI

Pathological Findings

Purulent material will be expressed from prostate during surgical drainage procedure:

- Gram stain and culture of material will give causative agent, most commonly bacterial

DIFFERENTIAL DIAGNOSIS

- Clinically can be hard to distinguish from UTI, acute prostatitis, or any other lower urinary tract infection.
- Should have clinical suspicion, which can be confirmed with TRUS

TREATMENT

Initial treatment should focus on broad-spectrum antibiotics, IV hydration, and pain control.

MEDICATION

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, fluoroquinolones are good choices
- Some sources advise addition of clindamycin for additional anaerobic coverage until the cultures return.
- Some recommend suprapubic cystotomy drainage as adjunct.
- Fungal infections may require 4–6 wk systemic therapy in addition to drainage.

SURGERY/OTHER PROCEDURES

TUR unroofing (preferred) or transperineal drainage with US guidance followed by urethral catheter drainage

ADDITIONAL TREATMENT

- Relates to predisposing conditions
- For patients with bladder outlet obstruction, therapy should be started to relieve obstruction, (ie, -blockers or 5-reductase inhibitors)

ONGOING CARE

PROGNOSIS

Should recover fully once definitive therapy undertaken

COMPLICATIONS

Urinary tract fistulae, urosepsis, death if diagnosis not made in timely manner

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Supportive once definitive therapy performed
- Once acute events resolves, monitoring focuses on optimizing medical comorbidities and improving voiding symptoms.

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See Also (Topic, Algorithm, Electronic Media Element)

Prostatitis, Acute, Bacterial (NIH I)

CODES

ICD9

- 041.4 Escherichia coli (E. coli) infection in conditions classified elsewhere and of unspecified site
- 041.11 Methicillin susceptible Staphylococcus aureus
- 601.2 Abscess of prostate

ABBREVIATIONS

- AFB: Acid-fast bacteria
- AIDS: Acquired immunodeficiency syndrome
- CBC: Complete blood count
- CT: Computed tomography
- DRE: Digital rectal exam
- HIV: Human immunodeficiency virus
- IV: Intravenous
- MRI: Magnetic resonance imaging
- PCR: Polymerase chain reaction
- PSA: Prostate-specific antigen
- TB: Tuberculosis
- TRUS: Transrectal ultrasound
- TUR: Transurethral

- US: Ultrasound
- UTI: Urinary tract infection

PROSTATE, BENIGN HYPERPLASIA/HYPERTROPHY (BPH)

Steven A. Kaplan, MD

Stacy M. Scofield, BS

BASICS

DESCRIPTION

- BPH refers to histologic changes within the prostate gland and may not imply the presence of an enlarged prostate or symptoms. It can be associated with EP (aka, BPE) and/or BOO.
- LUTS are 1 manifestation of BPH.
- Synonym(s): Nodular hyperplasia

EPIDEMIOLOGY

Prevalence of LUTS in men increases with age:

- LUTS commonly includes urinary frequency, urgency, hesitancy, and a weak stream. (The term prostatism was previously used to refer to this symptom complex.)
- LUTS often has a significant negative impact on a patient's quality of life. A survey of >5,000 community-dwelling men age 65 in the US without history of prostate cancer found that 46% reported moderate to severe LUTS.

RISK FACTORS

- Although family history and advancing age are risk factors for BPH, evidence for comorbidity, environmental, dietary, or lifestyle related risk factors is generally weak.
- The Massachusetts Male Aging Study found that cigarette smoking and increased physical activity were protective against BPH, whereas heart disease correlated with development of BPH. There may also be a positive association between obesity and prostate volume and LUTS.

Genetics

Some men with younger age of onset and larger glands have a family history of BPH.

GENERAL PREVENTION

- Randomized clinical trials (MTOPS) have suggested that the combination of an -blocker with a 5-reductase inhibitor can reduce the lifetime risk of acute urinary retention and may prevent symptomatic disease progression.
- Bladder decompensation may be prevented by treatment of BOO.

PATHOPHYSIOLOGY

- The development of BPH/LUTS begins with abnormal microscopic hyperplasia and macroscopic growth. This, along with the active force generation of prostatic and bladder

neck smooth muscle, contributes to urine outflow obstruction and the classic obstructive voiding symptoms of decreased force of stream, intermittent stream, and hesitancy.

- The detrusor response to increased resistance is initially to generate higher pressures to overcome the outlet resistance. This leads to a variety of cellular and morphologic changes in the bladder. The common storage symptoms of frequency, urgency and nocturia are likely the sequelae of these alterations in bladder physiology.
- Progression of the disease may eventually lead to bladder decompensation, in which the bladder is no longer able to generate sufficient pressures to empty.
- Increasing prostate volume is considered a normal part of ageing. The prostate grows rapidly from birth to puberty and in the 3rd decade reaches a size of 20 g on average.
- The primary site for this androgen-dependent growth process involves the periurethral and transition zones of the prostate.

COMMONLY ASSOCIATED CONDITIONS

- OAB (urinary frequency, urgency, nocturia, urge incontinence)
- Sexual dysfunction (erectile and/or ejaculatory dysfunction)

DIAGNOSIS

HISTORY

- Family history of prostate diseases
- Prior intervention/evaluation of LUTS
- Current medications that may modify voiding pattern (ie, diuretics, cold medications)
- Other medical conditions that may complicate urinary function (ie, diabetes)
- Any risk factors for bladder cancer (smoking)
- Any previous neurologic symptoms, injury or disease (ie, Parkinson disease, disk disease, etc.)
- Onset, duration and severity of symptoms:
  - Voiding symptoms (previously called obstructive symptoms): Hesitancy, intermittency, weak stream, abdominal straining to void, post void dribbling, incomplete emptying, double voiding)
  - Storage symptoms (previously called irritative symptoms): Daytime frequency, nocturia, urgency, urge incontinence, enuresis, dysuria)
- The IPSS is a reproducible, validated index designed to determine disease severity and response to therapy:
  - Similar to the AUASS, consists of 7 questions related to voiding symptoms (See Section VII).
  - Scores of 0–7, 8–19, and 20–35 signify mild, moderate, and severe symptoms, respectively.

– In addition, the IPSS includes a quality of life score as a single 7-point scale question asking the patient how he would feel if he were to spend the rest of his life with his current urinary condition.

PHYSICAL EXAM

- Evaluation of the abdomen, pelvis, perineum
- Attempt to recreate activities that typically cause incontinence in the patient.
- 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

- Urinalysis to exclude hematuria or evidence of infection
- PSA:
  - May be a proxy for prostate size
  - In a large screening trial, prostate volume/mean PSA were as follows:14 cm3/1; 25.cm3/1; 13/52 cm3/1.45
  - Prostate cancer detection; discuss risk benefits of PSA screening
- Urine cytology: Not considered standard; only if there is a predominance of irritative symptoms, hematuria and/or risk factors for bladder cancer such as smoking

Imaging

- Not indicated unless there is evidence of upper tract deterioration or a need to further evaluate hematuria
- TRUS may be beneficial in determining accurate size readings for certain minimally invasive procedures or if evaluation is suspicious for a clinically significant prostate cancer to direct prostate biopsy

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 accumulation:
  - Combined with a measurement of PVR volume (see below), it is an excellent screening tool for BOO in men with LUTS.
  - Uroflowmetry measures voided volume, voiding time, average flow rate, and maximum flow rate (Qmax), also called the PFR.

– Qmax: 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/sec is often considered normal, whereas a value of <7 mL/sec is suggestive of significant obstruction.

– Occasionally may not be able to differentiate obstruction from poor bladder contractility. In these cases, a formal urodynamic study that incorporates a pressure flow measurement is useful:

Urethral catheterization with transrectal pressure transducer

Obstruction confirmed with low flow (Qmax, <15 mL/sec) and high voiding pressure >60 cm water.

• PVR: Although generally used, PVR does not convincingly correlate with the severity of LUTS, the presence of BOO, or treatment outcomes:

– An elevated PVR is found with obstruction, but may also indicate detrusor decompensation due to various causes, including chronic BOO.

– PVR does not provide diagnostic information for OAB.

• Voiding diary for several 24-hr periods may help quantify the degree of frequency and volume output. Helps evaluate for possible 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.

Pathological 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

• For obstructive symptoms:
  – Detrusor sphincter dyssynergia
  – Foreign body
  – Meatal stenosis
  – Neuropathic bladder
  – Pelvic floor dysfunction
  – Prostate cancer

- Prostatic abscess
- Prostatitis syndromes
- Urethral obstruction (stricture, condylomata)

• For irritative/storage symptoms:
- Bladder cancer
- Detrusor hyperreflexia/OAB
- Interstitial cystitis
- Polyuria/polydipsia
- Prostatitis syndromes

TREATMENT

• Unless there is evidence of significant chronic damage to the urinary tract that requires intervention (hydronephrosis, bladder calculi, recurrent infections, etc.) treatment is primarily for quality of life issues.

• 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

• -Blocker and 5-reductase inhibitors often prescribed together

MEDICATION

• -Blockers (reduce muscle tone in prostate/bladder neck):
- Terazosin (start 1 mg/d to max 20 mg)
- Doxazosin (start 1 mg/d to max 8 mg)
- Tamsulosin (start 0.4 mg to max 0.8 mg)
- Alfuzosin (10 mg/d)
- Silodsin (8 mg/d)

• 5-Reductase inhibitors (block intracellular DHT conversion; generally best for larger glands, may take 6–12 mo for improvement):
- Finasteride (5 mg/d)
- Dutasteride (0.5 mg/d)

• Antimuscarinic agents may help with bladder overactivity:
- Tolterodine ER (2–4 mg/d)
- Solifenacin (5–10 mg/d)

SURGERY/OTHER PROCEDURES

• Often considered 2nd-line after failure of medical therapy; may be 1st-line in retention or if very large prostate.

- TURP represents gold standard against which all other therapies are compared.
- Open simple prostatectomy usually for glands >100 g:
  - Suprapubic prostatectomy: Enucleation of adenoma through bladder; useful with coexisting problems such as very large bladder calculi or to repair diverticulum
  - Retropubic simple prostatectomy: Enucleation 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), laser prostatectomy (holmium, KTP)

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Prostatic stents; best if need TURP but poor surgical risk
- Phytotherapy (plant extracts) includes saw palmetto, Pygeum africanum; -sitosterols have limited support in the literature

ONGOING CARE

PROGNOSIS

- Symptoms usually well managed by medications
- Progression of disease, when risk factors identified, can be well managed

COMPLICATIONS

- Generally accepted sequelae of untreated, undertreated, or progressive BPH
- Historically, many men typically had complications of BPH including UTIs, hematuria, bladder calculi, bladder decompensation, incontinence, and upper-tract deterioration. With modern awareness and management techniques, this is less common.
- The most commonly used endpoints in medical trials are symptom deterioration, BPH-related surgery, and AUR. AUR continues to be the most widely accepted and most scientific endpoint, although the exact pathophysiologic mechanism is not completely understood.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Outlet Obstruction (BOO)
- Lower Urinary Tract Symptoms (LUTS)

CODES

ICD9

– 600.00 Hypertrophy (benign) of prostate without urinary obstruction and other lower urinary tract symptoms (LUTS)

– 600.01 Hypertrophy (benign) of prostate with urinary obstruction and other lower urinary tract symptoms (LUTS)

ABBREVIATIONS

- AUASS: American Urological Association's Symptom Score
- AUR: Acute urinary retention
- BPE: Benign prostate enlargement
- BPH: Benign prostatic hypertrophy
- BOO: Bladder outlet obstruction
- DRE: Digital rectal exam
- EP: Enlarged prostate
- IPSS: International Prostate Symptom Score
- LUTS: Lower urinary tract symptoms
- MTOPS: Medical Therapy of Prostatic Symptoms
- OAB: Overactive bladder
- PFR: Peak flow rate
- PVR: Post void residual
- TURP: Transurethral resection of prostate
- TRUS: Transrectal ultrasound
- UTI: Urinary tract infection

PROSTATIC INTRAEPITHELIAL NEOPLASIA (PIN)

Marc C. Smaldone, MD

Joel B. Nelson, MD

BASICS

DESCRIPTION

- Characterized by architecturally benign prostatic acini or ducts lined by cytologically atypical cells confined within the epithelium
- It is sub-classified as low-grade PIN (LGPIN) and high-grade PIN (HGPIN).
- LGPIN was formerly referred as PIN 1 and HGPIN as PIN 2 and 3.
- Many pathologists are no longer reporting the presence of low-grade PIN as the significance is not clear and should not be commented on in diagnostic reports.
- Men with LGPIN diagnosed on needle biopsy are at no more risk of having adenocarcinoma on repeat biopsy than are men with a benign biopsy.
- Literature written before 1989 described PIN as intraductal hyperplasia, hyperplasia with malignant change, large acinar atypical hyperplasia, marked atypia, ductal-acinar dysplasia. These terms are no longer used.
- ASAP is another histologic finding that suggests a focus of atypical glands are suspicious for cancer. ASAP is distinct from HGPIN, and the 2 should not be used interchangeably.

EPIDEMIOLOGY

- Incidence of HGPIN on prostatic biopsy is 4–7%.
- The incidence and extent of PIN increases with age. Estimated prevalence figures are in men from 40–49, 15%, to as high as 70% in men 80–89 yr of age.
- Incidence of carcinoma detection on repeat biopsy following identification of PIN on needle biopsy is 21–36%.
- HGPIN adjacent to atypical glands confers an increased risk of subsequent diagnosis of carcinoma of >50%.
- Recent data suggest that detection of carcinoma on subsequent biopsy is directly associated with the number of cores with HGPIN involvement on initial biopsy.

RISK FACTORS

Currently, no known risk factors for PIN other than prostate cancer elsewhere in the gland

Genetics

- Biomarker studies indicate that HGPIN is related more closely to prostate cancer than benign epithelium.
- Frequent changes in HGPIN include both increases and decreases in chromosome 8 (loss 8p, gain 8q).

• Other common changes include gains of chromosomes 7, 10, 12 and Y, and losses of 10q, 16q, and 18q.

• Incidence of aneuploidy in HGPIN is 50–70%.

• Telomerase activity has been reported to occur in 16% of HGPIN lesions and 85% of invasive prostatic carcinomas.

GENERAL PREVENTION

• Unknown; HGPIN offers promise as an intermediate histologic marker to indicate subsequent likelihood of carcinoma in chemoprevention studies.

• Use of HGPIN as a surrogate endpoint is problematic due to sampling errors on repeat biopsies.

• Many studies, such as using green tea extracts, under way.

PATHOPHYSIOLOGY

• A strong association exists between HGPIN and prostatic adenocarcinoma.

• Both HGPIN and adenocarcinoma preferentially involve the peripheral zone and are often multifocal.

• The frequency, severity, and extent of HGPIN increases in the presence of prostate cancer.

• Biomarkers and molecular changes show similarity between HGPIN and carcinoma.

• PIN does not need to be present for carcinoma to arise.

• Low-grade carcinomas, especially those detected within the transition zone, are not closely related to HGPIN.

• Rates of cell proliferation and death are raised in HGPIN and prostate cancer compared to normal prostates.

• HGPIN and prostate cancer are phenotypically and morphometrically similar.

• Some genetic and molecular alterations are common to both HGPIN and prostate cancer.

• HGPIN may offer a short-term surrogate marker in prostate cancer prevention trials.

• In patients treated with hormonal therapy before radical prostatectomy (neoadjuvant hormonal therapy), a marked reduction in PIN is noted.

COMMONLY ASSOCIATED CONDITIONS

Prostatic adenocarcinoma

DIAGNOSIS

HISTORY

• History of previous prostate biopsy

• Family history of prostate cancer

PHYSICAL EXAM

- There are no abnormalities on DRE directly associated with PIN.
- DRE findings are variable in patients with PIN.
- Abnormalities (induration, nodule) may be detected on DRE in patients with concurrent prostatic adenocarcinoma or other pathology.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PIN itself does not give rise to elevated serum PSA values.
- PSA levels are variable in patients with PIN.

Imaging

- There are no specific imaging (CT, MRI, TRUS) findings associated with PIN.
- TRUS findings in patients with PIN do not enhance the prediction of which patients are more likely to have carcinoma on repeat biopsy.
- Round or oval hypoechoic lesion on TRUS may indicate concurrent prostate cancer.

Diagnostic Procedures/Surgery

- Transrectal US-guided prostatic needle biopsy to evaluate for prostate cancer
- Repeat biopsy of the prostate should entail at least systematic sextant biopsy of the entire gland.

Pathological Findings

- Predominant location of HGPIN is the peripheral zone of the prostate.
- Diagnostic criterion for LGPIN:
  - Epithelial cell crowding and stratification with irregular spacing
  - Nuclei enlarged with marked size variation
  - Normal chromatin
  - Very rarely prominent nucleoli
  - Both basal cell layer and basement membrane intact
- Diagnostic criterion for HGPIN:
  - Epithelial cell crowding, irregular spacing and stratification
  - 4 patterns identified:
    Tufting (most common)
    Micropapillary
    Cribriform
    Flat
  - Nuclei enlarged, with some size and shape variation
  - Prominent nucleoli

– Basal cell layer is often disrupted but the basement membrane is intact.

• Immunostaining of histologic sections with HMW-CK to document presence of intact basal layer and thus absence of carcinoma.

DIFFERENTIAL DIAGNOSIS

• Atypica induced by inflammation, infarction, or radiation
• Cribriform hyperplasia
• Cribriform, ductal endometrioid and urothelial carcinoma
• Lobular atrophy and post atrophic hyperplasia
• Radiation induced atypia
• Normal anatomic structures and embryonic rests
• Transitional cell metaplasia
• Typical and atypical basal cell metaplasia

TREATMENT

• For patients diagnosed with HGPIN on extended initial core sampling, results of current studies indicate that a repeat biopsy within the 1st yr may be unnecessary in the absence of other clinical indicators of cancer.

• Patients with unifocal HGPIN can be managed conservatively with serial estimates of PSA level and DREs.

• Patients with multifocal HGPIN on initial biopsy should be rebiopsied within 3–6 mo of the initial biopsy, regardless of PSA level or DRE.

• If a repeat biopsy is performed, it should sample the entire prostate, and not just the initial sextant site where HGPIN was detected.

• Men with LGPIN diagnosed on needle biopsy are at no more risk of having adenocarcinoma on repeat biopsy than are men with a benign biopsy.

ALERT

It is critical that the patient understand that the word neoplasia in prostatic intraepithelial neoplasia is not a diagnosis of cancer.

MEDICATION

• No currently FDA approved medications for the treatment of PIN; finasteride and dutasteride have been shown in studies to reduce the incidence of PIN, but the implications of this are not clear at present.

• As a target for chemoprevention of prostate cancer, many trials are planned or under way to treat HGPIN.

• SERMs such as toremifene and others are under investigation.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Green tea extracts (catechins) are under study in clinical trials.
- Lycopenes are unproven.

ONGOING CARE

COMPLICATIONS

HGPIN is a likely a precursor lesion to many intermediate to high-grade adenocarcinomas and in and of itself does not produce any known complications beyond the risks of biopsy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Current recommendation is for patients with multifocal HGPIN undergo repeat biopsy 0–6 mo after initial biopsy, irrespective of serum PSA level and DRE findings, then every 6 mo for 2 yr, and every 12 mo thereafter.
- LGPIN, in and of itself, does not require any specific follow-up.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Atypical Small Acinar Proliferation, Prostate (ASAP)
- Prostate Cancer, General
- Prostate Nodule

- PSA Elevation, General

CODES

ICD9

602.3 Dysplasia of prostate

ABBREVIATIONS

- ASAP: Atypical small acinar proliferation
- CT: Computed tomography
- DRE: Digital rectal exam
- FDA: Food and Drug Administration
- HGPIN: High-grade prostatic intraepithelial neoplasia
- HMW-CK: High-molecular-weight cytokeratin
- LGPIN: Low-grade prostatic intraepithelial neoplasia
- MRI: Magnetic resonance imaging
- PIN: Prostatic intraepithelial neoplasia
- PSA: Prostate-specific antigen
- SERM: Selective estrogen receptor modulators
- TRUS: Transrectal ultrasound

PROSTATITIS, ACUTE, BACTERIAL (NIH I)

Aisha K. Taylor, MD

Anthony J. Schaeffer, MD

BASICS

DESCRIPTION

- Acute bacterial prostatitis is a potentially life-threatening bacterial infection of the prostate that requires treatment with IV antibiotics.
- Much less common than chronic prostatitis because of the mode of presentation
- Prostatic abscess is a well recognized but infrequent complication.

EPIDEMIOLOGY

- Incidence of acute prostatitis: 6%
- Adult men are most frequently affected, as this disease rarely involves prepubertal or pubertal boys.

RISK FACTORS

- Acute epididymitis
- BOO secondary to benign prostatic hyperplasia
- Immunocompromise and or immunosuppression
- Phimosis
- Recent prostate biopsy
- Recent urologic instrumentation
- Unprotected anal intercourse (meatal inoculation with fecal contents)
- Urethral catheterization or chronic condom catheter

GENERAL PREVENTION

Safe sex practices may prevent some cases.

PATHOPHYSIOLOGY

- Intraprostatic urinary reflux of infected urine
- Ascending urethral infection:
  - Meatal inoculation during unprotected anal intercourse
  - Urologic instrumentation
  - Prolonged catheterization
  - Direct invasion or lymphogenous spread from the rectum
  - Direct hematogenous infection
  - Most infections caused by single bacterial uropathogenic organism (ie, E. coli, Klebsiella, Pseudomonas)
  - Up to 10% by enterococci

– Occasionally can be polymicrobial
– MRSA in increasingly becoming an important nonuropathogenic source
– If sexually active and <35 yr, consider N. gonorrhea
– With severe immunocompromise such as HIV more unusual organisms such as Tuberculosis, Cryptococcus, Histoplasma, and Candida should be considered.

- NIH classification and definitions of prostatitis:
  – I: Acute bacterial prostatitis
  – II: Chronic bacterial prostatitis: Recurrent infection
  – III: Chronic abacterial prostatitis/CPPS: No demonstrable infection:

IIIA: Inflammatory CPPS: WBCs present in semen/expressed prostatic secretions or voided bladder urine (VB3)

IIIB: Noninflammatory CPPS: WBCs not present in semen/expressed prostatic secretions or voided bladder urine (VB3)

– IV: Asymptomatic inflammatory prostatitis: Detected by prostate biopsy or presence of WBCs in prostatic secretions during evaluation for other disorders

COMMONLY ASSOCIATED CONDITIONS

- BPH
- Urethral stricture disease
- Immunosuppressive diseases (diabetes, HIV)

DIAGNOSIS

HISTORY

- An acute illness associated with fever, chills, low back, perineal/rectal pain, irritative voiding symptoms, generalized malaise
- Arthralgia and myalgia common
- May present with acute urinary retention

ALERT

Avoid vigorous prostatic exam or massage in a patient with suspected acute bacterial prostatitis. Not only very painful but may cause bacteremia and sepsis. Likewise urethral instrumentation should be avoided if possible.

PHYSICAL EXAM

- Signs of sepsis including fever, tachycardia, and hypotension
- Palpable bladder or abdominal fullness may imply acute urinary retention.
- DRE should be performed cautiously as noted:
  – Findings including enlarged, exquisitely tender, warm, boggy, swollen prostate gland

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC demonstrates moderate to severe leukocytosis.
- Urinalysis shows leukocytes, bacteria, or other findings consistent with UTI.
- Blood cultures may reveal evidence of bacteremia.
- PSA should not be obtained in this setting as it will likely be elevated.

Imaging

- CT or TRUS may reveal presence of prostatic abscess but are not usually necessary as the diagnosis is primarily clinical.
- The use of TRUS in the acute setting should be used cautiously if at all.

Diagnostic Procedures/Surgery

Prostate biopsy is contraindicated in the presence of acute bacterial prostatitis

DIFFERENTIAL DIAGNOSIS

- Chronic bacterial prostatitis
- Granulomatous prostatitis
- Perirectal abscess
- Prostate cancer
- Prostatic abscess
- Prostatodynia
- UTI

TREATMENT

- Most patients are ill and will require admission and IV antibiotics.
- Analgesics
- Antipyretics
- Bed rest
- Increased fluid intake
- Sitz baths
- Stool softeners
- Bladder drainage if there is evidence of retention:
  - A urethral catheter should be placed cautiously. With any difficulty or if the patient is too uncomfortable, percutaneous suprapubic tube should be placed.
  - Remove all catheters as soon as possible.

MEDICATION

- Fluoroquinolones (eg, ciprofloxacin 400 mg IV b.i.d.)
- Trimethoprim-sulfamethoxazole, 8–10 mg/kg/d (based on trimethoprim component) in 2–4 IV doses

- Ampicillin with gentamicin (ampicillin 3–5 mg/kg/d IV; gentamicin 1–2 mg/kg IV q8–12h or daily dosing 4–7 mg/kg q24h IV)
- If suspect STD such as gonorrhea in male <35, ceftriaxone 250 mg IM in 1 dose with doxycycline 100 mg b.i.d.
- Change to culture-specific oral antibiotics based on bacterial susceptibilities when afebrile for 24 hr.
- Continue oral agents for 4 wk.
- Some common agents useful in the urinary tract may include ciprofloxacin, levofloxacin, ofloxacin.

SURGERY/OTHER PROCEDURES

- Suprapubic tube placement via suprapubic punch cystostomy catheter cannot be passed easily in setting of acute urinary retention.
- Surgical drainage of prostatic abscess if this complication develops (transrectal, perineal aspiration, or transurethral resection). In general, the abscess should be >1 cm to derive maximum benefit.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Allopurinol 600 mg/d initially for short duration decreasing to 300 mg/d has been shown to improve discomfort.
- -Blockers (terazosin, doxazosin, tamsulosin, alfuzosin, silodosin) may improve symptoms

ONGOING CARE

PROGNOSIS

- If initial response to therapy is favorable then patient prognosis is excellent.
- Studies using quinolone antibiotics suggest that a negative culture after 7 days of therapy is predictive of a long-term response.
- ~5% of acute bacterial prostatitis will convert to chronic bacterial prostatitis.
- If the patient with suspected bacterial prostatitis is not responding to initial empiric therapy, consider prostatic abscess.

COMPLICATIONS

- Decreased fertility
- Epididymitis
- Progression to chronic prostatitis
- Prostatic abscess with inadequate or delayed treatment of acute prostatitis episode
- Pyelonephritis
- Septicemia

- Urinary retention

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up urine cultures to verify that the infection has cleared and that chronic bacterial prostatitis is not present.
- A PSA test must not be performed for at least 1–2 mo after the episode resolves due to the possibility of a falsely elevated reading that raises concern for prostate cancer.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate, Abscess
- Prostatitis, General
- Prostatitis, Mycotic
- Prostatitis, Tuberculous
- Prostatitis, Chronic, Bacterial (NIH II)
- Urinary Tract Infection (UTI), Adult Male

CODES

ICD9

- 041.9 Bacterial infection, unspecified, in conditions classified elsewhere and of unspecified site
- 601.0 Acute prostatitis

ABBREVIATIONS

- BOO: Bladder outlet obstruction
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- CPPS: Chronic pelvic pain syndrome
- CT: Computed tomography

- DRE: Digital rectal exam
- HIV: Human immunodeficiency virus
- IV: Intravenous
- MRSA: Methicillin-resistant Staphylococcus aureus
- PSA: Prostate-specific antigen
- STD: Sexually transmitted disease
- TRUS: Transrectal ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

PROSTATITIS, CHRONIC BACTERIAL (NIH II)

Jason P. Gilleran, MD

Robert R. Bahnson, MD

BASICS

DESCRIPTION

- Chronic bacterial prostatitis (NIH II) includes symptoms of prostatitis with positive urine culture and no signs of systemic infection.
- Occasionally, no local symptoms are present.
- Recurrent UTI with a single organism that persists is the classic hallmark.
- Overlap of symptoms makes it difficult to distinguish clinically from chronic nonbacterial prostatitis (NIH Type III, CP/CPPS); about 10% of these patients with type III prostatitis will have positive cultures.
- NIH classification and current definitions of prostatitis:
  - Type I: Acute bacterial prostatitis
  - Type II: Chronic bacterial prostatitis; recurrent infection
  - Type III: Chronic abacterial prostatitis/CPPS; no demonstrable infection:

    IIIA: Inflammatory CPPS: WBCs present in semen/expressed prostatic secretions or voided bladder urine (VB3)

    IIIB: Noninflammatory CPPS: WBCs not present in semen/expressed prostatic secretions or voided bladder urine (VB3)
  - Type IV: Asymptomatic inflammatory prostatitis: Detected by prostate exam or presence of WBCs in prostatic secretions during evaluation for other disorders

EPIDEMIOLOGY

- Prostatitis in general is the most common urologic diagnosis in men <50 yr old, and the 3rd most common diagnosis in men >50 yr old.
- Affects 10–14% of men of all ages and accounts for 2 million office visits annually
- Chronic bacterial prostatitis is the most common cause of recurrent UTI in the adult male population.

RISK FACTORS

- Inadequately treated episodes of acute bacterial prostatitis may increase risk for developing chronic prostatitis syndromes.
- Older men with BPH/bladder outlet obstruction
- Urethral strictures
- Urethral catheterization
- Possibly reduced sexual activity with resulting prostatic congestion

GENERAL PREVENTION

- Adequate treatment of acute bacterial prostatitis
- Protected intercourse

PATHOPHYSIOLOGY

- With progressive benign prostatic enlargement, obstruction causes reflux into prostatic ducts.
- Obstructive, turbulent, and/or high-pressure voiding combined with intraprostatic ductal reflux, leads to acute intraductal inflammation.
- Progresses to chronic intraductal inflammation.
- Bacteria are present in inflamed ducts in protected bacterial aggregates or bacterial biofilms.
- Increased incidence of prostatic calculi may serve as a nidus of infection.
- Prostatic zinc levels (zinc is thought to be antibacterial) are lower in patients with chronic bacterial prostatitis; however, it is not clear if this a cause of or due to the infection.
- pH of prostatic fluid may increase from a normal of ~6.5 to >8.0 with infection
- Common pathogens: Escherichia coli (most common), Enterococcus faecalis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus spp.
- Others: Staphylococcus epidermatitis, S. saprophyticus, Corynebacterium, and Ureaplasma urealyticum, Chlamydia trachomatis, Candida, trichomonas, Mycobacterium hominis, and Tuberculosis:
  - Chlamydia, Ureaplasma, Mycoplasma spp. can cause prostatitis but do not grow in routine culture.

COMMONLY ASSOCIATED CONDITIONS

- BPH
- Detrusor/sphincter dyssynergia
- Sexual dysfunction
- STDs
- Subfertility/infertility
- Urethral stricture

DIAGNOSIS

HISTORY

- Fever and chills are not usual and suggest acute bacterial prostatitis.
- Dysuria, urgency, nocturia, weak stream
- Perineal, penile, scrotal, suprapubic, or groin pain; pain with or after ejaculation
- ED, decreased libido

- Prior UTIs, STDs
- Unprotected intercourse, new partners, sexual orientation
- Urethral catheterization or other lower genitourinary surgery
- NIH-CPSI, a self-administered validated-symptom index, may be useful.

PHYSICAL EXAM

- Exam of the genitalia may reveal vague widespread pelvic discomfort.
- Perineal tenderness may be present.
- DRE may reveal a minimally tender or boggy prostate.
- Prostatic calculi may be palpable.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and culture:
  - Routine urine culture may be negative. A positive culture may be obtained as part of the Mears-Stamey 4-glass test (see below):
  - Pyuria and bacteruria may be present
  - Hematuria should prompt workup for other causes.
- PSA may be elevated in the setting of prostate infection and should not be obtained until the infection clears.

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.
- Transrectal US performed in patients with pain on ejaculation may reveal enlargement of the prostate or seminal vesicle. Prostatic calculi may be visualized.

ALERT

In the setting of possible acute bacterial prostatitis or prostatic abscess, prostatic massage should not be performed.

Diagnostic Procedures/Surgery

- Mears-Stamey 4-glass test considered gold standard for the diagnosis of chronic bacterial prostatitis and involves isolated cultures of different portions of the lower urinary tract:
  - Make sure that the patient has a full bladder
  - Clean the glans thoroughly with antimicrobial solution. Retract foreskin as necessary.
  - Void 10 mL into sterile container (VB1). Represents urethral flora sample.
  - After voiding 100 mL, collect 10 mL midstream urine in another sterile container (VB2). Represents bladder flora sample.

– Perform prostatic massage to collect EPS from the urethra; submit for culture and examine on a glass slide under 40×. Represents prostate flora.

– Collect the next voided 10 mL in a sterile container. Represents a combination of prostate and blader flora.

– Normal:

Negative urethral, prostatic, and bladder cultures (VB1, VP2, EPS, and VB3 negative)

Normal prostatic secretions show no evidence of excess WBCs (<10 WBC cells per high-power field).

– Positive:

If EPS or VB3 colony counts are 10× higher than VB1 or VB2, bacterial prostatitis is present.

If all cultures are positive, then bacterial cystitis is likely present and the test should be repeated after 5 days of antibiotics (prostatitis and cystitis can coexist, and cystitis in men is often secondary to prostatitis).

EPS result is >10–20 WBC per high-power field or clumping of WBC. It is not diagnostic for bacterial infection as it can also be seen with NIH Class IIIA prostatitis.

- A modified Mears Stamey test (2-glass test) can also be performed that is considered more convenient and practical by most:

– After cleansing the glans, obtain 10 mL of a mid stream urine for culture (preprostate massage). Represents bladder flora. Should also be dipped for white cells.

– Perform prostate massage and obtain 10 mL of urine (postprostate massage) for culture and microscopic exam. Represents prostate and bladder flora. If white cell are present, they may represent bacterial prostatitis or NIH type IIIA.

– If post massage colony counts are 10× higher than premassage 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

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis/prostatic abscess
- Bladder outlet obstruction/BPH
- Chronic nonbacterial prostatitis (NIH IIIA/B)
- Cystitis

- Interstitial cystitis
- Prostatic cyst
- Seminal vesiculitis
- STDs
- Tuberculous/granulomatous prostatitis
- Urethritis or urethral pathology (stricture)

TREATMENT

- Antibiotic course normally extends for 6–8 wk and sometimes longer with refractory infections. Goal is to eradicate the nidus of infection in the prostate. Follow culture results.
- 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

Fluoroquinolones preferred. No difference in bacterial eradication between levofloxacin and ciprofloxacin, although prostatic fluid concentration of levofloxacin is higher than ciprofloxacin.

- Fluoroquinolones:
  - Ciprofloxacin, levofloxacin 500 mg/d for at least 6–8 wk
  - Trimethoprim-sulfamethoxazole
  - 60/80 mg b.i.d. for at least 6–8 wk
  - Tetracycline derivatives (eg, doxycycline) only if Chlamydia or Mycoplasma suspected

Second Line

Anti-inflammatories (ibuprofen) for symptoms:

- -Blockers (doxazosin, tamsulosin, alfuzosin, silodosin) may help with LUTS

SURGERY/OTHER PROCEDURES

- Not generally recommended
- TURP: Can be considered in select cases of refractory prostatitis with infected calculi and/or obstruction.

ADDITIONAL TREATMENT

Radiotherapy

Not recommended

Additional Therapies

- Frequent ejaculation (in patients with enlarged, symptomatically congested glands)
- Dietary modifications of common comestibles found to irritate the lower urinary tract
- Sitz baths for symptomatic relief

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Prostate massage (controversial):
  - May work by stimulating hibernating bacterial biofilms (making them more susceptible to antimicrobials), draining the obstructed inflamed ducts (allowing for better antimicrobial penetration), and stimulating blood supply to the area.
- Zinc supplements: Questionable benefit
- Phytotherapy:
  - Plant extracts and herbal medications (ie, saw palmetto) popular but may only be as effective as placebo

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 (3–6 mo) with a lower daily dose.
- Treating underlying obstruction or prostatic calculi if necessary may prevent further infections.

COMPLICATIONS

- Recurrent cystitis, epididymitis, urethritis
- CPPS
- Infertility (effect on semen quality debatable)
- Primarily effects QOL
- Unknown if predisposes to prostate cancer

FOLLOW-UP RECOMMENDATIONS

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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Asymptomatic Inflammatory (NIH IV)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Prostatitis, Chronic, Nonbacterial, Noninflammatory (NIH CP/CPPS III B)
- Prostatitis, General
- Prostatitis, Granulomatous
- Stamey Test (Meares-Stamey Test)

CODES

ICD9

– 041.9 Bacterial infection, unspecified, in conditions classified elsewhere and of unspecified site

– 601.1 Chronic prostatitis

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- CP/CPPS: Chronic prostatitis/chronic pelvic pain syndrome
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- EPS: Expressed prostatic secretion
- LUTS: Lower urinary tract syndrome
- NIH-CPSI: NIH Chronic Prostatitis Symptom Index
- PSA: Prostate-specific antigen
- PVR: Post void residual
- QOL: Quality of life
- STD: Sexually transmitted disease
- TURP: Transurethral resection of prostate
- US: Ultrasound
- UTI: Urinary tract infection
- VB 1: Voided bladder 1

- VB 2: Voided bladder 2
- VB 3: Voided bladder 3
- WBC: White blood cell

PROSTATITIS, CHRONIC NONBACTERIAL, NONINFLAMMATORY (NIH CP/CPPS III B)

Aisha K. Taylor, MD
Michael J. Wehle, MD
Anthony J. Schaeffer, MD

BASICS

DESCRIPTION

- CPPS or NIH Type III B is unexplained pelvic pain involving the groin, genitalia, or perineum, and may be associated with voiding symptoms occurring in the absence of pyuria or bacteruria.
- This was previously described by some as prostatodynia; the use of this term is currently discouraged.
- Many believe that the symptoms of CPPS in men closely relate to the similar symptom complex in women with interstitial cystitis.
- NIH classification and current definitions of prostatitis:
  - Type I: Acute bacterial prostatitis
  - Type II: Chronic bacterial prostatitis; recurrent infection
  - Type III: Chronic abacterial prostatitis/CPPS; no demonstrable infection:

    IIIA: Inflammatory chronic pelvic pain syndrome: WBCs present in semen/expressed prostatic secretions, or voided bladder urine (VB3)

    IIIB: Noninflammatory CPPS: WBCs not present in semen/expressed prostatic secretions or voided bladder urine (VB3)
  - Type IV: Asymptomatic inflammatory prostatitis: Detected by prostate exam or presence of WBCs in prostatic secretions during evaluation for other disorders

EPIDEMIOLOGY

- ~1 in 5 men with lower urinary tract symptoms typical of BPH likely have CPPS at the same time
- The annual prevalence in the general population of CPPS is 0.5%.
- CPPS is most prevalent in men 36–50 yr old, showing no apparent racial predisposition.

RISK FACTORS

- Psychologic stress and depression are associated with flare-ups of CPPS.
- Suggestion that inadequately treated episodes of acute prostatitis may increase risk for developing chronic prostatitis syndromes

PATHOPHYSIOLOGY

- Exact etiology is not determined, many theories:
  - 1 theory is that intraprostatic urinary reflux occurs, which may be secondary to dysfunctional voiding, causing high intraprostatic urine pressures.
  - Postulated that dysregulation of pro- and anti-inflammatory cytokines leads to inflammation from otherwise normal prostate bacteria
  - Dysfunction of the perineal afferent nerves causes heightened pain responses to otherwise normal stimuli in this region
  - Pelvic muscle tension myalgia or inflammation may be present.
- Other theories suggest fastidious organisms that cannot be easily cultured, autoimmune factors, or neuropathy.

COMMONLY ASSOCIATED CONDITIONS

- Anxiety, depression
- Chronic fatigue syndrome
- Chronic pain syndromes
- Functional somatic syndromes
- Myofascial pain syndrome
- Sexual dysfunction

DIAGNOSIS

HISTORY

- Severe pain characterized by:
  - Pelvic pain
  - Lower back pain
  - Perineal pain
  - Penile/scrotal pain
  - Pelvic floor muscle spasms
- Decreased libido
- Sexual dysfunction
- Painful ejaculation
- Irritative and obstructive voiding symptoms
- Impact of symptoms on QOL
- Identify specific triggers of symptoms: Foods, beverages, activities (physical, sexual)
- NIH-CPSI, a self-administered validated symptom index

PHYSICAL EXAM

- No uniformly distinguishing physical exam characteristics

- Exam of the genitalia may reveal vague widespread pelvic discomfort.
- DRE may reveal high anal sphincter tone.
- DRE revealing a severely tender prostate or bogginess may suggest acute bacterial prostatitis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Negative urethral, prostatic, and bladder cultures (VB1, VP2, EPS, and VB3 negative) (see Section II: “Stamey Test”)
- Normal prostatic secretions with no evidence of excess WBCs: Negative result is 10 WBCs per high-power field. Positive result is >10–20 WBCs per high-power field.
- Hematuria should prompt workup for other causes, such as carcinoma in situ.
- PSA may not be useful for CPSS but should be considered as part of prostate cancer screening.

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.
- Transrectal US performed in patients with pain on ejaculation may reveal enlargement of seminal vesicle caused by obstruction of ejaculatory duct as source of chronic pain.

Diagnostic Procedures/Surgery

- Mears-Stamey 4-glass test
- Videourodynamic evaluation sometimes reveals spastic dysfunction of the bladder neck or prostatic urethra, and can rule out underlying neurologic dysfunction.
- Cystoscopy to rule out interstitial cystitis as source of pain
- Anal sphincter electromyography and or sphincter function profiles can help diagnosis hypertonicity and failure of the pelvic floor musculature to relax.
- Uroflowmetry may demonstrate diminished flow with intermittency.

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis
- Anal fistula
- Bladder cancer or carcinoma in situ
- Bladder outlet obstruction/BPH
- Chronic bacterial prostatitis
- Chronic nonbacterial prostatitis
- Coccydynia
- Epididymo-orchitis

- GI diseases (diverticulosis, irritable bowel, celiac disease)
- Hernia (ventral, groin, sports hernia):
  - Sports hernia is a weakening of the posterior inguinal wall without a palpable hernia.
- Interstitial cystitis
- Myofascial pain syndrome
- Pelvic joint dysfunction
- Prostatic abscess
- Prostatic cyst
- Seminal vesiculitis
- STDs
- Tuberculous prostatitis
- Urethritis or urethral pathology

TREATMENT

- Management of NIH III A and NIH IIIB CPPS is similar.
- Attempt to identify specific and hopefully treatable causes for the symptoms.
- CPPS is generally considered a diagnosis of exclusion.
- Good physician–patient relationship is essential as many patients with CPPS have difficult-to-manage symptoms.
- Patient should understand that this is not a traditionally treatable disease but rather a chronic condition that can often be controlled.
- Use of NIH-CPSI or voiding diaries can be useful in monitoring progress.
- Multimodal therapy is usually required.
- Medical therapy is directed toward symptomatic relief.
- Empiric antibiotic therapy has a role in selected patients, although it may be more effective in NIH IIIA chronic prostatitis.
- -Blockers have become a primary therapy in the treatment of CPPS.

MEDICATION

First Line

- -Blockers:
  - Doxazosin 1–4 mg, then effective dose daily for 12 wk (can cause decrease in BP, headache)
  - Tamsulosin 0.4 mg once daily for 12 wk (can cause decreased ejaculate volume, headache; rarely, absent ejaculate, decrease in BP)
  - Alfuzosin 10 mg b.i.d. for 12 wk (can rarely cause decrease in BP, headache

– Contraindication: Moderate hepatic insufficiency, or with cytochrome P-450 3A4 inhibitors)

- Antimicrobial therapy:
  - Fluoroquinolones:

    Ciprofloxacin, levofloxacin 500 mg/d for 4 wk

    Common adverse events include dizziness, restlessness, headache, diarrhea, nausea, rash; rarely, convulsion, psychosis, severe hypersensitivity, tendon rupture
  - Trimethoprim-sulfamethoxazole:

    160/80 mg b.i.d. for 4 wk

    Common adverse events: Anorexia, nausea, vomiting, rash, urticaria

    Rarely: Blood dyscrasias, hypersensitivity, or photosensitivity, hepatic necrosis
- 5-Reductase inhibitors:
  - Finasteride 5 mg/d PO
  - Dutasteride 0.5 mg/d PO:

    Common adverse events: Decreased libido

Second Line

- Anti-inflammatories (ibuprofen)
- Pentosan polysulfate a semisynthetic mucopolysaccharide that may also have some anti-inflammatory properties. Dose used is 900 mg/d vs. standard dose of 100 mg PO t.i.d.
- Treatments directed at neuropathic-like pain:
  - TCAs:
  - Nortriptyline 10 mg PO q.h.s. working up to a maximum of 75–100 mg PO at bedtime (less sedation than amitriptyline)
  - Gabapentin or pregabalin
  - Opioids should not be widely used.

SURGERY/OTHER PROCEDURES

Not generally recommended:

- Transurethral microwave thermotherapy as a last option

ADDITIONAL TREATMENT

- Biofeedback
- Acupuncture
- Frequent ejaculation (in patients with enlarged, symptomatically congested glands)
- Prostatic massage; not currently popular
- Physical therapy
- Myofascial or trigger point release

- Acupuncture
- Physiologic counseling in cases with severe debilitating pain, stress, or tension with impact on overall psychologic functioning
- Low-dose diazepam (muscle spasm relief and anxiolytic) may help relieve myalgia in the pelvic floor muscles.
- TUMT and transurethral needle ablation have not been successful.
- Dietary modifications of common comestibles found to irritate the lower urinary tract

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Quercetin: A bioflavonoid with antioxidant properties that was reported to produce significantly greater improvement than placebo according to scores on the NIH-CPSI

ONGOING CARE

PROGNOSIS

Variable course with remissions and flare-ups

COMPLICATIONS

- None known
- Primarily effects QOL
- Unknown if CPPS predisposes to prostate cancer

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Long-term supportive care
- Following prostate cancer screening guidelines is recommended.

ADDITIONAL READING

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- Schaeffer AJ. Chronic prostatitis and the chronic pelvic pain syndrome. N Engl J Med 2006;355: 1690–1698.

See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Asymptomatic Inflammatory (NIH IV)

- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Prostatitis, General
- Stamey Test (Meares-Stamey Test)

CODES

ICD9

601.1 Chronic prostatitis

ABBREVIATIONS

- BP: Blood pressure
- BPH: Benign prostatic hypertrophy
- CP/CPPS: Chronic prostatitis/chronic pelvic pain syndrome
- DRE: Digital rectal exam
- EPS: Expressed prostatic secretion
- GI: Gastrointestinal
- NIH-CPSI: NIH Chronic Prostatitis Symptom Index
- PSA: Prostate-specific antigen
- QOL: Quality of life
- STD: Sexually transmitted disease
- TCA: Tricyclic antidepressant
- TUMT: Transurethral microwave thermotherapy
- US: Ultrasound
- VB 1: Voided bladder 1
- VB 2: Voided bladder 2
- VB 3: Voided bladder 3
- WBC: White blood cell

PROSTATITIS, CHRONIC NONBACTERIAL INFLAMMATORY (NIH CP/CPPS III A)

Aisha K. Taylor, MD

Anthony J. Schaeffer, MD

BASICS

DESCRIPTION

- NIH III A is classified as inflammatory CP/CPPS
- Formerly called chronic nonbacterial prostatitis (Stamey-Mears classification)
- Perineal, groin, and genital pain associated with the presence of WBCs in the semen after prostate massage urine specimen (VB3)
- Differentiated from NIH III B noninflammatory CPPS in NIH III B (WBCs are not present in semen/expressed prostatic secretions or voided bladder urine [VB3])
- The symptoms can have a significant impact on QoL.

EPIDEMIOLOGY

- Annual prevalence of CPPS in general population is 0.5%.
- Mean age is 42, but can present from age 20 onward.

RISK FACTORS

Not known

Genetics

Polymorphisms in the genes or promoters for IL-10 and TNF that result in decreased TNF production

PATHOPHYSIOLOGY

- Unknown but several theories
- Atypical infectious agent not routinely cultured
- It has been postulated that dysregulation of pro- and anti-inflammatory cytokines lead to inflammation from otherwise normal prostatic bacteria.
- A dysfunction of the nervous system leading to pain
- Psychologic factors also appear to be involved in producing symptoms.
- NIH classification and definitions of prostatitis:
  - I: Acute bacterial prostatitis
  - II: Chronic bacterial prostatitis; recurrent infection
  - III: Chronic abacterial prostatitis/CPPS; no demonstrable infection:

    IIIA: Inflammatory CPPS; WBCs present in semen/expressed prostatic secretions or voided bladder urine (VB3)

IIIB: Noninflammatory CPPS; WBCs not present in semen/expressed prostatic secretions or voided bladder urine (VB3)

– IV: Asymptomatic inflammatory prostatitis; detected by prostate biopsy or presence of WBCs in prostatic secretions during evaluation for other disorders

COMMONLY ASSOCIATED CONDITIONS

- Anxiety, depression
- Chronic pain and fatigue syndromes
- Fatigue
- Fibromyalgia
- Functional somatic syndromes
- Irritable bowel
- Sexual dysfunction
- Neurologic disease (often vertebral disk disease)
- Cardiovascular disease

DIAGNOSIS

HISTORY

- The symptoms of CP/CPPS are identical to those of a true prostatic infection.
- Pain, often severe, characterized by:
  - Pelvic pain
  - Lower back pain
  - Perineal pain
  - Penile/scrotal pain
  - Pelvic floor muscle spasms
  - Decreased libido
  - Sexual dysfunction
  - Painful ejaculation
  - Irritative and obstructive voiding symptoms
- Identify any comestibles that may aggravate the condition (dairy, caffeine, alcoholic beverages, breads, spicy foods, etc.).
- NIH-CPSI is a self-administered validated symptom index.

PHYSICAL EXAM

- Exam of the genitalia may reveal vague widespread pelvic discomfort.
- DRE may reveal high anal sphincter tone.
- DRE revealing a severely tender prostate, or bogginess may suggest acute bacterial prostatitis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Routine urine analysis and culture
- Negative urethral, prostatic, and bladder cultures (VB1, VP2, EPS, and VB3 all negative) (see Section II: “Stamey Test”)
- Normal prostatic secretions with evidence of excess WBCs (negative result is <10 WBC cells per HPF; positive result is >10–20 WBC per HPF)

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.
- TRUS performed in patients with pain on ejaculation may reveal enlargement of seminal vesicle caused by obstruction of ejaculatory duct as source of chronic pain.

Diagnostic Procedures/Surgery

- Stamey test (Mears-Stamey 4-glass test) (see Section II)
- Videourodynamic evaluation reveals spastic dysfunction of the bladder neck or prostatic urethra, and rules out underlying neurologic dysfunction.
- Cystoscopy rules out interstitial cystitis as source of pain.
- Anal sphincter electromyography and/or sphincter function profiles can help diagnosis hypertonicity and failure of the pelvic floor musculature to relax.
- Uroflowmetry may demonstrate diminished flow with intermittency.

Pathological Findings

Lymphocytic infiltrate of prostatic stroma suggestive of chronic inflammation

DIFFERENTIAL DIAGNOSIS

- Acute bacterial prostatitis (NIH I)
- Bladder cancer/CIS
- Chronic bacterial prostatitis (NIH II)
- Chronic nonbacterial inflammatory prostatitis (NIH III B)
- Coccydynia
- Epididymo-orchitis, chronic orchalgia
- GI diseases (diverticulosis, irritable bowel, celiac disease)
- Hernia (ventral, groin, sports):
  - Sports hernia is a weakening of the posterior inguinal wall without a palpable hernia.
- Interstitial cystitis
- Nerve root irritation (vertebral disk disease)

- Pelvic joint dysfunction
- Prostatic abscess
- Prostatic cyst
- Pudendal nerve entrapment
- STDs
- Tuberculous prostatitis

TREATMENT

- Management of NIH III A and NIH IIIB CPPS is similar.
- Attempt to identify specific and hopefully treatable causes for the symptoms.
- CPPS is generally considered a diagnosis of exclusion.
- Good physician–patient relationship is essential, as many patients with CPPS have difficulty managing symptoms.
- Patient should understand that this is not a traditionally treatable disease but rather a chronic condition that can often be controlled.
- Use of NIH-CPSI or voiding diaries can be useful in monitoring progress.
- Multimodal therapy is usually required.
- Medical therapy is directed toward symptomatic relief.
- Empiric antibiotic therapy has a role in selected patients, although may be more effective in NIH IIIA than NIH III B chronic prostatitis.
- -Blockers have become a primary therapy in the treatment of CPPS.

MEDICATION

First Line

- -Blockers:
  - Doxazosin 1–4 mg then effective dose daily for 12 wk
    Adverse events: Decrease in BP, headache
  - Tamsulosin 0.4 mg/d for 12 wk
    Adverse events: Decreased ejaculate volume, headache; rare, absent ejaculate, decrease in BP
  - Alfuzosin 10 mg b.i.d. for 12 wk
    Adverse events, rare: Decrease in BP, headache
    Contraindication: Moderate hepatic insufficiency, or with cytochrome P-450 3A4 inhibitors
- Antimicrobial therapy:
  - Fluoroquinolones:
    Common adverse events: Dizziness, restlessness, headache, diarrhea, nausea, rash

Rare: Convulsion, psychosis, severe hypersensitivity, tendon rupture

– Ciprofloxacin, levofloxacin 500 mg/d for 4 weeks

– Trimethoprim-sulfamethoxazole 160/80 mg b.i.d. for 4 wk:

Common adverse events: Anorexia, nausea, vomiting, rash, urticaria

Rare: Blood dyscrasias, hypersensitivity, or photosensitivity, hepatic necrosis

- 5-Reductase inhibitors:
  - Finasteride 5 mg/d PO or dutasteride 0.5 mg/d PO:

    Common adverse events: Decreased libido

Second Line

- Anti-inflammatory agents (eg, ibuprofen)
- Pentosan polysulfate:
  - Semi-synthetic mucopolysaccharide that may also have some anti-inflammatory properties
  - Dose used is 900 mg/d vs. standard dose of 100 mg PO t.i.d.
- Treatments directed at neuropathic-like pain:
  - TCAs:

    Nortriptyline 10 mg PO q.h.s. working up to a maximum of 75–100 mg PO at bed-time [C]

    Less sedation than amitriptyline
  - Gabapentin [C] or pregabalin [C]
  - Opioids [C] should not be widely used

ADDITIONAL TREATMENT

- Biofeedback
- Acupuncture
- Frequent ejaculation (in patients with enlarged, symptomatically congested glands)
- Prostatic massage; not currently popular
- Physical therapy
- Myofascial or trigger point release
- Acupuncture
- Physiological counseling in cases with severe debilitating pain, stress, or tension with impact on overall psychologic functioning
- Low-dose diazepam (muscle spasm relief and anxiolytic) may help relieve myalgia in the pelvic floor muscles.
- TUMT and transurethral needle ablation have not been successful.
- Dietary modifications of common comestibles found to irritate the lower urinary tract

ONGOING CARE

COMPLICATIONS

- Primarily effects QoL
- Unknown if predisposes to prostate cancer

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Long-term supportive care
- Following prostate cancer screening guidelines is recommended.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Asymptomatic Inflammatory (NIH IV)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III B)
- Prostatitis, General
- Stamey Test (Meares-Stamey Test)

CODES

ICD9

601.1 Chronic prostatitis

ABBREVIATIONS

- BP: Blood pressure
- CIS: Carcinoma in situ
- CP: Chronic prostatitis

- CPPS: Chronic prostatitis/Chronic pelvic pain syndrome)
- DRE: Digital rectal exam
- EPS: Expressed prostatic secretion
- GI: Gastrointestinal
- HPF: High-power field
- NIH-CPSI: NIH Chronic Prostatitis Symptom Index
- QoL: Quality of life
- STD: Sexually transmitted disease
- TCA: Trycyclic antidepressants
- TNF: Tumor necrosis factor
- TRUS: Transrectal ultrasound
- TUMT: Transurethral thermotherapy
- VB 1: Voided bladder 1
- VB 2: Voided bladder 2
- VB 3: Voided bladder 3
- WBC: White blood cell

PROSTATITIS, GENERAL

Michael S. Cookson, MD

Benjamin M. Whittam, MD

BASICS

DESCRIPTION

- Traditionally classified as: Acute bacterial prostatitis, chronic bacterial prostatitis, non-bacterial prostatitis, and prostatodynia

)[A]:

  - NIH Class I: Acute bacterial prostate; infection of prostate, sudden onset, often associated with UTI
  - NIH Class II: Chronic bacterial prostatitis; insidious onset, relapsing, recurrent UTI
  - NIH Class III: Chronic prostatitis (CP)/Chronic pelvic pain syndrome (CPPS):

    IIIA: Inflammatory: Inflammatory cells in prostatic secretion, seminal fluid, post prostatic massage urine

    IIIB: Noninflammatory: Insignificant inflammatory cells
  - NIH Class IV: Asymptomatic inflammatory prostatitis, incidental biopsy finding

- This section provides a brief overview of prostatitis. See each specific type for details of diagnosis and management

EPIDEMIOLOGY

- 2 million cases annually
- 9–16% men have had diagnosis of prostatitis
- 3–12% male outpatient urology visits
- Predominant age: 20–50 and >70 yr

RISK FACTORS

- Acute epididymitis
- Chronic catheterization (indwelling, condom)
- Dysfunctional voiding
- Immunocompromised states
- Intraprostatic ductal reflux
- Phimosis
- Prostatic calculi
- Transurethral surgery/instrumentation
- Unprotected anal sex
- UTI

Genetics

No known genetic patterns

GENERAL PREVENTION

- Proper treatment of acute bacterial prostatitis may reduce chronic bacterial prostatitis (NIH II)
- Safe sex practices

PATHOPHYSIOLOGY

- Extension of UTI
- Manipulation of urinary tract or prostate
- Bacterial:
  - Ascending infection through urethra
  - Refluxing urine into prostate ducts
  - Direct extension or lymphatic spread from rectum
  - Hematogenous spread
  - Calculi serving as nidus for infection
  - Aerobic gram-negative bacteria (Escherichia coli, Pseudomonas, Klebsiella, Proteus),

Neisseria gonorrhea, Enterobacteriaceae, Burkholderia pseudomallei)

  - Miscellaneous:

Chlamydia trachomatis

  - Gram-positive bacteria (Streptococcus faecalis, Staphylococcus aureus)
  - Organisms suspected, but unproven (Staphylococcus epidermidis, micrococci, non-group D Streptococcus, diphtheroids)
  - Uncommon:

Mycobacterium TB, parasitic, mycoses (blastomycosis, coccidioidomycosis, cryptococcus, histoplasmosis, paracoccidiomycosis, candidiasis)

- Nonbacterial:
  - Nonrelaxation (spasm) of the internal urinary sphincter and pelvic floor striated muscles leading to increased prostatic urethral pressure and intraprostatic urinary reflux; leading theory
  - Ureaplasma, Trichomonas vaginalis, and Chlamydia postulated, but not proven

COMMONLY ASSOCIATED CONDITIONS

- Cystitis (secondary to bacterial prostatitis)
- Epididymitis
- Prostatic hypertrophy
- STD

- Urethritis/urethral stricture
- UTI

DIAGNOSIS

HISTORY

- Acute bacterial prostatitis (NIH I):
  - Fever, chills, malaise
  - Perineal, suprapubic pain
  - Irritative voiding symptoms: Urgency, frequency, dysuria
  - Obstructive voiding symptoms: Hesitancy, intermittent stream, acute urinary retention
  - Rare sepsis
  - 5% will develop chronic prostatitis
- Chronic bacterial prostatitis (NIH II):
  - Recurrent UTIs
  - Asymptomatic or CPPS (see below)
- CP/CPPS (NIH IIIA/B):
  - Pain in perineum, suprapubic, penis, testicles, groin, low back
  - Pain especially after or during ejaculation
  - Irritative/obstructive voiding symptoms lasting >3 mo
  - ED, sexual disturbances, severe effect on quality of life
- NIH Class IV: None; usually only elevated PSA or nodule that prompts biopsy

ALERT

Do not perform massage or aggressive rectal exam in the face of acute prostatitis or prostatic abscess.

PHYSICAL EXAM

- Acute bacterial prostatitis (NIH I):
  - Suprapubic pain
  - Possible acute urinary retention
  - DRE: Hot, boggy, exquisite tenderness
  - Sepsis: Febrile, tachycardic
- Chronic bacterial prostatitis/CPPS (NIH II/IIIA/IIIB):
  - Unremarkable, except pain
  - DRE: May be normal or soft/boggy, variable amounts of pain, prostatic calculi

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PSA may be falsely elevated with prostatitis
- Suspected acute bacterial prostatitis:
  - Urine analysis, urine culture, CBC, blood culture
- Suspected CBP/CP/CPPS (NIH II/III):
  - Urine analysis, urine culture
  - Mears-Stamey 4-glass test

)[A]: Pre/post prostatic massage:

Urine microscopy and culture of midstream urine specimen prior to prostate massage (Pre-M)

Urine microscopy and culture of 10 mL urine post prostate massage (Post-M)

With NIH II(chronic bacterial):

Pre-M: ± urine WBC, ± culture

Post-M: + urine WBC, + culture

- NIH IIIA inflammatory CP/CPPS:
- Pre-M: – urine WBC, – culture
- Post-M: + urine WBC, – culture

- NIH IIIB non-inflammatory CP/CPPS:
- Pre-M: – urine WBC, – culture
- Post-M: – urine WBC, – culture

Imaging

- CT: Suspicion of abscess/malignancy or fail appropriate antimicrobial treatment
- Transrectal US: Suspicion of abscess or failure antibiotic therapy (rule out abscess, calculi)

Diagnostic Procedures/Surgery

- PVR if sensation of incomplete emptying
- Urodynamics: CPPS patients; debatable
- Cystoscopy: CPPS patients with hematuria; rules out bladder neck pathology, lower tract malignancy

Pathological Findings

- Sheets, clusters, nodules of lymphocytes, plasma cells in fibromuscular stroma
- No relationship to the ducts and acini
- Infiltrates of inflammatory cells restricted to the glandular epithelium and lumen found in prostatitis and BPH
- Variable appearance of inflammatory changes

DIFFERENTIAL DIAGNOSIS

- Acute urinary retention
- Cystitis (bacterial, interstitial)
- Obstructive bladder calculus
- Prostate cancer
- Prostatic abscess
- Pyelonephritis
- Urethritis

TREATMENT

- NIH I acute prostatitis:
  - IV antibiotics, then switch to oral agents
  - Acute retention may be treated with in-and-out catheter or small-caliber Foley for <12 hr or suprapubic drainage with acute prostatitis.
  - Acute bacterial prostatitis that does not resolve with conventional measures; must rule out prostate abscess
- NIH II: Long-term antibiotic therapy
- NIH IIIA/B: Similar management; empiric antibiotics often used with variable success; focus on symptomatic and supportive therapy
- NIH IV is only histologic diagnosis and no specific therapy necessary

MEDICATION

First Line

- Antibiotics:
  - Acute bacterial prostatitis (inpatient):
    Ampicillin IV 1–3 g q6h AND gentamicin
    Afebrile 24–48 hr may change to oral antibiotics
  - Acute bacterial prostatitis (outpatient):
    Trimethoprim-sulfamethoxazole DS PO b.i.d. for 4–6 wk
    Ciprofloxacin 500 mg PO b.i.d. for 4–6 wk
  - Chronic bacterial prostatitis:
    Ciprofloxacin 500 mg PO b.i.d. for 12 wk; levofloxacin may have better prostate penetration and q.d. dosing
    Fluoroquinolones more cost effective and may be superior to TMP/SMX
  - CP/CPPS:
    NIH IIIA: Antibiotics may reduce symptoms, but should work within 4–6 wk

)[A]

- -Adrenergic blockers:

)[B]

)[A]

- Anti-inflammatory agents:
  - NSAIDs
  - Analgesics
  - Antipyretics
- Stool softeners

Second Line

- Antibiotics: Erythromycin, azithromycin, clarithromycin if C. Trachomatis implicated
- Finasteride or dutasteride: Only if associated BPH in patients with CP/CPPS

SURGERY/OTHER PROCEDURES

- Transurethral resection: Prostatic abscess or prostate in intractable chronic bacterial disease
- Transurethral microwave therapy: Refractory chronic prostatitis

ADDITIONAL TREATMENT

- Numerous unproven therapies have been suggested with little to no evidence for treatment of CP or CPPS including: Allopurinol, balloon dilation, TUNA, acupuncture, neuromodulation (as below)
- Frequent ejaculation (in patients with enlarged, symptomatically congested glands), prostatic massage (not in acute prostatitis)
- Dietary modifications of common comestibles found to irritate the lower urinary tract
- Sitz baths for symptomatic relief

COMPLEMENTARY AND ALTERNATIVE MEDICINE

)[B]

- Neuromodulation (CP/CPPS): Amitriptyline, gabapentin, acupuncture, biofeedback, massage, neurostimulation

ONGOING CARE

PROGNOSIS

- Prolonged course, often difficult to cure
- 50–97% cure rate, depending upon category
- 20% with recurrent or persistent infection

COMPLICATIONS

- Acute urinary retention
- Chronic bacterial prostatitis with incomplete treatment of acute bacterial prostatitis
- Epididymitis, orchitis, seminal vesiculitis (rare)

- Gram-negative sepsis, bacteremia
- Prostatic abscess

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Most improve with antibiotic in 3–4 wk with infection
- Long-term management of CP/CPPS requires multimodality therapy and supportive care

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH I)
- Prostatitis, Asymptomatic Inflammatory (NIH IV)
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Prostatitis, Chronic, Nonbacterial, Noninflammatory (NIH CP/CPPS III B)
- Prostatitis, General Algorithm
- Prostatitis, Granulomatous
- Stamey Test (Meares-Stamey Test)

CODES

ICD9

- 601.0 Acute prostatitis
- 601.1 Chronic, subacute prostatitis
- 601.9 Prostatitis not otherwise specified

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- CP: Chronic prostatitis
- CPPS: Chronic pelvic pain syndrome
- CT: Computed tomography
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- NSAID: Nonsteroidal anti-inflammatory drug
- PSA: Prostate-specific antigen
- PVR: Post void residual
- STD: Sexually transmitted disease
- TMP/SMX: Trimethoprim sulfamethoxazole
- TUNA: Transurethral needle ablation
- US: Ultrasound

- UTI: Urinary tract infection

PROSTATITIS, GRANULOMATOUS

Stephen E. Strup, MD

Bradley W. Warner, MD

BASICS

DESCRIPTION

- Inflammation of the prostate associated with granuloma formation. Often confused with carcinoma of the prostate
- Can be caused by infectious and noninfectious etiologies

ALERT

The DRE cannot differentiate between prostate nodules due to granulomatous prostatitis and prostate cancer. Biopsy is essential to differentiate the 2 entities.

EPIDEMIOLOGY

0.8–1% of benign inflammatory prostatic specimens

RISK FACTORS

- Infectious: Bacterial, viral, fungal, parasitic, including Mycobacterium, STDs
- HIV infection may increase risk for tuberculous prostatitis
- Iatrogenic causes: TURP, BCG instillation therapy for bladder cancer. 40% of patients receiving intravesical BCG may develop granulomatous prostatitis
- Systemic granulomatous diseases: Wegener granulomatosis, Churg-Strauss syndrome, sarcoidosis, rheumatoid arthritis, polyarteritis nodosa, malakoplakia
- Idiopathic: No specific cause identified, theorized that blockage causes prostatic secretions to escape into the stroma and cause a granulomatous reaction. May account for the majority of cases.

PATHOPHYSIOLOGY

- Specific subtype: Caused by identifiable infectious agent (mycobacterium, fungi, syphilis, brucellosis, virus, parasites). With TB often associated with systemic infection. With HIV TB may cause prostatic abscess.
- Nonspecific subtype: Usually an incidental finding on biopsy (0.3–3.0%)
- Iatrogenic: After TURP or needle biopsy, necrotizing lesions may resemble lesions associated with rheumatoid diseases
- Eosinophilic subtype: Very rare, may suggest allergic etiology:
  - Usually associated with systemic condition (asthma, Wegener, Churg-Strauss syndromes)
- Autoimmune-based: HLA-DR15 linked T-cell–mediated response against PSA

COMMONLY ASSOCIATED CONDITIONS

May be associated with systemic conditions (asthma, Wegener granulomatosis, Churg-Strauss syndrome, sarcoidosis, rheumatoid arthritis, polyarteritis nodosa, malakoplakia)

DIAGNOSIS

HISTORY

- Often asymptomatic
- Previous UTI or STD:
  - Syphilis, TB, or other infectious agent
  - Often associated with UTI 2–3 mo prior to onset of symptoms
- History of LUTS:
  - Irritative voiding symptoms, including urgency, frequency, dysuria
  - Obstructive voiding symptoms, including acute urinary retention
- Systemic granulomatous disease:
  - If associated with systemic vasculitis or granulomatous disease, may have constitutional symptoms or signs
- History of prostate surgery or bladder cancer:
  - BCG or TURP can cause granulomatous prostatitis.
- Fever, chills, or other constitutional signs:
  - Suggest infectious, systemic etiology

PHYSICAL EXAM

Rectal exam: Hard, indurated gland with/without nodule:

- Tender vs. painless
- Tuberculous prostatitis should be suspected with a draining perineal fistula.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Leukocytes may be present during UTI.
- Urine cultures are often sterile.
- Blood sampling may reveal elevated sedimentation rate, acid phosphatase, or eosinophilia
- May have transient rise in PSA
- If evidence of TB or mycotic disease, appropriate tests should be ordered:
  - AFB stain of urine and semen
  - TB cultures may take up to 10 wk
  - PCR: Genomic amplification of M. tuberculosis–specific DNA allows rapid identification of TB. High sensitivity and specificity, with results in 48 hr.

Imaging

- Transrectal US has limited utility.
- Granulomatous prostatitis can appear as a focal hypoechoic area with a nodular appearance similar to prostate cancer.

Diagnostic Procedures/Surgery

Prostate biopsy is definitive test.

Pathological Findings

- Histologically, shows noncaseating granuloma, prominent macrophage infiltrate with occasional multinucleated giant cells (Langerhans cells) that are characteristic of all granulomas:
  - Immunohistochemistry for cytokeratin (CAM 5.2) may stain glands positive, but not the infiltrate. Infiltrate stains for the macrophage marker, CD68.
- Fibrotic tissue replaces parenchyma.

DIFFERENTIAL DIAGNOSIS

- Nodular rectal exam (neoplasm, malignant):
  - Lymphoma: Primary and secondary
  - Prostatic adenocarcinoma
  - Sarcoma, small-cell carcinoma, and other rare tumors and metastases
  - Transitional cell carcinoma
- Nodular rectal exam (benign):
  - Benign prostatic hyperplasia
  - Calculus/calcification
  - Ejaculatory duct cyst
  - Granulomatous prostatitis
  - Prostatic intraepithelial neoplasia
  - Scarring from previous surgery or infection
- Rectal wall lesions (thrombosed hemorrhoid, carcinoma, etc.)

TREATMENT

- Spontaneous resolution of symptoms usually occurs, but rectal exam findings may persist.
- May need to rule out prostate cancer.
- Antibiotics for documented UTI.
- Symptomatic treatment may be given:
  - Sitz baths, fluids, anti-inflammatory and other symptomatic medications
- Temporary transurethral urinary catheterization if symptoms are severe or retention of urine is present

MEDICATION

- Antibiotics
- Antituberculous agents:
  - Used only if documented infectious cause
  - Isoniazid, rifampin, pyrazinamide, and either ethambutol or streptomycin should be the initial regimen, with change based on the isolate sensitivities. Pyridoxine (vitamin B6) 25–50 mg/d to prevent INH neuropathy.

SURGERY/OTHER PROCEDURES

10% of cases can be refractory to conservative management and eventually require prostatectomy.

ADDITIONAL TREATMENT

Some advocate corticosteroids and antihistamines in idiopathic cases.

ONGOING CARE

PROGNOSIS

Most will spontaneously resolve; physical exam, DRE findings may persist for years.

COMPLICATIONS

- Undetected prostate cancer
- Acute urinary retention
- If infectious in etiology, may pass organism to sexual partner
- Infertility possible

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Despite a previous history of granulomatous prostatitis on biopsy, abnormal glands may need to be rebiopsied so as not to miss a concomitant cancer.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate Nodule
- Prostatitis, General
- Prostatitis, Tuberculous

CODES

ICD9

601.8 Other specified inflammatory diseases of prostate

ABBREVIATIONS

- AFB: Acid-fast bacillus
- BCG: Bacillus Calmette-Guérin
- BPH: Benign prostatic hyperplasia
- DRE: Digital rectal exam
- HIV: Human immunodeficiency virus
- LUTS: Lower urinary tract symptoms
- PCR: Polymerase chain reaction
- PSA: Prostate-specific antigen
- STD: Sexually transmitted disease
- TB: Tuberculosis
- TURP: Transurethral resection of prostate
- US: Ultrasound
- UTI: Urinary tract infection

PROTEINURIA

Neil H. Grafstein, MD
Oluyemi Akin-Olugbade, MD

BASICS

DESCRIPTION

- Persistent abnormal amounts or types of protein in the urine:
  - May be 1st indication of renal disorders either primary (eg, proliferative glomerulonephritis) or secondary (eg, HTN, lupus nephritis, 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:
    Earliest sign of diabetic nephropathy
    Identifies those at risk of cardiovascular disease in both diabetic and nondiabetic populations
- Important to distinguish between benign (no long-term renal significance) and pathologic causes of proteinuria. Can often differentiate based on:
  - Associated clinical findings (eg, known diabetes or HTN; edema and lipiduria in nephrotic syndromes)
  - Persistency of proteinuria:
    Transient or intermittent proteinuria is unlikely to be associated with significant renal pathology.
    Example etiologies: Exercise, emotional stress, fever, orthostatic proteinuria
    Document proteinuria on >1 visit
  - Degree of proteinuria:
    500 mg/24 hr usually heralds significant glomerular disease
    Proceed to quantitative measurement when dipstick is persistently positive

EPIDEMIOLOGY

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- Increases with age
- Higher in patients with DM:

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- African Americans afflicted with higher levels of proteinuria due to increased risk of associated diseases

- Orthostatic proteinuria in 2–5% of adolescents:
  - Uncommon in age >30 yr:

    Increased protein excretion in the upright position. Resolves in supine position.

    No therapy required, often resolves with time

RISK FACTORS

- DM
- HTN
- Obesity (BMI >35 kg/m2), but progression to renal disease not proven

Genetics

Disease-specific

GENERAL PREVENTION

):

  - Not cost effective in patients without risk factors

)

- Screening for proteinuria during prenatal care to rule out preeclampsia, nephrotic syndrome

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 hypoalbuminemia, lipiduria, edema, ascites)
- Tubular proteinuria:
  - Inability of proximal convoluted tubule to absorb low-molecular-weight proteins such as immunoglobulin light chains, 2-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 immunoglobulins and low-molecular-weight proteins.
- Tissue proteinuria:
  - Associated with acute inflammation of urinary tract due to cystitis, acute prostatitis, and urinary tract tumors
- Transient proteinuria:
  - Glomerular permeability and decreased tubular reabsorption have both been proposed as possible mechanisms.

COMMONLY ASSOCIATED CONDITIONS

- See “Differential Diagnosis.”
- Hypercoagulability, lipiduria, edema, and hypoalbuminemia (nephrotic syndrome)

DIAGNOSIS

HISTORY

- Presence of underlying systemic disease:
  - DM, HTN, autoimmune disorders, cardiac disease, multiple myeloma
- Triggers of transient proteinuria:
  - 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)

PHYSICAL EXAM

- BP measurement to rule out HTN
- Edema with nephrotic syndrome, heart failure
- Papilledema: Uncontrolled HTN
- Jugular venous pressure elevation, heart sounds (heart failure, HTN)
- Abdominal bruits: Renal artery stenosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- 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)
  - False positive: Alkaline urine; concentrated urine; contamination with blood; recent IV contrast dye
  - False negative: Dilute urine; dipstick only detects albumin and will miss other plasma proteins (eg, Bence-Jones proteinuria in multiple myeloma)
- Urinalysis for associated hematuria, casts (glomerulonephritis)
- 3% sulfosalicylic acid:
  - Detects all types of proteinuria
  - Strongly consider in patients with acute renal failure and negative or trace protein on dipstick to rule out myeloma
- Split urine collection: Daytime (7 AM to 11 PM) and overnight (11 PM to 7 AM) to rule out orthostatic proteinuria

- Albumin-to-creatinine ratio or total protein-to-creatinine ratio in a random urinary sample:
  - Quantitative test that is reliable and not dependent on concentration. Less cumbersome than 24-hr collection
  - Corresponds to 24-hr albumin excretion in a linear manner (eg, ratio of 3 = 3 g/24 hr)
  - Serial measurements monitor therapeutic response
  - Preferred screening strategy for diabetic patients
  - 2 out of 3 positive tests separated by 3–6 mo considered persistent proteinuria
- Serum creatinine to rule out renal insufficiency
- Albumin, cholesterol: Nephrotic syndrome
- Blood glucose: DM
- Urine protein electrophoresis: To assess for light chain immunoglobulins/Bence-Jones proteins associated with multiple myeloma
- Others as indicated: Hepatitis and/or HIV testing, autoantibodies (ANA, etc.)

Imaging

- Renal US in cases of persistent proteinuria to rule out anatomic abnormality
- 3-phase CT if renal function sufficient and associated hematuria

Diagnostic Procedures/Surgery

Tissue analysis:

)[C]:

- Proteinuria with hematuria
- Prolonged ARF of unknown etiology
- Nephrotic proteinuria
- Transplanted kidney

Pathological Findings

Depends on underlying etiology

DIFFERENTIAL DIAGNOSIS

- Glomerular proteinuria:
  - IgA nephropathy
  - Diabetic nephropathy
  - Medications (eg, NSAIDs, captopril, lithium)
  - Minimal change
  - Primary glomerulonephritides
  - Autoimmune (eg, SLE, amyloidosis)

- Tubular proteinuria:
  - Obstructive uropathy
  - Toxins and drugs
  - Fanconi syndrome
- Overflow proteinuria:
  - Multiple myeloma
  - Monoclonal gammopathy of unknown significance
  - Rhabdomyolysis causing myoglobinuria
  - Any hemolytic state causing hemoglobinuria
- Transient proteinuria:
  - Fever
  - Strenuous exercise
  - Emotional stress
  - Pregnancy
  - Cold exposure
  - Orthostatic proteinuria

TREATMENT

- Treat specific underlying etiology.
- All patients with persistent proteinuria should be referred to a nephrologist.
- Hematology-oncology evaluation for patients with Bence-Jones protein for treatment of multiple myeloma

)[B]

- Strict glycemic and BP control in diabetics
- Salt/fluid restriction for edema associated with nephrotic syndrome

MEDICATION

First Line

)[A]:

- Can reduce protein excretion by 35–45%
- Lisinopril 2.5 mg/d PO; increase as tolerated
- Ramipril 2.5–5 mg/d PO, 20 mg/d max
- Captopril 12.5–25 mg PO b.i.d./t.i.d., 50 mg t.i.d. max

Second Line

Angiotensin II receptor antagonists:

- Use if side effects such as cough and angioedema develop from ACE inhibitors
- Candesartan, eprosartan, irbesartan, losartan, valsartan

- Calcium channel blockers: May be better for HTN with less renal effect in the relatively ischemic kidney

ONGOING CARE

PROGNOSIS

Isolated proteinuria; degree-dependent:

- Nonnephrotic proteinuria has low risk of progressive kidney disease
- 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

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COMPLICATIONS

- Progression to renal failure
- Proteinuria is a marker for overall cardiovascular health.

FOLLOW-UP RECOMMENDATIONS

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

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See Also (Topic, Algorithm, Electronic Media Element)

- Glomerulonephritis, Acute
- Glomerulonephritis, Chronic
- Proteinuria Algorithm
- Renal Failure, Acute
- Renal Failure, Chronic
- Section IV: Urinalysis and Urine Studies

CODES

ICD9

- 593.6 Postural proteinuria
- 791.0 Proteinuria

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ANA: Antinuclear antibody
- ARF: Acute renal failure
- BP: Blood pressure
- DM: Diabetes mellitus
- ESRD: End-stage renal disease
- HIV: Human immunodeficiency virus
- HTN: Hypertension
- NSAID: Nonsteroidal anti-inflammatory drug
- PCT: Proximal convoluted tubule
- SLE: Systemic lupus erythematosus

PRUNE BELLY (TRIAD) SYNDROME

Richard Natale, II, MD
Michael J. Erhard, MD

BASICS

DESCRIPTION

- Prune belly refers to the classic appearance of abdominal wall wrinkling and budging flanks caused by varying degrees of abdominal wall deficiency, found almost exclusively in males.
- Triad:
  - Deficient abdominal musculature
  - Bilateral cryptorchidism
  - Urinary tract anomalies (eg, dilated prostatic urethra, renal dysplasia, hydroureteronephrosis)
- Incomplete variants lack abdominal wall features; females lack gonadal anomalies
- 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; moderate renal insufficiency and moderate hydroureteronephrosis; pulmonary hypoplasia not prominent
  - Type III: Mild features of triad or incomplete variant; no evidence of pulmonary hypoplasia
- Synonyms: Eagle-Barrett or Triad syndrome

EPIDEMIOLOGY

- 1:29,000–1:40,000 live births
- 95% males
- Higher incidence in blacks, children born to young mothers

RISK FACTORS

Exact mechanism unknown:

- Early in utero posterior urethral obstruction
- Primary defect in lateral plate mesoderm
- Yolk sac defect

Genetics

- Most cases are sporadic, with normal karyotype.
- Potential inheritance patterns in familial cases (2-step autosomal dominant; sex-influenced autosomal recessive; X-linked)

- Majority of twins discordant for PBR suggests nongenetic basis

GENERAL PREVENTION

Aimed at preserving renal function and preventing UTI

PATHOPHYSIOLOGY

- Basic defect thought to be related to fetal developmental anomaly of intermediate and lateral mesoderm
- Abdominal defects due to deficient musculature medially and inferiorly:
  - May be partial hypoplasia of the abdominal wall to complete absence of musculature
- Testes:
  - Usually intra-abdominal (over iliac vessels)
  - Epididymis poorly attached
  - Descent in part affected by mechanical forces (eg, large bladder, low intra-abdominal pressures)
- Kidneys:
  - Dysplasia in 50%, to varying degrees
  - Nonobstructive hydronephrosis is common; does not correlate to degree of dysplasia
- Ureters:
  - Dilated, tortuous, and redundant; distal > proximal
  - Increased ratio of collagen to smooth muscle
  - Poor peristalsis and ureteral coaptation lead to stasis and reflux
- Bladder:
  - Enlarged with no significant hypertrophy
  - May have urachal pseudodiverticulum
  - Urachus patent in up to 30%
  - Increased ratio of collagen to smooth muscle
  - Urodynamics commonly show normal compliance, delayed sensation, large capacity; 50% void with normal pressures and flow, and have low postvoid residuum
- Prostatic urethra:
  - Dilated urethra due to prostatic hypoplasia
  - 20% can have distal obstructive lesions (eg, valves, atresia, stenosis)
- Anterior urethra:
  - Usually normal
  - Most common abnormalities: Megalourethra and urethral atresia (latter can be fatal unless urachus is patent)

- Megalourethra can be caused by transient obstruction
- Fusiform: Defect in corpus cavernosum and spongiosum; entire phallus dilates on voiding
- Scaphoid: Defect in corpus spongiosum; only ventral urethra dilates

- Fertility:
  - Usually infertile (rare cases of paternity with sperm retrieval) due to azoospermia
  - Histologic defect in testes
  - Atretic vas deferens and seminal vesicles
  - Retrograde ejaculation from incompetent bladder neck

COMMONLY ASSOCIATED CONDITIONS

- Turner syndrome, trisomy 13 and 18, Beckwith-Wiedemann syndrome
- Malrotation of gut
- Imperforate anus (rare)
- Pulmonary complications at birth (hypoplasia, pneumothorax) due to oligohydramnios
- Cardiac anomalies

DIAGNOSIS

HISTORY

- Gestational history (eg, oligohydramnios, prenatal hydronephrosis)
- 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
- Lungs/chest: Auscultate for pneumothorax; evaluate for pectus excavatum/carinatum
- GI: Associated with gastroschisis or omphalocele; imperforate anus; intestinal malrotation, atresia, or stenosis
- Urologic: Evaluate meatus, observe urinary stream, attempt to palpate testes
- Abdomen: Wrinkled, redundant skin over lower abdomen with bulging flanks
- Extremities: Observe for dimpling on lateral aspect of knees, knock knees, clubfoot, hip dislocation, scoliosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Serum electrolytes, urea nitrogen, and creatinine:

- Nadir creatinine <0.7 ng/dL is predictive of adequate renal function through childhood.
- Urinalysis and urine culture

Imaging

- Chest x-ray (pneumothorax)
- Renal/bladder US (degree of renal dysplasia and hydroureteronephrosis)
- Radioisotope studies (technetium-99m/99Tc):
  - DMSA at 4–6 wk to assess renal parenchymal function
  - MAG3 scan to assess presence/degree of obstruction
  - Consider magnetic resonance urography

Diagnostic Procedures/Surgery

VCUG:

- Perform while on antibiotic prophylaxis
- Reflux in up to 75% of cases
- Large bladder and dilated prostatic urethra tapering to membranous urethra

Pathological Findings

Renal dysplasia on biopsy

DIFFERENTIAL DIAGNOSIS

- Megacystis microcolon
- Intestinal hypoperistalsis syndrome (marked female predominance)

TREATMENT

- Demonstrate proper bladder emptying
- UTI prophylaxis
- Avoid instrumentation early to reduce UTI risk
- Follow renal function

MEDICATION

UTI prophylaxis:

- Ampicillin 25 mg/kg/d as neonates
- Then, trimethoprim-sulfamethoxazole 2 mg/kg once daily or nitrofurantoin 1–2 mg/kg once daily beyond 2 mo of age

SURGERY/OTHER PROCEDURES

- Prenatal: Vesicoamniotic shunting for oligohydramnios (controversial)
- Circumcision to reduce incidence of UTI
- Urinary tract reconstruction (eg, reimplant) is controversial due to potential for improvement or resolution, stabilization of function, or need for eventual renal transplantation
- Early intervention may be warranted with progressive/severe hydronephrosis, progressive renal failure, or recurrent UTIs:

– Temporary cutaneous vesicostomy or bilateral cutaneous pyelostomies (avoid proximal ureterostomies)

– Ureteral reimplantation with/without tapering

- Reduction cystoplasty reserved for large urachal diverticulum or as part of extensive reconstruction, since large-capacity bladders with large residual volumes tend to recur
- Orchidopexy:

– Transabdominal, Fowler-Stephens, or microvascular autotransplantation, preferably done by 1 yr of age or in combination with other procedures:

– Rare cases of germ cell neoplasia

- Abdominal wall reconstruction for cosmesis, may help pulmonary and bladder function

ONGOING CARE

PROGNOSIS

- Degree of renal dysplasia most important determinant of long-term survival
- Up to 1/3 develop renal failure and will require dialysis/renal transplantation

COMPLICATIONS

- Renal failure
- Respiratory failure (early)
- Urosepsis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Serial evaluation of renal function and for UTIs
- Imaging is individualized

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Polyhydramnios/Oligohydramnios
- Undescended Testes (Cryptorchidism)

CODES

ICD9

756.71 Prune belly syndrome

ABBREVIATIONS

- DMSA: Dimercaptosuccinic acid
- GI: Gastrointestinal
- MAG3: Mercaptoacetyltriglycine
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

PSA ELEVATION FOLLOWING LOCAL THERAPY FOR PROSTATE CANCER

Amit R. Patel, MD
Eric A. Klein, MD

BASICS

DESCRIPTION

- Rising PSA after local therapy for nonmetastatic CaP that occurs after initial local therapy, otherwise known as biochemical recurrence or PSAR:
  - Definition varies with respect to treatment modality.
  - RP eliminates the source of PSA, and serum PSA values should become undetectable within 6 wk of surgery (<0.2 ng/mL standard assay)
  - After RP: PSA >0.2 ng/mL and rising as confirmed on a repeat test (AUA guidelines for T1/T2/N0/M0 disease)
  - RT does not eliminate all prostatic epithelium and may take 1–2 yr to reach posttreatment nadir
  - After RT: 3 consecutive PSA rises after reaching a nadir with the date of failure defined as the midpoint between the PSA nadir and the 1st rise (ASTRO definition); or PSA nadir + 2 ng/mL (Phoenix definition); the Phoenix definition is now preferred

EPIDEMIOLOGY

- In 2009, 192,280 men were diagnosed with CaP in the US:
  - 90% will undergo local therapy.
  - ~35% (70,000 patients) will have biochemical recurrence within 10 yr.
  - ~50,000 patients have PSA-only recurrence each year.
- Natural history:
  - Following biochemical recurrence, long but variable:
    Recent studies demonstrate >16 yr median time to CaP specific mortality.

RISK FACTORS

- Following RP, risks factors for PSA progression include pathologic Gleason score, positive surgical margins, extracapsular extension, seminal vesicle invasion
- Following RT, risk factors for PSA progression include Gleason score, percentage of positive biopsy cores, clinical stage, androgen deprivation duration, and radiotherapy dose.
- PSADT, pathologic Gleason score, and time to PSA recurrence are all individual risk factors for CaP death following PSA recurrence after RP:
  - All 3 variables are highly correlated.

- PSADT is a significant factor to risk-stratify patients:
  - PSADT <3 mo associated with high risk of death from CaP
  - PSADT should be evaluated on a continuum rather than on a set cutoff value.
- Gleason score:
  - Patients with score of 8 have >2.2 times risk of death from CaP than those with <8 on RP specimen with PSA recurrence.
- Years from RP to PSA recurrence:
  - Patients with <3 yr to PSA recurrence have >3.5 times risk of death from CaP than patients with >3 yr time to PSA recurrence.

DIAGNOSIS

HISTORY

- Cancer-specific history:
  - Initial PSA
  - Biopsy information
  - Primary local therapy details (ie, XRT dose)
  - Pathologic stage, Gleason, margin status if RP performed
  - Post-treatment PSA values/dates
  - Current symptoms
- Beware PSA bounce: Transient rise in PSA (typically <1 ng/mL) in 10–12% of men following radiation therapy, typically 24 mo after treatment; usually returns to baseline
- PSA levels remaining undetectable for 2–4 yr after RP and then gradually rising likely indicate local recurrence:
  - If PSA never falls or rapidly rises following RP, suspect systemic disease

PHYSICAL EXAM

DRE for evidence of recurrence

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- The 1st preoperative PSA should be obtained 6 wk–3 mo following therapy (AUA guidelines).
- Ultrasensitive PSA may detect serum PSA sooner than conventional PSA tests, but PSA kinetics will determine clinical significance.

Imaging

- Imaging (CT abdomen/pelvis or bone scan) limited in the setting of early PSA recurrence:
  - Low yield to detect occult micrometastatic disease that may be the source of PSA recurrence

– The tests have significant value when the PSA is >50 ng/mL or there is a rapid PSA velocity (>0.5 ng/mL/mo).

• ProstaScint scan (Indium111 capromab pendetide) uses a monoclonal antibody against the PSMA to determine the site of recurrence. FDA-approved for use in men with a PSA recurrence after RP. Variable results for fossa or nodal recurrence may limit use in clinical decision making.

• Endorectal MRI and PET scans are not yet mainstream tests to evaluate biochemical recurrence.

Diagnostic Procedures/Surgery

• TRUS-guided biopsy (TRUS biopsy) has a limited role in localizing the recurrence and guiding secondary treatment options:

– Doppler flow in fossa indicate likely recurrence.

– Prostatic fossa biopsies are not correlated with radiation therapy response after RP.

DIFFERENTIAL DIAGNOSIS

• Benign source of prostate tissue either left behind with surgery or ectopic benign prostate tissue

• Local recurrence of CaP

• Local recurrence with micrometastatic disease

• Systemic/metastatic disease

TREATMENT

The key is to determine whether:

• The PSA rise is due to local recurrence, systemic recurrence, or both; and

• Distinguish between high- and low-risk patient to prevent disease progression or CaP mortality.

MEDICATION

• ADT, also referred to as hormonal therapy:

– Controversial in PSA-only recurrence due to the lack of existing studies demonstrating benefit in this setting

– Not benign therapy, as significant side effects exist affecting QoL: Hot flashes, bone loss, increased fracture risk, sexual dysfunction, loss of libido, memory loss, increased fat deposition, loss of muscle mass, metabolic changes (ie, insulin resistance, hypercholesterolemia) that increases risk of heart disease

– Benefits may include delayed time to metastasis and prolonged survival.

• CAB:

– Consists of combination LHRH agonist with androgen receptor blockage

– Meta-analysis for use in metastatic disease suggests a 7–20% relative reduction in CaP death.

– May be used for PSA-only CaP recurrence after evaluative risk stratification suggests poor prognosis

- Surgical castration provides unimodal androgen blockage:

– Numerous studies have compared castration to CAB with mixed results; the studies support the use of either in metastatic disease

– Costs of castration is <CAB

– The risks of androgen deprivation vs. the benefits must be evaluated prior to castration.

- Retrospective studies evaluating the timing of ADT in PSA-only recurrence support the use of early therapy, especially in high-risk patients:

– For failed RT, men started on ADT with PSA <20 ng/mL have a 12-mo survival advantage over men started on ADT with PSA >20 ng/mL

– In high-risk men (Gleason >8, PSADT <12 mo), ADT started when the PSA <10 ng/mL may provide a 50% risk reduction for metastasis at 3-yr follow-up.

SURGERY/OTHER PROCEDURES

Salvage RP is an option for local recurrence after seeds or external radiation:

- Contemporary studies demonstrate cancer-specific survival rates of 63–73%.
- Complications rates are worse than primary RP.
- QoL measures are worse than primary RP.
- Time from PSA failure to salvage RP has been historically long; thus 20% require cystoproctostomy.
- 50–75% of men may have long-lasting or permanent incontinence.

ADDITIONAL TREATMENT

- Salvage RT:

– After RP:

Large series have reported 5-yr progression-free probabilities at 40–45%.

Long-term progression-free survival may be suboptimal, with 10-yr rates at 20%.

Absolute PSA at treatment initiation is an important variable in outcomes: Treatment initiated earlier has better outcomes.

Predictors of death from CaP, including rapid PSADT, high-grade disease, and early recurrence may not predict salvage RT outcomes. Thus, these patients may be candidates for salvage RT.

Impact of salvage RT for survival remains unknown.

Generally, dose should be 64–70 Gy.

Studies suggest it may be best to radiate before PSA >2.0 ng/mL, but some advocate starting RT at lower PSA levels.

– Salvage RT after RT:

The use of salvage brachytherapy following the failure of RT is highly controversial and should only be performed in the setting of a clinical trial.

- Salvage cryotherapy:
  – After RT failure:

3rd-generation cryotherapy probes have decreased in size, using an approach similar to brachytherapy.

Incontinence rates have been reported as low as 10%; this is an appealing option for men who are reluctant to undergo salvage RP due to high risk of incontinence and other morbidity.

Recurrence rates range from 25–60%, with a 5-yr recurrence rate of 60%, with recurrence defined as PSA nadir + 2 ng/mL.

Factors predicting favorable response include pre-cryotherapy PSA <10 ng/mL, PSADT <16 mo, preradiation clinical stage T1/T2, biopsy Gleason 7, and no hormonal treatment during the initial radiation treatment.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- COX-2 inhibitors:
  – Initial studies demonstrated decreased PSA velocity compared to placebo.
  – Increased cardiac risks with therapy have halted clinical trials using these medications.
- Pomegranate juice:
  – Increasing in popularity as a chemo-preventative agent as well as an alternative to hormonal therapy for PSA recurrence.
  – Phase II trials demonstrate excellent tolerability as well as increased PSADT compared to placebo.

ONGOING CARE

PROGNOSIS

Prognosis depends on numerous factors, including the initial treatment modality, baseline tumor characteristics, clinical stage, as well as the risk factors discussed above:

- PSADT, pathologic Gleason score, and time to recurrence are important variables in determining prognosis and treatment.

• PSADT <3 mo has been shown to be a significant poor prognostic sign for cancer-specific and overall survival.

COMPLICATIONS

All therapies have unique complications and must be weighed with the patient's QoL in mind. These are discussed above.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Prostate Cancer, Locally Advanced (T3, T4)
• Prostate Cancer, Metastatic (N+, M+)
• Prostate Cancer Risk Calculators
• PSA Velocity and Doubling Time
• PSA Elevation, General

CODES

ICD9

• 185 Malignant neoplasm of prostate
• 790.93 Elevated prostate specific antigen (psa)

ABBREVIATIONS

• ADT: Androgen deprivation therapy
• AUA: American Urology Association

- CAB: Combined androgen blockade
- CaP: Adenocarcinoma of the prostate
- CT: Computed tomography
- DRE: Digital rectal exam
- LHRH: Luteinizing hormone releasing hormone
- MRI: Magnetic resonance imaging
- PAD: Peripheral androgen blockage
- PET: Positron emission tomography
- PSA: Prostate-specific antigen
- PSADT: PSA doubling time
- PSAR: PSA recurrence
- PSMA: Prostate-specific membrane antigen
- QoL: Quality of life
- RP: Radical prostatectomy
- RT: Radiation therapy
- TRUS: Transrectal ultrasound
- XRT: External-beam radiation therapy

PSA ELEVATION, GENERAL

Joseph R. Zola, MD

Leonard G. Gomella, MD

BASICS

DESCRIPTION

- The main use of PSA is the diagnosis and treatment of CaP. This section reviews the current use of PSA in the diagnosis of CaP.
- Definition of normal PSA is controversial.
- Elevated PSA traditionally >4.0 ng/mL based on the Baltimore Longitudinal Study of Aging
- Elevated PSA >2.5 ng/mL is advocated by some; especially for African Americans >40 or with family history of CaP in men >40
- Age-specific and race-specific guidelines proposed, but controversial

Range (yrs)	Asian	Black	White
40–49	0–2.0	0–2.0	0–2.5
50–59	0–3.0	0–4.0	0–3.5
60–69	0–4.0	0–4.5	0–4.5
70–79	0–5.0	0–5.5	0–6.5

- Median PSA (per Catalona):
  - 4th decade, 0.7 ng/mL

- 5th decade, 0.9 ng/mL
- 6th decade, 1.3 ng/mL
- 7th decade, 1.7 ng/mL

• Based on the PCPT biopsy trial (done regardless of PSA), men can have CaP despite low PSA levels. Therefore, there is no lower cutoff or normal PSA to indicate that no cancer is present. PCPT data:

PSA (ng/mL)
CaP Rate
PSA (ng/mL)
CaP Rate
0–0.5
6.6%
3.1–4.0
26.9
0.6–1.0
10.1%
4.0–10.0
25%
1.1–2.0
17%
>10.0
>50%
2.1–3.0
23.9%

• The challenge: Lower the normal PSA to recommend biopsy where life-threatening cancer is present, but not to a point where overdetection of incidental cancers occurs.

• A variety of PSA derivatives have been described to overcome this problem, but none are absolute. These may be useful in the intermediate PSA elevation range of 4.0–10 ng/mL: Age/race specific PSA, PSA density, PSA velocity, newer forms of PSA assay (free, molecular forms)

• PSA changes over time have gained more interest than a single PSA in screening for CaP.

• New data suggest a single PSA of >1.2 ng/mL before age 50 predicts increased CaP risk.

- PSA is a better predictor of cancer than findings on DRE or TRUS alone.
- PSA >10 indicates elevated risk of advanced disease.
- PSA is proportional to prostate volume; prostate volume/mean PSA were as follows: 14 cm3/1; 25 cm3/1.13/52 cm3 1.45 in 1 study
- CaP can only be diagnosed through tissue biopsy and not by PSA alone.

ALERT

PSA should not be done in the setting of untreated bacterial prostatitis or within 3–4 wk of prostate instrumentation due to risk of false elevation.

EPIDEMIOLOGY

- Across all races, age >50, 7.9% of men randomly screened have PSA >4.0 ng/mL
- Regardless of PSA level, CaP (2008) in US: 186,320 new cases, 28,660 deaths, 1 in 6 lifetime risk (15.8% of men); US prevalence 2,106,499 men, or 1.5% all ages and races

RISK FACTORS

- Advancing age
- Benign enlargement of the prostate
- Infection
- Presence of CaP
- Prostatic infarction
- Recent instrumentation (TURP, cystoscopy, catheterization, prostate biopsy)

Genetics

- PSA associated with 1 of 15 distinct genes in the kallikrein family localized to the long arm of chromosome 19 within the region spanning q13.2–q13.4.
- PSA is also called human kallikrein 3 (hKLK3)

PATHOPHYSIOLOGY

- PSA is a serine protease produced by the prostatic epithelium and periurethral glands that liquefies the seminal coagulum.
- Seminal fluid has high PSA concentrations (mg/mL); PSA is much lower (ng/mL) in serum.
- Complexed to antiproteases 1-ACT and 2-MG; small proportion is unbound (FPSA)
- PSA bound to ACT; the free portion is detected by assay, while that bound to MG is not detected by routine assay.
- Complexed PSA hepatic clearance (1/2-life 2–3 days); FPSA is cleared by glomerular filtration (1/2-life 2–3 hr).
- PSA elevation is due to disrupted prostatic architecture and compromised integrity of the basal layer or basement membrane.

- CaP actually produces less PSA per gram compared to benign tissue.
- Androgens influence PSA levels.
- Sources of fluctuation in PSA:
  - No PSA analytic standard; can vary by lab and test method; best to use same lab to compare values more reliably
  - 15% coefficient of variation in PSA assay
  - Physiologic variation in PSA 15–30% in the short term; BPH can vary up to 30%.
  - 26–37% with elevated PSA return to normal 1 yr later, and 45–55% return to normal within 4 yrs
  - Seasonal variation: PSA is higher in summer
  - Infection, infarction, trauma, ejaculation within 24 hr, or prostate instrumentation or massage can produce elevations (not routine DRE).
  - Finasteride (5 mg for BPH and 1 mg for alopecia) and dutasteride are 5-reductase inhibitors; they lower PSA by 50% over 6 mo; correct PSA by doubling to maintain utility for screening.

DIAGNOSIS

HISTORY

- Difficulty with urination, such as hesitancy, straining, weak stream, or intermittency
- Dysuria, frequency, or urgency
- Previous PSA levels or prostate biopsies
- Known history of CaP
- Family history of prostate carcinoma
- Medications, including herbals
- Markedly elevated PSA >20 ng/mL associated with bone, back, or hip pain could suggest metastatic CaP

PHYSICAL EXAM

- DRE: Nodules, induration, asymmetry, bogginess, tenderness
- Palpable bladder with obstruction
- Adenopathy, supraclavicular
- Bony pain, point tenderness with metastasis
- Neurologic, especially lower extremity weakness, sensation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Routine urine analysis to rule out UTI
- Consider evaluation for prostatitis by modified Stamey-Mears test or exam of EPS (See Section I: “Chronic Bacterial Prostatitis NIH II”)

- PSA, TPSA: Chronologically organized summary of all available values
- FPSA, %FPSA:
  - With CaP lower FPSA; postulated that CaP cells produce more ACT
  - Measured as the percent of FPSA/TPSA
  - FPSA is more specific in men with prostates <50 g; not valid if TPSA >10
  - TPSA (4.0–10.0 ng/mL) together with % FPSA can stratify risk of CaP (see table)

PSA (ng/mL)
CaP Rate
%FPSA
CaP Prob
0–2
1%
0–10
56%
2–4
15%
10–15
28%
4–10
25%
15–20
20%
>10
>50%
20–25
16%

>25
8%

- PSAD: PSA divided by TRUS volume:
  - Correlates PSA to TRUS prostatic size to distinguish BPH from CaP:
  - Useful with PSA levels 4–10 ng/mL and a previous negative biopsy
  - Cut off of 0.15 ng/mL/cm3 improves specificity by 50%, misses 27– 48% of cancers

– Cut off of 0.1 avoids 31% of biopsies, misses 10% of cancers

– Cut off of 0.8 avoids 12% of biopsies, misses 5% of cancers

- PSAV:

– Rate of PSA increase per year, based on the theory that PSA rises more rapidly if clinically significant CaP present:

for

PSA1 = 1st PSA measurement (ng/mL)

PSA2 = 2nd PSA measurement (ng/mL)

PSA3 = 3rd PSA measurement (ng/mL)

Time1 = interval between PSA1 & PSA2 (yr)

Time2 = interval between PSA2 & PSA3 (yr)

– Baltimore Longitudinal Study: 72% with CaP had a PSA rise >0.75 ng/mL/yr vs.10% with BPH

– Prospective trials: 47% with PSAV >0.75 ng/mL/yr had CaP vs.11% with PSAV <0.75

– Minimum 18 mo interval with 3 repeat PSAs are necessary for accurate PSAV determination.

– Other PSAV values are under study (see below).

Imaging

- TRUS:

– Determine prostatic size; calculate PSAD; evaluate for extraprostatic extension; most useful to guide systematic needle biopsy

– Contrast-enhanced, Doppler, and MicroFlow TRUS may improve biopsy yield and identify more high-grade cancers.

- MRI with endorectal coil: May be useful with clinical suspicion despite negative TRUS biopsy:

– Requires endorectal coil (at 3 Tesla), thin cuts, and T2-weighted images

– Varying sensitivity (13–95%) and specificity (49–97%) for CaP detection; MRI with SPECT imaging improves detection

- CT: No role in primary CaP detection:

– Only with high suspicion of advanced CaP (positive nodal disease by CT >1 cm): PSA >20 ng/mL or Gleason 8, cT3

– Used to monitor metastases after diagnosis

- Bone scan: Suggested only if PSA >20 ng/mL or high-grade disease or cT3 or pain

– Positive <0.8% with CaP and PSA <15 ng/mL and 2.6% with PSA 15.1– 20.0 ng/mL

Diagnostic Procedures/Surgery

TRUS-guided prostate biopsy with 18G biopsy needle and local anesthesia:

- Historic sextant (6-core) biopsy inadequate
- Extended biopsy (8–13 cores) with laterally directed samples is now standard.
- Most hypoechoic lesions are not CaP, but are 2 times more likely to contain CaP as isoechoic areas (25–50% are CaP missed with hypoechoic-only biopsies).
- Suspicious lesions should be biopsied,
- Transition zone samples may be considered with >50 mL volume prostate or for repeat biopsy.

Pathological Findings

See Section I: “Prostate Cancer, General.”

DIFFERENTIAL DIAGNOSIS

- Adenocarcinoma of the prostate
- BPH
- Prostatitis (usually bacterial infection)
- Prostatic infarction: Idiopathic or after shock, sepsis, or recent cardiac bypass surgery
- Iatrogenic urethral manipulation, recent cystourethroscopy, Foley catheter placement
- Prostatic massage (but not routine DRE)
- Trauma (cycling, extensive ambulation)
- Ejaculation within 24 hr of PSA test

TREATMENT

- Prostate cancer screening 2009 guidelines from the AUA: PSA and DRE should be offered annually, beginning at age 40, to men who have at least a 10-yr life expectancy:
- Due to PSA fluctuations, confirm an elevated PSA with a 2nd reading before biopsy. Patient should not ejaculate for 48 hr before test.
- Empiric antibiotics for elevated PSA is controversial but advocated by some, especially with major short-term fluctuations in PSA.
- Published indications to perform prostate biopsy:
  - Prostate nodule, regardless of PSA
  - PSA >10 ng/mL in the absence of prostatitis
  - PSA >4.0 ng/mL and PSAV >0.75 ng/mL/yr
  - PSA <4.0 ng/mL and PSAV >0.3–0.5 ng/mL/yr
  - PSA >2.5 ng/mL and PSAV >0.60 ng/mL/yr
  - PSA 4–10 and F/T PSA<10%
  - F/T PSA <20% and PSAV >0.75 ng/mL/yr

- AUA 2009 PSA Best Practice Statement:
  - There is no single threshold PSA which should prompt prostate biopsy. Biopsy decision based PSA and DRE and consider multiple factors (F/T total PSA, age, PSA velocity, PSA density, family history, ethnicity, prior biopsy, history, comorbidities).
  - The use of a specific PSA cutpoint in combination with DRE alone can lead to an overestimation/underestimation of risk

MEDICATION

With evidence of bacterial prostatitis, treat with antibiotics and repeat PSA 4 wk after:

- Fluoroquinolone (eg, ciprofloxacin 500 mg b.i.d.) or trimethoprim-sulfamethoxazole (180/800 mg b.i.d.) or doxycycline (100 mg b.i.d.)

SURGERY/OTHER PROCEDURES

For repeat biopsy, some advocate the following:

- TUR of transition zone; not commonly used today
- Saturation biopsy (15–45), based on size of the prostate under IV sedation or formal anesthesia

ADDITIONAL TREATMENT

- CaP risk calculators are available on the Internet to predict outcome of biopsy.
- EPCA-2 (investigational), may discriminate BPH from CaP.
- PCA3 gene detected in the urine after prostate massage suggests CaP; may be a useful tool after negative biopsy (FDA approved).

COMPLEMENTARY AND ALTERNATIVE MEDICINE

No consistent evidence for effects of herbal medications on PSA (eg, saw palmetto) but these may contain illicit compounds that lower PSA (eg, PC SPES); identify in the patient history.

ONGOING CARE

PROGNOSIS

- With elevated PSA, positive biopsy rate is 6–25%; elevated PSA and nodule rate is 18–60%
- Overall, if 2nd biopsy is performed, detection rate is 10–35%.

COMPLICATIONS

Failure to diagnose cancer; patient anxiety over repeat testing; risk of biopsy and drugs

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- PSA <2.5 ng/mL, low PSAV: Annual DRE/PSA
- PSA 2.6–10 ng/mL, low PSAV:

- Consider biopsy or obtain FPSA
- F/T PSA >25%: Repeat PSA/DRE in 6 mo

• Based on TRUS biopsy results:

- Negative :Repeat DRE/PSA in 6 mo; consider F/T PSA as guide for another biopsy
- HGPIN or ASAP:

Repeat biopsy (3–6 mo) with ASAP; not clear if repeat biopsy necessary with HGPIN

- Consider transition zone sampling with any repeat biopsy.
- Positive biopsy (CaP): Staging studies, discuss treatment options

• Persistent PSA elevation (PSA >10 ng/mL):

- Repeat biopsy; transition zone sampling

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

• Prostate Cancer, General

• PSA Elevation Following Definitive Therapy for Localized Prostate Cancer

CODES

ICD9

790.93 Elevated prostate specific antigen (PSA)

ABBREVIATIONS

• ACS: American Cancer Society

• ACT: Antichymotrypsin

• ASAP: Atypical small acinar proliferation

• AUA: American Urology Association

• BPH: Benign prostatic hypertrophy

- CaP: Adenocarcinoma of the prostate
- CT: Computed tomography
- DRE: Digital rectal exam
- EPCA-2: Early prostate cancer antigen-2
- EPS: Expressed prostatic secretion
- F/T: Free total ratio
- FPSA: Free PSA
- HGPIN: High-grade prostatic intraepithelial neoplasia
- MG: 2-Macroglobulin
- MRI: Magnetic resonance imaging
- PCPT: Prostate Cancer Prevention Trial
- PSA: Prostate-specific antigen
- PSAD: PSA density
- PSAV: PSA velocity
- SPECT:
- TPSA: Total PSA
- TRUS: Transrectal ultrasound
- TURP: Transurethral resection of prostate
- UTI: Urinary tract infection

PSEUDOHERMAPHRODITISM, MALE AND FEMALE

Steve J. Hodges, MD
Anthony Atala, MD

BASICS

DESCRIPTION

- Pseudohermaphrodite is an older expression that referred specifically to conditions in which the phenotypic sex was inconsistent with the gonadal sex.
- Disorders of sexual development (DSDs) the more general preferred term today, which refers to congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical.
- Female pseudohermaphrodite (now called 46 XX DSD):
  - Karyotype 46XX
  - Gonads: Histologically normal ovaries
  - External genitalia: Varying degrees of masculinization
  - Causes:

    CAH is most common cause in females. Results from block in cortisol synthesis pathway with exogenous virilization

    Other causes: Progestational agents given in the 1st trimester; virilizing tumors such as maternal ovarian/adrenal tumors
- Male pseudohermaphrodite (now called 46 XY DSD):
  - Karyotype: 46XY
  - Gonads: Histologically normal testes
  - External genitalia: Incomplete masculinization
  - Causes: Androgen insensitivity, 5-reductase deficiency, disordered steroidogenesis (testosterone)
- True hermaphrodite (now called ovotesticular DSD): See Section II topic.

EPIDEMIOLOGY

- Female pseudohermaphrodite:
  - 21-Hydroxylase deficiency; 90% of CAH; 1 in 15,000 births
  - 11-Hydroxylase deficiency; 5–8% of CAH (rare)
  - 3-Hydroxysteroid dehydrogenase deficiency
- Male pseudohermaphrodite:
  - Androgen insensitivity; 1 in 20,000–64,000 incidence with complete testicular feminization; complete form 10 times more common than incomplete form
  - 5-reductase deficiency: Rare

– Disordered steroidogenesis (testosterone): Rare

RISK FACTORS

- Maternal progestational agents
- Family history

Genetics

- Female pseudohermaphrodite:
  – Recessively inherited:
    21-Hydroxylase deficiency: Locus on 6p
    11-Hydroxylase deficiency: Locus on 8q
    3-Hydroxysteroid dehydrogenase deficiency: Locus on chromosome 1
- Male pseudohermaphrodite:
  – Androgen insensitivity: X-linked
  – 5-Reductase deficiency: Autosomal recessive
  – Disordered steroidogenesis (testosterone): Autosomal or X-linked recessive

GENERAL PREVENTION

- Prenatal genetic counseling
- Prenatal steroid therapy

PATHOPHYSIOLOGY

- Female pseudohermaphrodite:
  – CAH: Disruption in cortisol synthetic pathway; cortisol unable to provide negative feedback control of ACTH release

21-Hydroxylase deficiency: 11-deoxycortisol and cortisol. Resultant increase in ACTH production: 17-hydroxyprogesterone and 17-hydroxypregnenolone: Metabolized to dehydroepiandrosterone and androstenedione (converted to testosterone peripherally)

11-Hydroxylase deficiency: Occurs later in cortisol synthetic pathway. Accumulation of precursors including DOC, and 17-hydroxyprogesterone; DOC: HTN in 2/3

3-Hydroxysteroid dehydrogenase deficiency: Early block in cortisol synthetic pathway. Accumulation of dehydroepiandrosterone (not converted to testosterone). Less virilization than with other forms of adrenogenital syndrome

  – Exogenous progestational agents:

Ethisterone and Norlutin administered to prevent miscarriage. Similar to testosterone; causes virilization if given in 1st trimester

  – Virilizing maternal tumors: Luteoma, arrhenoblastoma

- Male pseudohermaphrodite:
  – Androgen insensitivity: Faulty androgen receptor with elevation of LH and testosterone

– 5-Reductase deficiency: Failure of conversion of testosterone to dihydrotestosterone:

Resultant failure of virilization of genital tubercle and urogenital sinus

LH levels normal or slightly elevated; testosterone levels normal

– Disordered steroidogenesis:

CAH: Disruption in cortisol synthetic pathway

20,22-Desmolase deficiency: Deficiency prior to synthesis of pregnenolone; cholesterol major secreted steroid; impaired testosterone synthesis

3-Hydroxysteroid dehydrogenase deficiency: Early block in cortisol synthetic pathway; accumulation of dehydroepiandrosterone (not converted to testosterone); impaired testosterone synthesis

17-Hydroxylase deficiency: Accumulation of corticosterone and 11-deoxycorticosterone

17,20-Desmolase deficiency: Normal adrenocortical function; failure of conversion of 17-hydroxyprogesterone to androstenedione

17-Hydroxysteroid dehydrogenase deficiency: Normal adrenocortical function; failure of conversion of androstenedione to testosterone

COMMONLY ASSOCIATED CONDITIONS

- Hypospadias
- Cryptorchidism

DIAGNOSIS

HISTORY

- Maternal progestational agents
- Family history: Ambiguous genitalia, unexplained infant mortality, hirsutism, infertility, amenorrhea

PHYSICAL EXAM

- Female pseudohermaphrodite:
  - Genitalia exam:
    Clitoral hypertrophy with chordee
    Single urogenital sinus emptying at base of clitoris
    Rugose and pigmented labial scrotal folds
  - Somatic (untreated):
    Advanced bone age with early epiphyseal closure and short stature
    Precocious pubic and axillary hair
    Acne, amenorrhea, failure of breast development

- Male pseudohermaphrodite:
  - Genitalia exam:

Androgen insensitivity, complete form: Complete feminization; undescended testes/absent wolffian duct remnants; vagina short or rudimentary

Androgen insensitivity, incomplete form: Some virilization of external genitalia (labial fusion, clitoromegaly, vagina rudimentary, Wolffian duct remnants) may be present.

5-Reductase deficiency: Severe hypospadias; blind vaginal pouch; testes with wolffian duct development; no müllerian structures; enlargement of phallus at puberty

Disordered steroidogenesis (testosterone): Wide range from mild hypospadias to full feminization

  - Somatic findings:

Androgen insensitivity: Breast development; scant pubic hair with complete form

5-Reductase deficiency: Female habitus but without breast development; muscle development at puberty

- In general, suspect pseudohermaphrodite in the newborn when there is:
  - Unclear genital sex
  - Clitoromegaly
  - Bilateral undescended testes
  - Hypospadias with unilateral or bilateral cryptorchidism
  - Presence of a palpable gonad: Excludes diagnosis of pseudohermaphrodite
  - Rectal exam with palpable uterus: Excludes diagnosis of male pseudohermaphrodite
  - Increased pigmentation of labioscrotal folds/areola: Consistent with CAH
  - Hypotension/dehydration: Consistent with CAH
- In general, suspect pseudohermaphrodite in the adolescent when there is:
  - Gynecomastia/female habitus in the male
  - Amenorrhea in the female

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Karyotype: Peripheral blood leukocyte analysis has replaced the buccal smear.
- Plasma 17-hydroxyprogesterone: Elevated with 21-hydroxylase deficiency
- Urinary 17-ketosteroids and pregnanetriol: Elevated with 21-hydroxylase deficiency
- Plasma testosterone:
  - Pre- and post-hCG administration (in the male pseudohermaphrodite):

Level of poststimulation testosterone/dihydrotestosterone (if suspicious of 5-reductase deficiency)

- Fibroblast skin cultures (if suspicious of androgen insensitivity)
- Female pseudohermaphrodite:
  - Electrolytes:
    1/2–1/3 with salt-wasting form (21-hydroxylase and 3-hydroxylase deficiency)
    Hypotension, hyponatremia, hyperkalemia, elevated renin
    Increased severity of hypotension with 3-hydroxylase deficiency
    11-hydroxylase deficiency: Salt retention, HTN, hypernatremia
- Male pseudohermaphrodite:
  - Electrolytes:
    Androgen insensitivity: Normal
    5-Reductase deficiency: Normal
    Disordered steroidogenesis
    CAH: 20,22-desmolase deficiency: Salt wasting
    3-hydroxysteroid dehydrogenase deficiency: Salt wasting
    17-hydroxylase deficiency: Hypokalemic alkalosis, HTN
    17,20-desmolase deficiency: Normal adrenocortical function
    17-hydroxysteroid dehydrogenase deficiency: Normal adrenocortical function

Imaging

- Genitogram: Water-soluble contrast media injected through feeding tube into perineal opening usually under fluoroscopy:
  - Configuration of urogenital sinus
  - Cervical impression/fallopian tubes excludes diagnosis of male pseudohermaphrodite
- Abdominal/pelvic US:
  - Müllerian structures may be detected.

Diagnostic Procedures/Surgery

- Endoscopy: Configuration of urogenital sinus. Visualized cervix excludes diagnosis of male pseudohermaphrodite
- Exploratory laparotomy: Consider if other studies inconclusive. Gonadal biopsy to rule out dysgenesis or true hermaphrodite

Pathological Findings

Discordant phenotypic and genotypic sex

DIFFERENTIAL DIAGNOSIS

See Section I: “Disorders of Sexual Differentiation.”

TREATMENT

- Sex assignment is based on ability to construct functioning genitalia.
- Fertility is secondary consideration.
- Sex assignment is completed prior to discharge.
- Multidisciplinary team care is generally found in tertiary centers: Subspecialists in pediatric endocrinology, pediatric urology, psychology/psychiatry, gynecology, genetics, neonatology, and if available, social work, nursing, and medical ethics

ALERT

CAH (salt wasting) may present with neonatal shock due to profound hypovolemia, hyperkalemia and hyponatremia

MEDICATION

- Female pseudohermaphrodite:
  - CAH:

    Fluid/salt repletion if salt-wasting variant

    Glucocorticoid/Florinef replacement

    Monitoring of BP and electrolytes

    Serial measurements of plasma renin 17a-hydroxyprogesterone; androgens can monitor therapy

    Antihypertensives may be needed for 11b-hydroxylase deficiency
- Male pseudohermaphrodite:
  - Glucocorticoid, mineralocorticoid, and antihypertensives may be needed.

SURGERY/OTHER PROCEDURES

- Female pseudohermaphrodite:
  - CAH:

    Reduction clitoroplasty

    Vaginoplasty: Hormonal therapy may normalize clitoral size so reduction may not be necessary. Timing of surgery controversial, many moving to early repair
- Male pseudohermaphrodite:
  - Androgen insensitivity (complete): Orchiectomy: Timing controversial, raised as female
  - Disordered steroidogenesis and 5-reductase deficiency:

    Sex assignment based on ability to reconstruct phallus/testosterone response
- Bilateral orchiectomy usually performed at time of hernia repair after workup for delayed puberty or female sex assignment
- Hypospadias and scrotal surgery in male-assigned patients can be performed at 6 mo preoperative testosterone may help with phallus size.

ADDITIONAL TREATMENT

- CAH is genetic, so prenatal genetic counseling is required.
- Prenatal therapy with dexamethasone may help.

ONGOING CARE

PROGNOSIS

Generally good with appropriate care

COMPLICATIONS

- Infertility
- Psychological trauma

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Family counseling critical during evaluation
- Sensitivity essential
- Explain that genital formation is incomplete and that reconstructive efforts will complete normal development.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Disorders of Sexual Differentiation (DSD)
- True Hermaphrodite

CODES

ICD9

- 255.2 Adrenogenital disorders
- 259.51 Androgen insensitivity syndrome
- 752.7 Indeterminate sex and pseudohermaphroditism

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone
- BP: Blood pressure
- CAH: Congenital adrenal hyperplasia
- DOC: Deoxycorticosterone

- DSD: Disorders of sexual development
- hCG: Human chorionic gonadotropin
- LH: Luteinizing hormone
- US: Ultrasound

PYELONEPHRITIS, ACUTE

David J. Kaplan, MD
Michel A. Pontari, MD

BASICS

DESCRIPTION

- An infectious process that has progressed from involving the lower urinary tract to involving the renal pelvis and parenchyma.
- 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 of outpatient acute pyelonephritis is highest among young women, infants, and the elderly, respectively.
- Women peak 15–29, with decline after. In men, uncommon before age 35, with increase up to 80 yr, where it equals female rates
- >250,000 episodes annually in the US:
  - 12–13/10,000 in outpatient females
  - 3–4/10,000 in inpatient females
  - 2–3/10,000 in outpatient males
  - 1–2/10,000 in inpatient males

RISK FACTORS

- Anatomic or functional abnormalities: Incomplete emptying of the bladder; urine is more easily infected:
  - Vesicoureteral reflux, neurogenic bladder, BOO
- Foreign body: Bacterial colonization occurs, and the foreign body acts as a nidus for infection
  - Calculous disease, medullary sponge kidney
  - Indwelling catheters
- Medical conditions:
  - Diabetes mellitus, immunosuppression, alcohol abuse
- Social:
  - Poor perineal hygiene, soiling
  - Variables in sexual behavior (new or multiple partners) and use of spermicide
  - Previous episode of pyelonephritis

Genetics

Related to vesicoureteral reflux

GENERAL PREVENTION

- Eliminate anatomic/functional abnormalities.
- Patients with recurrent infections may require low-dose prophylactic antibiotics.
- Proper indwelling catheter management

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 organisms are gram-negative rods:
  - Escherichia coli accounts for the majority of cases (80% in women, 70% in men)
  - Klebsiella pneumoniae is the 2nd most common organism (5–10%)
- Bacteria enter urinary tract:
  - Ascending infection: Urethra and bladder
  - Results from colonization of the vaginal introitus with fecal flora in females
  - Lymphatic and hematogenous dissemination to the kidneys is uncommon.
- Bacteria adhere to the urothelium, with subsequent invasion and inflammatory response.
  - Adhesins and fimbriae: Allow bacteria to adhere to urothelium
  - Lipopolysaccharides: 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

COMMONLY ASSOCIATED CONDITIONS

See “Risk Factors.”

DIAGNOSIS

HISTORY

- Fevers, chills, malaise, nausea, or vomiting
- Flank or abdominal pain
- Dysuria, urgency or frequency, gross hematuria
- Prior episodes of UTIs
- History of renal calculi or urinary tract abnormalities
- History of diabetes, immunosuppression, or alcoholism
- History of recent instrumentation
- Children may present with failure to thrive.

PHYSICAL EXAM

- Vital signs for signs of sepsis
- CVA tenderness
- Abdominal distension with decreased bowel sounds may be present
- Pelvic exam in women may help differentiate gynecologic disease.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis with neutrophil predominance (90%)
- Serum chemistry: Renal failure uncommon unless obstruction or sepsis present
- Blood culture: 12% of hospitalized pyelonephritis patients will have bacteremia.
- Pregnancy test in women
- Urinalysis: Pyuria >5–10 WBCs/HPF:
  - WBC casts indicate 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 the causative organism; 10,000 bacteria/mL suggest acute pyelonephritis in patients with cath urine.

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 ureteral obstruction, which, with fever and infection, is a surgical emergency.
- 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 scarring and should undergo imaging.
- Abdominal x-ray (KUB):
  - Evaluate for renal or ureteral calculi
  - Intraparenchymal gas: Emphysematous pyelonephritis
  - Renal shadow may be enlarged and poorly defined secondary to parenchymal edema
- ExU:
  - 75% of patients with uncomplicated acute pyelonephritis will have a normal ExU
  - ExU shows an enlarged kidney (>15 cm in length or 1.5 cm greater than the unaffected side with decreased nephrogram and delayed excretion).

– Cortical striations may be seen.

– Focal enlargement of the kidney is consistent with focal bacterial nephritis, or acute lobar nephronia may be confused with tumor or abscess.

– Nonobstructive dilation of the renal pelvis and ureter may be present (endotoxins impair ureteral peristalsis).

- US:
  – Renal enlargement with hypoechoic parenchyma and loss of corticomedullary differentiation
  – Noninvasive; no ionizing radiation
- CT:
  – Noncontrast CT of the abdomen reveals an enlarged kidney with decreased attenuation parenchyma, and perinephric fat streaking.
  – Contrast administration shows delayed enhancement with delayed excretion.
- Radionuclide scan:
  – Cortical agents (eg, DMSA) reveal decreased activity in the affected kidney.
  – Useful to identify areas of scarring

Diagnostic Procedures/Surgery

Determine residual urine if retention suspected

DIFFERENTIAL DIAGNOSIS

- Any intraabdominal inflammatory process:
  – Appendicitis, cholecystitis, diverticulitis, pancreatitis, peptic ulcer disease
- Gynecologic conditions:
  – Pelvic inflammatory disease, ectopic pregnancy, ruptured ovarian cysts
- Urologic conditions:
  – Renal colic with fever
  – Renal and perinephric abscesses
- Lower lobe pneumonia
- Musculoskeletal pain

TREATMENT

- Supportive care consists of hydration, antipyretics, and analgesics.
- Empiric antibiotics that are active against the possible causative organisms and achieve adequate levels in the renal parenchyma and urine are used.

MEDICATION

- Outpatient therapy:
  – In uncomplicated acute pyelonephritis, those who are reliable, tolerate oral intake, and do not have signs of sepsis do not require hospitalization.

– Oral fluoroquinolones (ciprofloxacin 500 mg PO b.i.d., or levofloxacin 750 mg/d PO) are adequate for empiric treatment. Levofloxacin is approved for a 5-day regimen.

– An alternative antibiotic is trimethoprim-sulfamethoxazole (TMP-SMZ).

– Therapy should be continued for 10–14 days. Mild cases may be treated for 7 days.

– Recent studies suggest an increase in quinolone resistance as well as susceptibility to TMP-SMZ.

- Inpatient therapy:

– If signs of sepsis, bacteremia, or cannot tolerate oral medications: Hospitalize

– Also recommended for children, the elderly, pregnant patients, diabetics, and the immunocompromised and with complicated pyelonephritis

– Parenteral antibiotic therapy uncomplicated:

Ampicillin (2 g IV q6h) and gentamicin (1.5 mg/kg IV q8h) is traditional treatment; OR

Ceftriaxone (1 g/d IV) empirically; OR

IV fluoroquinolones ciprofloxacin 400 mg q12h or levofloxacin 750 mg q24h; aztreonam is also an acceptable alternative

– Most patients continue to have fever or flank pain for several days after appropriate therapy has been started.

– IV therapy continued until the patient is afebrile or cultures indicate another appropriate antibiotic.

– When able to tolerate oral intake, the patient is switched to an oral antibiotic as for oral therapy above.

– Pregnant patients: Place on suppression therapy (eg, nitrofurantoin 100 mg/d PO, cephalexin 250 mg/d PO) after treatment until delivery, due to a relapse rate of up to 60% in nonsuppressed patients.

– Patients with a delayed response to therapy should be treated with a longer course of antibiotics (14–21 days), even without evidence of complicated disease.

- Complicated pyelonephritis: Assess for underlying urologic abnormalities (obstructive uropathy, stones, etc.)

– Parenteral antibiotic therapy in complicated cases:

Piperacillin-tazobactam 3.375 g q6h, ticarcillin-clavulanate 3.1 g q6h, cefepime 1 g q12h

Alternates include meropenem, and imipenem. Dose-adjust with renal failure.

– After transitioning to species-specific antibiotics, therapy should be continued for 14–21 days.

SURGERY/OTHER PROCEDURES

Diversion with indwelling stent or percutaneous drain may be necessary in patients with urinary obstruction.

Pregnancy Considerations

Ampicillin, amoxicillin and, PO cephalosporins have proven to be safe; amoxicillin/clavulanic acid (Augmentin) is recommended for resistant organisms; nitrofurantoin is safe for the fetus but potentially toxic to the mother; fluoroquinolones should be avoided in pregnancy.

ONGOING CARE

PROGNOSIS

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 scarring (20%)
- Children with developing kidneys are at significant risk of scarring from even 1 episode of acute pyelonephritis.
- Diabetics are at significant risk of developing emphysematous pyelonephritis, a more fulminant process with a high mortality:
  - Characterized by renal intraparenchymal gas and detectable on KUB
- Patients with calculi or urinary tract obstruction who have recurrent episodes of pyelonephritis may develop xanthogranulomatous pyelonephritis:
  - Characterized by large nonfunctioning renal mass
  - Stones are present in 80% of cases.
- Pregnant patients are at high risk because of the physiologic changes of pregnancy to the urinary tract:
  - Sepsis
  - Adult respiratory distress syndrome
  - Preterm delivery with low-birth-weight infants

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Urine cultures 4–6 wk after completion of antibiotics to verify infection cleared
- 10–30% suffer a relapse and may be treated with a 2nd 14-day course of antibiotics.
- Occasionally, a 6-wk course is necessary for cure.
- Check for clearing of hematuria if initially present.

ADDITIONAL READING

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- Warren JW, Abrutyn E, Hebel JR, et al. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in children. Clin Infect Dis 1999;29:745.

See Also (Topic, Algorithm, Electronic Media Element)

- 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

– 041.4 Escherichia coli (E. coli) infection in conditions classified elsewhere and of unspecified site

– 041.85 Other specified bacterial infections in conditions classified elsewhere and of unspecified site, other gram-negative organisms

– 590.10 Acute pyelonephritis without lesion of renal medullary necrosis

ABBREVIATIONS

- BOO: Bladder outlet obstruction
- CBC: Complete blood count
- CT: Computed tomography
- CVA: Costovertebral angle
- DMSA: Dimercaptosuccinic acid
- ExU: Excretory urogram

- IV: Intravenous
- KUB: Kidneys, ureters, bladder
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

PYELONEPHRITIS, CHRONIC

Christa Abraham, MD

Michael Perrotti, MD

BASICS

DESCRIPTION

- Injury to the kidney with inflammation and fibrosis of the renal parenchyma, pelvis, and calyces. It is most often caused by recurrent or chronic renal infection.
- Not usually diagnosed based on clinical presentation, chronic pyelonephritis is usually a radiologic or pathologic diagnosis.
- Clinical signs and symptoms are often vague but can be related to the infection and the severity and location of injury within the kidney:
  - Often an incidental finding, it may present as asymptomatic bacteriuria, dysuria and frequency (lower urinary tract symptoms), vague complaints of flank or abdominal discomfort, and intermittent low-grade fevers.
  - Synonym(s): Chronic interstitial nephritis

EPIDEMIOLOGY

- Occurs in males and females of all ages:
  - More common in childhood, especially with congenital anomalies such as VUR
- Infectious chronic pyelonephritis accounts for 15–20% of cases of chronic renal failure.
- Less common in patients having no underlying functional or structural urinary tract abnormalities, renal, or urinary tract disease

RISK FACTORS

- Female sex
- In 50% of cases, history of a previous episode of acute pyelonephritis
- VUR/reflux nephropathy
- Congenital urinary tract anomalies
- Neurogenic bladder dysfunction
- Pregnancy
- Urinary tract obstruction with complicated UTI can result in renal insufficiency:
  - Mechanical obstruction includes prostatic hyperplasia, calculi, retroperitoneal fibrosis, neoplasms, and congenital anomalies.

Genetics

Evidence suggests that susceptibility to acute pyelonephritis may have a familial component and may be associated with decreased CXCR1 expression.

GENERAL PREVENTION

- Upper urinary tract evaluation in patients with recurrent bacteriuria or recurrent acute pyelonephritis
- Early detection, evaluation, and treatment of childhood UTIs
- Prompt detection and management of VUR
- Detection and treatment of obstructive uropathy

Geriatric Considerations

Chronic pyelonephritis can present with atypical symptoms and signs in the debilitated elderly patient. Diagnosis requires an astute clinical acumen.

Pregnancy Considerations

- Antibiotic prophylaxis during pregnancy in patients with risk factors including:
  - History of acute pyelonephritis during pregnancy
  - Recurrent bacteriuria after treatment during pregnancy
  - History of recurrent UTIs on previous antibiotic prophylaxis before being pregnant

Pediatric Considerations

- Assess UTI with:
- ExU
- VCUG
- Serial DMSA scanning for scar detection and progression
- Renal US

PATHOPHYSIOLOGY

- Progressive localized immune response to bacterial infection
- Hyaline casts in tubule may cause resemblance to thyroid colloid known as renal thyroidization.
- Fibrosis around the glomeruli replaces kidney parenchyma in patches:
  - Calyceal clubbing with nonuniform localized scarring

COMMONLY ASSOCIATED CONDITIONS

- VUR
- Spinal cord injury
- XGP is a form of chronic pyelonephritis.
- Presents with foamy lipid laden macrophages
- Often unilateral and associated with longstanding obstructing nephrolithiasis.

DIAGNOSIS

HISTORY

- Frequently asymptomatic and discovered incidentally
- UTIs in childhood and during pregnancy

- Presence of HTN, especially in children with known reflux nephropathy
- Proteinuria, polyuria, nocturia, frequency
- Patients with spinal cord injury present with cloudy or malodorous urine, vague abdominal discomfort, malaise, lethargy, leakage between catheterizations, or increased spasticity or autonomic dysreflexia.
- Fever of unknown origin
- Failure to thrive in infant or child

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 pyuria or proteinuria. 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.
- Creatinine elevation may be associated with significant intrinsic renal damage.

Imaging

- Imaging studies (ExU or CT) reveal the typical findings of chronic pyelonephritis:
  - Small or atrophic kidney, unilateral or bilaterally
  - Compensatory hypertrophy with unilateral atrophy
  - Blunted 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. Pyonephrosis or abscesses are usually identified if present.
- Plain radiographs useful to evaluate abnormal calcifications and gas patterns.
- Tc-DMSA (technetium-99m DMSA) renal scanning is considered among best studies to evaluate for renal scarring.

Diagnostic Procedures/Surgery

- Cystoscopy in selected cases

- Renal biopsy

Pathological 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 colloid, hence the description renal thyroidization.

DIFFERENTIAL DIAGNOSIS

- Analgesic nephropathy
- Diabetic nephropathy
- Gouty nephritis
- Hypertensive renal disease
- Interstitial nephritis
- Lower UTI
- Psoas and subdiaphragmatic abscess
- Renal artery stenosis
- Renal malakoplakia
- Renal TB
- Urolithiasis
- XGP

TREATMENT

- Chronic pyelonephritis is difficult to manage as it is an irreversible process.
- With mild VUR, suppressive antibiotics until resolution or puberty in children
- Severe reflux may require reimplantation.
- Correct anatomic anomalies or stones if possible.

MEDICATION

- Acutely episodes of pyelonephritis should be treated (See Section I: “Pyelonephritis, Acute”).
- Suppressive antibiotics for mild cases of VUR in children:
  - In children <3–6 mo, use low-dose amoxicillin or cephalexin, cefazolin, or other 1st-generation cephalosporin
  - In children >6 mo, switch to nitrofurantoin, trimethoprim-sulfamethoxazole, or trimethoprim alone

• HTN is best treated by ACE inhibitors (lisinopril, enalapril, ramipril) that may also protect the kidney from progressive renal failure:

– ACE inhibitors increase the risk for congenital anomalies when used in the 2nd and 3rd trimesters and are therefore contraindicated.

SURGERY/OTHER PROCEDURES

• Correction of reflux may be necessary in children with high-grade reflux. Low-grade reflux may resolve with time.

• Nephrectomy for persistent/recurrent infection unresponsive to systemic treatment, markedly decreased function (ie, 10%), pain, or refractory HTN

ADDITIONAL TREATMENT

• If XGP diagnosed, Proteus sp. is often involved.

• Nephrectomy usually chosen but partial nephrectomy can also treat focal disease.

ONGOING CARE

PROGNOSIS

• 24-hr protein excretion may be an important prognostic indicator of progressive deterioration of renal function due to focal and segmental glomerulosclerosis superimposed on tubulointerstitial disease.

• Radionuclide renal scan can assess renal function and scarring.

COMPLICATIONS

Emphysematous pyelonephritis:

• ESRD: In children with reflux, a small percentage can have renal failure.

• Focal segmental glomerulosclerosis

• HTN

• Perinephric abscess: Requires surgical drainage.

• Polyuria, nocturia from loss of tubular concentrating ability

• Pregnancy-related miscarriages in women with chronic reflux

• Proteinuria

• Pyonephrosis

• XGP

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Repeat urine cultures 2 wk after therapy to check for persistent infection and follow-up at 3-mo intervals.

• Serial US every 1–2 yr

• Serum creatinine.

- BP checks; good control of BP may limit renal damage over time:
  - 15% of patients with reflux nephropathy who reach adulthood have HTN.
  - Some advocate screening renal US of siblings who have reflux

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Pyelonephritis, Acute
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Vesicoureteral Reflux, Adult
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

- 041.9 Bacterial infection, unspecified, in conditions classified elsewhere and of unspecified site
- 590.00 Chronic pyelonephritis without lesion of renal medullary necrosis

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- BP: Blood pressure
- CVA: Costovertebral angle
- DMSA: Dimercaptosuccinic acid
- ESRD: End-stage renal disease
- ExU: Excretory urogram
- FSGS: Focal segmental glomerulosclerosis
- HTN: Hypertension
- US: Ultrasound

- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux
- WBC: White blood cell
- XGP: Xanthogranulomatous pyelonephritis

PYELONEPHRITIS, EMPHYSEMATOUS

Scott G. Hubosky, MD

BASICS

DESCRIPTION

- A rare but potentially lethal, acute, necrotizing infection involving the renal parenchyma, renal pelvis, and perinephric tissues caused by a gas-forming organism.
- Highest risk in those with diabetes and patients with obstructing renal or ureteral stones
- Mortality rates in described series range from 10–40%.
- Synonym(s): Renal emphysema, Pneumonephritis

EPIDEMIOLOGY

- Only a few hundred cases have been reported in the English literature since 1966.
- Female > Male (6:1)
- Most patients are >60
- Bilateral cases are very unusual but reported.
- The left renal unit is slightly more likely to be involved.
- No documented cases in children.

RISK FACTORS

- DM found in >80–90%:
  - Poor glycemic control is common
- Urinary tract obstruction usually found in nondiabetic cases:
  - Stones
  - Papillary necrosis
  - Calyceal stenosis
- Alcohol abuse
- Malnutrition
- Immune compromise and neoplasia

GENERAL PREVENTION

- Strict glycemic control of pre-existing DM helpful
- Adequate treatment of pre-existing pyelonephritis
- Expedient resolution of urinary tract obstruction if present

PATHOPHYSIOLOGY

- Emphysematous pyelitis (gas in the renal pelvis) may occur with or without emphysematous pyelonephritis (gas in the renal parenchyma)
- Infection with gas-producing organism. Gas collection in both collecting system and renal parenchyma. Occasionally gas may be seen in perinephric tissues.

- Escherichia coli is most common (70–90%).
- Klebsiella, Proteus, Clostridium, and Candida also isolated. Polymicrobial infections in 10%
- Entamoeba histolytica and Aspergillus fumigatus are newly emerging pathogens, particularly in immunocompromised patients.
- Bacterial fermentation of glucose produces hydrogen and carbon dioxide gas
- Low oxygen tensions facilitate ascending UTI (Facultative anaerobes: E. coli, Proteus, Klebsiella) proliferation.
- DM predisposes to gas formation due to high tissue concentrations of glucose, microangiopathic disease resulting in hypoxic conditions, and an immunodeficient-like state preventing adequate leukocyte response.

COMMONLY ASSOCIATED CONDITIONS

- DM
- Immunocompromised states, including renal transplant recipients in transplanted kidney
- Urinary tract obstruction due to stones or papillary necrosis and sloughed papilla

DIAGNOSIS

HISTORY

- Fever, chills, rigors
- Nausea, vomiting
- Severe abdominal and flank pain
- Urgency, frequency, dysuria
- Malaise
- Mental status changes
- Pneumaturia is uncommon unless secondary emphysematous cystitis present
- Past medical history with focus of diabetes and HgbA1c as a marker for glycemic control
- Immunocompromising diseases or medications
- History of urolithiasis

PHYSICAL EXAM

- Pyrexia
- Septic shock with tachycardia and hypotension
- Occasionally flank and/or subcutaneous emphysema may be present but is not typical

ALERT

Emphysematous pyelonephritis is a life-threatening urologic emergency that requires prompt diagnosis and intervention to prevent mortality.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Leukocytosis
- Thrombocytopenia in up to 50% of cases at presentation and may be related to early DIC and in some series, platelet counts of <60,000/uL were associated with an increased risk of death.
- Elevated creatinine
- Hyperglycemia
- Lactic acidosis
- Significant pyuria and bacteruria on urinalysis
- Positive blood and urine cultures for causative organism

Imaging

- CT is modality of choice and shows gas in renal parenchyma, collecting system, and/or perirenal tissue:
  - Contrast not essential for diagnosis and may be contraindicated with renal impairment
  - Stones may be detected. Look for evidence of sloughed papilla.
  - Gas may also be seen in the renal vein or extending into the retroperitoneum.
  - Descriptors used in describing the CT findings include streaky and bubbly shadows in and surrounding the kidney. Crescent-shaped gas distribution surrounding the kidney.
  - Emphysematous pyelitis refers to gas in the renal collecting system.
  - Dry-type emphysematous pyelonephritis refers to gas only in the parenchyma and is often best treated by immediate nephrectomy.
- KUB may show gas over renal silhouette but is nonspecific and has low sensitivity. CT is preferred imaging modality. Ileus pattern is common.
- MRI is not a recommended study.
- Many classification systems based on imaging have been described. The most recent version is noted here:
  - Class 1: Gas confined to the collecting system
  - Class 2: Gas confined to the renal parenchyma alone
  - Class 3A: Perinephric extension of gas or abscess
  - Class 3B: Extension of gas beyond the Gerota fascia
  - Class 4: Bilateral emphysematous pyelonephritis or emphysematous pyelonephritis in a solitary renal unit.
  - This system may provide prognostic and therapeutic implications. For class 1 and 2 disease percutaneous drainage was successful and mortality was very low. For class 3 and

4 disease, mortality was higher, and the success of percutaneous drainage was much less.

Diagnostic Procedures/Surgery

Diagnosis made radiographically

Pathological Findings

- Gross kidney shows multiple abscesses in parenchyma with empty central area.
- Microscopic exam shows glomerulosclerosis, arteriosclerosis, intrarenal vascular thrombi, and papillary necrosis.

DIFFERENTIAL DIAGNOSIS

- Emphysematous cystitis
- Necrotic renal tumor
- Pyelonephritis
- Pyonephrosis with urinary tract obstruction
- Renal abscess
- Xanthogranulomatous pyelonephritis: May also produce gas in the kidney, but usually not to the degree of emphysematous pyelonephritis
- Intrarenal gas following urologic intervention (ureteroscopy, retrograde pyelogram)
- Reno-alimentary or broncho-renal fistulas
- Occasionally overlying bowel gas can be confused with intrarenal gas collection.

TREATMENT

- Severe pyelonephritis and emphysematous pyelonephritis may have similar presentations.
- Fluid resuscitation
- IV pressors with ICU monitoring if needed
- Insulin drip if needed to control blood sugars
- Foley catheter to monitor urine output and maximize drainage
- Antibiotics should be initiated before initiating any radiologic investigation
- A combination of percutaneous drainage with antibiotics is often the preferred management of emphysematous pyelonephritis today

MEDICATION

- Broad-spectrum IV antibiotics empirically, then tailor choice based on cultures
- Intravenous ampicillin, gentamicin, and metronidazole initial choices. In patients with penicillin allergy, use vancomycin in place of ampicillin.
- Alternatively, quinolones have excellent tissue penetration and good gram-negative coverage.

SURGERY/OTHER PROCEDURES

- Emergent nephrectomy was former gold standard; patient needs adequate resuscitation and stabilization before anesthesia.
- Flank approach preferred to avoid abdominal cavity; extensive inflammation may be associated with high blood loss.
- Nephrectomy may still be required if patient does not improve with drainage and IV antibiotics.
- In dry-type emphysematous pyelonephritis where the gas is limited to only the parenchyma, percutaneous drainage may not be as effective as immediate nephrectomy.
- Delayed, elective nephrectomy may be necessary for nonfunctioning kidneys; however, a nonfunctioning kidney may not respond well to antibiotic therapy and should be considered for immediate nephrectomy.
- Recent meta-analysis of 10 retrospective series on 210 patients showed 13.5% mortality in those percutaneously drained vs. 25% mortality in emergent nephrectomy.

ADDITIONAL TREATMENT

Relief of obstruction is paramount in management. Although percutaneous drainage is the mainstay, ureteral stenting may also have a role in selected cases.

ONGOING CARE

PROGNOSIS

- Mortality highest in those patients presenting with these risk factors: Shock, mental status changes, acute renal failure or thrombocytopenia
- Index of suspicion must be high in diabetic patients with fever and flank pain.

COMPLICATIONS

- Septic shock due to urosepsis
- Loss of renal unit and renal insufficiency
- Perinephric abscess
- Postoperative wound infections due to contamination
- Complications due to percutaneous drainage or nephrectomy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow up CT in few days if percutaneous drainage performed
- Blood and urine cultures must be followed for sensitivities.
- Nuclear renal scan to determine split renal function and to determine if elective nephrectomy is required when patient stable.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Pyelonephritis, Acute
- Pyelonephritis, Chronic
- 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

ABBREVIATIONS

- CT: Computed tomography
- DIC: Disseminated intravascular coagulation
- DM: Diabetes mellitus
- ICU: Intensive care unit
- IV: Intravenous
- KUB: Kidneys, ureters, bladder
- MRI: Magnetic resonance imaging
- UTI: Urinary tract infection

PYELONEPHRITIS, XANTHOGRANULOMATOUS (XGP)

Margaret S. Pearle, MD, PhD

BASICS

DESCRIPTION

- A rare, severe form of chronic renal infection that culminates in diffuse renal destruction and a nonfunctioning kidney.
- Xanthogranuloma is the characteristic nodular infiltration by lipid-laden macrophages.
- Sometimes described as a pseudotumor because of its local growth characteristics; can sometimes be mistaken for a malignancy on imaging studies.

EPIDEMIOLOGY

- Rare disorder that occurs in 0.6–1.4% of patients with renal inflammatory disorders evaluated pathologically.
- Female > Male (3:1)
- Peak incidence in 5th–7th decade of life but can occur at any age
- Described in children
- Both sides affected equally, but typically unilateral process

RISK FACTORS

- Diabetes
- History of stones
- History of UTIs
- Urologic instrumentation

GENERAL PREVENTION

Adequate treatment of known UTI may limit development

PATHOPHYSIOLOGY

- 3 key pathogenetic factors are stones, obstruction, and infection:
  - Obstruction followed by infection can lead to tissue destruction and ultimately renal loss.
  - Sloughed renal papilla may also cause obstruction.
- Likely involves an altered host acute inflammatory response due to obstruction or ischemia.
- Proteus mirabilis is most common associated organism followed by E. coli.
- Diabetics, with altered immune response, are affected most commonly.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- Renal calculi, including staghorn calculi

- Immunosuppression

ALERT

XGP has been called the “great imitator” because it often cannot be distinguished clinically or radiographically from renal cell carcinoma.

DIAGNOSIS

HISTORY

- Nonspecific signs and indolent course

)[B]

- Persistent bacteriuria despite treatment with appropriate antibiotics
- ~1/3 of XGP patients have a history of stones
- Diabetes common
- HTN in about 20% of patients

PHYSICAL EXAM

- Fever
- Elevated BP in rare cases
- Flank tenderness
- Palpable flank mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[B]

- Renal function normal or unaffected
- Urinalysis: WBC, RBC, bacteria, protein
- Urine cytology may show foam cells but predictive value of this finding is controversial.
- Urine culture may be negative, but Proteus and E. coli are common pathogens:
  - Mixed urine cultures occur in 10% of XGP patients
  - May require tissue culture to identify organism
- Liver enzymes abnormal in as many as 1/2 of XGP patients (Stauffer syndrome)

Imaging

- CT is imaging study of choice:
  - Can diagnose stones and hydronephrosis
  - Multiple renal calculi or staghorn calculi may be seen.
  - Shows enlarged kidney/mass
  - Renal parenchyma replaced with low attenuation cystic structures and renal abscesses
  - Walls, but not cavities, of these cystic structures enhance

- IV urogram shows nonvisualization of kidney in 30–80% of patients:
  - Stone visible in 30–80% of patients
  - Common finding is a reniform mass with distorted calyces.
- Renal US shows an enlarged kidney with an echogenic focus representing the stone and anechoic areas of parenchyma.
- Retrograde pyelogram is usually not necessary but would show distortion of the collecting system.
- MRI provides little additional information over CT.
- Tc-DMSA (technetium99m dimercaptosuccinic acid) or MAG-3 (mercaptotriglycine) renal scans can be used to evaluate differential renal function. Renal scan may confirm nonfunction of the involved kidney.

Diagnostic Procedures/Surgery

Diagnosis is made on the basis of clinical suspicion and radiographic imaging studies.

Pathological Findings

- Diffuse involvement of entire kidney is present in up to 80% of cases.
- Segmental involvement is less common:
  - XGP can cause extensive local tissue invasion and destruction. Occasionally adjacent organs are involved. Pyelocutaneous and uretero-cutaneous fistulae can be found.
- Gross findings:
  - Massively enlarged kidney
  - Hydronephrosis
  - Obstructing stone(s)
  - Pus-filled calyces and parenchymal abscesses
  - Yellow nodules surrounding the calyces represent lipid-laden macrophages
- Microscopic findings:
  - Thin cortex with extension of inflammatory response beyond kidney
  - Lipid-laden macrophages (xanthoma cells) admixed with lymphocytes, plasma cells, and giant cells form sheets around the calyces and parenchymal abscesses
  - On gross sectioning, the mass may resemble a renal cell carcinoma with hemorrhage, necrosis, and the characteristic yellow appearance.
  - Nonfunctioning kidney is often the end result.

DIFFERENTIAL DIAGNOSIS

- Pyonephrosis
- Renal abscess
- Renal lymphoma

- Renal tumor
- TB

TREATMENT

- Primarily managed by nephrectomy
- Culture-specific antibiotics should be continued until urine cultures are negative.
- Antibiotics should be altered based on the results of the tissue culture

MEDICATION

- Broad-spectrum antibiotics pending urine culture, such as ampicillin 1 g q8h and an aminoglycoside (ie, gentamicin 5 mg/kg q24h) is usually effective until culture-specific antibiotics can be initiated.
- Negative urine cultures are common, and tissue cultures taken at the time of surgery may be necessary to identify the offending organism.
- Some recommend continuing oral antibiotics for up to 1 wk following nephrectomy.

SURGERY/OTHER PROCEDURES

- Nephrectomy is the usual treatment because of the diffuse nature of the inflammatory process, nonfunctioning kidney, or concern for malignancy
- Nephrectomy can be extremely difficult due to intense inflammatory reaction.

)[B]

- Flank approach preferred so as to avoid contaminating the peritoneal cavity:
  - Full mechanical and antibiotic bowel prep is recommended since XGP may involve any surrounding organs or tissues.
  - Drains should be placed in the renal bed.

)[B]

ONGOING CARE

PROGNOSIS

- With removal of the stone and infected tissue, the prognosis for preserved renal function is good, provided patient has normal contralateral kidney.
- Likelihood of a recurrence in the contralateral kidney is very low.
- Likelihood of recurrent stones is high.

COMPLICATIONS

- Renal insufficiency if the contralateral kidney is compromised
- Recurrent stone formation
- Respiratory complications after surgery
- Wound infection
- Injury to adjacent organs such as the spleen requiring splenectomy or the liver, colon, or duodenum may occur during nephrectomy.

- Major vascular injury due to inflammatory process
- Fistulas (often form the drain site) or abscesses may occur postoperatively, requiring drainage and further antibiotic therapy based on cultures.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Serum creatinine, CBC, and liver enzymes (if abnormal) should be repeated to assure normalization.
- Histopathology of kidney guides need for further radiographic studies

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See Also (Topic, Algorithm, Electronic Media Element)

- Pyelonephritis, Acute
- Pyelonephritis, Chronic
- Pyelonephritis, Emphysematous
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

590.00 Chronic pyelonephritis without lesion of renal medullary necrosis

ABBREVIATIONS

- BP: Blood pressure
- CBC: Complete blood count
- CT: Computed tomography
- HTN: Hypertension
- IVU: Intravenous urogram
- MRI: Magnetic resonance imaging
- RBC: Red blood cell
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell
- XGP: Xanthogranulomatous pyelonephritis

PYURIA

Bilal Chughtai, MD

Michael Perrotti, MD

BASICS

DESCRIPTION

- The presence of WBCs in the urine; implies the presence of an inflammatory response.
- Normally, men have <2 WBC/HPF and women <5 WBC/HPF
- Definition of significant pyuria varies but most sources indicate the following definitions:
  - Unspun urine: >1 WBC/HPF (400×) or >10 WBC/mm3
  - Centrifuged urine: >10 WBC/HPF in the resuspended sediment of a centrifuged aliquot of urine (10–15 mL of urine spun at 1,500–3,000 rpm for 5 min). The supernatant then is decanted and the sediment resuspended in the remaining liquid and placed on a slide.
- Sterile pyuria is the presence of WBCs without the presence of bacteria and suggests either partially treated UTI therapy or other disorders such as cancer, stones, or atypical infection with TB or another atypical organism. Other inflammatory disorders, possibly outside of GU tract should be considered.

EPIDEMIOLOGY

Association between pyuria and bacteriuria:

- 96% of patients who are symptomatic from a UTI and are bacteruric have >10 WBCs/HPF

RISK FACTORS

- Urolithiasis
- Previous history of UTI

PATHOPHYSIOLOGY

- Clean-catch midstream urine may contain contaminants of bacteria and WBCs.
- Significant pyuria may represent true infection.
- Bacteria in urinary tract leading to inflammatory response
- Bacterial factors
- Bacteria successfully colonize the urinary tract in a retrograde manner
- Certain bacteria are efficient at adhering to mucosal cells.

COMMONLY ASSOCIATED CONDITIONS

- Bacteruria
- UTI
- Renal calculi

ALERT

Persistence of sterile pyuria in the setting of symptoms relating to pyelonephritis and no identifiable anatomic lesion should prompt an evaluation for the tubercle bacillus or other atypical pathogen such as Chlamydia or Ureaplasma.

DIAGNOSIS

HISTORY

- Dysuria, frequency, urgency, malaise, rarely low-grade fever.
- Occasionally, hematuria (gross): Especially in the female patient; uncommon in children and men
- Fever and flank pain with upper tract origin: Pyelonephritis
- Asymptomatic or atypical symptoms: Young and old patients
- Young patients: Abdominal discomfort, failure to thrive, fever, vomiting, jaundice
- Older patients: May be asymptomatic or have incontinence, fevers, frequency, and urgency
- Varied symptoms with sterile pyuria associated with varied pathology
- History of childhood fevers: May imply UTIs and associated congenital abnormalities
- Problems with toilet training, urgency, incontinence
- Family history of UTIs: Mothers, daughters, sisters
- History of a risk factor for bacteriuria

PHYSICAL EXAM

- Suprapubic tenderness: Cystitis
- Flank tenderness: Pyelonephritis
- Fever: Usually with upper-tract infection
- Children may have abdominal discomfort, tenderness, or distention

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Dipstick: Best for screening. Note that the LE read time for most test strips is up to 2 minutes, whereas other analytes can be read in 30–60 seconds.
- LE test:
  - Detects the presence of WBCs in the urine; normal test is negative.
  - LE is produced by granulocytic leukocytes that catalyze the hydrolysis of an indoxyl carbonic acid ester to indoxyl. The indoxyl reacts with a diazonium salt to produce a purple color on the reagent strip.
  - Sensitivity 72–97%, specificity 41–86% for detection of culture-positive UTI
  - Test not affected by red cell concentrations up to 10,000/L. Glucose >1 g/dL, albumin >500 mg/dL, formaldehyde, cephelalexin, and gentamicin may interfere with test.

– False-negative LE (pyuria present but negative dipstick): Very concentrated urine, glycosuria, presence of urobilinogen, large amounts of ascorbic acid, cephalexin, cephalothin, and tetracycline.

– False-positive LE (pyuria absent, but positive dipstick): Contamination (vaginal, etc.) or after instrumentation of the urinary tract, presence of imipenem, meropenem, clavulanic acid

– Pyuria and a positive LE test can be seen in the absence of bacteruria. This sterile pyuria can be seen in infection with atypical organisms (TB, Chlamydia, Ureaplasma), urolithiasis, glomerulonephritis, interstitial cystitis, CIS, exercise, steroid use, cyclophosphamide, and in partially treated infection. LE test may be truly positive and suggest a significant disease process but with no evidence of a pyogenic (bacterial) infection.

- Determine the presence of nitrites, blood, or protein. If present, may indicate UTI in the setting of pyuria
- Microscopic exam: Presence of crystals or bacteria
- Gram stain: May increase identification of bacteria
- Culture technique:
  – Clean-catch midstream urine: Most commonly used
  – Catheterized urine: May be necessary to assure diagnosis or in special situations (ie, children, patients unable to void, the debilitated, the obese)
- Segmented urine specimen:
  – Voided specimen 1,2,3 to localize to urethra, bladder, prostate
  – Also called Stamey test (Meares-Stamey Test). For full discission see Section I: “Prostatitis, Chronic, Bacterial (NIH II)” and “Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)”
- Rapid in-office test:
  – Semi-quantitative screening culture devices for detecting, enumerating, and identifying specific bacteria in urine:
  – 80% accurate; usually fresh unspun sample
- Urine cytology: If urothelial carcinoma suspected

Imaging

- Childhood: US, VCUG, radionuclide cystogram, IV pyelogram
- Adult: Only indicated if suspicious of pathology history, obstruction, stone disease, hematuria
- Imaging in routine UTIs involving normal adult females: Very low yield of pathology:
  – Sterile pyuria evaluation for other causes

Diagnostic Procedures/Surgery

- Localization of bacteria: Segmented urine, ureteral catheterization, immunologic antibody studies
- Isotopic function studies and cystogram
- CT: Localization of nidus or abnormality responsible for bacteriuria/pyuria (ie, abscess)

DIFFERENTIAL DIAGNOSIS

- Contamination of specimen with vaginal organisms and/or cells
- Cystitis
- Epididymitis
- Genitourinary TB
- Interstitial cystitis
- Interstitial nephritis (eg, analgesic nephropathy)
- Kawasaki disease
- Neoplasm: Urothelial carcinoma, renal cell carcinoma
- Nonuropathogenic cause: As in sterile pyuria
- Prostatitis
- Pyelonephritis: Acute, chronic, emphysematous, tuberculous, xanthogranulomatous
- Renal abscess
- Renal papillary necrosis
- STD
- Transplant rejection
- Urethral diverticulum
- Urethritis
- Urinary diversions and foreign bodies in the urinary tract (stents, etc.)
- Urinary tract fistula
- Vulvovaginitis

TREATMENT

- Identify leading cause of inflammatory response.
- Treatment is directed at the cause of pyuria.
- Most commonly, UTI will be the cause.

MEDICATION

In infection, treat with appropriate antibiotics based on empiric therapy or culture results. See Section I: “Urinary Tract Infection (UTI)” topics.

SURGERY/OTHER PROCEDURES

- Correct underlying disorder.

- Treat kidney stone, foreign body, etc.

ADDITIONAL TREATMENT

- Bacteriuria with pyuria is treated as a UTI in childhood and premenopausal women.
- Persistent or recurrent bacteriuria: May need treatment for more prolonged periods followed by chronic low-dose medication
- High-risk patients (children with congenital abnormalities and adults with significant risk factors): May need chronic suppressive antimicrobial treatment
- Postmenopausal: Treated only if symptomatic or associated with complicating factors
- Diabetics and those with obstruction or on immunosuppression may need other means to address ongoing pyuria.

ONGOING CARE

PROGNOSIS

Based on etiology

COMPLICATIONS

Possible ascending infection, sepsis, renal failure, death if there is significant delay in treatment of UTI

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Repeat exam: 2 wk post-treatment for UTI:
  - Ensure asymptomatic
- Microscopic: Urinalysis, urine culture
- Periodic urinalysis to verify clearing of pyuria

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bacteruria and Pyuria

- Pyelonephritis, Chronic
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Prostatitis, Chronic, Bacterial (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Prostatitis, General
- Pyuria Algorithm
- Tuberculosis, Genitourinary
- Urinary Tract Infection (UTI), Adult Female
- Urinary Tract Infection (UTI), Adult Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

- 041.9 Bacterial infection, unspecified, in conditions classified elsewhere and of unspecified site
- 599.0 Urinary tract infection, site not specified
- 791.9 Other nonspecific findings on examination of urine

ABBREVIATIONS

- CIS: Carcinoma in situ
- CT: Computed tomography
- GU: Genitourinary
- HPF: High-powered field
- LE: Leukocyte esterase
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourogram
- WBC: White blood cell

RENAL AND PERIRENAL ABSCESS

Marc C. Smaldone, MD

Joel B. Nelson, MD

BASICS

DESCRIPTION

- Renal abscess/carbuncle: Collection of purulent material confined to the renal parenchyma.
- Perirenal abscess: Results from extension of an acute cortical abscess into the perinephric space; confined by Gerota fascia.
- Pararenal/perinephric abscess: Results from the rupture of a perinephric abscess through Gerota fascia into the pararenal space

EPIDEMIOLOGY

Perinephric and renal abscesses are uncommon but potentially lethal complications of UTI.

RISK FACTORS

- 2/3 of gram-negative abscesses are associated with renal calculi or kidneys with poor function.
- Diabetes mellitus, polycystic kidney disease, hemodialysis, neurogenic bladder
- Ascending infection: Associated with distal obstruction, complicated UTIs associated with stasis, or vesicoureteral reflux
- Hematogenous renal seeding: Skin infection with gram-positive organisms, IV drug abuse, immunocompromised status
- Pregnant women with untreated bacteriuria are associated with a higher incidence of pyelonephritis and subsequent diagnosis of abscess.
- Renal infection is among the most common sites for extrapulmonary disease in patients with TB.

GENERAL PREVENTION

Increased clinical suspicion, prompt recognition, and treatment of infection, especially in the face of obstruction or high-risk patients.

PATHOPHYSIOLOGY

- Gram-negative organisms have been implicated in the majority of adults with renal abscesses.
- Escherichia coli, Proteus mirabilis, and Staphylococcus aureus (in descending order of occurrence) account for the majority of infections.
- Hematogenous renal seeding by gram-negative organisms may occur, but this is not likely to be the primary pathway for gram-negative abscess formation.

• Ascending infection associated with tubular obstruction from prior infections, vesicoureteral reflux, or calculi appears to be the primary pathway for the establishment of gram-negative abscesses.

DIAGNOSIS

HISTORY

- Significant chronic or acute illnesses including diabetes, neurogenic bladder dysfunction, chronic renal failure, hemodialysis, and polycystic renal disease
- Renal calculi
- IV drug abuse
- Gram-positive source of infection 1–8 wk before the onset of urinary tract symptoms (preceding infection can occur in any area of the body)
- 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
- Abdominal and/or flank mass
- CVA or flank tenderness
- Distended or palpable bladder
- Skin carbuncles or dermatologic evidence of IV drug abuse
- Heart murmurs

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum creatinine:
  - Variable findings, dependent on concurrent obstruction and underlying renal dysfunction
- CBC:
  - Patients typically have marked leukocytosis
- 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
- 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 bloodborne, urine cultures in these cases typically show no growth or a microorganism different from that isolated from the abscess.

- Blood cultures:
  - Gram-negative organisms are most commonly cultured.
  - Gram-positive organisms are not routinely similar to those cultured from abscess.

Imaging

- Differentiation between early renal abscess and acute pyelonephritis is difficult due to small size.
- IV urography:
  - 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
  - Absence of psoas shadow on affected side
  - Bubbles of extraluminal gas can be seen surrounding the kidney in large perinephric abscesses.
- Abdominal US:
  - Quickest and least expensive diagnostic imaging study
  - Common findings include an echo-free or low-echodensity space-occupying lesion with increased transmission, which is poorly marginated during the acute phase.
  - Well-defined discrete lesion during chronic stages, which is difficult to distinguish from a renal mass.
- Abdominal CT:
  - Diagnostic procedure of choice
  - Can often delineate the route of spread of infection into surrounding tissues
  - Abscesses are characteristically well-defined both before 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 (perinephric) 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).

Diagnostic Procedures/Surgery

CT- or US-guided needle aspiration may be necessary to differentiate an abscess from a hypervascular tumor; aspirated material can be cultured and appropriate antimicrobial therapy

instituted.

DIFFERENTIAL DIAGNOSIS

- Pyelonephritis
- Pyonephrosis
- Xanthogranulomatous pyelonephritis
- Emphysematous pyelonephritis
- Renal TB
- Bowel perforation with retroperitoneal spread of infection

TREATMENT

- 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 tailored 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.
- Obstruction, if present, must be relieved.

MEDICATION

- Antibiotic therapy: May prevent surgical intervention unless abscess involves perinephric space.
- Initiate empiric treatment with fluid resuscitation and broad-spectrum IV antibiotics.
- IV 3rd-generation cephalosporins, aminoglycosides, or antipseudomonal penicillins
- Adjust antibiotic coverage according to culture/sensitivity results.
- Adjust dose for renal function.
- For a suspected hematogenous source, expand coverage to include penicillin-resistant Staphylococcus.

SURGERY/OTHER PROCEDURES

- Standard treatment for renal abscesses >5 cm or those that fail to respond to percutaneous drainage and IV antibiotic therapy has been rapid incision and drainage.
- 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

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.

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 5–12%.

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, genitourinary fistulas to the lung, colon, skin, etc.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Address the underlying medical conditions to prevent recurrent infections.
- Repeat radiographic studies to confirm repeat resolution.
- Extended antibiotic therapy is often required.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Pyelonephritis, Acute
- Pyelonephritis, Chronic
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Pyonephrosis
- Retroperitoneal Abscess

CODES

ICD9

590.2 Renal and perinephric abscess

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle
- IV: Intravenous
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection

RENAL AND URETERAL CALCULI (NEPHROLITHIASIS)

Nicholas T. Leone, MD

Demetrius H. Bagley, MD

BASICS

DESCRIPTION

- The upper urinary tract includes the kidney and ureter and is a common location for the clinical presentation of urolithiasis.
- Sites of calculi in the upper urinary tract include the calyx, renal pelvis, and the ureter (upper, mid, lower).
- Nature of the colic can often denote the location of the stone.
- Synonym(s): Nephrolithiasis

EPIDEMIOLOGY

- 12 cases per 10,000 persons in US
- 4% for women, 12% for men
- Peak incidence 30–60 yr
- Increasing incidence in developed countries due to high dietary protein intake
- Whites > Hispanics > Asians > Blacks

RISK FACTORS

- Male > Female (1.3:1); traditional ratio of Male > Female (3:1) is narrower due to life-style changes.
- Family history: 3 times normal risk
- Increased BMI increases risk.
- Prior stone history: Recurrence increases with time:
  - Year 1: 10–15% risk
  - Year 5: 50–60% risk
  - Year 10: 70–80% risk
- Sedentary lifestyle, immobilization, dehydration, inflammatory bowel disease
- UTI with urea-splitting organisms (eg, Proteus)

Genetics

- Urolithiasis: A polygenetic defect and partial penetrance not completely defined
- Cystinuria: Homozygous recessive disorder
- Renal tubular acidosis is inherited.

GENERAL PREVENTION

- High fluid intake: Urine output goal 2 L/d.
- Restrict sodium: Increased sodium intake of 100 mEq/d increases urinary calcium 50 mg/d.

- Moderate oxalate restriction: Spinach, tea, chocolate, nuts
- Moderate calcium intake: 800–1,000 mg/d
- Meat intake 2 servings/d
- Avoid high doses of vitamin C (>500 mg/d).

PATHOPHYSIOLOGY

- Supersaturation: Urine becomes supersaturated with stone-forming salts, which precipitate out of solution and form crystals that can aggregate and develop stones; highly dependent on urine volume and pH.
- Inhibitors: Allow for a higher urinary concentration of stone-forming salts to be held in solution before precipitation occurs, inhibiting stone formation; low urinary inhibitors (citrate, magnesium, urea, etc.) can lead to stone formation.

COMMONLY ASSOCIATED CONDITIONS

- Generic conditions related to stone formation
- Urinary obstruction or stasis, chronic diarrhea, foreign material in urinary tract
- Specific conditions and stone composition:
  - Calcium oxalate stones: Absorptive hypercalciuria, renal hypercalciuria, hyperparathyroidism, dietary calcium excess, sarcoidosis, inflammatory bowel disease, hyperuricosuria, hyperoxaluria, hypocitraturia
  - Calcium phosphate stones: Type I renal tubular acidosis, medullary sponge kidney
  - Uric acid stones: Gout, Lesch-Nyhan disease, myeloproliferative disorders, neoplastic disorders requiring chemotherapy
  - Struvite stones: UTI with urease-splitting organisms (ie, Proteus, Klebsiella, etc.)
  - Cystine stones: Defective renal tubular reabsorption of dibasic amino acids (cystinuria)
- Stones that are not moving or are only partially obstructing may cause minimal discomfort. Obstructing stone often asymptomatic as upper tract decompresses due to pyelovenous and lymphatic absorption and decompression.
- Upper tract characteristics of calculi location:
  - Calyx: Flank pain with obstruction of ostia; dull ache, may not radiate
  - Renal pelvis: Often asymptomatic; stones >1 cm unlikely to pass; with symptoms, CVA and flank pain radiating to upper abdomen (can be confused with cholecystitis or gastritis)
  - Proximal ureteral stone: Flank pain or CVA tenderness; often radiates to abdomen or groin
  - Mid-ureteral stone: Lower abdominal pain

– Distal ureteral stone: Groin, bladder, scrotum, or labial pain

• 3 sites of upper-tract narrowing can hinder stone progression: UPJ, the iliac vessels, and UVJ. Stones 5 mm usually pass spontaneously. Ureteral stones 6 mm to 1 cm. If >1 cm, the stone will not pass.

DIAGNOSIS

HISTORY

• Pain: Varies from asymptomatic to mild ache to acute colic requiring hospitalization and parenteral analgesia:

– Acute colic: Paroxysms of sudden acute pain that intensifies, often associated with nausea/vomiting, then resolves after 30–60 min

• Microscopic or gross hematuria: Seen in 80%; gross hematuria rarely continues after few days

• Irritative symptom (frequency, urgency, dysuria) suggests bladder stones, distal ureteral stones, or associated UTI.

• Prior history of urolithiasis suggests recurrence.

• Family history of urolithiasis suggests calculi.

PHYSICAL EXAM

• Abnormal vital signs or altered sensorium: Evidence of urosepsis

• Flank tenderness: Can be due to obstructing stone or pyelonephritis

• Fever: Evidence of systemic infection

DIAGNOSTIC TESTS & INTERPRETATION

Lab

• Urinalysis: Hematuria in 85%, pyuria, crystalluria

• pH <6 suggests uric acid stone; pH >8 urea-splitting organism

• Leukocytosis: Evidence of systemic infection

• Azotemia: Evidence of dehydration, bilateral obstruction, or obstruction of solitary kidney

Imaging

• Spiral CT of the abdomen:

– Most common study in setting of acute symptoms, 97% sensitive, 96% specific

– Stone protocol: 3 mm cuts through abdomen and pelvis without contrast

– Assesses number, size, and location of stones; presence of hydronephrosis, forniceal rupture, perinephric stranding

– Density of stone can suggest chemical composition (uric acid ~300 HU, calcium stone ~650 HU)

– Does not provide functional information (hydronephrosis is suggestive of obstruction but not diagnostic)

– CT urogram done with and without contrast

- Intravenous urography:

– Requires IV contrast; historically, best study to define intrarenal and ureteral anatomy; provides information on stone location and degree of obstruction; estimates gross renal function; patients should strain urine due to diuretic effect of IV contrast

- Plain film (KUB):

– 90% sensitive for detecting urinary calculi; quick, inexpensive, minimal radiation exposure; unable to detect small stones (<2 mm) or radiolucent stones (pure uric acid, cystine, indinavir, and xanthine stones)

- US:

– Study of choice for children, pregnant females, and patients with contrast allergy; difficult to detect small stones; can visualize radiolucent stones and hydronephrosis; useful for serial imaging of patients with known stones due to lack of radiation

Diagnostic Procedures/Surgery

Retrograde pyelography is reserved for concomitant endoscopic treatment of stones or placement of ureteral stent to relieve urinary obstruction; rarely necessary for diagnosis.

DIFFERENTIAL DIAGNOSIS

- Abdominal aortic aneurysm
- Appendicitis
- Bowel obstruction
- Cholecystitis or biliary colic
- Gastritis, pancreatitis, peptic ulcer
- Mesenteric ischemia
- Musculoskeletal back pain
- Pyelonephritis
- Sloughed renal papilla
- UPJ obstruction

TREATMENT

- Determine if urolithiasis is associated with urinary obstruction or infection. Infection with obstruction or signs of sepsis requires emergent decompression of upper urinary system, broad-spectrum antibiotics, analgesics; delay definitive surgical treatment until systemic infection is resolved.
- Consider admission for refractory pain, nausea/vomiting/extremes of age or with comorbidities.

• Obstruction in the absence of infection and if renal function is stable (ie, contralateral renal unit healthy and compensating): May consider trial of analgesics and conservative medical management

• Noninfected, nonobstructed stone <5–6 mm, asymptomatic or symptomatic but controlled with oral medication:

– Trial of analgesics and conservative medical management

– Fluid replacement: Treat dehydration but avoid excessive fluid intake as this does not increase the likelihood of stone passage and may aggravate discomfort

• The period of observation for partially obstructing stone is controversial; in general, intervene if stone has not passed within 4–6 wk.

• Strain urine to monitor for spontaneous passage and to collect stone for chemical analysis.

• Stones >6–7 mm usually will require urgent or elective intervention; a period of observation is reasonable. Stones >1 cm almost never pass.

• For the management of calyceal and staghorn calculi, see the specific section in this book.

MEDICATION

• Broad-spectrum antibiotics tailored to urine culture results; may consider trial of conservative medical management

• Analgesia:

– Parenteral route if pain is severe and associated with nausea and vomiting

– NSAIDs can be superior to narcotics for acute renal colic, but should be avoided in patients with azotemia, dehydration, or pregnancy

• Antiemetics if acute colic is associated with nausea and vomiting

• Medical expulsive therapy:

– -Blockers (ie, terazosin, tamsulosin) or calcium-channel blockers (ie, nifedipine) can relax musculature of the ureter and lower urinary tract. Recent studies support their benefit in reducing pain associated with stone passage, increasing frequency of stone passage, and reducing need for surgical intervention.

• Uric acid stones and cystine stones can be dissolved with medical therapy; calcium stones and struvite stones cannot be dissolved:

– Uric acid stones: Alkalinize urine with potassium citrate or bicarbonate to maintain urinary pH at 6.5–7.0:

Urinary pH >7.5 can precipitate calcium phosphate with resulting stone formation

May dissolve up to 1 cm/mo

– Cystine stones: Alkalinize urine with potassium citrate or bicarbonate to maintain urinary pH >7.5. Difficult to dissolve.

SURGERY/OTHER PROCEDURES

- Indications for surgical intervention:
  - Infection with obstruction
  - Intractable pain, nausea, or vomiting
  - Progressive renal deterioration, bilateral obstruction, or obstruction of solitary functional kidney
  - Failure of conservative medical management
  - Occupational: Pilots regardless of stone burden cannot fly with stone
- With systemic infection or infection of obstructed system: Emergent decompression with percutaneous nephrostomy tube or ureteral stent
- ESWL:
  - Success rate 80–90% for stones <2 cm; lower success for lower-pole calyceal stones and impacted ureteral stones
  - Contraindications: Pregnancy, bleeding diathesis, and distal urinary obstruction
- Percutaneous nephrolithotomy:
  - Large stone burdens >2 cm, staghorn calculi, lower-pole stones, cysteine stones, upper urinary tract anatomic abnormalities, transplant kidney stones
  - Success rate approaches 100%, although repeat procedures may be necessary.
  - Contraindications: Bleeding diathesis and untreated infection
- Flexible and semirigid ureteroscopy:
  - Gold standard for mid/distal ureteral stones
  - Flexible ureteroscopy capable of accessing entire upper urinary tract
  - Options: Basket extraction, holmium laser ablation, electrohydraulic lithotripsy, and US lithotripsy
- Open surgical removal: Historical gold standard for urolithiasis, now used <1% of all stone cases. Appropriate for large staghorn calculi, especially in setting of concomitant UPJ obstruction

ONGOING CARE

PROGNOSIS

- Historical probability of stone passage based on location and size:
  - Proximal ureter: >5 mm, 0%; 5 mm, 57%; <5 mm, 53%
  - Mid-ureter: >5 mm, 0%; 5 mm, 20%; <5 mm, 38%
  - Distal ureter: >5 mm, 25%; 5 mm, 45%; <5 mm, 74%

- Excellent prognosis for treatment of existing calculi, given the highly successful surgical options available should medical therapy fail
- 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.

COMPLICATIONS

Untreated stones can predispose to recurrent local or systemic infection, pyelonephritis, urosepsis, and irreversible renal impairment.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- If stone is passed or extracted, it should be analyzed for chemical composition.
- A metabolic abnormality is diagnosed in 97% of stone-forming patients after proper evaluation.
- Patients with asymptomatic, clinically inactive stones can be monitored with semiannual US to watch for metabolic activity (ie, growth in size or number of stones) and should be counseled on reasons for seeking immediate medical attention.

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See Also (Topic, Algorithm, Electronic Media Element)

- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General

CODES

ICD9

- 592.0 Calculus of kidney
- 592.1 Calculus of ureter
- 592.9 Urinary calculus, unspecified

ABBREVIATIONS

- BMI: Body mass index
- CT: Computed tomography
- CVA: Costovertebral angle
- ESWL: Extracorporeal shock wave lithotripsy
- HU: Hounsfield units
- KUB: Kidneys, ureters, bladder
- NSAID: Nonsteroidal anti-inflammatory drug
- UPJ: Ureteropelvic junction
- US: Ultrasound
- UTI: Urinary tract infection
- UVJ: Ureterovesicular junction

RENAL ANGIOMYOLIPOMA

Stanley Zaslau, MD, MBA

Can Talug, MD

BASICS

DESCRIPTION

- AML:
  - A benign renal tumor (hamartoma) composed of adipose tissue, muscle cells, and vascular structures
  - Tumors <4 cm are less likely to be symptomatic.
  - Increased risk of spontaneous bleed
  - Can be sporadic but most often associated with TSC
  - 50–80 % of patients with TSC will develop AML
- TSC: Autosomal dominant disorder comprised of mental retardation, epilepsy, angiofibromas of the face (adenoma sebaceum), hamartomas in kidney, brain, eye (retinal phakomas), heart, lung, and bone.
- LAM: Seen in woman of reproductive age and a subset of males and females with TSC; associated findings include hamartomas of smooth muscle in the lungs leading to respiratory failure
- Wunderlich syndrome: May be the 1st manifestation of AML. This is spontaneous, nontraumatic renal hemorrhage, usually confined to the subcapsular and perirenal spaces.

EPIDEMIOLOGY

- Uncommon: Prevalence of 0.13%; comprises 2–3% of all renal tumors.
- 20–30% of cases are seen in patients with TSC
- Mean age:
  - Sporadic AML: 5th or 6th decade
  - TSC patients: Age 30
- Female > Male (4:1) overall
- Female > Male (2:1) in TSC patients
- Right side more common than left

RISK FACTORS

- TSC (50% develop AML)
- LAM (40% develop AML)
- AML in TSC more likely to be larger, bilateral, multicentric, grow rapidly, and bleed spontaneously

Genetics

TSC:

- Prevalence 1 in 5,000–15,000
- Autosomal dominant with variable expression
- 2/3 of cases result from sporadic mutations
- 2 known genetic loci (both tumor suppressor genes): TSC1 (Cs 9q34) or TSC2 (Cs 16p13)

PATHOPHYSIOLOGY

- Renal: Renal insufficiency due to replacement of parenchyma with tumor
- Hematologic: Anemia due to hemorrhage
- Cardiovascular: Hypotension due to hemorrhage

COMMONLY ASSOCIATED CONDITIONS

- TSC
- LAM

DIAGNOSIS

HISTORY

- Most AML are asymptomatic and discovered incidentally.
- Occasionally, severe flank pain with hypotension with spontaneous hemorrhage
- Personal or family history of TSC
- History of LAM
- Flank/abdominal pain
- GI complaints due to mass effect
- Anemia, HTN, hematuria

PHYSICAL EXAM

- HTN or hypotension (due to hemorrhage)
- TSC: Mental retardation, adenoma sebaceum, ungual/subungual fibromas, lung disease:
  - Funduscopic exam for retinal hamartomas
- Flank/abdominal tenderness/mass:
  - Palpable mass can be seen in ~50% of symptomatic patients

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Anemia
- Gross/microscopic hematuria may be present
- Renal function (if multiple AMLs compress and replace normal parenchyma)
- Genetic testing for TSC

Imaging

- More likely to be bilateral and multicentric in TSC patients
- 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:

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- US: Well-circumscribed, hyperechoic mass with shadowing (other RCTs may also be echogenic)
- IVP: Similar appearance to other RCTs
- Angiogram: Increased vascularity (also seen in many malignant renal lesions); 50% of AMLs are found to have aneurysmal dilation
- MRI: Adipose tissue has high signal intensity on T1-weighted images and lower on T2-weighted images.

Diagnostic Procedures/Surgery

Fine-needle aspiration (biopsy) may be helpful:

- Nuclear atypia or pleomorphism in AML might be mistaken for malignancy.
- Negative biopsy does not exclude malignancy.
- AMLs may be at increased risk for bleeding with percutaneous procedures.

Pathological Findings

- Gross appearance: Yellow (extensive fat) to pink (extensive muscle), sometimes associated hemorrhage, rare cases of tumor thrombus
- Microscopic appearance: Varying amounts of mature fat cells, smooth muscle, and blood vessels:
  - Fat cells are of usual morphology.
  - Muscle cells have variable arrangements.
  - Blood vessels are thick walled.
  - May have regions of cellular atypia
- HMB-45: Monoclonal antibody against a melanoma-associated antigen seen in AML and can differentiate cases from other RCTs
- Commonly positive for actin and CD-68
- Retroperitoneal nodes may occasionally be involved with AML similar to the primary tumor and are not considered to be metastases.
- Malignant epithelioid AML: Very rare malignant variant that can metastasize

DIFFERENTIAL DIAGNOSIS

- Renal masses:
  - Renal cysts
  - Oncocytoma
  - Renal and retroperitoneal liposarcoma
  - Renal cell carcinoma
  - Renal lipoma
  - Sarcoma (including fibrosarcoma, leiomyosarcoma, and liposarcoma)
  - Teratoma
  - Upper-tract urothelial carcinoma
  - Wilms tumor
  - Xanthogranulomatous pyelonephritis
- Renal/retroperitoneal hemorrhage:
  - Arteriovenous malformation
  - Coagulopathy
  - Hemorrhage of other renal mass such as renal cell carcinoma
  - Iatrogenic
  - Ruptured aneurysm
  - Traumatic injury
  - Vasculitis

Pregnancy Considerations

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TREATMENT

- Many controversies concern management.
- Absolute indications for intervention include suspicion of malignancy, hemorrhage with significant hypotension or symptoms, persistent hematuria

SURGERY/OTHER PROCEDURES

- Indications: Diagnostic uncertainty, hemorrhage causing significant symptoms, pain, hematuria, risk of rupture
- Asymptomatic AML <4 cm:

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- Asymptomatic AML >4 cm:

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  - The risk of spontaneous hemorrhage appears greatest in masses >4 cm.
- Symptomatic AML/lesion >4 cm:

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- Acute hemorrhage:
  - Initially treated with embolization (stabilizes patient and often eliminates need for more intervention)
  - If explored emergently, total nephrectomy usually necessary

ADDITIONAL TREATMENT

Limited reports of treatment using cryoablation and radiofrequency ablation

ONGOING CARE

PROGNOSIS

- Local recurrence rare after removal
- Extrarenal lesions are multicentric and not metastatic.
- Extended follow-up is necessary after selective embolization due to complications and recurrence risk.

COMPLICATIONS

- Flank/abdominal pain
- Hematuria
- Hemorrhage (may cause anemia or shock)
- Mass effect on surrounding organs

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Controversial in patients with newly diagnosed AML; screen for TS.
- Conservative management: Serial imaging (usually with CT or US) every 6–12 mo
- Growth rate typically 5% per year for solitary AML
- TSC patients and those with multicentric AMLs have growth rate of 20% per year

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Cell Carcinoma, General
- Renal Mass
- Retroperitoneal Hematoma
- Tuberous Sclerosis Complex

CODES

ICD9

223.0 Benign neoplasm of kidney, except pelvis

ABBREVIATIONS

- AML: Angiomyolipoma
- CT: Computed tomography
- HTN: Hypertension
- IV: Intravenous
- LAM: Lymphangiomyomatos
- MRI: Magnetic resonance imaging
- RCC: Renal cell carcinoma
- RCT: Renal cortical tumor
- TSC: Tuberous sclerosis complex
- US: Ultrasound

RENAL ARTERY STENOSIS/RENOVASCULAR HYPERTENSION

Amit R. Patel, MD
Eric A. Klein, MD

BASICS

DESCRIPTION

- RAS refers to an anatomic renal arterial lesion causing decreasing renal blood flow that may or may not be associated with HTN.
- When associated with atherosclerotic disease, it is known as ARAS.
- RVH is HTN caused by renal hypoperfusion due to a flow-limiting vascular stenosis.

EPIDEMIOLOGY

- RAS:
  - Exact prevalence is unknown, and numbers may be underdiagnosed and underreported.
  - Incidentally found in patients with aorto-occlusive disease (33%), coronary artery disease (20%), and diabetes mellitus (43%)
  - ARAS has a higher prevalence in males
- RVH:
  - <1% prevalence in the mild to moderate HTN population
  - Increases with severity of HTN and population age
- Studies suggest prevalence of RAS is higher than that of RVH.
- Natural history:
  - FMD:

    Rarely leads to renal artery occlusion

    ~10% of FMD cases involve intimal or adventitial layers, which are commonly associated with dissection and thrombosis.
  - ARAS:

    Progression occurs in <5% of lesions that are <50% stenotic; increases to 39% progression in lesions that are >75% stenotic.

    ~50% of progressions occur within 2 yr of initial diagnostic angiogram.

    Progression may lead to renal atrophy; increases with degree of stenosis (up to 21% with stenosis >60%)

    Progression also leads to renal dysfunction; however, this is less common (up to 10% of patients with >70% stenosis of renal artery).

– Clinically significant progressive disease occurs within a small subset of RAS. It is important to identify patients who will benefit from invasive treatment.

RISK FACTORS

- Atherosclerotic disease
- Older age
- Males
- Difficult-to-control HTN:
  - On multiple antihypertensive medications
  - Accelerated HTN, malignant HTN, or association with pulmonary edema
- Increase in serum creatinine during BP reduction:
  - Frequently associated with ACE inhibition or ARB.
  - Suggestive of perfusion-dependent renal function.

PATHOPHYSIOLOGY

- RVH:
  - Results from critical vascular stenosis causing renal ischemia
  - Elevated renin leads to increased ATII, which controls BP and extracellular volume.
  - ATII elevates BP by causing generalized vasoconstriction.
  - ATII stimulates aldosterone secretion, causing sodium reabsorption and potassium and hydrogen ion secretion.
  - ATII causes efferent arteriolar vasoconstriction, maintaining pressure for glomerular filtration even under conditions of reduced blood flow such as RAS.
- RAS:
  - 70–90% of all renovascular lesions are secondary to atherosclerosis.
  - ARAS lesions are usually located at the ostia or proximal renal artery.
  - ARAS usually affects individuals >55 with manifestations of HTN, renal failure, congestive heart failure, and pulmonary edema.
  - 10% lesions are caused by FMD.
  - FMD lesions are usually located at the distal 2/3 of the renal artery.
  - FMD lesions are characterized by angiographic and histologic appearance according to the layer of artery affected.
  - FMD is predominant in females age 15–50

COMMONLY ASSOCIATED CONDITIONS

The cooperative study of renovascular HTN in 1972 examined clinical and radiographic features of RVH:

- High-grade retinopathy (reported 31% prevalence)
- Abdominal or flank bruits (sensitivity 39–63% and specificity 90–99%)
- Atherosclerotic disease
- Peripheral vascular disease
- Absence of family history of HTN
- Onset of HTN >50

DIAGNOSIS

HISTORY

Patient history should include aspects covering the risk factors discussed earlier.

PHYSICAL EXAM

- BP measurement
- Abdominal exam including auscultation
- Urinalysis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- PRA with captopril stimulation:
  - PRA is usually elevated with RVH due to renal hypoperfusion
  - Captopril stimulation improves PRA testing due to ACE inhibition and subsequent decrease in BP; this enhances the release of renin from the stenotic kidney.
  - Patient should not be on diuretics or ACE inhibitors
  - Positive test: PRA >12 ng/mL, or an absolute increase in PRA of at least 10 ng/mL, or an increase in PRA levels of >150%.
  - Specificity, 96%; sensitivity, 55%: Not a good screening test, but RVH can be excluded in patients with a negative test and low clinical suspicion.

Imaging

- Renal arteriography:
  - Gold standard for diagnosis of renovascular disease: Sensitivity/specificity, 99%
  - Provides detailed anatomy of main renal artery and distal branches
  - Various types of FMD lesions are depicted (ie, beaded, aneurysmal)
  - Invasive; not considered a primary test
  - Complications: CIN, local bleeding, renal artery dissection, pseudoaneurysm, atheroembolism
- Captopril renography:
  - Uses technetium99m DMSA and MAG3 to image renal perfusion activity of each kidney.

– Best if the patient is well hydrated, with liberal salt intake, off ACE inhibitors for 3–5 days

– Delayed time to maximal activity (>11 min), significant asymmetry of peak activity in each kidney, cortical retention of radionuclide, and marked GFR decrease of the ipsilateral kidney are specific signs of RV disease.

– Sensitivity and specificity for detecting lesions >75% is 83% and 93%, respectively

– The negative predictive value of a normal captopril renogram without any evidence of vascular disease is 100%; excludes RVH if negative in the setting of a normal renal function

- DUS:

– Inexpensive, widely available. Provides direct visualization of the renal arteries with hemodynamic information

– Successful imaging depends on operator, bowel gas, and body habitus.

– Peak systolic velocity of the renal artery >80 cm/sec; a ratio of the renal artery to the aorta >3.5 is diagnostic of stenosis: Sensitivity 90%

- MRA:

– Excellent detail of location and severity of disease in the renal vessels in addition to renography

– Noninvasive with minimal radiation exposure and non-nephrotoxic contrast agent use

– Claustrophobia or magnetic implants are contraindications for its use.

– Distal lesions are more difficult to diagnose.

– Advances in technology, 3D reconstruction, and echo gradient imaging will improve the accuracy and usefulness of MRA.

– Reported sensitivity and specificity ranges from 83–100% and 92–97%, respectively.

– In prospective studies using angiography as a reference, MRA has outperformed DUS and captopril renogram with sensitivity of 94%.

- CTA:

– Provides potential advantages over MRA in wide availability, cost-effectiveness, and convenience

– Drawbacks include the use of iodinated contrast agents that may increase the risk of CIN.

– Reported sensitivities of over 90%

– Can depict proximal branches of the renal artery better than MRA and DUS

- Test selection:
  - Clinician must 1st assess the degree of suspicion of RVH based on symptoms and the goals of potential treatment.
  - If 3 risk factors (from above) exist, patient should be considered high-risk and should undergo arteriography and simultaneous endovascular treatment.
  - If only 1 of the high-risk features exists, patient is considered low-risk and should be evaluated using a noninvasive test. Negative tests require no further evaluation. Positive tests should be followed by renal arteriography.

Diagnostic Procedures/Surgery

Renal vein renin sampling:

- Allows selective renal venous sampling to measure renin levels
- Net renin secretion is measured by subtracting the outflow from the inflow renin value
- Useful test for localizing the ischemic kidney
- Invasive test requiring percutaneous catheterization
- Currently, this test is reserved for assessing bilateral lesions, to localize which kidney contributes more significantly to RVH.

Pathological Findings

Renal histopathologic evaluation is warranted in patients with serum creatinine >4 mg/dL:

- Can be done at time of open revascularization with wedge biopsy
- Predominant morphologic changes are arteriolar nephrosclerosis and atheroembolic renal disease.
- Findings of tubular atrophy, interstitial fibrosis, and arteriolar sclerosis do not preclude recovery of renal function.
- Widespread glomerular hyalinization is indicative of irreversible renal injury.

TREATMENT

MEDICATION

- ACE inhibitor/ARB:
  - Shown to improve BP in up to 96% of patients with RVH.
  - May not prevent progression of ARAS lesion
- Multifaceted regimen should be implemented in ARAS due to concomitant cardiovascular risk:
  - Anti-platelet agents
  - Statins or other lipid-lowering agents
  - Smoking cessation
  - Weight loss

- Generally, medical management is reserved for high-risk patients who are at high risk for intervention, refuse therapy, or have irreversible atrophy of the affected renal unit:
  - These patients should be followed with serial renal function tests and DUS to assess for disease progression.
- Studies have shown the long-term efficacy of pharmacotherapy for HTN and renal function in patients with ARAS.
- PTA and intravascular stents:
  - PTA alone: Shown to improve BP and improve renal function. Has not been shown to provide significant benefit over pharmacologic therapy with respect to BP
  - PTA with stenting: Shown to reduce restenosis rate and to seals dissections caused by the PTA:

    Multicenter trial: 100% technical success, 75% 4–yr survival

    Other trials: Improved BP control in 75% after 1 yr

    Ostial lesions have higher restenosis rates.

    Complications: 7%; includes atheroembolic showering of distal tissue, hematoma, arteriovenous fistula, pseudoaneurysm, infection, and hemorrhage

    Improved techniques and products (ie, distal temporary atheroembolic filters and drug coated stents) may improve success rates.
- When to treat:
  - Patients with high-grade stenosis (>75%)
  - Disease involving entire renal unit (bilateral disease or disease in a solitary kidney)
  - Patients with worsening HTN or declining renal function
  - CHF unexplained by cardiac function
  - Recurrent pulmonary edema

SURGERY/OTHER PROCEDURES

Aortorenal bypass with autogenous graft vessel or polytetrafluoroethylene graft in the absence of a diseased aorta is the procedure of choice:

- Thorough angiographic evaluation of aorta and its branches is required
- Common alternative approaches include the splenorenal bypass for the left side and hepatorenal bypass for the right side (given patent celiac and splenic arteries).
- Reported >90% improvement or cure of HTN in patients
- Reported low mortality rates (2.6%–6.1%)
- Good long-term patency rates in ARAS

ONGOING CARE

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Based on risk factors; management should be followed. High-risk patients on medical or following surgical management should be followed with serial metabolic and renal function laboratories in addition to DUS.

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CODES

ICD9

- 405.91 Unspecified renovascular hypertension
- 440.1 Atherosclerosis of renal artery

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ARAS: Atherosclerotic renal artery stenosis
- ARB: Angiotensin receptor blocker
- ATII: Angiotensin II
- BP: Blood pressure
- CHF: Congestive heart failure
- CIN: Contrast induced nephropathy
- CTA: Computed tomography angiography
- DMSA: Dimercaptosuccinic acid
- DUS: Duplex ultrasonography
- FMD: Fibromuscular dysplasia
- GFR: Glomerular filtration rate
- HTN: Hypertension
- MAG3: Mercaptoacetyltriglycine
- MRA: Magnetic resonance angiography
- PRA: Plasma renin activity
- PTA: Percutaneous transluminal angioplasty
- RAS: Renal artery stenosis

- RVH: Renovascular hypertension

RENAL CAPSULAR NEOPLASMS

Manlio A. Goetzl, MD

J. Brantley Thrasher, MD

BASICS

DESCRIPTION

- Mesenchymal neoplasms primarily arising from components of the renal capsule
- Renal capsule consists of fibrous tissue, nerves, smooth muscle, blood vessels, perirenal fat, and lymph tissue

EPIDEMIOLOGY

- Extremely rare tumors
- Typically present after age 40
- Small percentage are found on autopsy alone
- Male = Female

RISK FACTORS

Possible that increased imaging frequency and technologies may lead to the increased detection of these lesions in the future

PATHOPHYSIOLOGY

- Benign:
  - Lipoma, fibroma, leiomyoma, hemangioma, solitary fibrous tumor, myolipoma
- Malignant:
  - Liposarcoma, fibrosarcoma, leiomyosarcoma, malignant fibrous histiocytoma, hemangiopericytoma, fibromyxoid sarcoma

DIAGNOSIS

HISTORY

- Many renal capsular neoplasms are asymptomatic.
- Hematuria, abdominal or flank pain
- Anorexia, weight loss, malaise, fevers, or bone pain may signify metastatic disease.
- History of diabetes mellitus, HTN may mandate more conservative surgical therapy.

PHYSICAL EXAM

Usually unremarkable

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Can see microscopic hematuria although less common than with parenchymal lesions

- Serum chemistries:
  - Elevated creatinine signifies underlying renal disease thus possibly mandating conservative surgical therapy
- CBC:
  - Anemia may indicate a bleeding lesion

Imaging

- Abdominal CT:
  - Preferred imaging choice

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  - Can show apparent origin from the renal capsule
  - Growth of large size in the absence of lymphadenopathy
  - Presence of fat suggestive of liposarcoma
  - Can be used to evaluate for metastatic disease
- Chest x-ray:
  - Rule out metastatic disease

Diagnostic Procedures/Surgery

- Angiography:
  - Benign lesions lack neovascularity and show sharp border.

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- Fine-needle aspiration may establish the diagnosis in selected cases.

Pathological Findings

- Leiomyoma:
  - Gross: Well-encapsulated, well-circumscribed
  - Microscopic: Interlacing bundles of smooth muscle with no mitotic figures, pleomorphism
  - Stain strongly positive for desmin and SMA
- Leiomyosarcoma:
  - Cell of origin is the smooth muscle cell of the capsule.

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  - Microscopic features include spindle cells, blunt-ended nuclei, eosinophilic cytoplasm, pleomorphism, mitotic figures
- Solitary fibrous tumor:

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  - Microscopic: Bland, spindle-shaped cells with scant cytoplasm accompanied by prominent hyalinized collagenous tissue

  - Diffuse positive expression of CD34, Bcl-2, CD99
- Malignant fibrous histiocytoma:
  - Gross: Solid, well-demarcated pinktan mass

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  - Stain positive for -1 antitrypsin, vimentin
- Liposarcoma:
  - Classifications include well-differentiated, myxoid, pleomorphic
  - Gross: Brownish nodular structure

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DIFFERENTIAL DIAGNOSIS

- Benign inflammatory tumors (xanthogranulomatous pyelonephritis)
- Abscesses
- Cystic nephromas
- Cysts (hemorrhagic, infected)
- Angiomyolipoma (fat poor)
- Focal pyelonephritis
- Hemangioma
- Leiomyoma
- Metanephric adenoma
- Metastasis from other primary tumor
- Oncocytoma
- Pseudotumors (column of Bertin, others)
- Renal cell carcinoma
- Renal lymphoma
- Renal medullary carcinoma
- Renal sarcoma
- Reninoma (JG apparatus tumors)
- Urothelial carcinoma
- Vascular malformations
- Wilms tumor

TREATMENT

- Frequently need pathologic exam to make accurate diagnosis
- Surgical management is the mainstay and can be diagnostic and therapeutic.
- Surgical excision appears to offer best hope of cure for malignancy of the renal capsule such as sarcoma:

– Frequently, multi-modality therapy is needed in an adjuvant setting.

MEDICATION

Chemotherapy for locally advanced and metastatic lesions:

- Cyclophosphamide, adriamycin, vincristine, actinomycin D, dacarbazine have all been used in various regimens for sarcoma.

SURGERY/OTHER PROCEDURES

- Radical nephrectomy is gold standard:
  – Can be performed open or laparoscopically
- However, benign capsular neoplasms may be easily amenable to partial nephrectomy.
- In patients with a solitary kidney or with chronic renal insufficiency, partial nephrectomy may be attempted.
- If perirenal in location, important to excise renal capsule with the mass

ADDITIONAL TREATMENT

Radiotherapy

Radiotherapy has been used in some settings to the renal bed and adjoining lymphatic area for the management of sarcoma.

Additional Therapies

Angioinfarction may be used in some patients for symptom relief.

ONGOING CARE

PROGNOSIS

- Benign lesions rarely recur after excision.
- Most studies show a poor prognosis in the setting of sarcoma:
  – Early local and distant recurrences are common.
  – In renal leiomyosarcomas, patients exhibited a median overall survival of 25 mo, with a 25% 5-yr overall survival.

COMPLICATIONS

After radical surgery, can include injury to contiguous organs, bleeding, wound infection, atelectasis, renal failure, myocardial infarction, pulmonary embolus, death

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Serial CT scans, chest x-ray, bone scan, liver enzymes to evaluate for metastatic disease
- Serum creatinine to monitor renal function

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See Also (Topic, Algorithm, Electronic Media Element)

Renal Mass

CODES

ICD9

- 189.0 Malignant neoplasm of kidney, except pelvis
- 214.3 Lipoma of intra-abdominal organs
- 223.0 Benign neoplasm of kidney, except pelvis

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- HTN: Hypertension
- JG: Juxtaglomerular
- SMA: Smooth-muscle actin

RENAL CELL CARCINOMA WITH TUMOR THROMBUS

Christopher L. Amling, MD
Sean J. Clark, MD

BASICS

DESCRIPTION

- RCC can invade the renal vein lumen, sometimes extending to suprarenal IVC and right atrium.
- The term thrombus is actually a misnomer, as it is actually an intraluminal growth of the tumor that may or may not be adherent to the vein wall.
- Although luminal growth is most common, tumor can also directly invade the vessel wall
- T3b: Renal vein or IVC below diaphragm
- T3c: IVC above diaphragm or into wall of IVC
- Whereas increasing size of primary renal mass may correlate with tumor thrombus, smaller tumors may also present with thrombus.

EPIDEMIOLOGY

- IVC involvement is found in 4–10% of cases of RCC.
- Right atrial involvement occurs in 1%.

RISK FACTORS

- Smoking
- Obesity
- Environmental exposure: Asbestos, cadmium, benzene, trichloroethylene
- No specific risk factors for tumor thrombus other than delayed diagnosis and high-grade, advanced disease

Genetics

No specific genetic factors predispose to venous involvement.

GENERAL PREVENTION

Modification of above risk factors for RCC

PATHOPHYSIOLOGY

- For staging, see “Section VII: TNM Classification.”
- The cephalad extent of the tumor is related to the degree of local extension.
- Bland thrombus must be differentiated from tumor thrombus:
  - Bland thrombus refers to a simple blood clot, it often occurs behind the tumor thrombus. MRI may be able to differentiate.

)[B]:

- Level 0: Tumor confined to renal vein
- Level I: Tumor extending up to 2 cm above the renal vein
- Level II: Extending beyond 2 cm above the renal vein but limited to the infrahepatic IVC
- Level III: Involving the retrohepatic IVC up to the diaphragm
- Level IV: Extending above the diaphragm or to the right atrium

COMMONLY ASSOCIATED CONDITIONS

- Bland thrombus of the infrarenal IVC
- Lower-extremity DVT
- Lower-extremity edema
- 33% of patients with tumor extending into IVC will have at least 1 synchronous metastasis
- Varicocele or caput medusa

DIAGNOSIS

HISTORY

)[B]:

- Hematuria
- Flank pain
- Abdominal mass
- Weight loss
- GI complaints

- Findings specific to IVC involvement:
  - Pulmonary embolus
  - Right atrial mass
  - Nonfunctioning involved kidney

PHYSICAL EXAM

- Bilateral lower-extremity edema may be present with IVC occlusion.
- Acute onset of varicocele can result from left renal vein or IVC involvement.
- Testicular exam to assess for a varicocele, which can develop due to venous outflow obstruction from a renal vein thrombus
- Dilated superficial abdominal veins (caput medusa due to collaterals)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- LFTs, creatine, electrolytes, CBC, and urine analysis are standard initial evaluation.
- Elevated ESR, elevated CRP may be present

- Proteinuria

Imaging

- Routine chest x-ray and bone scan as standard staging studies
- 3-phase helical CT can adequately evaluate the renal vein, but is less accurate for delineating the cephalad extent of tumor thrombus.
- Contrast inferior venacavography can define extent of tumor but is invasive and may require both antegrade and retrograde caval access:
  - May be appropriate if contraindications to MRI exist (metal implants, claustrophobia)

)[B]

- Renal arteriography can define a well-vascularized IVC tumor thrombus; renal embolization may lead to tumor shrinkage and facilitate resection of the tumor thrombus.
- Intraoperative TEE can evaluate tumor extent and adequacy of resection during surgery

Pathological Findings

Clear-cell is most common RCC subtype associated with vein thrombus.

DIFFERENTIAL DIAGNOSIS

- Renal mass:
  - Cysts (hemorrhagic, infected)
  - Fat-poor angiomyolipoma
  - Focal pyelonephritis
  - Hemangioma
  - Leiomyoma
  - Metastasis from other primary tumor
  - Oncocytoma
  - RCC
  - Renal lymphoma
  - Renal sarcoma
  - Urothelial carcinoma
  - Xanthogranulomatous pyelonephritis
- Intravascular filling defect:
  - Tumor thrombus
  - Bland thrombus of IVC

TREATMENT

- In the absence of obvious metastasis, the management is usually surgical.

• Essential to determine extent of thrombus proximally; intraoperative TEE may help.

• Caval thrombectomy, especially when bypass is required, is a major surgical procedure associated with morbidity.

• Comprehensive cancer care including nutrition, social support, and multidisciplinary patient care is advantageous.

MEDICATION

)[C]

• Immunotherapy (IL-2 and IFN-) has not shown the ability to reduce the size or extent of tumor thrombus.

SURGERY/OTHER PROCEDURES

• Precise determination of cephalad extent of tumor thrombus is essential to determining the optimal surgical approach.

• Subcostal incision may be adequate if IVC involvement in minimal.

• Chevron incision provides adequate abdominal exposure and can be extended with a midline sternotomy.

• Alternatively, a thoracoabdominal incision can provide adequate exposure to kidney and mediastinum, which may be more appropriate in case of prior sternotomy incision.

• Kidney is dissected and mobilized without disturbing or excessively manipulating the renal vein or IVC.

• Renal artery is controlled and divided early:

  – Division of the renal artery often results in shrinkage of the highly vascular tumor thrombus

• Suprarenal IVC, infrarenal IVC, and contralateral renal vein are mobilized and encircled.

• Liver is mobilized off the IVC and caudate lobe vessels are controlled and divided to reflect liver to the right and cephalad.

• Clamps are applied in the following order:

  – Infrarenal IVC
  – Contralateral renal vein
  – Suprarenal IVC

• Renal vein or IVC is incised over thrombus, thrombus is separated from the vessel wall and milked from the distal vessel

• Renal vein is divided, and kidney with attached thrombus is removed.

• Suprarenal IVC clamp is removed while anesthesia provides positive thoracic pressure to flush air and debris from the vena cava.

• Cavotomy is closed with 5–0 nonabsorbable suture. Caval lumen can be narrowed up to 50% without negative effect. If significant caval resection is necessary, a PTFE or pericardial graft can be applied.

• Pringle maneuver (compression of the hepatic portal) may be necessary to control backbleeding if suprahepatic clamping is needed.

• If supradiaphragmatic IVC or right atrial involvement is present, cardiopulmonary bypass with cold cardioplegia may be necessary to resect tumor thrombus.

• Level III tumors can be addressed with venovenous bypass, which has been shown to reduce operative times and may result in a lower complication rate than cardiopulmonary bypass.

• If IVC is completely occluded with thrombus, bypass techniques may not be necessary as adequate collaterals have already formed.

ADDITIONAL TREATMENT

Radiotherapy

• RCC is generally radioresistant.

• Preoperative radiation has not shown a survival advantage.

• Radiation therapy may be used in a palliative setting, especially for painful bony metastasis or symptomatic brain metastasis.

Additional Therapies

Preoperative embolization can be employed to reduce the size of the tumor as well as the level of tumor thrombus.

ONGOING CARE

PROGNOSIS

• 5-yr survival rate for patients with IVC involvement without metastasis is 18–68%.

• In the absence of lymph node metastasis, several investigators have found an equivalent prognosis for patients with and without vascular tumor thrombus.

)[C]

• Invasion of the vessel wall confers a poor prognosis.

COMPLICATIONS

)[B]

• Late complications are not significantly different between tumor thrombus levels.

• Complications include:

  – Cardiac and pulmonary embolic events related to tumor embolism

  – IVC occlusion

• Cardiopulmonary bypass for suprahepatic tumor extension is associated with additional complications:

- Acute renal failure
- ARDS
- Bowel necrosis
- Cerebrovascular accident
- Coagulopathy
- Multisystem organ failure
- Myocardial infarction

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Postoperative surveillance:

- Labs: Creatinine, LFTs
- Imaging: CT every 6 mo of the abdomen and chest x-ray standard follow-up

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Cell Carcinoma, General
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cell Carcinoma, Locally Advanced (T3–T4)

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- ARDS: Acute respiratory distress syndrome
- CBC: Complete blood count
- CRP: C-reactive protein
- CT: Computed tomography
- DVT: Deep vein thrombosis
- ESR: Erythrocyte sedimentation rate
- GI: Gastrointestinal
- IFN-: Interferon-
- IL-2: Interleukin-2
- IVC: Inferior vena cava
- LFT: Liver function test
- PTFE: Polytetrafluoroethylene
- RCC: Renal cell carcinoma
- TEE: Transesophageal echocardiography

RENAL CELL CARCINOMA, GENERAL

Adam R. Metwalli, MD
Peter A. Pinto, MD

BASICS

DESCRIPTION

- RCCs are tumors of the kidney arising from different parts of the nephron, resulting in several distinct histologic types.
- RCC is responsible for the majority of renal neoplasms (>80%).
- RCC is primarily a surgical disease because most tumors are largely resistant to conventional chemotherapies and radiation.

EPIDEMIOLOGY

)[B]
)[B]

- 10–20% higher incidence in African Americans
- Male > Female (3:2)
- Primarily occurs in 6th or 7th decade
- 2.3–6.6% of pediatric renal tumors are RCC.
- 4% of RCC are familial; majority are sporadic.

RISK FACTORS

)[C]

- A positive family history of RCC in a 1st- or 2nd-degree relative carries a relative risk of 2.9 of developing RCC.
- HTN has a 1.4–2-fold increased risk of RCC.
- Obesity, low socio-economic status, and urban background have been associated with an increased risk of RCC.

Genetics

- Clear-cell RCC is associated with deletion of chromosome 3p and/or mutations of the VHL gene.

)[A]

- Nonhereditary papillary RCC has been linked with changes in both chromosome 7 and 17.
- HPRCC arises from mutation of the met proto-oncogene on chromosome 7p34.
- Chromophobe RCC is a result of loss of chromosome 17.
- Birt-Hogg-Dubé syndrome develops from changes in the BHD1 gene on chromosome 17 p11.2.

GENERAL PREVENTION

Cessation of smoking can reduce the relative risk of developing RCC from 20–50%

PATHOPHYSIOLOGY

- Clear-cell and papillary RCC arise from the proximal convoluted tubules of the nephron.
- Local invasion is common with RCC; 20% of cases have invasion of the capsule or collecting system, 10% will have tumor thrombus.
- 2–4% of sporadic RCC will be bilateral either at the time of diagnosis or metachronously.
- Chromophobe and collecting-duct RCC develop from the distal convoluted tubule and collecting duct, respectively.
- Growth factors (VEGF, TNF-) are altered in the development and progression of RCC
- The older term renal adenoma referred to a mass histologically similar to RCC but <2 cm. These are now classified as RCC.
- See Section VII: TNM Classification.

COMMONLY ASSOCIATED CONDITIONS

- Acquired renal cystic disease in conjunction with ESRD has a 1–2% risk of developing RCC, an overall 5–20-fold increase in risk of RCC for ESRD patients.
- Retinal angioma, cerebellar and spinal hemangioblastoma, pancreatic cysts, and neuroendocrine tumors are associated with VHL-related RCC.
- Facial fibrofolliculomas in the malar region, lung cysts, and spontaneous pneumothoraces are associated with BHD-related RCC.
- Dermal leiomyomas are associated with HLRCC-related RCC.
- Possibly an increased risk of RCC in individuals with TS.

DIAGNOSIS

HISTORY

- Most locally confined RCC are asymptomatic.
- >50% of RCCs are detected incidentally by imaging studies ordered for other reasons.
- The classic triad of symptoms: Flank pain, palpable flank mass, and hematuria are all manifestations of advanced disease and are rarely seen since the advent of CT scanning.
- Associated symptoms are due to local tumor growth, hemorrhage, paraneoplastic syndromes, or metastatic disease and generally indicate advanced disease:
  - Paraneoplastic syndromes: Found in 20% of patients and may result in hypercalcemia, hyperparathyroidism, hyperinsulinemia, or other systemic abnormalities.
  - Paraneoplastic syndromes are thought to be responsible for constitutional symptoms such as fever, weight loss, and anemia.

PHYSICAL EXAM

- RCC is now known as a “radiologist’s tumor” due to the relative lack of physical exam findings.
- Abdominal exam should include deep palpation for any upper-quadrant masses, as well as auscultation for renovascular bruit.
- A careful testicular exam should be performed to assess for varicocele, which can develop due to venous outflow obstruction from a renal vein thrombus or epididymal mass in VHL disease.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- LFTs, creatine, electrolytes, CBC, and urine analysis are standard initial evaluation.
- Elevated ESR is present in 55.6%.
- Abnormal LFTs are found in 14.4%, which is called Stauffer syndrome if elevation is due to paraneoplastic syndrome and not due to liver metastases:
  - Stauffer syndrome is characterized by elevated alkaline phosphatase, PTT, low albumin, and sometimes elevated bilirubin or transaminases.
- Elevated serum calcium is seen in up to 13% overall and in 4.9% as a result of paraneoplastic syndromes.
- Polycythemia can be detected in 3.5%; anemia can also be seen due to blood loss.

Imaging

- A dedicated thin-slice renal CT scan is the best test for detecting renal masses.
- Any renal mass that enhances with IV contrast on CT or MRI should be considered RCC until proven otherwise.
- Any renal mass with negative CT attenuation (<20 HU) consistent with fat density is an angiomyolipoma:
  - CT or MRI is adequate for metastatic evaluation of abdomen
  - Chest X-ray is sufficient for pulmonary metastatic evaluation
  - Nuclear bone scan should be performed to rule out bony metastases in patients with elevated alkaline phosphatase or bone pain

Diagnostic Procedures/Surgery

- Historically, renal biopsy has not been part of workup for renal masses due to false-negative rate, risk of bleeding, and small risk of biopsy tract seeding with tumor cells:
  - Difficult to distinguish between oncocytoma and RCC on biopsy specimens
  - 83–90% of solid renal masses thought to be RCC on scanning prove to be RCC on pathologic analysis.

– Sensitivity and specificity of FNA biopsy is 80% and 95%, which is not better than radiologic evaluation alone.

- Biopsy or FNA has a role in differentiating RCC from a renal metastasis from another primary and from renal lymphoma:
  – With watchful waiting for small RCC, renal biopsy is also being used for surveillance with 90% accuracy of adequate specimens.

)[B]

Pathological Findings

- All RCC are adenocarcinomas, arising from renal tubular epithelial cells.
- Clear cell RCC is 70–80% of all solid enhancing renal tumors.
- Papillary (chromophilic) RCC: 10–15% and has 2 sub-types:
  – Type 1: Associated with HPRCC
  – Type 2: Very aggressive and associated with HLRCC
- Chromophobe RCC is 3–5% of solid renal masses and may be less aggressive biologically with good prognosis.
- Collecting (Bellini) duct rare (<1%) but lethal
- Renal medullary carcinoma is associated with sickle cell trait in young African Americans, is often advanced and metastatic at the time of diagnosis, and death occurs within a few months of diagnosis.

)[B]

- Sarcomatoid variants of all subtypes have been described; associated with a worse prognosis.

DIFFERENTIAL DIAGNOSIS

- Adrenal mass
- Angiomyolipoma (fat poor)
- Collecting duct tumor (Bellini)
- Cystic nephromas (multilocular cystic nephroma)
- Cysts (hemorrhagic, infected)
- Focal pyelonephritis
- Hemangioma
- Inflammatory masses (xanthogranulomatous pyelonephritis, abscess)
- Leiomyoma
- Metanephric adenoma
- Metastasis from other primary tumor
- Oncocytoma

- Pseudotumors (column of Bertin, others)
- Renal cell carcinoma
- Renal lymphoma
- Renal medullary carcinoma
- Renal sarcomas
- Reninoma (JG apparatus tumors)
- Urothelial carcinoma
- Wilms tumor (nephroblastoma)

TREATMENT

- Partial or radical nephrectomy is primary treatment for enhancing solid renal masses.
- Radical nephrectomy is removal of the entire kidney, surrounding perinephric fascia, lymph nodes and, if a large or upper-pole tumor, ipsilateral adrenal gland.

MEDICATION

Systemic therapy is for the patient with metastatic RCC and has no defined role for clinically localized RCC.

SURGERY/OTHER PROCEDURES

- Partial nephrectomy is becoming standard of care for masses <4 cm.
- Enucleation for small/multiple renal masses
- Radical nephrectomy is standard of care for larger tumors (highly selected partial).
- Small renal masses can be observed in patients who are not surgical candidates, particularly if they are <2 cm (~30% benign).
- Minimally invasive ablation techniques such as radiofrequency ablation or cryoablation are considered investigational by some but may be used for selected cases.

ADDITIONAL TREATMENT

Radiotherapy

Radiation has no role in the management of clinically localized RCC; may palliate mets

Additional Therapies

- Resection of solitary metastasis useful in select cases.
- There is no proven benefit to adjuvant systemic therapy in clinically localized RCC.

ONGOING CARE

PROGNOSIS

- Important prognostic factors for RCC are tumor stage, tumor size, Fuhrman nuclear grade, histologic sub-type:
  - Nomograms have been developed to predict risk of recurrence.
- Pathologic stage is the single most important prognostic factor for RCC:

  - T1a: 90–100% 5-yr survival
  - T1b: 80–90% 5-yr survival
  - T2: 70–80% 5-yr survival
- Paraneoplastic symptoms and signs, weight loss >10%, and poor performance status suggest a worse outcome.
- Ipsilateral adrenal involvement has a 0–40% 5-yr survival.
- Node-positive RCC has a 0–20% 5-yr survival.
- Metastatic RCC has a 0–10% 5-yr survival.

COMPLICATIONS

- Surgical complications: Bleeding, infection, injury to surrounding organs (liver, spleen, pancreas); prolonged urine leak for partial nephrectomy
- Metastases to lung, liver, bone, or other sites
- Paraneoplastic syndromes can result in cachexia, bleeding, HTN.
- Large tumors can also compromise GI or pulmonary function.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- See follow-up recommendations in “Renal Cell Carcinoma, Localized (T1–T2)”

)[B]:

  - T1: 0% local; 4% metastatic
  - T2: 2% local; 5.3% metastatic
- Peak time to recurrence: >48 mo for T2 RCC
- Surveillance is tailored to tumor stage:
  - T1: Yearly history and physical, labs
  - T2: Yearly history and physical, CXR, labs; biannual abdominal CT

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See Also (Topic, Algorithm, Electronic Media Element)

- Birt-Hogg-Dubé Syndrome
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cell Carcinoma, Locally Advanced (T3–T4)
- Renal Cell Carcinoma, Metastatic (N+, M+)
- Renal Cell Carcinoma, Pediatric
- Renal Mass
- Von Hippel-Lindau Disease/Syndrome

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- BHD: Birt-Hogg-Dubé syndrome
- CBC: Complete blood count
- CT: Computed tomography
- ESR: Erthyrocyte sedimentation rate
- ESRD: End-stage renal disease
- FNA: Fine needle aspiration
- GI: Gastrointestinal
- HLRCC: Hereditary leiomyomatous renal cell carcinoma
- HPRCC: Hereditary papillary renal cell carcinoma
- HTN: Hypertension
- HU: Hounsfield units
- JG: Juxtaglomerular
- LFT: Liver function tests
- MRI: Magnetic resonance imaging

- PTT: Prothrombin time
- RCC: Renal cell carcinoma
- TNF: Tumor necrosis factor
- TS: Tuberous sclerosis
- VEGF: Vascular endothelial growth factor
- VHL: Von Hippel Lindau syndrome

RENAL CELL CARCINOMA, LOCALIZED (T1–T2)

Robert G. Uzzo, MD

BASICS

DESCRIPTION

- RCC most commonly refers to adenocarcinoma, the most common type of renal neoplasm. Stage T1 and T2 are localized to the renal parenchyma with no obvious extension outside the renal capsule or involvement of regional lymph nodes or distant sites.
- Stage T1 has been further classified as T1a (tumor <4 cm) and T1b tumor (4–7 cm).

EPIDEMIOLOGY

- 57,760 new cases, with 12,980 deaths in 2009 in US
- Male > Female (~1.7:1):
  - 7th most frequent tumor in men (lifetime risk 1:61 in men and 1:103 in women)
- Disease of the elderly; peak incidence in the 6th and 7th decades of life
- 10–20% higher incidence in African Americans for unknown reasons
- 96% of cases are sporadic, whereas 4% are associated with familial syndromes.

RISK FACTORS

- Only accepted environmental risk factor is tobacco exposure: Increases relative risk by 1.4–2.5:
  - All forms of tobacco have been implicated.
  - Risk increases with cumulative exposure.

Genetics

- 3p25 (VHL gene) (tumor suppressor) implicated in 40–70% of all acquired cases of clear cell RCC
- 7q31 (cMet gene) (oncogene) implicated in cases of papillary RCC
- 17p11 (Birt-Hogg-Dubé gene; tumor suppressor) implicated in cases of chromophobe/oncocytoma
- 1q42 (HLRCC gene): HLRCC syndrome (type II papillary RCC)

PATHOPHYSIOLOGY

- Most RCC histologic types are believed to be derived from the proximal convoluted tubule, except chromophobe, oncocytoma, and papillary tumors, which are believed to arise from the distal tubule.
- Histologic grade and stage are independent factors that correlate with survival.
- Although tumor subtype (clear-cell vs. papillary vs. chromophobe carcinoma) does not have the same prognostic significance as histologic grade and tumor stage, some of these subtypes are more aggressive and have a shorter survival (collecting duct carcinomas, sarcomatoid clear-cell carcinomas, renal medullary carcinomas).

- Lesions <4 cm: Up to 20–30% can be benign. Progression to metastasis is <1% during a course of active surveillance (mean 34 mo) in a meta-analysis.
- Mean growth rate of a malignant lesion appears to be ~0.28 cm/yr.

COMMONLY ASSOCIATED CONDITIONS

- Extrarenal manifestations associated with RCC typically part of hereditary syndromes (VHL, BHD, HLRCC).
- Renal medullary carcinomas associated with sickle cell trait are highly aggressive and present in 3rd decade of life.

DIAGNOSIS

HISTORY

- Most stage T1/T2 lesions are asymptomatic, incidentally discovered
- Symptoms of more advanced disease include hematuria, flank pain, fever, weight loss (>10% of total body weight), bone pain.

PHYSICAL EXAM

- In stage T1/T2 disease, no typical physical findings
- Palpable abdominal mass, lymphadenopathy, left-sided nonreducing varicocele suggests advanced disease.
- Absence of findings on physical exam does not rule out advanced disease.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Anemia, polycythemia
- Serum creatinine: eGFR clearance better estimate of renal function
- Liver function tests: Possible Stauffer syndrome or metastasis
- Calcium: Elevated in paraneoplastic syndromes
- Alkaline phosphatase: Elevation suggests bone or liver involvement.

Imaging

- Pre- and postcontrast-based CT or MRI is essential.
- US can usually distinguish cystic from solid masses.
- Extent of disease evaluation includes CXR and CT chest/bone scan/CNS imaging if symptoms/signs mandate

Pathological Findings

Staging (see “TNM Staging” section)

DIFFERENTIAL DIAGNOSIS

- Adrenal mass
- Angiomyolipoma (fat poor)

- Collecting duct tumor (Bellini)
- Cystic nephromas (multilocular cystic nephroma)
- Cysts (hemorrhagic, infected)
- Focal pyelonephritis
- Hemangioma
- Inflammatory masses (xanthogranulomatous pyelonephritis, abscess)
- Leiomyoma
- Metanephric adenoma
- Metastasis from other primary tumor
- Oncocytoma
- Pseudotumors (column of Bertin, others)
- Renal cell carcinoma
- Renal lymphoma
- Renal medullary carcinoma
- Renal sarcomas
- Reninoma (JG apparatus tumors)
- Urothelial carcinoma
- Wilms tumor (nephroblastoma)

ALERT

Pseudotumors can be confused with renal malignancy. Hypertrophied column of Bertin can mimic a central tumor, particularly in congenitally solitary kidneys.

TREATMENT

- Assess global renal function (GFR) and strongly consider nephron-sparing approaches in many cases of localized RCC to avoid future chronic renal insufficiency.
- For T1 and T2 lesions, surgery is highly likely to result in a long-term cure.

MEDICATION

- Localized RCC is a surgical disease
- Limited role for tyrosine kinase inhibitors and antiangiogenic therapy in localized RCC
- No defined role for chemotherapy

SURGERY/OTHER PROCEDURES

- Approach is dictated by many factors including size of the mass, location of the tumor, number of lesions, and underlying renal disease.
- Excision: Partial or radical nephrectomy via open, laparoscopic, or robotic techniques
- Nephron-sparing surgery:
  - Partial nephrectomy becoming standard of care for masses T1a <4 cm. Implies removal of mass with a small rim of normal parenchyma:

Other accepted indications for partial nephrectomy include patients with bilateral renal masses, a tumor in a solitary kidney, renal insufficiency

– Enucleation (removal of mass by dissection between normal parenchyma and pseudocapsule of the tumor) may be acceptable for small and/or multiple renal masses as long as negative margins are achieved.

• Extended lymphadenectomy is controversial. At a minimum hilar lymphadenectomy should be performed with radical nephrectomy.

• Ablation: Cryoablation or RFA via laparoscopic, percutaneous, or open (rare) techniques. Generally reserved for masses <2–3 cm or in the setting of multiple renal masses, as in VHL. Ablation makes future resection extremely challenging.

• Active surveillance in the elderly or infirm. Especially useful in small asymptomatic masses.

ADDITIONAL TREATMENT

• Limited role in localized RCC outside clinical trials of focal radiotherapy (CyberKnife) or HIFU

• Used for painful bony metastases and CNS metastasis in advanced RCC

• Encourage smoking cessation.

• Minimize risk of hyperfiltration injury with pharmacologic and/or lifestyle changes to minimize effects of HTN and diabetes.

ONGOING CARE

PROGNOSIS

• Relative to stage, grade, histology

• Local recurrence after resection is ~2–3% after radical nephrectomy.

• 5-yr risks of recurrence for local or regional RCC fully excised are approximately:

– 5–9% for low-risk disease

– 20–25% for intermediate-risk disease.

– 60–80% for high-risk disease

• The prognosis for partial nephrectomy specimens with a positive margin is not clear. Every attempt should be made intraoperatively to avoid a positive surgical margin. If the final pathology reveals a focal positive margin, observation is indicated.

COMPLICATIONS

• Acute surgical/medical risks depend on treatments, techniques, and comorbidities.

• For partial nephrectomy: Acute renal failure, need for dialysis, urinary fistulas, and bleeding.

• Long term risk of chronic renal insufficiency after radical nephrectomy associated with increased cardio- and cerebrovascular morbidity:

– Increased risk of NSF with gadolinium and/or risk of contrast-induced nephropathy following use of iodinated contrast for radiographic surveillance

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- See Table for radical, partial nephrectomy, and ablation nephrectomy follow-up.
- All patients require periodic history, physical (including BP monitoring), and selected lab studies (calcium, hemoglobin, liver, renal profiles, urine analysis) at least yearly.
- Radiographic stage/grade/histology-specific surveillance mandatory. Based on clinical stage and mode of treatment. Surveillance scheme may be adjusted for other risk factors such as grade and histology:

– Following ablation, initial radiographic follow-up requires lack of enhancement on pre/post contrast-based CT or MRI at 3–6 mo after procedure. Biopsy confirmation of successful ablation is recommended. Occasionally after cryotherapy, an area of rim enhancement can be seen that usually resolves by 3 mo.

Stage

History, Exam, Labs

CXR

CT or MRI

T1NoMo

Yearly

Yearly for 5 yrs

None following excision for pT1a tumors

**At 3–6 mo postablation then every 12–24 mo for 5 yrs

Every 12–24 mo × 5 yrs (pT1b)

T2NoMo

Q6–12 mo for 5 yrs

Q6–12 mo for 5 yrs

Every 6–12 mo for 2 yrs then every 12–24 mo × 5 yrs

T3NoMo

Q3–6 mo for 2 yrs then yearly

Q3–6 mo for 2 yrs then yearly

Every 6–12 mo × 5 y then every 2 yrs

Every 3–6 mo for 3 yrs then every 6–12 mo × 5 yrs

Postoperative surveillance after radical nephrectomy, partial nephrectomy#, or ablation** of localized RCC

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See Also (Topic, Algorithm, Electronic Media Element)

- Birt-Hogg Dubé Syndrome
- Renal Cell Carcinoma, General
- Renal Cell Carcinoma, Locally Advanced (T3–T4)
- Renal Cell Carcinoma, Metastatic (N+, M+)
- Renal Cell Carcinoma, Pediatric
- Renal Mass
- Von Hippel-Lindau Disease/Syndrome

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- BHD: Birt-Hogg-Dubé syndrome
- CBC: Complete blood count
- CNS: Central nervous system
- CT: Computed tomography
- CXR: Chest x-ray
- eGFR: Estimated glomerular filtration rate
- GFR: Glomerular filtration rate

- HIFU: High-intensity ultrasound
- HLRCC: Hereditary leiomyoma renal cell carcinoma
- JG: Juxtaglomerular
- MRI: Magnetic resonance imaging
- NSF: Nephrogenic systemic sclerosis
- RCC: Renal cell carcinoma
- RFA: Radiofrequency ablation
- US: Ultrasound
- VHL: Von Hippel Lindau
- XGP: Xanthogranulomatous pyelonephritis

RENAL CELL CARCINOMA LOCALLY ADVANCED (T3–T4)

Adam R. Metwalli, MD

Peter A. Pinto, MD

BASICS

DESCRIPTION

Local advanced RCC that invades ipsilateral adrenal gland, perinephric fat, renal vein, vena cava, or beyond Gerota fascia:

- T3a: Adrenal or perinephric fat
- T3b: Renal vein or IVC below diaphragm
- T3c: IVC above diaphragm or into wall of IVC
- T4: Gross extension through Gerota fascia

EPIDEMIOLOGY

- RCC 57,760 new cases in the US annually in 2009; 8.9 new cases per 100,000 per year
- 12,980 deaths in 2007 in US in 2009
- 20% of patients present with locally advanced or node-positive RCC
- RCC with IVC involvement is seen in 4–10% of patients.

RISK FACTORS

- Cigarette smoking results in a 1.4–2.5 increased risk of RCC; risk increases with higher pack/yr consumption, may not be as much of a factor for women as men.
- A positive family history of RCC in a 1st- or 2nd-degree relative carries a relative risk of 2.9 of developing RCC.
- HTN has a 1.4–2-fold increase in risk of RCC.
- Obesity, low socio-economic status, and urban background have been associated with an increased risk of RCC.

Genetics

- Nonhereditary clear-cell RCC is associated with deletion of chromosome 3p and/or mutations of the VHL gene.
- VHL manifests clear-cell RCC due to alterations of the VHL gene on chromosome 3 p25–26.
- Nonhereditary papillary RCC has been linked with changes in both chromosome 7 and 17.
- HPRCC arises from mutation of the met proto-oncogeneon chromosome 7p34.
- Chromophobe RCC is a result of loss of chromosome 17.
- Birt-Hogg-Dube develops from changes in the BHD1 gene on chromosome 17 p11.2.

GENERAL PREVENTION

Smoking cessation, weight loss, annual physical examinations

PATHOPHYSIOLOGY

- Aggressive local invasion is common with RCC.
- 20% of cases will have frank invasion of the capsule or collecting system.
- 10% will demonstrate venous involvement with tumor thrombus.
- Adjacent organs are usually compressed by growing tumor, whereas direct invasion of liver, spleen, colon, pancreas, diaphragm, and duodenum are rare but associated with very poor prognosis.
- For staging, see Section VII: “TNM Classification.”

COMMONLY ASSOCIATED CONDITIONS

- Caput medusa
- Early satiety or emesis
- Flank pain
- Hematuria
- Pulmonary embolism
- Varicocele

DIAGNOSIS

HISTORY

- The classic triad of symptoms: Flank pain, palpable flank mass, and hematuria are all manifestations of advanced disease and are rarely seen since the advent of CT scanning.
- Associated symptoms are due to local tumor growth, hemorrhage, paraneoplastic syndromes, or metastatic disease and generally indicate advanced disease.
- Locally invasive RCC causes pain from invasion of posterior abdominal wall, nerve roots, or paraspinous muscles.
- History of pulmonary embolism should increase index of suspicion for venous thrombus in patient with kidney mass.

PHYSICAL EXAM

- Palpable abdominal mass
- Bilateral lower extremity edema
- Isolated right-sided varicocele, or 1 that does not decompress with recumbency
- Caput medusa (dilated abdominal veins)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- LFTs, creatine, electrolytes, CBC, and urine analysis are standard initial evaluation

- Elevated ESR is present in 55.6%
- Abnormal liver function tests are found in 14.4%, which is called Stauffer syndrome if elevation is due to paraneoplastic syndrome and not due to liver metastases:
  - Stauffer syndrome is characterized by elevated alkaline phosphatase, increased PTT, low albumin, and sometimes elevated bilirubin or transaminases
- Elevated serum calcium is seen in up to 13% overall and in 4.9% as a result of paraneoplastic syndromes.
- Polycythemia can be detected in 3.5%.

Imaging

- Sensitivity of CT for renal vein thrombus is 78%, for IVC thrombus is 96%

)[A]

  - Transabdominal US with color Duplex imaging can be used but may not be as sensitive for detection of cephalad extent of thrombus.

)[B]

- Venacavography is only for those who cannot have an MRI or have an indeterminate MRI.
- Nonfunction of affected kidney may indicate extensive venous thrombus formation.
- Staging of tumor thrombus:
  - Level I: At renal vein ostium
  - Level II: Up to short hepatic veins
  - Level III: Intrahepatic below diaphragm
  - Level IV: Above the diaphragm
- Chest CT: Evaluate for pulmonary metastases, more sensitive than chest x-ray
- Nuclear bone scan should be performed to rule out bony metastases in patients with elevated alkaline phosphatase or bone pain.

Diagnostic Procedures/Surgery

Biopsy or FNA has a role in differentiating RCC from a renal metastasis from another primary and from renal lymphoma.

Pathological Findings

- In patients with IVC thrombus, perinephric fat invasion decreased median survival by 69%.

)[B]

- All RCC are adenocarcinomas, arising for renal tubular epithelial cells.
- Clear cell RCC is 70–80% of all solid, enhancing renal tumors.
- Fuhrman nuclear grading is an independent prognostic factor with higher grade linked to worse outcome and more aggressive disease.

- Papillary RCC makes up 10–15% and has 2 subtypes:
  - Type 1: Associated with HPRCC and morphology suggestive of type 2
  - Type 2: Very aggressive and associated with HLRCC
- Chromophobe RCC is 3–5% of solid renal masses and may be less aggressive biologically.
- Collecting duct RCC is rare (<1%) but very lethal.
- Renal medullary carcinoma is 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

See Section I: Renal Cell Carcinoma with Tumor Thrombus

TREATMENT

Preoperative renal artery embolization may cause the tumor thrombus to regress and reduce the morbidity of surgery as a result.

MEDICATION

- Systemic therapy is for patients with metastatic RCC and has no role for locally advanced RCC with no evidence of metastasis.
- Several novel targeted therapies (eg, sunitinib, sorafenib, others) have shown promise in patients with metastatic disease and are being evaluated in adjuvant and neoadjuvant trials.

SURGERY/OTHER PROCEDURES

- Radical nephrectomy is standard of care.

)[B]

- 45–70% of T3b patients can be cured with aggressive surgery.

)[B]:

  - In patients with single lymph node metastasis or micrometastasis, a regional lymphadenectomy may be beneficial.
  - Aggressive lymphadenectomy may be beneficial in HLRCC as well.

ADDITIONAL TREATMENT

Radiotherapy

- 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

- Most trials of adjuvant therapy after nephrectomy have failed to demonstrate a survival benefit.
- Targeted agents to growth factors are being evaluated in both an adjuvant and neoadjuvant setting for patients at high risk for recurrence.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

There are no proven complementary or alternative therapies for locally advanced RCC.

ONGOING CARE

PROGNOSIS

- T3a: 60–80% 5-yr survival
- T3b/c: 40–60% 5-yr survival
- T4: 0–20% 5-yr survival
- Ipsilateral adrenal involvement has 0–40% 5-yr survival
- Node-positive RCC has 0–20% 5-yr survival.
- Metastatic RCC has 0–10% 5-yr survival.
- Overall median time to recurrence for locally advanced RCC is 6–8 yr.

)[B]

COMPLICATIONS

- Surgical complications are bleeding, infection, injury to surrounding organs (liver, spleen, bowel, pancreas).
- Pulmonary embolism from tumor thrombus
- Advanced tumors can bleed spontaneously either locally causing flank pain or into the urine resulting in hematuria and/or clot-induced urinary obstruction.
- Venous congestion resulting in bilateral lower extremity edema, varicoceles, or portal HTN from tumor thrombi into the renal, caval, or hepatic vasculature
- Metastases to lung, liver, bone, or other sites
- Postoperative bleeding or urine leak after partial nephrectomy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Peak time to recurrence for T3 tumors is 6–24 mo.
- T3: Every 6 mo history and physical exam, CXR, abdominal CT, and labs for 3 yr then yearly except for CT, which is biannual
- T3a: 8.2% local; 11.5% metastatic
- T3b: 10.6% local; 14.9% metastatic
- T4: Every 3 mo history and physical exam, CXR, labs; every 6 mo abdominal CT for 3 yr

- Long-term surveillance for T4 patients is rarely required due to high mortality.

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See Also (Topic, Algorithm, Electronic Media Element)

- Brit Hogg Dube Syndrome
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cell Carcinoma, Metastatic (N+, M+)
- Renal Cell Carcinoma, Pediatric
- Renal Mass
- Von Hippel-Lindau Disease/Syndrome

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- CXR: Chest x-ray
- ESR: Erythrocyte sedimentation rate
- ESRD: End-stage renal disease
- FNA: Fine-needle aspiration
- HLRCC: Hereditary leiomyomatous RCC
- HPRCC: Hereditary papillary RCC
- HTN: Hypertension
- IVC: Inferior vena cava
- LFT: Liver function tests

- MRI: Magnetic resonance imaging
- PTT: Prothrombin time
- RCC: Renal cell carcinoma
- US: Ultrasound
- VHL: Von Hippel Lindau syndrome

RENAL CELL CARCINOMA, METASTATIC (N+, M+)

Stephen B. Riggs, MD

Arie S. Belldegrun, MD

BASICS

DESCRIPTION

- Metastatic RCC is adenocarcinoma of the kidney that has spread to 1 regional lymph node <2 cm (N1), or >1 regional lymph node (N2). Distant metastatic sites (M1) include lung, liver, bone subcutaneous sites, and CNS.
- ~1/3 of patients with RCC present with metastatic disease.
- As many as 40–50% of patients will develop metastatic disease after initial diagnosis.

EPIDEMIOLOGY

- RCC accounts for 2–3% of all adult malignancies and is the most lethal of all urologic cancers.
- Typically presents in 6th–7th decade of life and is more common in African Americans
- 8.9 new cases of RCC/100,000 population
- Male > Female (3:2)

RISK FACTORS

- Smoking: ~2-fold increase
- VHL: RCC develops in about 50% of patients with VHL
- Patients with ESRD on dialysis

Genetics

- Majority of cases are sporadic
- VHL tumor suppressor gene located on 3p25–26 associated with clear-cell RCC
- 7q31 associated with papillary RCC

GENERAL PREVENTION

Smoking cessation

PATHOPHYSIOLOGY

- All RCCs are considered adenocarcinomas and are derived from renal tubular epithelial cells.
- Mode of spread is via direct extension, propagation into renal vein, or hematogenous.
- Rare reports of spontaneous regressions, usually pulmonary, following nephrectomy.

COMMONLY ASSOCIATED CONDITIONS

- VHL syndrome
- ESRD

DIAGNOSIS

HISTORY

- Gross hematuria
- Flank pain
- Weight loss, fever, night sweats, lethargy
- Family history of RCC
- Associated tumors, such as retinal angiomas, hemangioblastomas (VHL disease)
- Performance status

PHYSICAL EXAM

- Flank pain or abdominal mass
- Sudden onset of varicocele in men
- Epididymal lesion seen in VHL

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Anemia of chronic disease in up to 30%
- Urinalysis: Hematuria
- Complete metabolic panel
- Paraneoplastic syndromes (found in 20% of patients):
  - Hypercalcemia
  - Hypertension
  - Polycythemia
  - Nonmetastatic hepatic dysfunction (Stauffer syndrome)

Imaging

- Chest CT
- MRI or CT of abdomen and pelvis (~85% of enhancing renal masses are RCC)
- Most enlarged lymph nodes by abdominal and pelvic imaging prove to be inflammatory rather than neoplastic.
- CNS imaging is recommended in patients with symptoms or radiographic evidence of advanced disease.
- CT/PET has poor sensitivity but relatively good specificity and can be considered in equivocal cases.

Diagnostic Procedures/Surgery

Biopsy may be warranted in select cases; however, it carries a high false-negative rate:

- Used to determine primary RCC from metastatic dissemination to the kidney

Pathological Findings

- 5 histologic subtypes:

  - Clear cell: 70–80%
  - Papillary: 10–15%
  - Chromophobic: 3–5%
  - Collecting duct: 1%
  - Unclassified: 1%
- Sarcomatoid variants of all histologic subtypes have been described:
  - Represent poorly differentiated regions
  - Portends a much more aggressive biology with recurrence and resistance to systemic therapies the norm

DIFFERENTIAL DIAGNOSIS

- Renal masses:
  - Angiomyolipoma (fat-poor)
  - Collecting-duct tumors
  - Cystic nephromas
  - Cysts (hemorrhagic, infected)
  - Focal pyelonephritis
  - Hemangioma
  - Inflammatory masses (xanthogranulomatous pyelonephritis, abscess)
  - Leiomyoma
  - Metanephric adenoma
  - Metastasis from other primary tumor
  - Oncocytoma
  - Pseudotumors (column of Bertin, others)
  - Renal cell carcinoma
  - Renal lymphoma
  - Renal medullary carcinoma
  - Sarcomas
  - Reninoma (JG apparatus tumors)
  - Urothelial carcinoma
  - Wilms tumor (nephroblastoma)
- Lymphadenopathy:
  - Inflammatory related to RCC
  - Renal cell carcinoma
  - Infectious/inflammatory:

    Granulomatous: TB, sarcoidosis, histoplasmosis, lymphogranuloma venereum, Castleman disease, etc.

Nongranulomatous: Viral, bacterial (if abscess in local areas), sinus histiocytosis

– Primary lymphatic malignancy: Lymphoma (non-Hodgkin and Hodgkin, others)

– Other metastatic malignancies: GI (carcinoid, colorectal, lymphoma), urothelial, prostate, melanoma, penile, germ cell, cervical, ovarian, uterine

- Pulmonary nodules:
  - Breast cancer
  - Carcinoid tumors
  - Colon cancer
  - Granulomas (fungal, mycobacterial, others)
  - Hamartoma
  - Lung cancer (adenocarcinoma, squamous cell carcinoma)
  - Lymphomas
  - Melanoma
  - Renal cell carcinoma
  - Sarcoma
  - Testicular cancer

TREATMENT

- Patients should be evaluated in the context of being able to tolerate surgery and proceed with administration of systemic therapy.
- Non-clear cell RCC appears relatively resistant to currently available systemic treatment.

MEDICATION

First Line

- Immunotherapeutic-based strategies (best results in patients with good performance status):

– IL-2: Only agent shown to produce complete and durable responses in 6–8% of patients; PR 10–15%

– High-dose (bolus) IL-2 (Aldesleukin):

Typical regimen 600,000–720,000 IU/kg IV q8h for 5 days. Usually given as 2 cycles on days 1–5 and 15–19 of 28-day cycle (FDA-approved regimen). If patients do not progress, repeat approximately every 3 mo up to a max of 3 courses.

Significant toxicity includes fever, chills, nausea, vomiting, hypotension, arrhythmias, metabolic acidosis

– Low-dose IL-2:

Varying regimens, generally 10% of high-dose administered as outpatient

– Interferon-:

CR of 1%; PRR 10–15%:

Varying regimens described. SWOG intergroup regimen interferon alfa-2b: Induction:1.25 million IU/m2–5 million IU/m2 over 3 days and continued at 5 million IU/m2 Monday, Wednesday, Friday until progression. Dose modified based on toxicity.

Toxicity includes hematologic, hepatic, diarrhea, anorexia, and hypotension.

- Molecularly targeted therapies:
  – Sunitinib:

    FDA-approved for metastatic clear-cell RCC

    30% PRR, 6-mo improvement in PFS; although no CR reported

    Targets VEGF receptor tyrosine kinase and other pathways

    50 mg/d PO for 4 wk of 6-wk cycle (4 wk on, 2 wk off).

    Reports of MAHA when used with bevacizumab

  – Sorafenib: FDA-approved for metastatic clear-cell RCC

    Targets multiple tryosine kinases (VEGF receptor, PDGF receptor, FGFR1, others)

    400 mg PO b.i.d.

  – Temsirolimus:

    FDA-approved for 1st-line therapy in poor-risk patients; approximate 3-mo improvement in survival

    Parenteral rapamycin analogue inhibits mTOR kinase

    25 mg IV weekly (premedicate with diphenhydramine 25–50 mg IV)

  – Everolimus:

    FDA-approved in advanced RCC after failure of sunitinib or sorafenib

  – Bevacizumab:

    VEGF inhibitor: 10 mg/kg IV for 2 wk (not FDA-approved for RCC)

Second Line

- Sorafenib: FDA-approved for 2nd-line treatment after failed immunotherapy; 10% PRR, 3-mo improvement in PFS
- Sunitinib: Off label
- Clinical trials

SURGERY/OTHER PROCEDURES

- Cytoreductive nephrectomy to remove majority of disease burden in patients with metastatic disease is generally considered standard of care:
  – SWOG 8949 confirmed improved overall survival for debulking nephrectomy in interferon-treated patients with advanced RCC.

– Strongly consider metastasectomy for amendable and isolated metastasis (synchronous or metachronous)

– Lymphadenectomy should be performed in radiographically suspicious cases; however, ultimate role and benefit is yet to be defined

ADDITIONAL TREATMENT

Radiotherapy

Palliative role for osseous or CNS metastasis

Additional Therapies

- Combination of IL-2 and lymphocyte-activated killer cells equivalent to IL-2 alone
- Many other agents under study and reported: Nonmyeloablative allogeneic hematopoietic cell transplantation, IFN-, vaccines, other interleukins alone and in combination.
- Bevacizumab (VEGF inhibitor) with IFN- approved in Europe
- Multiple studies under way addressing sequencing and combination of targeted therapies along with immunotherapy and newer tryosine kinase inhibitors (everolimus, erlotinib, imatinib)

ONGOING CARE

PROGNOSIS

- 5-yr survival:
  - Any T stage N+ disease: 0–20%
  - Any T stage, any N, M+: 0–10%
  - Enhanced survival with the following characteristics: Long interval between nephrectomy and the appearance of distant metastases, a single metastatic site, and the absence of retroperitoneal adenopathy

COMPLICATIONS

- Related to treatment
- HD IL-2: Vascular leak syndrome
- Sunitinib, sorafenib: HTN, hand and foot syndrome
- Temsirolimus: Asthenia, rash

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Depends on grade and stage of tumor
- Usually chest and abdominal imaging every 3 mo for the 1st yr
- Serum chemistries and liver function tests

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Cell Carcinoma, General
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cell Carcinoma, Locally Advanced (T3–T4)
- Renal Cell Carcinoma, Pediatric

CODES

ICD9

- 189.0 Malignant neoplasm of kidney, except pelvis
- Secondary site:
  - 196.9 Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified
  - 197.0 Secondary malignant neoplasm of lung

ABBREVIATIONS

- CMP: Complete metabolic panel
- CNS: Central nervous system
- CR: Complete response
- CT: Computed tomography
- ESRD: End-stage renal disease
- FDA: Food and Drug Administration
- FGFR-1: Fibroblast growth factor receptor-1

- GI: Gastrointestinal
- HD: High dose
- IFN: Interferon
- JG: Juxtaglomerula
- MAHA: Microangiopathic hemolytic anemia
- MRI: Magnetic resonance imaging
- PDGF: Platelet-derived growth factor
- PET: Positron emission tomography
- PFS: Progression free survival
- PRR: Partial response rate
- RCC: Renal cell carcinoma
- SWOG: Southwest Oncology Group
- VEGF: Vascular endothelial growth factor
- VHL: Von Hippel-Lindau

Renal Cell Carcinoma, Pediatric

Phillip Mucksavage, MD

Douglas A. Canning, MD

BASICS

DESCRIPTION

A very rare childhood tumor arising from the renal tubular epithelium. This tumor type is distinct from the most common renal tumor in children (Wilms tumor).

EPIDEMIOLOGY

- Rare tumor comprising 2–6% of all 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 8–10 yr vs. <3 yr for Wilms tumor:
  - As common as Wilms tumor in 2nd decade of life
- Male = Female

RISK FACTORS

None known in the pediatric population

Genetics

)[C]:

- Rarely associated with VHL. If seen with VHL, more likely to be bilateral.

PATHOPHYSIOLOGY

- Thought to arise from renal tubular epithelium
- Distinct morphologic characteristics and unique genetic abnormalities when compared to adult RCC
- Most frequently papillary subtype with Xp11 translocation:

)[C]

- Lung and bone are the most common distant metastases.

COMMONLY ASSOCIATED CONDITIONS

- Some published reports of associations with tuberous sclerosis, urogenital malformations, chronic renal failure, neuroblastoma and teratoma with chemotherapy
- Rarely associated with adult familial RCC

DIAGNOSIS

HISTORY

)[C]

- Nausea, vomiting, malaise common

- Pain in up to 1/2

)[C]

PHYSICAL EXAM

)[C]

)[C]

)[C]

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[C]

- CBC: Rarely find polycythemia
- Liver and renal function tests: Baseline prior to treatment

Imaging

)[C]

- US demonstrates solid or cystic renal mass.
- CT or MRI with and without contrast reveal enhancing renal mass.
- IVP can demonstrate renal mass.
- Chest x-ray or chest CT scan for workup of metastatic disease
- Radionucleotide bone scan

Diagnostic Procedures/Surgery

Utility of biopsy prior to resection is unknown.

Pathological Findings

- Predominately papillary histologic features in children vs. clear-cell features in adults
- Average tumor size 6 cm.
- Pathologic staging based on modified Robson staging system

DIFFERENTIAL DIAGNOSIS

- Benign renal mass in children:
  - Choledochal cyst, intestinal duplication cyst
  - Congenital mesoblastic nephroma
  - Hydronephrosis
  - Mesenteric cyst
  - Multicystic dysplastic kidney
  - Polycystic kidney
  - Renal abscess
  - Splenomegaly
- Malignant renal masses in children:

- Hepatoblastoma
- Lymphoma
- Lymphosarcoma
- Neuroblastoma
- Renal cell carcinoma
- Rhabdomyosarcoma
- Wilms tumor

TREATMENT

Management is primarily surgical excision

MEDICATION

- Not adequately described in pediatric population
- Small series of patients treated with neoadjuvant chemotherapy according to Wilms tumor protocols

SURGERY/OTHER PROCEDURES

- Primary therapy for all cases

)[C]:

- Removal of entire kidney and portion of the ureter
- Common approaches in children include flank and abdominal.

)[C]:

- Laparoscopic radical or partial nephrectomy for RCC in children not adequately described

ADDITIONAL TREATMENT

Radiotherapy

Has been used for both initial treatment and recurrence but not well-characterized in pediatric populations

Additional Therapies

Il-2, adjuvant chemotherapy for metastatic disease has been tried in the pediatric population but not well-characterized.

ONGOING CARE

PROGNOSIS

Overall survival similar to adult RCC and depends on Robson stage:

- Best prognosis with stage I (>90%) and II (>80%)

)[C]

COMPLICATIONS

- Metastasis to lung and bone, multiple other sites

- Complications due to renal loss, secondary malignancy from chemotherapy or radiation have not been examined

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- No clear guidelines exist due to the small numbers of cases
- Should follow adult protocols:
  - Physical exam, chest x-ray, chemistry panel, CBC, and urinalysis every 6 mo for 5 yr.
  - CT on yearly basis for 5 yr
  - No long-term follow-up guidelines, but yearly PE, chest x-ray, laboratory studies, and alternate-year CT may be reasonable

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Cell Carcinoma, General
- Renal Cell Carcinoma, Localized (T1, T2)
- Renal Cell Carcinoma, Locally Advanced (T3–T4)
- Renal Cell Carcinoma, Metastatic (N+, M+)
- Renal Mass
- Robson Staging System
- Von Hippel-Lindau Disease/Syndrome

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- HTN: Hypertension
- IVP: Intravenous pyelogram
- MRI: Magnetic resonance imaging
- PE: Physical exam
- RCC: Renal cell carcinoma
- US: Ultrasound
- VHL: Von Hippel-Lindau

RENAL CYSTS (INTRARENAL, PERIPELVIC, AND PARAPELVIC)

Douglas M. Dahl, MD

Christopher J. Cutie, MD

BASICS

DESCRIPTION

- Fluid-filled structures in the kidney that are not continuous with the nephron or collecting system. There are several different types and descriptors of renal cysts.
- Simple cysts:
  - Most simple cysts are found incidentally on US or CT scan and arise from the renal parenchyma.
  - Often <2 cm (ranging from <1–>10 cm) and are round or oval
  - Can be single, multiple, and/or bilateral
  - If they grow very large, may impinge upon the renal pelvis, resulting in obstruction (parapelvic cysts).
- Complex renal cysts: Features not consistent with simple cyst; raise the possibility of malignancy:
  - Increased fluid density, internal thick-walled septations, thickened wall, nodular projections into the lumen, calcifications, and contrast enhancement
- Pyogenic cyst: Infected renal cyst
- Parapelvic renal cysts: Arise from the renal sinus
- Acquired renal cysts: Associated with chronic hemodialysis and occasionally may regress spontaneously
- The Bosniak classification is used to classify cysts further based on likelihood of malignancy.

EPIDEMIOLOGY

- 0.22% from birth–18 yr
- 20% by age 40
- 33% by age 60
- In autopsy series, 50% of patients >50 have 1 simple renal cysts.
- No clear difference among gender or race
- Simple cysts noted bilaterally are rare <50.

RISK FACTORS

- Polycystic kidney disease (autosomal dominant and recessive types)

- Hemodialysis:
  - In ESRD, cysts in 8–13% of patients before dialysis.
  - 10–20% have acquired cystic renal disease after 3 yr of dialysis, 40–60% after 5 yr, and > 90% after 10 yr.
  - Increasing age (7-fold increase from 4th–8th decade of life or an increased incidence from 5–36%)

Genetics

- ARPKD: PKHD1 gene, chromosome 6, protein product fibrocystin
- ADPKD: PKD1 and PKD2 genes, chromosome 16, protein products polycystin-1, -2
- Other genetic cystic diseases: Juvenile nephronophthisis, medullary cystic kidney disease, glomerulocystic kidney disease, Von Hippel-Lindau syndrome, tuberous sclerosis, Birt-Hogg Dube syndrome

GENERAL PREVENTION

Screening family members of patient with ADPKD and VHL

PATHOPHYSIOLOGY

- Simple cysts: Development of discrete fibrous saccules of clear fluid lined with cuboidal epithelium
- Some will involute and disappear over time
- In 1 study, simple cysts grew at a rate of 2.18 mm/yr.
- Some controversy over ability of simple cysts to cause HTN
- Parapelvic cysts (also called peripelvic cysts, parapelvic lymphatic cysts, parapelvic lymphangiectasia, renal sinus cysts) are found on <2% of kidneys on autopsy series. Can sometimes be confused with hydronephrosis.

COMMONLY ASSOCIATED CONDITIONS

- ADPKD
- ARPKD
- Birt-Hogg Dube syndrome
- ESRD
- Tuberous sclerosis: 50% have multiple renal angiomyolipomas; 20–25% of patients have renal cysts
- Von Hippel-Lindau disease: Individuals develop cysts in multiple organs (kidney, pancreas, liver, epididymis). Increased risk of RCC.

DIAGNOSIS

HISTORY

- Patients may present with an abdominal mass, pain, hematuria, or HTN.

- Family member with polycystic kidney disease or other inherited cystic disease

PHYSICAL EXAM

- Abdominal/flank mass (rare)
- Often a benign exam

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis
- Renal function tests

Imaging

- Simple cyst:
  - US: No internal echoes, distinct walls with defined margins, spherical shape with no internal echoes
  - CT: Sharp walls with smooth margins, spherical shape, homogenous throughout (HU ranging from 10 to + 20); no enhancement with IV contrast
  - CT diagnosis of a simple cyst is almost 100% if performed properly.
  - In the absence of these criteria, further workup of the lesion is necessary.
  - Enhancement is defined as an increase in HU by at least 15–20.
- Parapelvic cyst:
  - Appears on US as a medially located cystic mass with surrounding echogenic walls (located within the fatty renal sinus)
- MRI:
  - Bosniak classification of cystic renal masses was based on CT. Similar criteria can be applied to MRI, with the exception that calcifications may not be well seen.
  - Low signal on T1 and high signal intensity on T2 is consistent with benign simple cyst.
  - MRI may have a role in a subset of patients, such as those with multiple renal masses or those with VHL who may require multiple long-term imaging studies where excessive radiation is a concern.
  - May be superior to other imaging modalities in characterization of internal cyst contents (bleeding, mucin)
- CT with IV contrast is the gold standard for identifying parapelvic cysts:
  - Allows for discrimination 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:

– Category I: Benign simple cysts; thin wall without septa, calcifications, or solid components, water density, and no contrast enhancement. No further imaging needed.

– Category II: Benign cysts with a few thin septa; the wall or septa may contain fine calcification, sharp margins, nonenhancing, and usually <3 cm.

– Category IIF: Well-marginated 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 lesions >3 cm. These require follow-up (designated by the F designation).

– Category III: Indeterminate cysts with thickened irregular or smooth walls or septa; enhancement present. 40–60% percent are malignant (cystic RCC and multiloculated cystic RCC). Other class III lesions are benign and include hemorrhagic cysts, infected cysts, and multiloculated cystic nephroma.

– Category IV: Risk of malignancy is 85–100%. Characteristics of category III cysts plus they contain contrast enhancing soft-tissue components that are adjacent to and independent of the wall or septum.

Diagnostic Procedures/Surgery

Cyst aspiration and biopsy in selected indeterminate cases: Cytologic evaluation of fluid for malignancy or culture based on the indication and characteristics of the cyst

Pathological Findings

- Simple renal cyst: Single layer of cuboidal epithelium
- Not continuous with the collecting system

DIFFERENTIAL DIAGNOSIS

- ADPKD
- ARPKD
- Calyceal diverticulum
- Cystic degeneration (necrosis) of RCC
- Cystic malignancy (cystic RCC; sometimes called papillary cystadenocarcinoma)
- Hydronephrosis (parapelvic cysts)
- Juvenile nephronophthisis
- Medullary sponge kidney
- Multicystic dysplastic kidney
- Renal abscess
- Urinoma
- Xanthogranulomatous pyelonephritis

TREATMENT

• The major issue with renal cysts is differentiating a simple cyst from more serious diseases: Malignancy (RCC), polycystic kidney disease, complex cysts, and solid masses (such as a renal carcinoma or abscess).

• Bosniak classification raises concerns for risk of RCC with type Bosniak III and IV lesions.

• Bosniak type I (benign cyst): No action necessary; some clinicians consider 1 follow-up study (US) to confirm stability.

• Bosniak type II (septations and/or wall calcifications): Some clinicians consider 1 follow-up study (US) to confirm stability or if unable to differentiate from IIF cyst.

• Bosniak type IIF (increased, thicker walls and calcifications compared to type I): Follow-up studies for 2–3 yr

• Bosniak type III (irregular thick walls with calcification): Immediate surgery vs. other modality evaluation such as needle biopsy, or MRI

• Bosniak type IV (enhancement with contrast, malignancy likely): Surgical management

MEDICATION

Specific to those cystic diseases noted that cause HTN or renal insufficiency

SURGERY/OTHER PROCEDURES

• Radical or partial nephrectomy for complex or suspicious cysts

• Cyst decortication with marsupialization can be performed by multiple techniques including open, percutaneous resection, and laparoscopically.

ADDITIONAL TREATMENT

• Cyst aspiration and sclerotherapy therapy:

– Sometimes employed for large simple symptomatic renal cysts; it is not recommended for parapelvic/peripelvic cysts:

– This approach is supported by many authors as primary therapy for large symptomatic cysts before surgical management; others support laparoscopic management.

– Simple aspiration rarely leads to resolution.

– Negative cytology on the cyst fluid is usually required.

– Percutaneous injection of sclerosing agents increases success.

– Multiple sessions are usually required, and use of indwelling percutaneous catheter may increase success rates.

– Sclerosing agents described are multiple with ethanol, bismuth phosphate, n-butyl cyanoacrylate, povidone-iodine, and tetracycline commonly used. No data on which is best.

• See individual disease entities

ONGOING CARE

PROGNOSIS

- Up to 15% of patients with ADPKD will require hemodialysis.
- Benign simple cysts demonstrate little risk of progressing to malignancy.
- Correlation of Bosniak classification with risk of malignancy:
  - Bosniak I: No risk
  - Bosniak II: 0–5% risk
  - Bosniak III: 50% risk
  - Bosniak IV: 75–90% risk

COMPLICATIONS

- Rupture and hemorrhage with simple renal cyst; usually associated with flank pain and hematuria
- Infected renal cyst
- ADPKD: Cerebral berry aneurysms in up to 40% of patients (9% mortality due to subarachnoid hemorrhage)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up imaging of Bosniak type IIF cysts
- Multicystic dysplastic kidney/VHL observed with periodic sonography to monitor for neoplastic changes.
- Acquired renal cystic disease: Periodic imaging on dialysis

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Acquired Renal Cystic Disease
- Birt-Hogg Dube Syndrome
- Cystadenocarcinoma, Genitourinary
- Medullary Sponge Kidney
- Multicystic Dysplastic Kidney
- Polycystic Kidney Disease, Autosomal Dominant

- Polycystic Kidney Disease, Autosomal Recessive
- Renal Cell Carcinoma, General
- Renal Mass
- Tuberous Sclerosis
- Von Hippel Lindau Disease

CODES

ICD9

- 593.2 Cyst of kidney, acquired
- 753.12 Polycystic kidney, unspecified type
- 753.19 Other specified cystic kidney disease

ABBREVIATIONS

- ADPKD: Autosomal dominant polycystic kidney disease
- ARPKD: Autosomal recessive polycystic kidney disease
- CT: Computed tomography
- ESRD: End-stage renal disease
- HTN: Hypertension
- HU: Hounsfield unit
- IV: Intravenous
- MRI: Magnetic resonance imaging
- RCC: Renal cell carcinoma
- US: Ultrasound
- VHL: Von Hippel Lindau disease

Renal Dysplasia, Hypodysplasia, and Hypoplasia

Travis Shaw, MD

Douglas A. Canning, MD

BASICS

DESCRIPTION

- Renal dysplasia, hypoplasia, and hypodysplasia are forms of renal dysgenesis; namely, maldevelopment of kidney size, shape, or structure.
- Renal dysplasia: Chiefly 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, MCDK)

    Subtotal dysplasia: Segmental distribution in cortex and medulla

    Hereditary: Zellweger and Meckel syndromes
- Renal hypoplasia: Small kidneys that have a normal nephron density with less than normal number of calyces and nephrons and are not dysplastic:
  - Classification:

    True oligonephronia

    With normal ureteral orifice

    With abnormal ureteral orifice

    Oligomeganephronia

    Segmental (Ask-Upmark kidney)
- Renal hypodysplasia: Small kidneys that a have normal nephron density with less than normal number of calyces and nephrons and are dysplastic:
  - Classification:

    Normal ureteral orifice: With and without obstruction

    Ectopic ureteral orifice with or without ureterocele: Lateral, medial, or caudal

    With urethral obstruction

    Prune-belly syndrome

EPIDEMIOLOGY

- Renal dysplasia:
  - Unilateral or bilateral in 2–4 per 1,000 births
  - Male > Female (1.3:1)
  - Male > Female (1.9:1)

    Multicystic dysplastic kidney: 0.3–1 per 1,000 live births, incidence greater in males, left kidney more affected

- Renal hypoplasia:
  - Oligomeganephronia:
    Male > Female (3:1)
    Increased with low birth weight, often present by age 2.
  - Ask-Upmark kidney:
    Male < Female (1:2)
    Commonly present 10 yr of age
- Renal hypodysplasia:
  - Incidence is related to the underlying condition

RISK FACTORS

- Vesicoureteral reflux
- Posterior urethral valves
- Ureteral abnormalities: Primary megaureter, UPJO, ureterocele
- Prune belly syndrome

Genetics

- A majority of dysplastic and hypoplastic kidney disorders are sporadic and nonheritable
- Genetic pathways can affect ureteric bud formation, branching morphogenesis within the metanephric blastema, and normal nephrogenesis
- Familial renal adysplasia: Heterogenous autosomal dominant inheritance of renal agenesis, renal dysplasia, MCDK, etc. within 1 family

GENERAL PREVENTION

Early diagnosis and treatment of underlying urologic abnormality

Pregnancy Considerations

Antenatal US can detect renal dysgenesis in utero.

PATHOPHYSIOLOGY

- Normal metanephric differentiation requires induction via the ureteric bud.
- The branching of the collecting system, as well as nephron formation, are determined by the ureteric bud.
- Epithelial–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):
  - Aplastic dysplasia: Nubbin of nonfunctioning parenchyma
  - Congenital obstruction:
    Inhibition of nephron development

Increased TGF-

S-shaped bodies and cysts

Dedifferentiation of renal cells

– Bud defects:

Mackie-Stephens bud theory: Ectopic ureteric bud formation leads to abnormal ureteric orifice location and penetration of the ureteric bud into the metanephric blastema (lacks experimental evidence)

Defective genetic pathways: Defects in genetic pathways can affect ureteric bud formation, branching morphogenesis, and nephrogenesis (eg, RET, RAR, BMP4, SLIT2–ROBO2, AT2).

• 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 clear distinction between cortex and medulla, reduced number of renal segments, small renal artery, elongated nephrons

– Ask-Upmark kidney:

Likely secondary to reflux nephropathy

Deep groove(s) on lateral convexity with underlying tubules resembling thyroid tissue

Underdeveloped medulla

Arteriosclerosis and juxtaglomerular hyperplasia

• Hypodysplasia: 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 megaureter and UPJO

Without obstruction: Dwarf kidney; according to bud theory is the result of deficient metanephric blastema

– Abnormal ureteral orifice:

Pan-bud anomaly; abnormal budding leads to an ectopic ureteral orifice with thin renal parenchyma and ectatic calyces

Lateral ectopia: Often associated with reflux; rounded calyces are a result of premature termination of calyceal development

Medial or caudal ectopia and ureteroceles: Dilated ureter is the norm with thin renal cortex

– Urethral obstruction:

Position of ureteral orifices correlates with degree of renal dysgenesis in PUV: Orthotopic has normal histology; lateral orifice has hypoplasia; extremely lateral has hypodysplasia

– Prune belly syndrome: Large laterally displaced ureteral orifices with dysplastic kidneys explained by abnormal budding theory

COMMONLY ASSOCIATED CONDITIONS

- Branchio-oto-renal syndrome
- Ectopic ureteral orifice
- Fraser syndrome
- Jeune syndrome
- Kallmann syndrome
- Meckel-Gruber syndrome
- Oral-facial-digital syndromes
- Posterior urethral valves
- Potter syndrome
- Primary obstructing megaureter
- Prune belly syndrome
- Pulmonary hypoplasia
- Renal coloboma syndrome
- Simpson-Golabi-Behml syndrome
- Townes-Brocks syndrome
- UPJO
- Vesicoureteral reflux
- Zellweger syndrome

DIAGNOSIS

HISTORY

- Systemic:
  - Failure to thrive, abnormal growth, headache, fever, chills, shortness of breath, nausea, emesis, anorexia, skin pallor, vision change, mental status change
- Renal disease:
  - Polyuria, polydipsia, abdominal pain or mass, flank pain, hematuria
- Bladder disease:
  - LUTS, dysuria, nocturia, incontinence

PHYSICAL EXAM

- Abnormal weight or height
- Vital signs: Hypertensive, febrile
- Mental status: Encephalopathic
- HEENT: Retinopathy, papillary edema, dehydration
- Lungs: Crackles
- Abdomen: Distention, palpable mass, guarding, CVA tenderness, ascites
- Extremities: Pallor, peripheral edema

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Electrolytes, BUN, C, K+:
  - Elevated Cr, hyperkalemia, uremia
- Urinalysis: Proteinuria, hematuria, low specific gravity, bacteria
- Urine culture

Imaging

- Renal bladder US:
  - Kidney number and size, pelvocaliectasis, ureteral dilation, presence of cysts or mass, hyperechoic or hypoechoic parenchyma
  - Bladder volume, ureterocele
- CT of abdomen and pelvis:
  - Anomalous GU anatomy, presence of dilation, calculus disease
- Static-fluid and excretory MR urography:
  - GU anatomy, renal function, obstruction
- Renal scan:
  - Split function, obstruction
- VCUG: Anatomy, PUV, VUR
- Retrograde pyelography: Anatomy

Diagnostic Procedures/Surgery

- Cystoscopy
- Renal biopsy

Pathological Findings

- Gross findings:
  - Smaller renal size, mass, and contour
  - Renal lobulations and cysts
  - Pale and firm kidneys
  - Duplicated kidney or ureter

- Dilated collecting system
- Ectopic ureteral orifice
- Ureterocele
- Thickened bladder wall

- Histologic findings:
  - Dysplasia:
    Always with decreased nephron number
    Embryonic mesenchyme
    Primitive renal components
    Distortion of renal architecture
    Primitive glomeruli
    Nephron precursors: Comma and S-bodies
    Primitive ducts: Cartilage and tubules encircled by collars of fibromuscular cells
- Hypoplasia:
  - May have a normal nephron density
  - Oligomeganephronia: Reduction in nephron number with corresponding hypertrophy of the nephrons, nephron diverticula
  - Ask-Upmark kidney: Arteriosclerosis, juxtaglomerular hyperplasia, tubules resembling thyroid tissue
- Hypodysplasia:
  - Both dysplastic and hypoplastic

DIFFERENTIAL DIAGNOSIS

- ADPKD
- ARPKD
- Juvenile nephronophthisis
- Medullary sponge kidney
- Reflux nephropathy
- Renal vein thrombosis
- Simple cysts
- Sporadic glomerulocystic kidney disease
- Tuberous sclerosis
- UPJO
- Von Hippel-Lindau disease
- VUR
- Wilms tumor

TREATMENT

Consultation with nephrology and multimodality management

MEDICATION

Antibiotics for UTI or as prophylaxis for VUR

SURGERY/OTHER PROCEDURES

- Indications for nephrectomy: Pain, chronic infection, HTN, or increasing size
- Renal transplantation: ESRD
- Ureteral reimplantation: Reflux, primary megaureter
- Pyeloplasty: UPJO
- Valve ablation: PUV
- Cystoscopy: Diagnosis and treatment

ADDITIONAL TREATMENT

Peritoneal or hemodialysis for ESRD

ONGOING CARE

PROGNOSIS

Varies with degree of renal insufficiency and degree of comorbid conditions

COMPLICATIONS

Renal failure, anemia, UTI, failure to thrive

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- BP and growth chart annually
- Electrolytes, Cr, BUN annually
- Urinalysis and urine culture as indicated
- Bilateral disease: Renal US annually
- MCDK: Renal US every 2 yr to observe for involution

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

Individual diseases noted

CODES

ICD9

- 753.0 Renal agenesis and dysgenesis
- 753.15 Renal dysplasia

ABBREVIATIONS

- ADPKD: Autosomal dominant polycystic kidney disease
- ARPKD: Autosomal recessive polycystic kidney disease
- BP: Blood pressure
- BUN: Blood urea nitrogen
- Cr: Creatinine
- CT: Computed tomography
- CVA: Costovertebral angle
- ESRD: End-stage renal disease
- GU: Genitourinary
- HEENT: Head, eyes, ear, nose, throat exam
- LUTS: Lower urinary tract symptoms
- MCDK: Multicystic dysplastic kidney
- MR: Magnetic resonance
- PUV: Posterior urethral valves
- TGF: Transforming growth factor
- UPJO: Ureteropelvic junction obstruction
- US: Ultrasound
- UTI: Urinary tract infection
- VUR: Vesicoureteral reflux

RENAL ECTOPIA

Vanessa L. Elliott, MD
Jamie C. Messer, MD

BASICS

DESCRIPTION

- Renal ectopia (simple) describes a kidney outside of the normal position in the renal fossa and on the proper side of the body:
  - Pelvic kidney is the most common location.
  - Crossed renal ectopia describes the condition in which the kidney is located on the opposite side of where the ureter inserts:

In these cases, the ectopic renal unit is almost always fused to the opposite renal unit (90%) (cross-fused renal ectopia).

This is distinct from the horseshoe kidney, the most common renal fusion anomaly

EPIDEMIOLOGY

- Simple renal ectopia:
  - 1 in 500
  - 1 in 2,000–3,000 (pelvic renal ectopia)
  - Increased incidence on the left
  - Crossed renal ectopia is extremely rare, with no good epidemiologic data available.

RISK FACTORS

- Maternal illness early in pregnancy
- Teratogens

PATHOPHYSIOLOGY

- Renal ectopia (simple):
  - In the majority of cases, the contralateral kidney is in normal position.
  - Failure of ascent of the kidney into the renal fossa
  - Normal ascent involves craniad growth of the ureteral bud followed by migration of the metanephros. Several theories as to the cause of the arrested ascent.
  - Locations include:

Pelvic (most common): Overlies the sacrum, below the aortic bifurcation

Abdominal

Cephalad: Seen with omphalocele. Not a failure of ascent but a displacement of the kidney more superiorly near the diaphragm due to the herniation of the liver and intestines into the defect

)[A]

Crossed renal ectopia

No universally accepted embryologic theory as to why the kidney moves to the contralateral side

Usually with fusion to the contralateral renal unit (90%): Several different types of anomalies are described that depict how the kidneys are fused (inferior, S-shaped, lump, L-shaped, or disk/pancake).

The fused unit is typically in caudad position to the orthotopic renal unit (inferior type).

Without contralateral fusion in 10%

May be unilateral or bilateral

COMMONLY ASSOCIATED CONDITIONS

- 15–45% have genital abnormalities
- Cardiac anomalies
- Cloacal anomalies
- Contralateral renal agenesis:
  - Females: Uterine anomalies, duplication of the vagina
- Fusion abnormalities (eg, horseshoe kidney)
  - Males: Hypospadias, duplicated urethra, undescended testicles
  - Renal artery from lower aorta or iliac vessels
- Imperforate anus with cross-fused ectopia
- Skeletal anomalies
- UPJ obstruction
- Urolithiasis
- Vascular abnormalities

)[B]

DIAGNOSIS

HISTORY

- Typically asymptomatic; occasionally vague abdominal complaints.
- UTI may have been present
- Urolithiasis with renal colic
- Flank pain with UPJ obstruction
- With crossed fused ectopia, very few present clinically, and if so, usually later in life

PHYSICAL EXAM

- Typically normal

- Possible palpation of abdominal mass
- Examine for other associated genital anomalies

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No characteristic pattern
- BUN/Cr

Imaging

- Renal US: Identifies hydronephrosis in over 50% of cases
- CT
- VCUG to rule out reflux
- Diuretic renal scan if hydronephrosis present and negative VCUG

Diagnostic Procedures/Surgery

- Possible retrograde pyelogram if suspected UPJ obstruction
- Angiography if planning surgical intervention
- Cystoscopy is of limited value as the ureteral orifice is usually in normal position.

Pathological Findings

- May or may not assume the normal reniform shape
- Usually smaller than a normal kidney
- Renal pelvis is usually rotated anteriorly.
- Obstruction can result from either the UPJ or UVJ.
- Ureteral orifice is usually orthotopic.

DIFFERENTIAL DIAGNOSIS

- Horseshoe kidney
- Malrotated kidney
- Supernumerary kidney:
  - An accessory organ with its own blood supply and collecting system
  - It may or may not be reniform, but possesses a distinct capsule surrounding a parenchymal mass.
- Ptotic kidney

TREATMENT

Treatment is based on the presentation, such as urolithiasis, obstruction, or UTI

MEDICATION

Antibiotic prophylaxis for vesicoureteral reflux

SURGERY/OTHER PROCEDURES

- Urolithiasis:

)[A]

- UPJ obstruction:
  - Pyeloplasty
- Vesicoureteral reflux:
  - Ureteral reimplantation, injection of bulking agent

ONGOING CARE

PROGNOSIS

- The ectopic kidney is subject to increased risk of infection, obstruction, and stone disease.
- No increased risk of malignancy has been noted.
- With crossed ectopia there are rarely problems, as it is usually identified incidentally or at autopsy.

COMPLICATIONS

)[A]

- UTI

)[B]

- Vesicoureteral reflux

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Renal US/CT scan to evaluate for hydronephrosis, urolithiasis
- BUN/Cr

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See Also (Topic, Algorithm, Electronic Media Element)

- Horseshoe Kidney
- Ureteropelvic Junction Obstruction

CODES

ICD9

753.3 Other specified anomalies of kidney

ABBREVIATIONS

- BUN: Blood urea nitrogen
- Cr: Creatinine
- CT: Computed tomography
- ESWL: Extracorporeal shock wave lithotripsy
- PCNL: Percutaneous nephrolithotomy
- UPJ: Ureteropelvic junction
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

RENAL FAILURE, ACUTE

Wilmer B. Roberts, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- A relatively abrupt decline in renal function, over a period of hours to days, characterized by progressive azotemia and potentially accompanied by a decline in urine output
- Characterized by decreased GFR, increased BUN or Cr.
- Can be oliguric (urinary output <400 mL/d) or nonoliguric (>400 mL/d)
- 3 categories of ARF exist:
  - Prerenal azotemia
  - Intrinsic renal disease
  - Postrenal azotemia
- Some prefer the term acute kidney injury (AKI) and alternative criterion for ARF (and to detect more subtle changes in renal function) (see Section II: “RIFLE Criterion”).

EPIDEMIOLOGY

):

  - Prerenal disease: 21%
  - ATN: 66% of cases
- ARF requiring renal replacement therapy in the ICU was 5–6%

RISK FACTORS

Surgery, volume depletion, aminoglycoside therapy, CHF, contrast exposure, septic shock, nephrotoxic drugs

Genetics

Multifactorial

GENERAL PREVENTION

- Adequate hydration
- Preventing CIN:
  - N-acetylcysteine: 600 mg PO b.i.d. over 48 hr; data are conflicting, but benefit may be conferred

)[A]

PATHOPHYSIOLOGY

- Degree of renal dysfunction is directly proportional to the decrease in the GFR (mL/min)
- Prerenal azotemia:

– Hypoperfusion of the kidney characterized by return to baseline function within 24–72 hr, with appropriate systemic perfusion restoration

– Systemic hypotension stimulates the renin-angiotensin-aldosterone axis, ADH release, and the sympathetic nervous system.

– Results in redistribution of blood flow away from the renal cortex, avid resorption of sodium, water, and urea

– Urine and sodium output declines and osmolality increases.

– Reduction in blood flow decreases GFR.

– ATN can occur if hypoperfusion is sustained.

- Intrinsic renal disease:

– Tubular destruction occurs after traumatic injury releasing myoglobin from skeletal muscle.

– ATP depletion secondary to ischemia-reperfusion results in uncoupling of oxidative phosphorylation and cellular damage, with medullary areas containing renal tubules being most sensitive because of their normally reduced oxygen tension secondary to the countercurrent exchange mechanism.

– Decreased permeability of the GBM secondary to insult/toxin/inflammation

- Postrenal azotemia: Obstruction to urine flow (usually bilateral, but may occur in unilateral cases if pre-existing renal dysfunction present)

– Renal blood flow is reduced, as is GFR

– Impaired acid excretion

– Decreased concentrating ability

– With correction of obstruction, large volumes of urine containing sodium, potassium, and solute are excreted.

– Concentrating ability may be lost for days or weeks.

COMMONLY ASSOCIATED CONDITIONS

- ARPKD
- Diabetes
- Sepsis

DIAGNOSIS

HISTORY

- Evaluate drug exposure; onset and timing
- History of cardiac disease or other source of extracellular volume loss
- Fever or rash suggestive of allergy
- Irritative or obstructive symptoms, hematuria, stones, trauma

- Prior episodes of ARF, flank pain, abdominal pain, signs of uremia, oligo/anuria
- History of cancer or prior chemo/radiation therapy; bone pain in the elderly suggests multiple myeloma

PHYSICAL EXAM

- Assess volume status (skin turgor, weight, CVP, PCWP) and check patency of catheters or stents
- Peripheral edema, ventricular gallop, JVD: Suggestive of cardiac dysfunction
- Flank pain, suprapubic distension, and incontinence: Suggestive of obstruction
- Abdominal bruits or palpable aortic aneurysm: Suggests vascular causes
- Palpable purpura, pulmonary hemorrhage, and sinusitis: Suggests systemic vasculitis and glomerulonephritis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Proteinuria, hematuria, brown granular casts, renal tubular epithelial cells
  - Sediment: Granular, eosinophils (AIN), red cell casts (RPGN), crystals (lithiasis and obstruction)
- Urinary electrolytes/osmolality:
  - Urine sodium, fractional excretion of sodium, urine osmolality
- Serum electrolytes:
  - Calcium, magnesium and phosphorous, liver function tests, coagulation profile

Interpretation:

ATN

Prerenal

Urine/plasma Cr

<20

>40

Urine/plasma BUN

<3

>8

Urine/plasma osm

<1.2

>1.2

Urine sodium

>40

<20

Urinalysis

Casts

no casts

Imaging

- Renal US (sensitivity 90%, specificity 95%): For obstruction and medical renal disease
- Nuclear medicine renography (DMSA/DTPA scan): Functional assessment and presence of obstruction
- CT can reveal etiology of obstruction and hydronephrosis (IV contrast is generally contraindicated in ARF).

Diagnostic Procedures/Surgery

- Cystoscopy (evaluate bladder outlet)
- Angiogram (renovascular disease)
- Retrograde urethroscopy/ureterography (ureteral obstruction)
- Renal biopsy is indicated after excluding pre- and postrenal causes and toxic/ischemic causes.

Pathological Findings

- Medical renal disease: Normal-sized kidneys
- Ischemia: Size disparity
- Postrenal obstruction: Hydronephrosis

DIFFERENTIAL DIAGNOSIS

- Prerenal:
  - Intravascular volume depletion: Hemorrhage, shock, GI losses (vomiting, diarrhea, fistulas), renal losses (nephritis, glycosuria, diuretics)
  - Volume loss: Skin losses, respiratory losses, sequestration in 3rd spaces (pancreatitis, peritonitis, obstruction), inadequate fluid replacement, burns
  - Reduced cardiac output: Cardiogenic shock (MI, arrhythmia, malignant HTN), CHF, tamponade, valvular disease, cardiomyopathy, massive PE, sepsis
  - Systemic vasodilatation: Anaphylaxis, antihypertensive drugs, sepsis, overdose, anesthesia

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  - Hyperviscosity syndromes: Multiple myeloma or macroglobulinemia
- Intrinsic renal:
  - Renal (70% will have concurrent causes)
  - Hypoperfusion (50%)

– Toxic (25%)

– Multisystem diseases: Systemic lupus, Goodpasture, Henoch-Schönlein purpura, necrotizing vasculitis, Behçet disease, neoplasia, cryoglobulinemia (secondary to hepatitis B/C)

– Glomerulopathies: MPGN, membranous, IgA

– Infectious: Poststreptococcal glomerulonephritis, endocarditis, viral sepsis

– Medications: Antibiotics (aminoglycosides, cephalosporins, penicillins, tetracyclines, sulfa derivatives, rifampin, acyclovir, amphotericin), NSAIDS, diuretics, antihypertensives (captopril, -methyldopa), anticonvulsants (carbamazepine, phenytoin, phenobarbital, valproic acid), chemotherapeutic agents (cisplatin, methotrexate, mitomycin), cyclosporine, cimetidine, allopurinol, azathioprine, penicillamine, heavy metals (mercury, lead, arsenic), organic solvents

- Postrenal:

– Pediatric patients: Posterior urethral valves, bilateral ureteral obstruction, meatal stenosis

– Adults: Pregnancy, bilateral ureteral calculi, retroperitoneal disorders (fibrosis), hemorrhage, lymphocele, urinary extravasation or fistula (resorption), neurogenic bladder, iatrogenic (ureteral ligation), BPH, carcinoma (prostate, bladder, cervix, colon), papillary necrosis, coagulated blood, fungus ball

TREATMENT

- Based on etiology:
  – Correct underlying factors to restore renal perfusion.
  – Eliminate nephrotoxic drugs.
  – Maintain normal volume status.
- Ensure adequate urinary drainage and absence of extravasation.
- Restrict fluid intake to 500 mL/d, plus the daily urine volume; best if given orally.

MEDICATION

First Line

Mannitol and furosemide may be considered to improve urine output. Use at the time of ischemic insult to convert an oliguric to a nonoliguric state.

Second Line

Calcium channel blockers may have a role in the transplant kidney.

SURGERY/OTHER PROCEDURES

For obstruction:

- Ureteral stents

- Percutaneous nephrostomy/nephrostolithotomy
- Ureteroscopic stone extraction
- ESWL

ADDITIONAL TREATMENT

- Maintain adequate nutrition:
  - Carbohydrates >100 g/d to minimize ketosis
  - 1.0–1.8 g/kg/d of protein to curb catabolism and prevent negative nitrogen balance
- Monitor for infections and use GI prophylaxis to prevent GI bleeding (a major factor contributing to death).

COMPLEMENTARY AND ALTERNATIVE MEDICINE

):

- Severe refractory acidosis, electrolyte abnormalities, intoxicants/poisonings, volume overload, and symptomatic uremia

ONGOING CARE

PROGNOSIS

- ATN, the most common cause of in-hospital ARF, with adequate correction of underlying causes, usually begins to resolve within days.
- With prolonged obstruction, monitor electrolytes and volume status for sequelae of postobstructive diuresis.

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- Dialysis requirement associated with significant mortality.

COMPLICATIONS

Chronic renal insufficiency or failure:

- Dialysis dependence

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Monitor for infections.
- Avoid overexpansion of plasma volume by tracking daily weights.
- Track electrolytes and avoid abnormalities (hyponatremia, low bicarbonate, hyperkalemia, hyperphosphatemia, hypermagnesemia).
- Adjust drug dosages to account for impaired GFR.

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See Also (Topic, Algorithm, Electronic Media Element)

- Acute Kidney Injury (AKI)
- Contrast Induced Nephropathy (CIN)
- Renal Failure, Chronic
- Rifle Criterion

CODES

ICD9

- 584.5 Acute renal failure with lesion of tubular necrosis
- 584.6 Acute renal failure with lesion of renal cortical necrosis
- 584.7 Acute renal failure with lesion of renal medullary (papillary) necrosis

ABBREVIATIONS

- ADH: Antidiuretic hormone
- AIN: Acute interstitial nephritis
- AKI: Acute kidney injury
- ARF: Acute renal failure
- ARPKD: Autosomal recessive polycystic kidney disease
- ATN: Acute tubular necrosis
- BPH: Benign prostatic hyperplasia
- BUN: Blood urea nitrogen
- CHF: Congestive heart failure
- CIN: Contrast-induced nephropathy
- Cr: Creatinine
- CT: Computed tomography
- CVP: Central venous pressure
- DMSA: Dimercaptosuccinic acid
- DTPA: Diethylene triamine pentaacetic acid
- ESWL: Extracorporeal shock wave lithotripsy
- GBM: Glomerular basement membrane

- GFR: Glomerular filtration rate
- GI: Gastrointestinal
- HTN: Hypertension
- ICU: Intensive care unit
- IV: Intravenous
- JVD: Jugular-venous distension
- MI: Myocardial infarction
- MPGN: Membranoproliferative glomerulonephritis
- NSAID: Nonsteroidal anti-inflammatory drug
- PCWP: Pulmonary capillary wedge pressure
- PE: Pulmonary embolism
- RPGN: Rapidly progressive glomerulonephritis
- US: Ultrasound

RENAL FAILURE, CHRONIC

Deborah T. Glassman, MD

BASICS

DESCRIPTION

- A progressive loss of nephron number and function with the long-term inability of the kidney to filter toxins and nitrogen-containing compounds
- National Kidney Foundation formal definition: Either kidney damage or a decreased kidney GFR of <60 mL/min/1.73 m2 for 3 or more months
- Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.
- Elevation of serum creatinine and decrease in creatinine clearance
- May progress to ESRD: An irreversible loss of renal function requiring RRT.
- Untreated ESRD may lead to uremia and hyperkalemia, which are life-threatening.
- National Kidney Foundation/Kidney Disease Outcomes Quality Initiative classification of chronic renal failure stages:
  - Stage 1: Kidney damage, normal or increased GFR (>90 mL/min/1.73 m2)
  - Stage 2: Mild reduction in GFR (60–89 mL/min/1.73 m2)
  - Stage 3: Moderate reduction in GFR (30–59 mL/min/1.73 m2)
  - Stage 4: Severe reduction in GFR (15–29 mL/min/1.73 m2)
  - Stage 5: Kidney failure (GFR <15 mL/min/1.73 m2 or dialysis)
- Synonym(s): Chronic renal disease

EPIDEMIOLOGY

- Estimated 8 million people have GFR <60 mL/min/1.73 m2; data from the NHANES III
- Estimated 12 million have evidence of microalbuminuria
- ESRD in US in 2005: 106,912 (4):
  - 350.7 per 1 million population
  - Male > Female
  - African Americans > Caucasians (3:1)
  - 62.8 is mean age at start of ESRD therapy
- Increasing between 1988–2004 from 10.0–13.1%. Thought to be due, in part, to increasing prevalence of diabetes, increasing BMI and HTN.

RISK FACTORS

- Advanced malignancy
- Autoimmune diseases: Goodpasture syndrome, Wegener granulomatosis, SLE, TTP, amyloidosis

- Diabetes
- Familial syndromes: Polycystic kidney disease, Alport syndrome
- Glomerulonephritis, especially focal segmental, IgA nephropathy
- Hematologic diseases: Sickle cell anemia, blood cell dyscrasias
- HIV nephropathy
- Medications: Analgesics, chronic NSAIDs, aminoglycosides, lithium, lead exposure, chemotherapeutics, heroin
- Metabolic disease: Gout, Fabry disease, hyperoxaluria
- Obesity
- Persistent urinary dysfunction: Ureteral or prostatic obstruction, neurogenic bladder, vesicoureteral reflux with recurrent infections:
  - Primarily in pediatric and young adult population
- Renal lithiasis: Chronic ureteral obstruction, nephrocalcinosis
- Renal tubular disorders (cystinosis, oxalosis, Fanconi syndrome)
- Vascular disease: HTN, aneurysms, atheromatous disease, fibromuscular endovascular diseases

Pediatric Considerations

Obstructive uropathy and congenital aplasia/hypoplasia/dysplasia are responsible for almost 1/2 of all cases of CKD in children.

Genetics

Inherited diseases such as polycystic renal diseases, others

GENERAL PREVENTION

- Good BP and glucose control
- Relief of any obstructions or correction of anatomic anomalies in the urinary tract
- Prevention of and treatment of UTIs
- Proper dosing of nephrotoxic medications
- Reno-protective therapies: ACE inhibitor, angiotensin II receptor blocker; best if initiated before creatinine reaches 1.2 mg/dL (106 mmol/L) in women and 1.5 mg/dL (133 mmol/L in men)

PATHOPHYSIOLOGY

- Mechanisms leading to CRF:
  - Insulin resistance with compensatory hyperinsulinemia
  - Inappropriate activation of the renin-angiotensin-aldosterone system and increased oxidative stress
  - Endoplasmic reticulum stress

- Coagulability and impaired fibrinolysis

• The combined effects of these conditions induce in the kidneys impaired pressure natriuresis, glomerular HTN, endothelial dysfunction, and vasoconstriction, as well as matrix proliferation and expansion.

• Creatinine doubles with each 50% loss in GFR.

• Hyperkalemia usually occurs with GFR, 25 mL/min or if on high-potassium diet

• Metabolic acidosis: Inability of damaged kidneys to produce ammonia in the proximal tubules to excrete ammonium

• Anemia from decreased erythropoietin

• Renal bone disease: Extraskeletal calcifications, renal osteodystrophy: Hyperphosphatemia suppresses renal hydroxylation of inactive 25-hydroxyvitamin D to calcitriol; hypocalcemia and hyperphosphatemia stimulate secondary hyperparathyroidism

COMMONLY ASSOCIATED CONDITIONS

• Cardiovascular diseases

• Collagen vascular diseases

• Diabetes

• HTN

• Urinary tract obstruction or anomalies (vesicoureteral reflux, chronic pyelonephritis, hydronephrosis)

DIAGNOSIS

HISTORY

• Symptoms develop slowly and may not be apparent until renal failure is very advanced.

• Symptoms:
  - General: Fatigue. weakness, malaise
  - GI: Anorexia, nausea, metallic taste
  - Neurologic: Irritability, insomnia, difficulty concentrating, twitching, restless legs
  - Dermatologic: Pruritus
  - GU: Decreased urine output, decreased libido, menstrual irregularities
  - CV: Chest pain, shortness of breath

• History of HTN, diabetes

• Medication usage: NSAIDs; other nephrotoxins

• Occupational exposures to heavy metals

• Childhood renal infections or history of glomerulonephritis

• Gynecologic history of preeclampsia

- Family history of autosomal dominant polycystic kidney disease

PHYSICAL EXAM

- Hypertension: 85% of ESRD patients have primary or secondary
- Skin: Pallor (anemia), ecchymosis (platelet dysfunction)
- HEENT: Funduscopic abnormalities, hearing loss (Alport syndrome)
- CVA: Pulsus paradoxus (pericardial tamponade)
- Respiratory: Rales (volume overload)
- Abdomen: Palpable masses (ADPKD), CVA tenderness (pyelonephritis, ureteral obstruction)
- Extremities: Edema, tophi (gout), previous dialysis access, calciphylaxis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum chemistry:
  - Elevated creatinine
  - Low albumin levels
  - Elevated uric acid
  - Hyperkalemia
  - Low bicarbonate
- Hyperlipidemia
- Urinalysis, with microscopy:
  - Color: Red (hematuria), brown (rhabdomyolysis)
  - Protein: If very high, consider nephrotic syndrome
  - Casts: RBC (glomerulonephritis); WBC casts (interstitial nephritis)
  - Fat bodies: Nephrotic syndrome
- CBC: Decreased hemoglobin (normochromic normocytic anemia), low platelets
- 24-hr urine collections: Accurate calculation of creatinine clearance, proteinuria levels (see “Patient Monitoring”)
- Blood antibodies: ANA (lupus), hepatitis B and C, anti-GBM (Goodpasture, rapidly progressing glomerulonephritis)
- Calcium, phosphate, vitamin D, PTH for evidence of renal bone disease.

Imaging

- Renal US: Small kidneys, loss of corticomedullary differentiation, decreased echogenicity. May also show hydronephrosis of an obstructive cause
- Noncontrast CT: To narrow differential diagnosis of etiology, rule out renal masses
- Nuclear renal scans, arteriography, and cystography as clinically indicated

Diagnostic Procedures/Surgery

Renal biopsy to determine etiology

Pathological Findings

Based on specific disease

DIFFERENTIAL DIAGNOSIS

- Acute, reversible renal failure vs. chronic disease is the main differential.
- Cause of chronic renal failure is much more extensive (see “Risk Factors”).

TREATMENT

- Treat underlying disease to halt progression.
- Coordinate care with nephrology and renal dietitian.
- Control BP.
- Control blood sugar (HbA1C <7%).
- Restrict protein to <1 g/kg/d.
- Restrict salt to <2 g/d (nondialysis patients).
- Restrict water to <1–2 L/d.
- Restrict potassium to 60–70 mEq/d.
- Restrict phosphorus to 5–10 mg/kg/d.
- Dosage-adjust meds for reduced renal clearance.

MEDICATION

First Line

- HTN:
  - ACE inhibitors or angiotensin II receptor blockers (do not use ACE inhibitors if serum creatinine >3 mg/dL, renal artery stenosis, solitary kidney). May retard progression of renal failure.
  - Calcium channel blockers
  - Diuretics (also for congestive heart failure)
  - Clonidine, hydralazine, minoxidil as adjunct
- Metabolic Imbalances:
  - Acute hyperkalemia:

    Calcium chloride or gluconate IV with glucose IV, bicarbonate IV

    Sodium polystyrene sulfonate (Kayexalate) 15 g PO or 30 g PR. Contraindicated in GI obstruction, hypokalemia, or hypocalcemia; adverse reactions include bowel obstruction, necrosis (if given with sorbitol), and electrolyte imbalances
  - Chronic hyperkalemia: Kayexalate
  - Hyperphosphatemia: Phosphate binders (calcium acetate, calcium carbonate, lanthanum carbonate, sevelamer)

– Hypocalcemia: Calcium supplements with or without calcitriol

– Hyperparathyroidism: Calcitriol or vitamin D analogs (doxercalciferol, paricalcitol); calcimimetic agents (Cinacalcet)

- Anemia: Iron supplementation (ferrous sulfate, iron dextran, iron sucrose or ferric gluconate); erythropoietin (50 U/kg once or twice per week IV or SC.

Second Line

RRT for ESRD:

- Hemodialysis: For acute symptoms of fluid overload, refractory hyperkalemia, uremic symptoms, severe metabolic acidosis (pH 7.2), seizures
- Peritoneal dialysis
- Renal transplantation

SURGERY/OTHER PROCEDURES

- Vascular or peritoneal dialysis access as appropriate
- Renal transplantation as renal replacement therapies

ADDITIONAL TREATMENT

Monitor and treat hyperlipidemia.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Patient education
- Stop smoking.
- Establish and maintain a good support system.
- Register for renal transplantation.
- Appropriate placement of dialysis catheters and fistulas to avoid emergency situations

ONGOING CARE

PROGNOSIS

- Depends on patient ability to prevent continued decline of GFR. May progress to ESRD and death without replacement therapy.
- Predictors of accelerated progression: Greater proteinuria; higher BP; black race; lower serum HDL cholesterol; lower levels of serum transferrin

COMPLICATIONS

Malnutrition, sexual dysfunction, thyroid dysfunction, uremic neuropathy and encephalopathy, death

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Calculation of GFR:

- Modification of Diet in Renal Disease Study (MDRD):

Estimated GFR (eGFR) (mL/min/1.73 m2)

= GFR (mL/min/1.73 m2) = 1.86 × (SCR)1.154

× (Age)0.203 × (0.742 if female)

× (1.212 if African American)

- Cockcroft-Gault equation:

Multiply by 0.85 for women

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

Renal Failure, Acute

CODES

ICD9

- 585.1 Chronic kidney disease, stage I
- 585.2 Chronic kidney disease, stage II (mild)
- 585.3 Chronic kidney disease, stage III (moderate)

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- ADPKD: Autosomal dominant polycystic kidney disease
- ANA: Antinuclear antibodies
- BMI: Body mass index
- BP: Blood pressure
- CKD: Chronic kidney disease
- CRF: Chronic renal failure
- CT: Computed tomography
- CVA: Costovertebral angle
- eGFR: Estimated GFR
- ESRD: End-stage renal disease
- GBM: Glomerular basement membrane
- GFR: Glomerular filtration rate

- GI: Gastrointestinal
- GU: Genitourinary
- HDL: High-density lipoprotein
- HEENT: Head eyes, ear, nose, throat exam
- HIV: Human immunodeficiency virus
- HTN: Hypertension
- MDRD: Modification of Diet in Renal Disease study
- NHANES III: 3rd National Health and Nutrition Exam Survey
- NSAID: Nonsteroidal anti-inflammatory drug
- PTH: Parathyroid hormone
- RBC: Red blood cell
- RRT: Renal replacement therapy
- SLE: Systemic lupus erythematosus
- TTP: Thrombotic thrombocytopenic purpura
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

RENAL FUSION ANOMALIES

David D. Thiel, MD

BASICS

DESCRIPTION

- A congenital condition in which the renal units are joined
- Most are asymptomatic.
- Horseshoe kidney is the most common renal fusion anomaly:
  - In the horseshoe kidney, the fusion is at 1 pole, typically the lower (>90% of cases).
- Crossed-fused renal ectopia is the 2nd most common fusion anomaly:
  - Kidney is located on the opposite side of where the ureter inserts
  - In these cases, the ectopic renal unit is almost always fused to the opposite renal unit (90%).
  - Crossed-fused renal ectopia is distinct from the horseshoe kidney.

EPIDEMIOLOGY

- Horseshoe kidney occurs in 1 in 400–500 live births:
  - Male > Female
  - 90% are asymptomatic
- Crossed-fused ectopia occurs in 1 in 7,000 autopsies:
  - Male > Female
  - Crossing from left to right is the most common.

RISK FACTORS

Crossed-fused ectopia is frequently associated with vertebral anomalies such as myelomeningocele and sacral agenesis.

Genetics

Horseshoe kidney increased in trisomy 18:

- Consider karyotype in girls with horseshoe kidney.

PATHOPHYSIOLOGY

- Ureteral bud extends to the metanephric blastema during 4th–5th wk of gestation to induce kidney formation.
- The kidneys then ascend and rotate between the 4th and 9th wk of gestation. The metanephric blastema are closely associated during ascent.
- Failure of this blastema to separate during ascent results in fusion abnormality.
- Crossed-fused ectopia results when the ureteric bud crosses to the opposite side to induce the metanephric blastema on the side opposite of its trigonal insertion.

- Most kidneys that cross will be fused. Crossed ectopia without fusion is less common
- Criss-crossed ectopia very rare.
- Horseshoe kidney can be further classified based on the location of the isthmus:
  - Symmetric horseshoe kidney: Each kidney lies on opposite sides of the spine
  - Asymmetric horseshoe kidney (also referred to as L-shaped): Fused portion (isthmus) lies lateral to the midline.

COMMONLY ASSOCIATED CONDITIONS

- Other GU abnormalities associated with horseshoe kidneys:
  - Hypospadias
  - Undescended testicles
  - Vesicoureteral reflux seen in 50% of cases:
    VCUG is routine part of evaluation
- Horseshoe kidney also associated with imperforate anus and Meckel diverticulum.
- Crossed-fused ectopia may be associated with imperforate anus.

Pediatric Considerations

Most renal fusion abnormalities are asymptomatic. However, these anomalies predispose to infection, hydronephrosis, stone disease, and, in some cases, neoplasia in the pediatric population.

DIAGNOSIS

HISTORY

- History of UTI
- Hematuria
- Stone history
- Most renal fusion abnormalities are asymptomatic.

PHYSICAL EXAM

- Palpable abdominal mass (hydronephrosis)
- CVA tenderness (stone or pyelonephritis)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis (for hematuria)
- Serum creatinine (for obstruction)

Imaging

- Vesicoureteral reflux seen in 50% of horseshoe kidneys:
  - VCUG is routine part of evaluation.
- If question of UPJ obstruction on imaging, get MAG3 with Lasix to confirm obstruction

Diagnostic Procedures/Surgery

Karyotype recommended in females with horseshoe kidney to rule out chromosome 18 abnormalities

Pathological Findings

Wilms tumor in children and TCC in adults are more common in horseshoe kidneys:

- Unclear if carcinoma related to embryologic mechanisms, urinary sepsis, or infection

DIFFERENTIAL DIAGNOSIS

- Renal mass
- Supernumerary kidney:
  - An accessory organ with its own blood supply and collecting system
  - It may or may not be reniform, but possesses a distinct capsule surrounding a parenchymal mass.
- Malrotated kidneys can look like horseshoe kidney on imaging.

TREATMENT

No therapy usually needed if asymptomatic

MEDICATION

Antibiotics:

- Vesicoureteral reflux treated the same as in those without horseshoe kidneys in children. Antibiotic prophylaxis may be used until resolution for low-grade reflux.

SURGERY/OTHER PROCEDURES

- Wilms tumor in children and urothelial carcinoma in adults are more common in horseshoe kidneys.
- If surgical removal required, be aware of aberrant blood supply:
  - The number of arteries varies and may arise from the aorta or the iliacs.
  - In horseshoe kidney, the fusion is usually at the lower poles; this is called the isthmus. The isthmus can often be divided at time of surgery for removal.
  - The isthmus often lies just below the inferior mesenteric artery.
  - Arteriography is traditionally used to define vasculature before surgery but 3D CT angiography is adequate for operative planning.
- Ureter reimplant surgery for reflux no different than normal anatomy
- UPJ obstruction can be managed with dismembered pyeloplasty:
  - Endoscopic incision of UPJ is often difficult in horseshoe kidneys.
- Stones can be removed at time of pyeloplasty in cases of UPJ obstruction:
  - ESWL may not be as successful in horseshoe kidneys secondary to urinary stasis
  - PCNL is possible in horseshoe kidneys. Percutaneous access is often required in a more anterior and medial location than normal.

ONGOING CARE

PROGNOSIS

Most cases patients are asymptomatic; condition usually found incidentally or during evaluation for UTI or urolithiasis.

COMPLICATIONS

- Possible increased risk of malignancy
- Urolithiasis
- UTI
- UPJ obstruction
- Vesicoureteral reflux

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Due to slight increase in incidence of Wilms tumor in children and TCC in adults, some advocate imaging every 6 mo once diagnosis is made.
- The abnormalities and conditions for crossed-fused ectopia are similar to horseshoe kidneys, and treatment often follows similar lines.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Malrotated Kidney
- Horseshoe Kidney
- Renal Ectopia
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

753.3 Other specified anomalies of kidney

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle

- ESWL: Extracorporeal shockwave lithotripsy
- GU: Genitourinary
- MAG3: Mercaptoacetyltriglycine 3
- PCNL: Percutaneous nephrostolithotomy
- TCC: Transitional cell carcinoma
- UPJ: Ureteropelvic junction
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

RENAL INFARCTION

Stanley Zaslau, MD, MBA
Susan E. Saunders, MD

BASICS

DESCRIPTION

- Renal infarction is a rare condition that involves any process in which blood flow to the kidney becomes decreased and causes necrosis of the organ's tissue.
- Most commonly caused by thromboembolic phenomenon in conditions such as atrial fibrillation

EPIDEMIOLOGY

Has been estimated at 0.48–1.4% based upon autopsy data

RISK FACTORS

- Acute tubular necrosis
- Antiphospholipid antibody syndrome
- Atherosclerosis
- Atrial fibrillation
- Chagas disease
- Cocaine abuse
- Collagen vascular disease
- Congestive heart failure
- DM
- Dilated cardiomyopathy
- Endocarditis
- Hypercoagulable states
- HTN
- Iatrogenic (from surgical manipulation of the vascular)
- Intimal dissection
- Long-bone fracture (fat embolus)
- MI
- Pyelonephritis
- Renal artery aneurysm and stenosis
- Renal artery or vein thrombosis
- Sickle cell disease; can also cause papillary necrosis
- Trauma; usually rapid deceleration injury with intimal flap in renal artery
- Valvular heart disease

Genetics

More likely in patients with family history of coronary artery disease, DM, or any metabolic syndrome. Also associated with family history of collagen vascular diseases.

GENERAL PREVENTION

- Minimize risk of trauma by wearing seatbelts
- Treatment of atrial fibrillation or other embolic diseases with anticoagulant therapy
- Treatment of hypercholesterolemia with statins or other cholesterol-lowering medications.

PATHOPHYSIOLOGY

- Main mechanisms are embolization:
  - Clot emboli most common
  - Atherosclerotic emboli (cholesterol crystal embolism)
  - Vegetative emboli in SBE
  - Fat embolus

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COMMONLY ASSOCIATED CONDITIONS

- Angina
- Claudication
- Focal neurologic deficits due to emboli
- Mesenteric and intestinal ischemia
- Patent foramen ovale
- Papillary necrosis (especially with sickle cell disease)
- Polyarteritis nodosa with vasculitis

ALERT

Symptoms associated with acute renal infarction are very similar to other much more common causes of flank pain such as urolithiasis or pyelonephritis. This often results in a delayed diagnosis in most patients that impacts on long-term recovery of the kidney.

DIAGNOSIS

HISTORY

- Most patients have underlying heart disease or a history of recent trauma.
- The most common concomitant cardiac risk factor is atrial fibrillation.
- Recent MI can result in left ventricular thrombus.
- Acute flank pain: ~75%
- Nausea/vomiting: ~50%

- Gross hematuria may be seen.

PHYSICAL EXAM

- Fever
- Acute HTN is typical.
- Diffuse abdominal pain usually without peritoneal signs
- CVA tenderness
- Flank ecchymosis if patient experienced traumatic injury
- Abdominal bruit from aneurysm
- Peripheral vascular disease
- Decreased urine output

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Leukocytosis: In 70% of patients
- Creatinine level may be normal or elevated.
- Microscopic hematuria is found in 80% of patients.
- Proteinuria in 90% of patients
- LDH elevated in 100% of patients. If other liver transaminases are not elevated, when combined with the symptom complex, highly suggestive of renal infarction
- ALT elevated in 83% of patients
- AST elevated in 66% of patients

Imaging

- CT with and without contrast is the best study to demonstrate acute infarct:
  - Classic findings of renal infarction on CT:

    Low-attenuated areas secondary to local edema

    Wedge-shaped area of devascularized infarct with a sharp demarcation

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- US with Doppler flow
- Radionuclide scanning not very useful acutely but may have a role in follow-up of the infarcted kidney

Diagnostic Procedures/Surgery

- ECG to diagnose arrhythmia
- Echocardiography to identify atrial or ventricular thrombus
- Angiography can help diagnose any vascular occlusion; may also allow intervention.

Pathological Findings

• Histology acutely exhibits apoptotic cells as demonstrated by nuclear chromatin condensation.

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DIFFERENTIAL DIAGNOSIS

- Renal calculi
- Renal vein thrombosis
- Pyelonephritis
- Renal tumor
- Renal cystic disease
- Renal artery stenosis
- Other intra-abdominal process not involving the kidney

TREATMENT

- Prompt recognition through a high degree of suspicion is key to rapid treatment.
- Supportive therapy with IV fluids and pain control
- Optimum therapy is not clear.
- Acute treatment options include simple anticoagulation, thrombolytic therapy, or more invasive intervention
- Since most patients have acute renal infarction from thromboembolic causes, primary anticoagulation is usually considered 1st line.

MEDICATION

- Control HTN
- Anticoagulative therapy:
  - Begin with heparin. Initial bolus of 80 U/kg followed by continuous infusion 16 U/kg/hr and adjusted to PTT.
  - Convert to oral warfarin. Usual target INR is 2.0–3.0, at which time heparin can be discontinued.
  - Useful for thromboembolic conditions such as atrial fibrillation
- Thrombolytic therapy with tPA has been used but could be a consideration in an unstable patient:
  - Direct intra-arterial infusion may limit systemic side effects.
  - Contraindications include cerebral AVM or malignancy, any history of cerebral hemorrhage, aortic dissection, active hemorrhage, bleeding diathesis, others.
  - Relative contraindications: Major surgery within the past 3 wk, uncontrolled HTN, pregnancy, others

SURGERY/OTHER PROCEDURES

• Most traumatic arterial injuries have been traditionally managed by open surgical repair. In general, surgical intervention is not considered a primary option for thromboembolic renal infarction. In some cases, patients being explored for other injuries may have renal revascularization performed (see “Renal Trauma, Adult” and “Renal Trauma, Pediatric”).

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– Vascular reperfusion surgery is usually not indicated if there is significant renal atrophy.

• Patient attributes that make operative management a consideration for acute embolic renal infarct include:

– Young patient with an infarct discovered within 6 hr of the insult

– Patients with bilateral infarcts or a solitary kidney

ADDITIONAL TREATMENT

• Interventional angioplasty with balloon dilation of the artery or thrombectomy.

• Limited experience with other forms of percutaneous endovascular therapy such as stenting.

• Best results are seen when the intervention is performed within hours or days of the insult.

ONGOING CARE

PROGNOSIS

• Prognosis after renal infarct depends on concomitant medical conditions, cause of infarct, and amount of renal tissue affected.

• Most patients have restoration of normal function with prompt treatment.

• Due to comorbidities, patients can die of the related illness.

COMPLICATIONS

• Renal atrophy

• Chronic renal insufficiency

• HTN

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Follow-up imaging to monitor progression or remission of infarcted renal tissue

• Regular laboratory studies with serum creatinine

• General medical treatment of underlying condition that led to infarct

• Regular BP readings to evaluate for new-onset HTN after renal infarct

• Long-term anticoagulation with warfarin for chronic conditions such as atrial fibrillation

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4. Lessman RK, Johnson SF, Coburn JW, et al. Renal artery embolism, clinical features and long term follow-up in 17 cases. Ann Intern Med 1978;89: 477.

See Also (Topic, Algorithm, Electronic Media Element)

- Renal Trauma, Adult
- Renal Trauma, Pediatric
- Sickle Cell Disease, Urologic Considerations

CODES

ICD9

593.81 Vascular disorders of kidney

ABBREVIATIONS

- ALT: Alanine aminotransferase
- AST: Aspartate aminotransferase
- AVM: Arteriovenous malformation
- BP: Blood pressure
- CT: Computed tomography
- CVA: Costovertebral angle
- DM: Diabetes mellitus
- ECG: Electrocardiogram
- HTN: Hypertension
- IV: Intravenous
- IVP: Intravenous pyelogram
- LDH: Lactate dehydrogenase
- MI: Myocardial infarction
- PTT: Prothrombin time
- SBE: Spontaneous bacterial endocarditis
- tPA: Tissue plasminogen activator
- US: Ultrasound

RENAL MASS

Gregory Spana, MD

Gabriel P. Haas, MD

BASICS

DESCRIPTION

Lesions in kidney that can be benign or malignant, cystic or solid, unilateral or bilateral, single or multifocal, primary or metastatic:

- Most common benign renal mass in adults: Simple cyst
- Most common malignant renal mass in adults: Metastatic tumor
- Most common primary malignant renal mass in adults: RCC
- Most common renal mass in newborns: Hydronephrosis
- Most common primary renal malignancy in children: Wilms tumor

EPIDEMIOLOGY

- Increasing detection of renal masses in adults due to more extensive use of abdominal imaging
- ~31,000 new cases of RCC per year
- Most common in 6th–7th decades
- RCC is 2–3% of adult malignant neoplasms
- Simple renal cysts found in 50% >50

RISK FACTORS

- Simple renal cysts: Advanced age
- AML: 20–30% found in patients with TS
- Oncocytoma: Familial renal oncocytomatosis, BHD
- Renal abscess: Immunocompromised state, DM
- XGP: Middle-aged women, DM, chronic obstructing urinary calculi.
- RCC: Male gender, advanced age, tobacco use (RR 1.4–2.5), end-stage renal failure, positive family history, TS, VHL, familial papillary renal cell carcinoma, hereditary leiomyomatosis and renal cell carcinomas
- Urothelial carcinoma of the renal pelvis (TCC): Tobacco use, analgesic abuse (phenacetin), Balkan nephropathy, aniline dye exposure, cyclophosphamide exposure, history of bladder cancer

Genetics

- RCC is associated with mutations of the VHL tumor suppressor gene located on chromosome 3p.
- ARPKD

- ADPKD
- Other genetic cystic diseases: Juvenile nephronophthisis, medullary cystic kidney disease, glomerulocystic kidney disease, tuberous sclerosis, BHD

GENERAL PREVENTION

Screenings of patients with hereditary syndromes that lead to renal masses are recommended.

PATHOPHYSIOLOGY

- RCC arises from the proximal convoluted tubule cell. Growth is generally <0.5 cm/yr.
- Simple cysts grow at a rate of 2.18 mm/yr
- Some small renal masses may not grow.
- The majority of small renal masses <1.5 cm are either cystic or benign renal masses. The majority of solid renal masses >1.5 cm are RCC.

Pediatric Considerations

- Wilms tumor is most common malignant neoplasm; mean age 3.5 yr; associated with multiple congenital syndromes (eg, Beckwith-Wiedemann, Denys-Drash)
- Rhabdoid tumor: Malignant sarcoma
- Clear-cell sarcoma: Malignant sarcoma
- Cystic nephroma: Benign
- Multicystic dysplastic kidney: Benign, nonfunctioning kidney
- Mesoblastic nephroma: Most common renal tumor in newborns; benign but locally invasive and treated with surgical excision

COMMONLY ASSOCIATED CONDITIONS

- VHL: Retinal angiomas, CNS hemangiomas, pheochromocytomas, pancreatic cysts, epididymal cystadenomas
- TS: Mental retardation, epilepsy, adenoma sebaceum; 50% have multiple renal angiomyolipomas; 20–25% of patients have renal cysts

DIAGNOSIS

HISTORY

- >50% of RCC found incidentally
- Classic triad (flank pain, gross hematuria, palpable mass) is rarely found in RCC.
- Paraneoplastic syndromes found in 20% of patients with RCC: Increased ESR, HTN, anemia, weight loss, fever, abnormal LFTs, hypercalcemia, polycythemia, neuropathy, amyloidosis
- Fever and flank pain may suggest inflammatory condition such as renal abscess, XGP
- Family history of syndromes associated with renal masses (VHL, TS)

- If on dialysis, acquired cystic renal disease

PHYSICAL EXAM

- Abdominal mass
- Fever suggests inflammatory masses
- HTN
- Hypotension: Ruptured AML
- Varicocele: May suggest a renal tumor with extension into the IVC (right-sided) or left renal vein (left-sided).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - Hematuria: Not always present
  - Nitrite- or leukocyte esterase–positive suggests infection
- Urine culture
- Voided urine cytology: May detect TCC of urinary tract (good specificity):
  - Positive in only 7% of patients with RCC
- CBC
- Renal function tests (BUN and creatinine)
- LFTs: 20% of patients with RCC may have abnormal LFTs secondary to Stauffer syndrome (nonmetastatic reversible hepatic dysfunction).
- Serum calcium: May be elevated in RCC secondary to paraneoplastic syndrome.

ALERT

Although fat is a hallmark of AML, some RCCs can also have varying degrees of fat on imaging studies.

Imaging

- Bosniak classification is a radiologic system of classifying cystic renal lesions based on CT scan (see “Renal Cysts”).
- Chest x-ray: Preoperative clinical staging with a malignant renal tumor; diagnosing TB.
- KUB: Detects enlarged or malpositioned renal shadow, but nonspecific.
- IVP:
  - Evaluates upper urinary tract and kidney Commonly used in the workup of hematuria
  - Detects renal masses; sensitivity for <3 cm masses is only 67%
  - Filling defects in the collecting system are suspicious for tumor until proven otherwise.

- Renal US:
  - Characterizes renal masses as solid or cystic, simple or complex; initial upper urinary tract imaging of choice in children
- Abdominal CT:
  - Gold standard for renal masses
  - CT IVP (urogram) is rapidly gaining acceptance as the upper-tract imaging of choice for hematuria
  - Renal masses evaluated using CT scan with and without IV contrast and 5 mm thin-cut slices (renal mass protocol)
  - Enhancing renal masses are generally considered malignancy until proven otherwise.
  - Useful in cancer staging, defining surgical anatomy, evaluating contralateral kidney function
- Abdominal MRI:
  - Study of choice to evaluate renal vascular anatomy and presence of tumor thrombus in the renal vein or IVC; may help further characterize some renal masses
- Renal scintography (renal scan): Useful to determine split differential in renal function during preoperative assessment for nephrectomy/partial nephrectomy; detect hypertrophied column of Bertin (pseudotumor)

Diagnostic Procedures/Surgery

- Retrograde pyelogram: Used to evaluate the upper urinary tracts in patients who have a contraindication to IV dye
- Renal biopsy: Most useful in patients when there is a high suspicion for metastatic lesions to the kidney (eg, lymphoma); high false-negative rate; useful if imaging inconclusive; essential if ablation is being considered
- Renal cyst aspiration with cytology

DIFFERENTIAL DIAGNOSIS

- Renal masses in adults:
  - Adrenal mass
  - Angiomyolipoma: Presence of fat within a renal mass is diagnostic of AML; fat-poor AML may resemble RCC
  - Carcinoid tumors
  - Collecting duct tumor (Bellini)
  - Cystic nephromas (multilocular cystic nephroma)
  - Cysts (hemorrhagic, infected)

  - Focal pyelonephritis
  - Hemangioma
  - Inflammatory masses (xanthogranulomatous pyelonephritis, abscess)
  - Leiomyoma: Usually arise in renal capsule
  - Metanephric adenoma: Cannot be reliably distinguished from RCC on imaging studies; considered benign
  - Metastasis from other primary tumor: Lung, gastric, breast cancers are most common. Melanoma and other tumor types reported
  - Oncocytoma: Benign; cannot be reliably differentiated from RCC on imaging studies
  - Pseudotumors (column of Bertin, others)
  - RCC
  - Renal cortical adenoma: Controversial diagnosis; cannot be reliable distinguished from RCC on imaging studies: <2 cm
  - Renal lymphoma
  - Renal medullary carcinoma
  - Renal sarcomas: 1–2% of all renal masses (leiomyosarcomas, fibrosarcomas, malignant fibrous histiocytomas, anaplastic sarcoma)
  - Reninoma (JG apparatus tumors)
  - Urothelial carcinoma
  - Wilms tumor (nephroblastoma)
- Benign renal mass in children:
  - Choledochal cyst, intestinal duplication cyst
  - Congenital mesoblastic nephroma
  - Cystic nephroma (multiloculated cystic nephroma)
  - Hydronephrosis
  - Mesenteric cyst
  - Multicystic dysplastic kidney
  - Polycystic kidney: ARPKD presents usually in infancy; ADPKD usually presents later in life
  - Renal abscess
  - Splenomegaly
- Malignant renal masses in children:
  - Lymphoma
  - Lymphosarcoma

- Neuroblastoma (actually adrenal origin)
- Ossifying renal tumor of infancy
- RCC
- Sarcomas (clear cell sarcoma, rhabdomyosarcoma, others)
- Wilms tumor (nephroblastoma)

TREATMENT

- Imaging cannot reliably diagnose if a suspicious renal mass is benign or malignant, although larger size is more likely to be associated with malignant rather than a benign process.
- Solid masses <1.5 cm: Period of observation is reasonable as many of these may not grow.

MEDICATION

- Metastatic RCC treatment with targeted therapy against the VEGF pathway
- Immunotherapy for metastatic RCC with interferon or interleukin-2

SURGERY/OTHER PROCEDURES

- Painful simple renal cysts and infected cysts: Percutaneous aspiration and sclerotherapy
- Most authors recommend surgery for Bosniak III and IV cysts.
- AML >4 cm or small symptomatic lesions are treated by embolization, partial nephrectomy, or nephrectomy.
- Renal lesions suspicious for RCC are treated surgically (laparoscopically or open) usually with radical nephrectomy for masses >4 cm; partial nephrectomy (<4 cm), or ablation can be considered (cryosurgery, RFA).
- TCC of the renal pelvis is treated by endoscopic ablation for small superficial lesions or radical nephroureterectomy.

ADDITIONAL TREATMENT

- Palliation of bone or CNS metastases in RCC
- May have a role in some sarcomas in setting of residual disease

ONGOING CARE

PROGNOSIS

Prognostic factors for RCC include TNM stage, size, histologic type, nuclear grade, and performance status (nomograms available).

COMPLICATIONS

Surgical complications include hematoma, pneumothorax, infection, adjacent organ injury (liver, spleen, pancreas, duodenum, and bowel), urinary leak, myocardial infarction, thromboembolism, positive surgical margins.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Active surveillance: High-risk patients with small renal masses may be observed.
- Simple renal cysts: No further follow-up.
- Complex cysts (Bosniak IIF) require follow-up.
- Management of small renal masses is controversial and not generally agreed upon. Since many will continue to grow and may represent small RCCs, periodic imaging is recommended.
- Complex renal cysts require periodic follow-up with radiographic imaging or surgical intervention.
- AML <4 cm may be followed with imaging every 6–12 mo.
- Follow-up after RCC: Periodic abdominal imaging with associated laboratory and chest X-ray studies.
- Surveillance after upper-tract TCC: Periodic cystoscopy, urine cytologies, and IVP.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Cell Carcinoma, General
- Renal Cysts
- Renal Mass Algorithm

CODES

ICD9

- 223.0 Benign neoplasm of kidney, except pelvis
- 593.2 Cyst of kidney, acquired
- 593.9 Unspecified disorder of kidney and ureter

ABBREVIATIONS

- ADPKD: Autosomal dominant polycystic kidney disease
- AML: Angiomyolipoma

- ARPKD: Autosomal recessive polycystic kidney disease
- BHD: Birt-Hogg-Dube syndrome
- BUN: Blood urea nitrogen
- CBC: Complete blood count
- CNS: Central nervous system
- CT: Computed tomography
- DM: Diabetes mellitus
- ESR: Erythrocyte sedimentation rate
- HTN: Hypertension
- IV: Intravenous
- IVC: Inferior vena cava
- IVP: Intravenous pyelogram
- JG: Juxtaglomerular
- KUB: Kidney-ureter-bladder
- LFT: Liver function test
- RCC: Renal cell cancer;
- RFA: Radiofrequency ablation
- RR: Relative risk
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- TS: Tuberous sclerosis
- US: Ultrasound
- VEGF: Vascular endothelial growth factor
- VHL: Von Hippel-Lindau
- XGP: Xanthogranulomatous pyelonephritis

RENAL ONCOCYTOMA

Stephen A. Boorjian, MD
Robert G. Uzzo, MD

BASICS

DESCRIPTION

- Oncocytoma is the most common solid benign renal tumor of the kidney in adults.
- Renal oncocytosis: Condition of innumerable, bilateral oncocytomas with single dominant oncocytoma
- Most renal oncocytomas are asymptomatic and detected incidentally on imaging studies.
- Oncocytomas may occur in other organs (salivary gland, parathyroid, adrenal, thyroid).

EPIDEMIOLOGY

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- Epidemiology similar to RCC
- Male > Female (2:1)
- Median age at diagnosis is 62 yr
- 6% of oncocytomas bilateral
- 17% multifocal

RISK FACTORS

- Familial renal oncocytoma syndrome:
  - Described in relatively few families to date
- BHD syndrome (see below)

Genetics

- Most frequent abnormalities:
  - Loss of chromosome 1p
  - Loss of chromosome Y (in males)
- Less frequently, chromosomal translocations:
  - Breakpoint region on 11q13
  - Region encoding mitochondrial DNA
  - Unique to oncocytoma
- Loss of heterozygosity on chromosomes 1, 14, 21:
  - Seen in renal oncocytosis

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GENERAL PREVENTION

No preventative strategies have been described; screening of relatives with genetic syndromes

PATHOPHYSIOLOGY

Arise from intercalated cells in the collecting duct of the kidney (as does chromophobe RCC):

- Unlike clear-cell RCC, which arises from proximal renal tubule
- Occasionally, oncocytoma and oncocytic renal cell carcinoma may be found in the same kidney.

COMMONLY ASSOCIATED CONDITIONS

- Most oncocytomas sporadic
- BHD:
  - Autosomal dominant
  - Mutation in gene for folliculin protein
  - Renal tumors (chromophobe RCC + oncocytoma + unique hybrid tumor of chromophobe/oncocytoma)
  - Spontaneous pneumothorax, lung cysts
  - Skin lesions (fibrofolliculomas)

DIAGNOSIS

HISTORY

)[B]:

- Incidentally detected during workup for unrelated condition
- Gross hematuria, flank pain, flank mass rare
- Family history of renal tumors, fibrofolliculomas (benign skin tumors usually on the face), lung cysts/spontaneous pneumothorax: Rule out BHD

PHYSICAL EXAM

- No specific findings associated with sporadic oncocytoma:
  - Rare to have palpable flank mass
- Dermatologic exam if BHD is suspected

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No laboratory tests can identify renal tumor as an oncocytoma.
- Laboratory panel as with any newly diagnosed renal mass:
  - CBC, chemistry panel, LFTs

Imaging

- Cannot reliably distinguish oncocytoma from RCC on imaging
- CT with and without IV contrast:
  - Diagnostic test of choice for solid renal mass

– Central scar within mass often seen in oncocytoma, but not reliable to distinguish from RCC, as it can be confused with necrosis commonly seen in RCC

- MRI: Solid enhancing renal mass, ± central scar:
  - Test of choice if allergy to IV contrast, renal insufficiency
- Renal US:
  - Solid renal mass
  - Not typically helpful to identify mass as an oncocytoma
- Renal angiogram:
  - Spoke-wheel pattern of feeding vessels described in oncocytoma
  - Not definitive for diagnosis of oncocytoma
  - Test not typically helpful in evaluation of renal mass; may be useful in setting of partial nephrectomy
- Metastatic evaluation for solid renal mass:
  - Chest x-ray vs. chest CT
  - Additional studies (ie, bone scan, head CT) as indicated clinically

Diagnostic Procedures/Surgery

- Percutaneous biopsy:
  - May be useful to exclude metastasis to kidney based on patient history
  - May guide management if patient is poor surgical candidate
- Pitfalls of percutaneous biopsy:
  - Difficult to distinguish oncocytoma from chromophobe RCC
  - Coexistence of RCC and oncocytoma in same lesion/same kidney up to 10%

Pathological Findings

- Gross:
  - Well-circumscribed, mahogany brown; often with surrounding pseudocapsule
  - Average size reported in literature: 6–7 cm
  - 33% have central stellate scar (more common with larger tumors).
  - 20% demonstrate extension into perinephric fat.
  - Rarely, necrosis or calcifications
- Microscopic:
  - Round to polygonal, eosinophilic cells (oncocytes)
  - Characterized by abundance of mitochondria (seen best on electron microscopy)
  - Mitosis rare
  - Nuclei regular
  - Cells arranged in distinct nests

- May be difficult to distinguish oncocytoma from chromophobe RCC:
  - Colloidal iron stain positive in chromophobe RCC, negative in oncocytoma
  - Chromophobe RCC is vimentin-stain positive, oncocytoma is negative.

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ALERT

Although there are classic findings of oncocytoma on imaging, no radiographic studies can reliably differentiate the benign oncocytoma from the malignant RCC.

DIFFERENTIAL DIAGNOSIS

- Adrenal mass
- Angiomyolipoma
- Carcinoid tumors
- Collecting duct tumor (Bellini)
- Cystic nephromas (multilocular cystic nephroma)
- Cysts (hemorrhagic, infected)
- Focal pyelonephritis
- Hemangioma
- Inflammatory masses (xanthogranulomatous pyelonephritis, abscess)
- Leiomyoma
- Metanephric adenoma
- Metastasis from other primary tumor
- Oncocytoma: Benign; cannot be reliably differentiated from RCC on imaging studies
- Pseudotumors (column of Bertin, others)
- RCC
- Renal cortical adenoma: Controversial diagnosis; cannot be reliable distinguished from RCC on imaging studies: <2 cm
- Renal lymphoma
- Renal medullary carcinoma
- Renal sarcomas
- Reninoma (JG apparatus tumors)
- Urothelial carcinoma
- Wilms tumor (nephroblastoma)

TREATMENT

Mainstay of treatment for solid renal mass is surgical removal.

MEDICATION

No current medical management exists

SURGERY/OTHER PROCEDURES

- Establishes diagnosis of oncocytoma.
- Partial nephrectomy (open or laparoscopic) whenever technically feasible based on lesion size, location
- Radical nephrectomy rarely indicated unless very large, partial nephrectomy not possible, or diagnosis is uncertain

ADDITIONAL TREATMENT

Radiotherapy

No role for radiation therapy exists for this condition.

Additional Therapies

No additional therapies are recommended.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Renal cryotherapy and radiofrequency ablation:
  - Being studied as treatment options for solid renal masses
  - May be done laparoscopically or percutaneously
  - No long-term follow-up
  - Often can't differentiate lesion as oncocytoma from RCC before treatment
  - Currently best suited for poor surgical candidates
- Active surveillance in select patients with solid renal mass is being investigated as well; however, no size can reliably differentiate malignant from benign renal mass.

ONGOING CARE

PROGNOSIS

Oncocytoma is a benign tumor:

- Surgical extirpation is curative.

)

- Older, rare reports of metastisis may represent unrecognized low-grade RCC.

)

COMPLICATIONS

- Perioperative for partial/radical nephrectomy:
  - Bleeding, infection, urine leak (partial nephrectomy)
- Long-term after nephrectomy depending on remaining renal reserve:
  - Chronic renal insufficiency, dialysis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Long-term surveillance of renal units recommended semi-annually to annually:

- Metachronous ipsilateral and bilateral oncocytomas have been reported.
- Renal US is preferred modality, as it minimizes radiation exposure + no need for IV contrast.
- Urine analysis: Hematuria, proteinuria
- Serum creatinine

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See Also (Topic, Algorithm, Electronic Media Element)

- Birt-Hogg-Dubé Syndrome
- Renal Cell Carcinoma, General
- Renal Mass

CODES

ICD9

223.0 Benign neoplasm of kidney, except pelvis

ABBREVIATIONS

- BHD: Birt-Hogg-Dubé syndrome
- CBC: Complete blood count
- CT: Computed tomography
- IV: Intravenous
- JG: Juxtaglomerular
- LFT: Liver function test
- MRI: Magnetic resonance imagaing
- RCC: Renal cell carcinoma
- US: Ultrasound

RENAL PELVIC TUMORS

Brian M. Benway, MD
Robert S. Figenshau, MD
Gerald L. Andriole, MD

BASICS

DESCRIPTION

- Renal pelvic tumors that arise from the urothelium lining the renal collecting system and can be benign or malignant.
- Urothelial carcinoma (transitional cell carcinoma) is the most common malignant lesion (>90%).
- Other malignant tumors are rare and include squamous cell carcinoma, adenocarcinoma, and sarcoma.
- Benign tumors include fibroepithelial polyps, neurofibromas, plasmacytomas, and inverted papillomas.

EPIDEMIOLOGY

- 5–7% of all renal tumors
- 5% of all urothelial tumors
- Peak incidence in the 75–79 age group, with a diagnosis in 10 per 100,000 per year
- 80% of patients have had a previous urothelial malignancy in the bladder.
- 1–2% have bilateral tumors
- Male > Female (2:1)
- Whites > Blacks (2:1)
- Mortality rates higher in women and black men

RISK FACTORS

- Previous bladder cancer:
  - Risk highest for CIS, especially cases refractory to BCG
  - Other factors include multiple tumors, tumors near the ureteral orifice, high-grade or invasive disease, and vesicoureteral reflux.
- Smoking:
  - 7-fold increase for long-term smokers
  - 2-fold increase for former smokers; risk diminishes after quitting, but not completely
- Occupational exposure:
  - Aniline dyes, petroleum, plastics, coal, tar, asphalt.
  - Tumors can occur up to 15 yr after exposure

- Chronic inflammatory conditions:
  - Infections, stones, obstruction implicated in squamous cell carcinoma
- Analgesic abuse:
  - 22% of patients with renal pelvis tumors report history of abuse, usually within past 2 yr
  - Phenacetin, acetaminophen, salicylates, codeine implicated
  - Causes papillary scarring and thickening of basement membrane
  - Papillary necrosis is a synergistic risk factor.
- Cyclophosphamide therapy
- Balkan nephropathy
- Degenerative interstitial nephropathy
  - Unclear whether hereditary or environmentally induced
  - 100–200 times risk of upper-tract TCC, but no increase in bladder cancer risk
- Coffee consumption:
  - Nearly 2-fold risk reported in heavy coffee drinkers (>7 cups/d), however this may be due to increased prevalence of smoking in this population.

Genetics

- Risk factors appear to be mostly environmental.
- Possible hereditary influence in Balkan nephropathy
- HNPCC: Lynch II subset may have increased risk of upper-tract TCC.

GENERAL PREVENTION

- Smoking cessation
- Reduction or elimination of occupational exposure
- Careful surveillance of at-risk patients, or those with history of urothelial carcinoma, especially recurrent CIS

PATHOPHYSIOLOGY

- Tumor stage is more important prognostic factor than grade, although accurate staging can be difficult:
  - In general, higher-grade tumors are more likely to be higher-stage as well.
  - In-situ disease has high risk of progression.
- The thin muscular wall of the upper tract allows for earlier invasion and progression compared to the bladder.
- Invasive renal pelvis tumors have better prognosis than invasive ureteral tumors (54% vs. 24% 5-yr survival).
- Spread can be epithelial, lymphatic, or hematogenous:

- Lymphatic: Para-aortic, paracaval, iliac, pelvic
- Hematogenous: Liver > lung > bone > renal vein > IVC

COMMONLY ASSOCIATED CONDITIONS

- Urothelial carcinoma of the bladder; patients presenting with upper tract malignancy are at high risk of developing bladder cancer
- Contralateral upper tract TCC (1–2%)
- Inverted papilloma (18% risk of malignancy)
- HNPCC

DIAGNOSIS

HISTORY

- Gross or microscopic hematuria: 56–98%
- Flank pain (30%):
  - Usually dull, associated with obstruction from tumor; acute, colicky pain suggests an obstructing clot
- Asymptomatic: 15%
- History of smoking, occupational exposures, analgesic abuse, prior bladder cancer
- Anorexia, weight loss
- Bone pain
- Up to 19% of patients with malignancy are metastatic at the time of presentation.

PHYSICAL EXAM

- Flank tenderness
- Abdominal mass in advanced cases
- Most cases will have no gross physical findings.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis: Hematuria in 56–98%
- Cytology is best for higher-grade tumors:
  - Brush biopsies most accurate, followed by selective upper-tract washings, and voided specimens.
  - Contrast may distort specimens, so obtain cytology before performing retrograde pyelography.

Imaging

- CT urogram or IVP:
  - Filling defects, nonvisualization of 1 calyces, evidence of obstruction, soft-tissue mass

  - TCC has average density of 46 HU on CT
  - Obstruction portends invasive disease.
- Confirm with retrograde pyelography if necessary.
- Evaluate contralateral kidney for disease and for function.

Diagnostic Procedures/Surgery

- With clear filling defect on imaging and positive cytology, further diagnostic studies are not generally necessary.
- Ureteroscopy with biopsy:
  - Can be performed retrograde or antegrade
  - Biopsy may understage tumor
- Cystoscopy essential due to presence of bladder tumors in many patients with upper-tract urothelial carcinoma.

Pathological Findings

- p53 positivity, loss of heterozygosity of 9p21, NMP22, and increased telomerase activity associated with upper-tract urothelial carcinoma
- Lymphovascular invasion, tumor ploidy, and decreased p27 staining predict poor prognosis.
- Squamous cell carcinoma is 6 times more likely to be found in renal pelvis.

DIFFERENTIAL DIAGNOSIS

- Adenocarcinoma uncommon (<1%)
- Artifact (crossing vessel, air bubble, incomplete opacification of collecting system)
- Benign neoplasms: Fibroepithelial polyps, neurofibromas, and plasmacytomas
- Clot
- Extension of primary renal malignancy
- Fungus ball
- Inverted papilloma
- Sarcomas very rare
- Sloughed papilla
- Squamous cell carcinoma: Accounts for roughly 7% of malignancies.
- Stones, especially uric acid or matrix
- Transitional cell carcinoma: Most common malignant lesion (>90%)

TREATMENT

- Treatment based on proper identification of the tumor type
- Ureteroscopy has become the standard diagnostic and in many cases therapeutic tool for upper-tract tumors.

- Reduction of risk factors (stop smoking)
- Strict adherence to surveillance protocols

MEDICATION

Systemic medications are ineffective for the treatment of upper-tract urothelial malignancy. Topical agents (see below) may have a role.

SURGERY/OTHER PROCEDURES

- Gold standard for urothelial carcinoma (transitional cell and squamous cell carcinoma) remains nephroureterectomy:
  - Can be performed open or laparoscopically
  - Must remove entire ureter and cuff of bladder around ureteral orifice
  - Recurrence of 33–75% in ureteral stump if left behind
  - Lymph node dissection controversial, but may help direct further therapy
- Partial pelvectomy ± partial nephrectomy:
  - Laparoscopic approach increases risk for tumor spillage.
  - Consider for some patients with solitary kidney or poor renal reserve, but weigh risks vs. nephroureterectomy and dialysis
- Endoscopic management:
  - Most appropriate for low-grade, low-stage lesions or in patients with poor renal reserve
  - Retrograde or percutaneous
  - Percutaneous is better for larger lesions, although tract seeding is a concern.
  - Patients must be willing to undergo aggressive postoperative surveillance.

ADDITIONAL TREATMENT

Radiotherapy

- Adjuvant radiotherapy reduces the rate of local recurrence for surgically removed high-grade tumors, but does not impact recurrence rates for low-grade disease.
- The addition of platinum-based chemotherapy may enhance the efficacy of radiation.

Additional Therapies

- Topical chemotherapy and immunotherapy:
  - Can be used for definitive treatment in select cases, or as adjuvant therapy to reduce recurrence
  - Can give topical agents through percutaneous nephrostomy tube or ureteral catheter. Can also place ureteral stent and give intravesically, relying upon reflux.
- Chemotherapy:
  - Mitomycin C and thiotepa for topical use

– Systemic regimens favor combination therapy, such as MVAC. Combination therapy with gemcitabine and various agents is under investigation, and shows promise.

- Immunotherapy:

– BCG is 1st-line treatment for urothelial carcinoma; limited experience with -interferon

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Soy isoflavones have shown promise in in-vitro and animal models, but evidence in humans is lacking.

ONGOING CARE

PROGNOSIS

- Largely depends upon stage and treatment modality
- Nephroureterectomy: 97% overall disease-specific and 96% recurrence-free survival. Survival only 54% for T3 disease.
- Partial pyelectomy: 75% 5-yr survival for low-grade, 46% high-grade. Recurrence up to 70%.
- Endoscopic management: 31% chance of recurrence in upper tract, 43% chance subsequent bladder malignancy, 5–20% eventually require nephroureterectomy.

COMPLICATIONS

- Metastatic progression
- Renal insufficiency or failure
- Ureteral perforation during endoscopy
- Tumor spillage or tract seeding
- Secondary malignancy after adjuvant chemotherapy or radiation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Physical exam, cystoscopy, cytology every 3 mo for 2 yr, then every 6 mo for 2 yr, then annually.
- Chest x-ray and abdominal CT every 6 mo for 2 yr, then annually.
- If managed endoscopically or with partial resection, perform ureteroscopy every 6 mo for 2–3 yr, then annually.
- Cystoscopy to evaluate for bladder recurrence.

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See Also (Topic, Algorithm, Electronic Media Element)

- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Lynch Syndrome
- TNM Classification
- Ureter and Renal Pelvis, Squamous Cell Carcinoma
- Ureter and Renal Pelvis, Urothelial Carcinoma (Transitional Cell Carcinoma and CIS)

CODES

ICD9

- 189.1 Malignant neoplasm of renal pelvis
- 223.1 Benign neoplasm of renal pelvis

ABBREVIATIONS

- BCG: Bacillus Calmette-Guérin
- CIS: Carcinoma in situ
- CT: Computed tomography
- GU: Genitourinary
- HNPCC: Hereditary nonpolyposis colorectal cancer
- HU: Hounsfield unit

- IVP: Intravenous pyelogram
- MVAC: Methotrexate, vinblastine, doxorubicin, cisplatin
- TCC: Transitional cell carcinoma
- UTI: Urinary tract infection

RENAL SARCOMA, ADULT AND PEDIATRIC

Stephen B. Riggs, MD

Arie S. Belldegrun, MD

BASICS

DESCRIPTION

- Sarcomas of the kidney are rare solid tumors and represent 1–2% of all malignant renal tumors in adults. Sarcomas arise from mesenchymal tissue.
- In adults, leiomyosarcoma accounts for 50% of sarcomas.
- Renal sarcomas are more likely to be seen in childhood, represented almost exclusively by Wilms tumor (nephroblastoma).
- Other sarcomas of childhood include clear-cell sarcoma, malignant rhabdoid tumor, congenital mesoblastic nephroma, and fibrosarcoma.

EPIDEMIOLOGY

- Adults: 1% of renal cancer with peak incidence in 5th decade
- Children: 6–7% of childhood cancers represented mainly by Wilms tumor
- Wilms tumor occurs equally in boys and girls, with a median age of onset of 3.5 yr

RISK FACTORS

- Specific etiologies are not known.
- HIV is associated with Kaposi sarcoma of the kidney.
- Wilms tumor does have a small component of family history.

Genetics

- Adult renal sarcomas unknown; suggestion of familial tendency with angiosarcoma
- 1–2% of Wilms tumor patients have an inherited genetic predisposition:
  - WT1 located at 11p13 and is associated with renal and gonadal development.
  - WT2 located at 11p15 and is associated with BWS.
  - 90% of Wilms tumors arise from somatic mutations with overall genetic paradigm remaining unknown.

PATHOPHYSIOLOGY

- Most common adult renal sarcoma appears to be leiomyosarcoma, representing 50–60% of such tumors. A wide variety of other types, such as liposarcoma and fibrosarcoma, are also found.
- Aggressive local growth with high rate of local recurrence
- Later metastasis to the lung and liver can occur.
- Wilms tumor is categorized into favorable or unfavorable by histology; this has important implications regarding treatment.

COMMONLY ASSOCIATED CONDITIONS

Wilms tumor is associated with aniridia, hemihypertrophy, Beckwith-Wiedemann syndrome, Denys-Drash syndrome, and GU abnormalities (hypospadias and cryptorchidism).

DIAGNOSIS

HISTORY

- Age and sex of patient
- Family history
- History of mental retardation or GU anomalies
- Palpable and noticeable abdominal mass (especially in Wilms tumor)
- Shortness of breath, lethargy, abdominal pain, and weight loss may be present.

PHYSICAL EXAM

- Abdominal exam for mass:
  - In children, a palpable mass will be seen with Wilms tumor >80% of cases.
- Assess for associated lymphadenopathy.
- GU exam to assess for GU anomalies such as hypospadias or undescended testes

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Complete metabolic panel
- CBC
- Urinalysis may demonstrate microhematuria or pyuria.

Imaging

- Chest x-ray or CT to evaluate for metastatic disease
- CT or MRI to assess local extent of renal mass, status of contralateral renal unit, presence of adenopathy, and metastatic disease; no definitive defining features
- On MRI angiography, sarcomas tend to appear avascular.
- Renal US may be useful in evaluation of cystic renal mass.

Diagnostic Procedures/Surgery

Biopsy of limited utility

Pathological Findings

- Morphologically, renal sarcomas are similar to their extrarenal counterparts.
- In adults they can arise from both the parenchyma and capsule of the kidney.
- Wilms tumor:
  - Generally soft and friable with hemorrhage and necrosis
  - Classic: Coexistence of blastemal, epithelial, and stromal cells
  - Unfavorable histology is associated with extreme nuclear enlargement, hyperchromasia, and abnormal mitotic figures.

- Clear-cell carcinoma:
  - 3 defined components: Cord cells with mitotic figures, spindle-shaped septal cells, and a mucopolysaccharide intercellular matrix
- Leiomyosarcoma (most common):
  - Cell origin is smooth muscle of capsule or other perinephric structures.
  - Tend to displace rather than invade the parenchyma
- Leiomyosarcomas, fibrosarcomas, malignant fibrous histiocytomas, anaplastic sarcoma of the kidney are other histologic types.

DIFFERENTIAL DIAGNOSIS

- Children: Renal mass in childhood is Wilms tumor until proven otherwise:
  - Lymphoma
  - Lymphosarcoma
  - Neuroblastoma (actually adrenal origin)
  - Ossifying renal tumor of infancy
  - Renal cell carcinoma
  - Sarcomas (clear-cell sarcoma, rhabdomyosarcoma, others)
- Adult: Solid primary renal mass in adult is most likely to be a RCC; although, TCC or metastatic disease to the kidney are more likely considerations. The following types of sarcoma have been described. In general the management is the same:
  - Angiosarcoma
  - Chondrosarcoma
  - Clear-cell sarcoma
  - Ewing sarcoma/primitive neuroectodermal tumor
  - Fibrosarcoma
  - Kaposi sarcoma
  - Leiomyosarcoma (including the myxoid types)
  - Liposarcoma
  - Malignant fibrous histiocytoma
  - Malignant hemangiopericytoma
  - Malignant mesenchymoma
  - Malignant schwannoma
  - Osteogenic sarcoma
  - Rhabdomyosarcoma
  - Sarcomatoid renal cell carcinoma
  - Synovial sarcoma

– Wilms tumor

ALERT

Primary renal sarcoma is extremely rare. Primary retroperitoneal soft-tissue sarcoma (such as liposarcoma) with secondary renal invasion is the more common clinical presentation.

TREATMENT

- In adults, the lesions are usually approached as for RCC, as the lesion is rarely diagnosed preoperatively due to its rarity.
- Masses tend to be quite large, presumably due to rapid growth pattern.
- The primary treatment of renal sarcomas is surgical excision.

MEDICATION

- Dactinomycin and vincristine are used for more favorable stages of Wilms, with the addition of doxorubicin and abdominal radiation for more advanced stages.
- Doxorubicin for clear-cell sarcoma in children
- Doxorubicin, dacarbazine, and ifosfamide have been used with adult sarcomas; however, response rates at best are poor.

SURGERY/OTHER PROCEDURES

- Mainstay of treatment for all sarcomas is radical nephrectomy (some special cases partial nephrectomy).
- Wide excision is the preferred approach.
- 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 tumor to downstage prior to surgery, usually with external radiation therapy. In bilateral disease, nephron sparing is indicated.
- Sarcomas may require repeat surgical intervention for local recurrences.

ADDITIONAL TREATMENT

- Sometimes employed in management of Wilms tumor postop. Radiation of the tumor bed is indicated if the tumor extended beyond the renal capsule to involve adjacent organs or lymph nodes or with intraoperative tumor spillage.
- Adult sarcomas in adjuvant setting may reduce local recurrence.

ONGOING CARE

PROGNOSIS

- Adult sarcomas, especially high-grade, have a poor prognosis.

- Lower-grade sarcomas may exhibit a more indolent course.
- Pediatric patients with Wilms tumors can expect a >90% cure.
- Clear-cell sarcoma and especially rhabdoid tumors have a much worse prognosis overall.

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 RECOMMENDATIONS

Patient Monitoring

- Adults: Close follow-up for 2–5 yr:
  - Chest x-rays every 3–6 mo
  - Abdominal MRI or CT scanning every 3–6 mo
  - No specific tumor markers known for renal sarcomas
- Children: Same as adults. Try to limit studies such as CT due to long-term ionizing radiation risks.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Ossifying Renal Tumor of Infancy
- Renal Mass
- Wilms Tumor

CODES

ICD9

189.0 Renal sarcoma

ABBREVIATIONS

- BWS: Beckwith-Wiedemann syndrome
- CBC: Complete blood count
- CMP: Complete metabolic panel
- CT: Computed tomography
- GU: Genitourinary

- HIV: Human immunodeficiency virus
- HTN: Hypertension
- MRI: Magnetic resonance imaging
- RCC: Renal cell carcinoma
- TCC: Transitional cell carcinoma
- US: Ultrasound

RENAL TRAUMA, ADULT

Jamie C. Messer, MD

J. C. Trussel, MD

BASICS

DESCRIPTION

- Renal injuries can be caused by either blunt or penetrating trauma.
- Usually associated with other injuries
- Types of renal injuries in adults:
  - Contusions: 92%
  - Lacerations: 5%
  - Pedicle injuries: 2%
  - Ruptured/shattered kidneys: 1%

EPIDEMIOLOGY

- 10% of traumatic injuries involve the GU system; kidney most common
- 80% of renal injuries related to blunt trauma
- Often associated with multiple trauma
- 80–90% of renal injuries have another associated organ injury that may affect management.

RISK FACTORS

- Adult blunt trauma:
  - Degree of deceleration
  - Rapid deceleration
  - Higher grade (III to V) injury more likely to have complications
- Adult penetrating trauma:
  - Penetrating trauma to the upper abdomen increases risk of renal injury.
  - Factor in GSW is ballistics, weapon characteristics, and velocity

)[A]:

- Pediatric kidney relatively larger, less well protected, bones more mobile
- May be associated with congenital anomalies

GENERAL PREVENTION

General trauma preventative measures, such as restraints, etc.

PATHOPHYSIOLOGY

- Kidneys are generally protected in the retroperitoneum, surrounded by fat, substantial musculature, and the lower rib cage.
- For blunt trauma, significant forces are necessary to injury the kidney.

- Blunt trauma:
  - MVA, falls, athletic trauma, direct blows, and associated rib fractures may lead to renal injury
  - Deceleration is a large component of injury mechanism.
  - Deceleration may lead to intimal tearing of the renal artery, leading to thrombosis, then ischemia, or may avulse vessels completely.
- Penetrating trauma:
  - Contusion may occur in proximity of bullet path secondary to larger temporary cavity.
  - Stab wound degree of injury related to characteristics of weapon; 10% may not have hematuria

COMMONLY ASSOCIATED CONDITIONS

Injuries to other organ systems

DIAGNOSIS

HISTORY

- History is often limited, especially in the pediatric population
- Pediatric patient may have history of minimal trauma.
- Key elements:
  - Mechanism of injury; degree of deceleration
  - Blunt vs. penetrating trauma
  - Associated injuries; triage of severity of injuries and priorities for management
  - Associated fatalities
- Medical history (AMPLE trauma history): Allergies, Medications, Past Medical History, Last Meal, Event
- Contrast allergy, previous renal surgeries, stones, trauma, cancer

PHYSICAL EXAM

- Vitals signs:
  - Tachycardia and hypotension (SBP <90) in adults suggests major bleeding
- ABCDE exam:
  - Identify immediately life-threatening injuries
  - Renal injury is rarely immediately life-threatening with exception of shattered kidney and renal pedicle/vessel avulsion with significant hemorrhage.
- Secondary and tertiary survey:
  - Flank contusions/tenderness
  - Abdominal tenderness/distention

- Pelvic fractures
- Examine for blood at meatus, DRE

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urinalysis:
  - Hematuria >90% renal injuries
    Dipstick 98% sensitive and specific
    5 RBC per HPF significant
  - Hematuria absent in up to 36% renal vasculature injuries
  - Hematuria with hypotension positive predictor for major renal injury
- Basic labs: Hbg, HCT, Cr, electrolytes

Imaging

)[A]:

- Blunt trauma:
  Hypotension (SBP <90) and hematuria
  Gross hematuria
  Clinical indicators of renal injury from associated injury or mechanism
- Penetrating trauma:
  Any degree of hematuria
  Low threshold to image in penetrating trauma
- Pediatric:
  Any degree of hematuria
  Remember, higher risk of renal injury compared to adults

- US: Not usually useful in evaluation of acute trauma:
  - FAST is sonographic exam of the abdomen aimed at detecting the presence or absence of hemoperitoneum; used in some trauma centers but is not standard.
- CT: Best single study:
  - Contrast-enhanced is best
  - Useful to identify other organ injury; arterial/venous injuries
  - Delayed films to evaluate for urine leak, evaluate collecting system
  - Major injury suggested by medial hematoma, medial urine extravasation, lack of enhancement of renal parenchyma
- IV urography:
  - Largely replaced by CT scan
  - Exception is single-shot intraoperative IVP when preop imaging not available before abdominal exploration in the OR

– Single film 10 minutes after 2 mL/kg of IV contrast (max 150 mL)

– Can confirm function of contralateral kidney

– If film is not normal at 10 minutes, consider exploring kidney to stage and/or repair renal injury.

Diagnostic Procedures/Surgery

Angiography: Replaced largely by CT scanning but useful if embolization is being considered

DIFFERENTIAL DIAGNOSIS

Traumatic vs. spontaneous renal hemorrhage with conditions such as AML or renal cell carcinoma

ALERT

Degree of hematuria does not correlate with degree of injury in GU trauma.

TREATMENT

- General supportive care
- Staging: Determine the extent of renal injury:
  - 3 methods: Clinical, radiographic, and surgical
  - Low-risk patient may require only clinical staging.

)[A]:

Grade I: Microscopic or gross hematuria, normal radiographic studies, contusion/contained to subcapsular hematoma, no parenchymal laceration

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, avulsion of the renal hilum, devascularized kidney

)[A]:

– Blunt trauma:

A hemodynamically stable patient with well-staged renal injury may be managed nonoperatively.

98% of blunt renal injuries can be managed nonoperatively.

Grade IV and V injuries are more likely to require surgery.

Monitor with serial HCT and imaging

If bleeding persists, or delayed bleeding occurs, consider angiography and embolization as alternative to renal exploration.

– Penetrating trauma:

Well-staged select penetrating injuries can be managed nonoperatively.

55% of stab wounds and 24% of GSW can be managed nonoperatively.

If laparotomy is required for penetrating injury, surgically stage the patient

)[A]:

– Indications for operative management:

Absolute indications include persistent bleeding, expanding hematoma, pulsatile hematoma

Relative indications include urine extravasation, urinoma, nonviable parenchyma, delayed diagnosis or arterial injury, segmental arterial injury, incomplete staging

Urine extravasation can be managed nonoperatively with expectation of 87% resolution.

If nonviable tissue >20%, then complications greater; consider renal exploration

If unable to obtain a CT scan due to patient condition, perform single-shot IVP; if not normal renal exploration is indicated

– Isolated renal injuries:

Mostly managed nonoperatively, except major grade V pedicle avulsion injuries

Consider selective angioembolization, especially for segmental vessels.

If urine extravasation persists past 48 hr, consider placement of internal stent.

Bed rest is key; allow ambulation once gross hematuria has resolved.

– Renal exploration:

Transperitoneal approach best, allows identification of associated injuries

– Renal reconstruction:

Principles of renal reconstruction include debridement of nonviable tissue, hemostasis, closure of the collecting system, coverage of parenchymal defect.

If polar injury cannot be reconstructed consider partial nephrectomy, removal of all devitalized tissue.

– Renovascular injuries:

Prompt diagnosis by CT should lead to prompt renal exploration in attempt to salvage the kidney

Case reports of revascularization through use of endovascular stents

Diagnosis at >8 hr; kidney cannot typically be salvaged

Renal artery thrombosis revascularization may not be successful.

Segmental artery/vein injuries should be managed nonoperatively unless they affect >20% of parenchyma; then consider renal exploration.

Main renal vein may be repaired, may require occlusion of the vein and renal artery

– Indications for nephrectomy:

Nephrectomy indicated with normal contralateral kidney when renal injury is extensive and patient condition is not suitable to prolonged reconstruction.

– Damage control: Pack the kidney and plan re-exploration in 24–48 hr when patient stable.

SURGERY/OTHER PROCEDURES

See above for operative management

ONGOING CARE

PROGNOSIS

- Only 2–3% of blunt trauma requires surgical intervention.
- Prognosis for most renal injuries is excellent.

COMPLICATIONS

- Persistent urine extravasation, urinoma; can lead to perirenal infection and renal loss:
  - Internal stent may correct the problem.
- Delayed bleeding may occur up to 21 days; manage with bed rest:
  - Manage as per initial protocol for nonoperative management
- Perinephric abscess may be percutaneously drained.
- Hydronephrosis may occur; consider repeat imaging.
- HTN may be noted secondary to renal vessel injury, compression of kidney, posttraumatic AV fistula; fistula may resolve spontaneously, otherwise embolize.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Ambulate when urine clears; bed rest if hematuria recurs.
- Obtain follow-up imaging based on clinical course; consider repeat CT scan to verify resolution and absence of other abnormality.
- Serial HCT

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See Also (Topic, Algorithm, Electronic Media Element)

- Renal Trauma, Algorithm
- Renal Trauma, Pediatric
- Ureter, Trauma

CODES

ICD9

- 866.00 Unspecified injury to kidney without mention of open wound into cavity
- 866.01 Hematoma of kidney, without rupture of capsule, without mention of open wound into cavity
- 866.02 Laceration of kidney without mention of open wound into cavity

ABBREVIATIONS

- ABCDE: Airway, breathing, circulation, disability, exposure
- AV: Arteriovenous
- CT: Computed tomography
- DRE: Digital rectal exam
- FAST: Focused abdominal sonogram in trauma
- GSW: Gunshot wound
- GU: Genitourinary
- HCT: Hematocrit
- HPF: High-power field
- HTN: Hypertension
- IVP: Intravenous pyelogram
- MVA: Motor vehicle accident
- RBC: Red blood cell
- SBP: Systolic blood pressure
- US: Ultrasound

RENAL TRAUMA, PEDIATRIC

Tavis Shaw, MD

Pasquale Casale, MD

BASICS

DESCRIPTION

- Traumatic injury overall is the leading cause of childhood death in the US.
- Pediatric renal trauma is subdivided into blunt and penetrating mechanisms of injury.
- The pediatric kidney is believed to be more susceptible to trauma vs. an adult kidney.
- Over the past 2 decades, the management of pediatric renal trauma has shifted from operative intervention to conservative management.

EPIDEMIOLOGY

- 10–20% of all abdominal blunt trauma involves a renal injury.
- 90% 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.

RISK FACTORS

- Preexisting GU abnormalities (ie, ureteropelvic junction obstruction and horseshoe kidney):
  - 3–5-fold 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:
  - More pliable thoracic cage and weaker abdominal muscles
  - Less renal fat lower
  - Lie of the kidney within the abdomen

Genetics

Disorders that lead to an increase in GU anomalies have a greater risk for traumatic injury

GENERAL PREVENTION

Measures that decrease traumatic injury in general, such as seatbelts

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

COMMONLY ASSOCIATED CONDITIONS

Injury to other organ systems

DIAGNOSIS

HISTORY

- Mechanism of injury: Degree of actual traumatic injury may not correlate with the mechanism:
  - Blunt: Falls, automobile collision, sporting injuries, etc.
  - Penetrating: Gunshot wound, stabbing, etc.
- Vitals signs in the field:
  - Hypotension: Children will often have a normal BP despite a significant blood loss.
- Loss of consciousness
- Hematuria: Unlike adults, an unreliable indicator of underlying renal injury in children:
  - Up to 70% of children with grade II or higher renal injury may have neither gross nor microscopic hematuria.
- Medical history: Any acute or chronic medical conditions and any previous GU abnormality
- Surgical history: Previous urologic procedure for reflux, stone, hypospadias, etc.
- Iodine or latex allergy

PHYSICAL EXAM

- Vitals signs and ABCDE
- BP is often normal in severely hypovolemic children
- Exposure: Observe for obvious signs of abdominal/flank/thoracic trauma, abdominal/flank tenderness, flank ecchymosis, gross hematuria, pelvic instability
- DRE: Observe for perineal ecchymosis
- If blood at the urethral meatus do not insert Foley

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC, BMP, coagulation profile
- Urinalysis:

– Unreliable in determining the extent of GU trauma

– Up to 70% of children with grade II renal trauma will have neither gross or microscopic hematuria.

ALERT

The patient's hemodynamic status determines when and what type of imaging modality is indicated.

Imaging

- Indications for radiographic imaging: All penetrating abdominal trauma or blunt trauma victims with 1 of the following criteria:
  - Significant deceleration or high-velocity injury: MVA, fall from 15 feet
  - Trauma resulting in fracture of the thoracic cage, spine, pelvis, or femur, or bruising of the torso/perineum
  - Acute peritonitis
  - Gross hematuria
  - Microscopic hematuria (>50 RBC/HPF) associated with shock (SBP <90 mm Hg)
  - Delayed hemorrhage following renal trauma
- CT:
  - Triphasic abdominal and pelvic CT: Clinically stable patients; most sensitive method for diagnosing and classifying GU trauma; precontrast phase, nephrogram phase after injection of contrast, and delayed images at 15 min
  - Single-phase CT: Clinically labile patients; allows for determination of renal perfusion and major renal fractures
  - Delayed CT: Obtained postoperatively after patient is stabilized or after patient is resuscitated in the ICU for full trauma evaluation; also used to assess grade 3–5 renal injuries 2–3 days posttrauma to assess for baseline hematoma or urinoma.
- FAST:
  - Often combined with serial physical examinations as a screening modality after blunt trauma
  - Sensitivity ranges from 70–85% and specificity ranges from 93–100%; operator dependent
  - Option in areas with limited radiologic resources
- Arteriography:
  - Used for diagnosis of arteriovenous fistula in the setting of delayed hemorrhage following renal trauma
- Retrograde pyelography:

– Rule out presence of partial/total ureteral disruption

– Management of symptomatic urinoma

• Single-shot IVP:

– 2 mL/kg IV bolus given after patient is hemodynamically stable following trauma-exploratory laparotomy; allows for visualization of functioning contralateral kidney when considering unilateral nephrectomy

• Nuclear medicine:

– DMSA scan: Allows for quantification of renal function for grade 3–5 injuries; obtain at least 1 wk after traumatic injury, also indicated for posttraumatic HTN

• Follow-up imaging:

– Triphasic CT is indicated for patients with persistent fever, worsening flank pain, or gross hematuria >72 hr after injury.

DIFFERENTIAL DIAGNOSIS

Injury to other major abdominal viscera in the setting of acute trauma

TREATMENT

• The major conundrum facing the urologist in evaluating pediatric renal trauma is in determining when to surgically intervene.

• The decision to intervene operatively is based on 3 clinical indicators: Hemodynamic stability, accurate radiographic staging, presence of associated organ injuries

• 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 renorrhaphy 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 enteric tract by omentum or other tissue, and adequate drains are left in place.

ADDITIONAL TREATMENT

• Nonoperative management:

– Initially reserved for hemodynamically stable patients

– Admission to ICU for monitoring is warranted:

Bed rest, monitor urine output, serial abdominal exams, serial hemoglobin/HCT, resuscitate and transfuse as necessary

Broad-spectrum antibiotics for penetrating injury and blunt trauma with urinary extravasation or large retroperitoneal hematoma

– Ideal candidate will have grade I–II injury

– Patients with isolated grade III, IV, and V renal injuries are candidates for nonoperative treatment:

Angiographic, endoscopic, or percutaneous intervention will be required in up to 55% of patients.

Conservative management of isolated grade III–IV renal injuries will prevent 95% of patients from requiring operative intervention.

– Repeat CT of the kidney 2–3 days after trauma for grade III or higher renal injuries.

– Have low threshold for repeat CT if patient has decreasing hemoglobin/HCT despite blood transfusion or if child is hemodynamically unstable.

– Ambulation should resume when gross hematuria resolves.

– Strenuous physical activity should be avoided for 6 wk.

• Operative management:

– Absolute indications for renal exploration:

Hemodynamic instability from a renal source

Expanding or pulsatile retroperitoneal hematoma

Inability to stop persistent or delayed hemorrhage via selective vascular embolization

– Relative indications for renal exploration:

Patients with vascular instability resulting in an inability to obtain adequate preoperative radiographic studies

Retroperitoneal hematoma found at the time if surgical exploration

Known grade III or higher renal injury during concomitant abdominal exploration: Either perform renal exploration with renorrhaphy or separation of GI from GU tract and drain placement.

– Renal salvage via renorrhaphy or partial nephrectomy requires complete exposure of the injured kidney, debridement of nonviable tissue, repair of the collecting system, and ligation of all bleeding vessels.

– Renal pelvic or ureteral injuries should be closed water tight; if not, then ureteral stents or nephrostomy tube may be necessary.

– Nephrectomy should be considered in the setting of irreparable grade IV–V injures and in cases where nephrectomy would help control bleeding in the coagulopathic or hypothermic patient.

– Renal vascular injuries: The kidney is an end organ; segmental renal vessel repair should not be attempted, main renal artery reconstruction should only be considered if patients are hemodynamically stable and have either a solitary kidney or bilateral renal injuries.

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.
- ESRD:
  - Bilateral renal injury
  - May require peritoneal or hemodialysis

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ABBREVIATIONS

- ABCDE: Airway, breathing, circulation, disability, exposure
- BMP: Basic metabolic profile
- BP: Blood pressure
- CBC: Complete blood count
- CT: Computed tomography
- DMSA: Dimercaptosuccinic acid

- DRE: Digital rectal exam
- ESRD: End-stage renal disease
- FAST: Focused assessment with sonography for trauma
- GI: Gastrointestinal
- GU: Genitourinary
- HCT: Hematocrit
- HPF: High-power field
- HTN: Hypertension
- ICU: Intensive care unit
- IVP: Intravenous pyelogram
- MVA: Motor vehicle accident
- RBC: Red blood cell
- SBP: Systolic blood pressure

RENAL TUBULAR ACIDOSIS

Gaurav Bandi, MD

BASICS

DESCRIPTION

- RTA is a metabolic condition characterized by abnormal urinary acidification due to a defect in renal tubules, resulting in hyperchloremic nonanion gap metabolic acidosis, increased pH of the urine
- 4 major types of RTA:
  - 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

- RTA I: More common in adults (2/3 adults, 1/3 children) and women; endemic in certain regions of Thailand
- RTA II: Usually more predominant in males associated with Fanconi syndrome; urinary loss of glucose, amino acids, uric acid, phosphate, and bicarbonates
- Most RTAs are sporadic occurring at any age. Familial RTA are rare and usually occurs in childhood

RISK FACTORS

- Genetic
- Secondary to systemic disease. See “Commonly Associated Conditions.”

Genetics

- Familial RTA I:
  - AD form is associated with mutation is anion exchanger 1 gene
  - AR form is due to a mutation in the B1 or a4 subunit of H+-ATPase gene and associated with sensorineural deafness
- Familial RTA II:
  - AD form is rare
  - AR form associated with ocular abnormalities and mental retardation
  - AR form associated with osteopetrosis and cerebral calcification
  - AR form associated with Fanconi syndrome
- Familial RTA IV: Associated with pseudohypoaldosteronism type 1

PATHOPHYSIOLOGY

- Type I (distal) tubular acidosis: Secondary to impaired ability to secrete hydrogen ions into the distal tubule or collecting duct. Urine pH >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

COMMONLY ASSOCIATED CONDITIONS

- Acquired RTA type I:
  - Autoimmune disease: SLE, Sjögren syndrome, primary biliary cirrhosis, chronic active hepatitis
  - Chronic pyelonephritis
  - Diseases causing nephrocalcinosis
  - Drugs (amphotericin B, lithium, analgesics)
  - Ehlers-Danlos syndrome
  - Fabry disease
  - Glycogenosis type III
  - Hepatic cirrhosis
  - Hypercalcuria
  - Hypergammaglobulinemic syndrome
  - Leprosy
  - Malnutrition
  - Medullary cystic disease
  - Obstructive uropathy
  - Sickle cell disease, hereditary elliptocytosis
  - Toxins (toluene, glue)
  - Vitamin D intoxication
  - Wilson disease
- Acquired RTA type II:
  - Fanconi syndrome due to toxin-related or immunological nephrotoxic damage
  - Tubular toxicity causing acute tubular necrosis:
    Sepsis
    Rhabdomyolysis
    Hypotension
    Nephrotoxins: IV contrast, aminoglycoside antibiotics
  - Interstitial renal disease:
    Multiple myeloma
    Heavy metal poisoning (cadmium, lead, mercury)

Medications (methicillin, cisplatin, adefovir, tenofovir, COX-2 inhibitors, cimetidine, acetazolamide, sulfanilamide, ifosfamide, tetracycline, Topamax)

Infections: Leptospirosis, cornybacterium, diphtherial, polyoma virus, cytomegalovirus

Autoimmune disease: SLE, Sjögren's syndrome, sarcoidosis

- Amyloidosis

- Acquired RTA type IV:
  - Acute adrenal insufficiency
  - Addison disease
  - Diabetic nephropathy
  - Hypertension
  - Lupus nephropathy
  - Obstructive nephropathy
  - Tubulointerstitial nephropathies
- Gordon syndrome
- Sickle cell 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, UTIs, passage of stones in urine
- History of recurrent, familial, or childhood renal stone disease
- Ask about systemic diseases causing RTA

PHYSICAL EXAM

- Urologic examination of genitalia, suprapubic area for swelling and tenderness
- Examination for osteomalacia, hypokalemic muscle weakness, and growth retardation
- Examination for other systemic diseases

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Renal function test usually normal
- Electrolytes and blood gas reveal hyperchloremic, nonanion gap metabolic acidosis:
  - Hypokalemia or normokalemia in type I and II

- Hyperkalemia in type IV

- Urine pH (fasting, under oil, pH meter):
  - pH >5.5: Complete type I RTA

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  - Urine calcium: High in type I, normal in type II
  - Phosphaturia, glycosuria and aminoaciduria in Fanconi's syndrome

Imaging

Plain x-ray and CT urogram: For nephrocalcinosis and nephrolithiasis

Pathological Findings

- Nephrocalcinosis
- Nephrolithiasis
- Osteomalacia

DIFFERENTIAL DIAGNOSIS

)(C)

- Calcium phosphate stones
- Recurrent stones: >2/yr
- Bilateral stones
- Medullary nephrocalcinosis
- Medullary sponge kidney
- Hypocitraturia <0.5 mmol/24 hr
- Hypokalemia
- Chronic pyelonephritis
- Azotemia

TREATMENT

- 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

- Alkali therapy decreases stone formation and growth, prevents nephrocalcinosis, normalizes growth retardation in children, and corrects hypokalemia in most cases:

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Sodium bicarbonate (7.7 mEq HCO3/tab)

Bicitra (1 mEq Na, 1 mEq citrate/mL)

Polycitra (1 mEq Na, 1 mEq K, 2 mEq citrate/mL)

– Type I RTA generally requires lifelong treatment:

)(C)

May require potassium supplementation for hypokalemia

- Type II (proximal) RTA:
  - 5–20 mEq/kg/d in 4–6 doses/d due to the severe bicarbonate wasting.
  - Adults with bicarbonate levels >10 mEq/mL and no evidence of bone disease may not require treatment.
  - Supplemental potassium, calcium, vitamin D, and phosphate may become necessary.
- Type IV RTA treatment is directed toward correction of hyperkalemia rather than acidosis:
  - Dietary potassium restriction
  - Thiazide or loop diuretics
  - Mineralocorticoid replacement in cases of adrenal disease or hyporeninemia (fludrocortisone 0.1 mg/d)

SURGERY/OTHER PROCEDURES

- Management of stone by shock wave lithotripsy, ureteroscopy, percutaneous nephrolithotomy, and rarely, open surgery
- Management of obstructive uropathy

ONGOING CARE

PROGNOSIS

- Primary RTA I: Although a permanent disease, prognosis is excellent if diagnosis and treatment initiated early.
- Prognosis of other RTAs depends on associated disease

COMPLICATIONS

- Hypercalcuria
- Hyperkalemia or hypokalemia
- Nephrocalcinosis
- Nephrolithiasis
- Osteomalacia

Pediatric Considerations

Failure to thrive and rickets (in children)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Spot urine testing for NAG (N-acetyl--D-glucosaminidase) has eliminated the need for 24-hr urine collection. Levels increased secondary to renal tubular cell damage and hypercal-

ciuria

- Urinary calcium excretion should be kept <0.05 mmol/kg/d in infants and children
- Potassium levels should be monitored during alkali therapy and replaced appropriately
- Monitor underlying disease as indicated

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See Also (Topic, Algorithm, Electronic Media Element)

- Calcinosis, Renal
- Fanconi Syndrome
- Nephrocalcinosis
- Nephropathy, Obstructive

CODES

ICD9

588.89 Other specified disorders resulting from impaired renal function

ABBREVIATIONS

- AD: Autosomal dominant
- AR: Autosomal recessive
- CT: Computed tomography
- IV: Intravenous
- NAG: N-acetyl-0-D-glucosaminidase
- RTA: Renal tubular acidosis
- SLE: Systemic lupus erythematosus
- UTI: Urinary tract infection

RENAL VEIN THROMBOSIS

Costas D. Lallas, MD

BASICS

DESCRIPTION

- RVT is an acute or chronic blood clot in one or both renal veins or tributaries. May extend into the vena cava
- In infants, RVT presents as a severe illness typically, occasional colicky pain:
  - 60% enlarged kidneys on physical examination; gross hematuria and microangiopathic hemolytic anemia and thrombocytopenia
- In the adult, RVT presentation depends on onset of RVT:
  - Acute RVT: Sudden flank pain, costovertebral angle tenderness, and gross hematuria—classic triad—only present in minority of cases.
  - Chronic RVT: Generally asymptomatic; proteinuria and microscopic or gross hematuria.

EPIDEMIOLOGY

- Newborns and infants: Commonly associated with asphyxia, dehydration, shock and sepsis; usually acute and unilateral (more common on left side); although 30% bilateral:
  - Male-to-female ratio: 2:1 in the neonate, with no sex predilection beyond age 1
- Adults: Associated with nephrotic syndrome, renal carcinoma, oral contraceptives, steroids, or renal transplantation; usually chronic and unilateral

RISK FACTORS

- Infants:
  - Acute hypoxia, birth trauma
  - Cyanotic congenital heart disease with resultant polycythemia
  - Cytomegalovirus
  - Dehydration: Diarrhea, vomiting, and shock
  - Maternal diabetes, polyhydramnios, and toxemia
  - Performance of angiocardiography
  - Preterm (<36 wk) infants at risk
  - Sickle cell disease
- Adults:
  - Abdominal tumors, especially renal cell carcinoma
  - Endothelial damage
  - Hypercoagulable state
  - Intrinsic hypercoagulability (eg, Factor V Leiden deficiency)

– Nephrotic syndrome:

Membranous nephropathy: Lesion most frequently associated with nephrotic syndrome–related RVT

Other causes reported: Membranoproliferative glomerulonephritis, minimal change disease, rapidly progressive glomerulonephritis, amyloid, focal sclerosis, or lupus nephritis

– Oral contraceptives, steroids

– Renal transplantation, particularly in patients receiving treatment with OKT-3 and cyclosporine

– Shock, sepsis, dehydration

– Stasis

– Trauma

– Use of IV contrast agents

– Vasculitis

GENERAL PREVENTION

Adults: Long-term anticoagulation seems appropriate, only if RVT has recurred when patients discontinued anticoagulation

PATHOPHYSIOLOGY

• Newborn: Diminished intrarenal blood flow due to hypovolemia (sepsis, dehydration, diarrhea):

– Initiates thrombosis of the intrarenal venous radicles. Both antegrade and retrograde spread results in RVT.

– May become bilateral, produce vena caval occlusion and renal artery thrombosis

– 65% in neonates, 30% beyond 1 yr of age

– Associated with adrenal hemorrhage in 15% of cases

• Adults: Most often unilateral; acute and chronic forms described:

– Acute RVT: Severe hydration, sudden hypercoagulability, renal vein obstruction from tumor or transplant rejection

– Chronic RVT: Nephrotic syndrome (most often membranous glomerulonephritis):

Nephrotic syndrome: >3 g/d urinary protein loss, hypoalbuminemia, hypercholesterolemia, edema

RVT is a result of nephrotic syndrome and not the cause

Slow onset allows the development of collateral venous kidney drainage; therefore, symptoms are rare.

Nephrotic syndrome: Alterations in coagulation system that favors thrombosis

RVT in the nephrotic syndrome: 5– 62%

RVT highest in nephrotic syndrome due to membranous nephropathy; however, membrano-proliferative glomerulonephritis, lipoid nephrosis, and amyloidosis have also been associated with high rates of RVT.

COMMONLY ASSOCIATED CONDITIONS

- DVT in patients with nephrotic syndrome
- Pulmonary embolus

DIAGNOSIS

HISTORY

- Infant:
  - Risk factors: Mother's history, birth, and early postnatal course
  - Gross hematuria
- Adult:
  - Risk factors should be explored.
  - Sudden onset of hematuria and flank pain should raise the question of renal vein thrombosis, as should a history of nephrotic syndrome in the presence of hematuria

PHYSICAL EXAM

- Infant:
  - Unilateral, or often bilateral, flank masses. Evidence of dehydration and cyanotic heart disease
- Adult:
  - Evidence of blunt trauma, abdominal mass
  - Edema or anasarca suggestive of nephrotic syndrome.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Infants:
  - Thrombocytopenia, leukocytosis, hemolytic anemia
  - Consumptive coagulopathy (prolonged clotting time, elevated fibrinogen and fibrin split products)
  - Proteinuria
  - Elevated BUN and creatinine
- Adult:
  - Proteinuria and microscopic hematuria
  - Hemolytic anemia, consumptive coagulopathy, and thrombocytopenia may be present.

– Elevated BUN and creatinine; hypoalbuminemia

– Marked elevation in LDH with normal transaminases

Imaging

- Infant:

– Ultrasonography: Enlarged and echogenic kidneys (90%) with attenuation or loss of corticomedullary differentiation. Calcification and thrombus may be seen extending outside the kidneys to the inferior vena cava.

– Doppler studies may detect resistance or absence of flow in renal venous branches or collateral branches. Also, increased resistance in the renal artery may be present.

– IVP (if performed): Delayed opacification and renomegaly

– A renal scan may be obtained to assess the function of the involved kidney.

– The extent of thrombus may be assessed by duplex ultrasonography, and only rarely will CT, MRI, or renal venography be required for confirmation of the diagnosis or determination of the extent of thrombus.

- Adult:

– IVP: Faint or absent excretion of contrast and congested, enlarged kidney due to congestion:

Collateral circulation causes the collecting system opacification to varying degrees

The renal pelvis is usually stretched, distorted, and blurred, occasionally leading to confusion with polycystic disease

Notching of the ureter due to collateral circulation

Complete nonfunction may require retrograde pyelography that demonstrates a compressed, stretched, and distorted collecting system

– Inferior vena cavography with selective catheterization of the renal vein is the gold standard for the diagnosis.

– Doppler ultrasonography is helpful, especially in the transplanted kidney.

– MRI: Excellent imaging; avoids iodinated contrast, but concerns over use of gadolinium in patients with renal insufficiency

– CT findings are similar in noninvasive evaluation of acute RVT.

Sensitivity of CT angiography approaches 100%; considered current imaging modality of choice

Object of low attenuation within the renal vein and/or inferior vena cava and proximal venous enlargement

Capsular venous collaterals, thickened Gerota’s fascia and pericapsular stranding

Diagnostic Procedures/Surgery

Renal biopsy in the setting of nephrotic syndrome and RVT; may guide therapy and confirm etiology

Pathological Findings

- Membranous nephropathy is the most common finding in the setting of nephrotic syndrome and RVT.
- In infants the condition is pathologically more correctly described as “renal venous thrombosis” as the interlobular and arcuate renal veins are primarily affected rather than the main renal vein in adults.

DIFFERENTIAL DIAGNOSIS

- Other cause of acute renal colic (urolithiasis, etc.)
- Renal infarction
- Renal cell carcinoma with direct compression or tumor thrombus
- Renal vein leiomyosarcoma (filling defect)

TREATMENT

- Evaluate and treat all underlying causes.
- Aggressive rehydration and treatment of sepsis, diarrhea, and electrolyte abnormalities

MEDICATION

- Infants:
  - Thrombolytic agents (urokinase/streptokinase) reported but controversial
  - Systemic heparinization: Prevents thrombus propagation into inferior vena cava (risk of propagation low with fluid and electrolyte repletion). Also used in neonates with bilateral involvement.
  - The use of heparin is controversial, as it has been shown to preserve renal function and has not been demonstrated to prevent loss of renal function.
- Adults:
  - Unilateral RVT: Heparin anticoagulation and long-term anticoagulation with warfarin:

The optimum duration of anticoagulation therapy is unknown; many believe that anticoagulation should be continued until the chronic state of dehydration is reversed (as evidenced by maintenance of serum albumin levels >2.5 g/L) or until resolution of nephrotic syndrome.

  - Asymptomatic patients with unilateral RVT may be treated expectantly with supportive measures.
  - Acute clot dissolution (streptokinase/urokinase), systemically or with selective renal vein infusion, may be useful, especially in RVT of a renal transplant, bilateral RVT, or uni-

lateral RVT in a solitary kidney.

– Long-term antihypertensive treatment may be required

– Steroid or immunosuppressive use may be indicated in cases of systemic disease.

SURGERY/OTHER PROCEDURES

- Infants: No role for surgical thrombectomy
- Adults:

– Rarely used, because neither renal preservation nor improved survival documented

– Surgical thrombectomy (either open or percutaneous) in patients with acute bilateral RVT who are not expected to survive, especially if pulmonary emboli occur despite anticoagulation therapy; can also be combined with thrombolytic agents in select patients.

– Nephrectomy in highly selected patients for life-saving measures.

– Thrombectomy postop posttransplant RVT

– Radical nephrectomy and thrombectomy in renal cell carcinoma

ADDITIONAL TREATMENT

- Infants with acute renal failure: Peritoneal dialysis as necessary
- IVC filters are indicated in high-risk adult patients for pulmonary embolism. Need to be placed in suprarenal vein position.

ONGOING CARE

PROGNOSIS

- Neonates: Mortality rate of 3%
- The kidney may recover completely, atrophy to a small scarred kidney, or recover partially, resulting in renovascular hypertension or chronic tubular dysfunction.
- Nephrectomy may be required if renovascular hypertension or chronic infection develops.
- ACE inhibitors and/or angiotensin II receptor blockers may decrease proteinuria from nephrotic syndrome as decreased urinary protein loss decreases hypercoagulability. Treat hypercholesterolemia.

COMPLICATIONS

- Consumptive coagulopathy, pulmonary embolism
- In the transplant patient, loss of graft

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Infants:

– Renal function may be followed, using nuclear scanning. Often scarring atrophy is detected long term. About 5% of affected neonates progress to dialysis or transplantation.

– Monitor blood pressure, as renovascular hypertension may occur after RVT, even with normal renal function. Occurs ~20% of the time.

- Adults:
  – Treat nephrotic syndrome.
  – Because RVT may be asymptomatic, all patients with nephrotic syndrome should be monitored for the development of RVT-related hypertension and hematuria.
  – Long-term anticoagulation as a preventative in nephrotic syndrome not supported

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See Also (Topic, Algorithm, Electronic Media Element)

Nephrotic Syndrome

CODES

ICD9

453.3 Embolism and thrombosis of renal vein

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- BUN: Blood urea nitrogen
- CT: Computed tomography
- DVT: Deep vein thrombosis
- IV: Intravenous
- IVP: Intravenous pressure
- LDH: Lactate dehydrogenase
- MRI: Magnetic resonance imaging
- RVT: Renal vein thrombosis

RETROGRADE EJACULATION

Hector Pimentel, MD

Craig S. Niederberger, MD

BASICS

DESCRIPTION

- Absent or low-volume ejaculate caused by the expulsion of semen into the bladder
- Ejaculatory dysfunction should be suspected in any male with no ejaculate or a volume of ejaculate <1 mL.
- Differentiate from anejaculation, defined as absence of antegrade semen production despite achievement of orgasm

EPIDEMIOLOGY

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RISK FACTORS

- Bladder neck procedures (TURP, TUIP)
- Neuropathic disorders:
  - Diabetes
  - Multiple sclerosis
  - Pelvic surgery (abdominal-perineal resection, etc.)
  - Retroperitoneal surgery
  - SCI including spinal disk surgery
- Medications:
  - -Blockers: Reduce muscle tone in prostate/bladder neck and slightly reduce seminal emission
  - Alfuzosin: Possibly less risk than others
  - Doxazosin
  - Silodosin
  - Tamsulosin
  - Terazosin
  - Psychotropic medications
  - Antidepressants such as SSRIs (up to 62% experience RE)
  - Antipsychotics (eg, risperidone)

GENERAL PREVENTION

- Avoidance of retroperitoneal surgery, bladder neck surgery, and antiadrenergic medications

- Nerve-sparing retroperitoneal lymphadenectomy (ie, template, others)

PATHOPHYSIOLOGY

- Normal male ejaculation is stimulated by the sympathetic nervous system:
  - The effector nerves that cause seminal emission and bladder neck closure are sympathetic fibers arising from T10–L2, travelling through the sympathetic ganglia, hypogastric plexus, and peripheral pelvic nerves.
  - Seminal emission and bladder neck closure are both controlled by -adrenergic neurons.
  - Contraction of the epididymis, vas deferens, seminal vesicles, and prostate causes seminal fluid to enter the urethra.
  - Bladder neck closure occurs simultaneously with the deposition of the seminal fluid in the posterior urethra.
  - Seminal fluid emission is followed by relaxation of the external sphincter and rhythmic contractions of the bulbocavernosus and ischiocavernosus muscles, leading to ejaculation.
- With RE, all components are in place, but tight closure of the bladder neck does not occur.
- Abnormal closure of the bladder neck is the main mechanism for RE:
  - Failure to fully coapt the bladder neck causes the sperm to follow the path of least resistance and enter the bladder rather than pass antegrade through the urethra.
  - Caused by neural disruption (SCI, diabetes, RPLND) or iatrogenic (medications, prostate surgery such as TURP).
  - Sexual dysfunction (ED, delayed ejaculation, and decreased libido) may be the leading cause of discontinuation of antidepressants.
  - V-Y plasty was a procedure performed in the past for boys with recurrent UTIs that has been abandoned but may be a cause of RE.
- Note that most cases of failure to ejaculate in the man with SCI and in patients who have undergone retroperitoneal lymphadenectomy is actually failure of emission and not retrograde ejaculation.
- Abnormal peristaltic function of the vas deferens may contribute.
- Androgen deficiency may also result in lack of emission by decreasing the amount of prostate and seminal vesicle secretions.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- Multiple sclerosis

- SCI and/or herniated disk
- Testicular cancer
- Rectal cancer

DIAGNOSIS

HISTORY

- Sexual history: Important to differentiate a low-volume or absent ejaculate from ED, anorgasmia, or an improper semen analysis collection.
- Patients may complain about cloudy urine after sexual activity.
- Medical history: Ask about antiadrenergic drugs, diabetes, neurologic, or spinal cord disorders.
- Surgical history: Retroperitoneal, bladder neck, or back/spinal surgery.

PHYSICAL EXAM

- Patients with RE typically have a normal GU exam.
- Absent vas, small testis, or seminal vesicle dilation suggest other cause for low-volume ejaculate.
- Muscle weakness or impaired sensation suggests a neurologic disorder as the cause of RE.

ALERT

Ensure that patient is collecting semen analysis specimen correctly. Verify that at least 2 semen analyses have shown low-volume ejaculate <1.5 mL.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Routine laboratory testing is of limited utility.
- A routine urine analysis that demonstrated high sperm concentration after ejaculation is suggestive. Note that some sperm may be seen in the urine after routine normal ejaculation.

Diagnostic Procedures/Surgery

- Postejaculatory urine is sufficient for diagnosis of RE.
- In patients with low-volume ejaculation, the postejaculatory urine specimen should be compared to original semen analysis:
  - After a period of abstinence (24–48 hr), ask patient to empty bladder.
  - Ejaculate and capture fluid in a container; label container as “Ejaculate.”
  - Void immediately after and capture all fluid; label as postejaculation urine

Pathological Findings

Normal semen parameters:

- Volume: >2 mL or more
- pH: >7.2 or more
- Sperm concentration: >20 × 106 or more spermatozoa/mL
- Total sperm number: 40 × 106 or more spermatozoa per ejaculate
- Motility: >50% with grade a + b motility or >25% or more with grade a motility
- Morphology: >15% by strict criteria
- Viability: >75% sperm viable
- WBCs: <1 million/mL

DIFFERENTIAL DIAGNOSIS

- Absence of vas deferens
- Anejaculation
- Anorgasmia
- Ejaculatory duct obstruction
- Improper semen analysis collection technique

TREATMENT

- Treatment is initiated for patients who are interested in their fertility status.
- Medical treatment is most successful for patients without bladder neck injury.
- Stop potentially offending medications if possible.
- Medical therapy is given 7 days before the 1st planned ejaculation.

MEDICATION

First Line

- Pseudoephedrine 60 mg q.i.d.
- Ephedrine 25 mg q.i.d.
- Imipramine 25 mg b.i.d.
- Phenylpropanolamine 75 mg b.i.d.

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Second Line

Patients with failure of medical therapy require urine sperm retrieval in conjunction with assisted reproductive techniques:

- Prior to urine sperm retrieval, the urine is alkalinized to a pH of 7.0:
  - Sodium bicarbonate 650 mg q.i.d. OR
  - 1–3 tsps of baking soda 12–48 hr before ejaculation
- Urine sperm retrieval is then achieved by bladder catheterization or spontaneous voiding.
- Assisted reproductive technologies include intrauterine insemination, in vitro fertilization, or intracytoplasmic sperm injection

SURGERY/OTHER PROCEDURES

Young-Dees and similar operations are no longer used because of their invasive nature and the success of other techniques.

ONGOING CARE

PROGNOSIS

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COMPLICATIONS

- The main problem related to RE is infertility.
- Medical treatment with sympathomimetics is associated with palpitations and headaches:
  - Imipramine can be associated with dizziness and nausea.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Periodic semen analysis is used after a few weeks on medical therapy to evaluate efficacy.

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See Also (Topic, Algorithm, Electronic Media Element)

- Anorgasmia/Dysorgasmia
- Ejaculatory Disturbances (Delayed, Decreased, or Absent)
- Infertility, Urologic Considerations
- Semen Analysis, Abnormal Findings and Terminology
- Seman Analysis, Technical and Normal Value

CODES

ICD9

608.87 Retrograde ejaculation

ABBREVIATIONS

- ED: Erectile dysfunction
- GU: Genitourinary
- RE: Retrograde ejaculation
- RPLND: Retroperitoneal lymph node dissection
- SCI: Spinal cord injury
- SSRI: Selective serotonin reuptake inhibitor
- TUIP: Transurethral incision of prostate
- TURP: Transurethral resection of prostate
- UTI: Urinary tract infection

RETROPERITONEAL ABSCESS

Alexander Kutikov, MD
Robert G. Uzzo, MD

BASICS

DESCRIPTION

- An infectious process found in 1 of 4 retroperitoneal compartments:
  - Anterior retroperitoneum:
    Esophagus, duodenum, pancreas, bile duct, portal and splenic veins, appendix, ascending/descending colon, rectosigmoid
  - Posterior retroperitoneum (aka, perinephric/perirenal):
    Kidneys, ureters, gonadal vessels, aorta, inferior vena cava, lymphatics
    See “Renal and Perirenal Abscess”
  - Retrofascial:
    Iliopsoas, 12th rib, spine, paraspinous musculature
  - Pelvic:
    Prevesical, retrovesical, presacral, and perirectal spaces
- Most common type is perinephric abscess and is from renal source

EPIDEMIOLOGY

Reported highest in 3rd–6th decades

RISK FACTORS

- Diabetes
- Diverticulitis
- Existing osteomyelitis or epidural infection
- GU tract obstruction
- Immunosuppression
- Inflammatory bowel disease (Crohn disease)
- Malignancy
- Osteomyelitis
- Pyelonephritis
- Recent instrumentation or surgery of GU or GI tract
- TB

GENERAL PREVENTION

Perioperative antibiotic prophylaxis

PATHOPHYSIOLOGY

- Intraperitoneal abscesses are more common than retroperitoneal abscesses.

- Infection seeds a contained space in retroperitoneum:
  - Usually anaerobic and aerobic organisms are present.
  - Usual source is normal flora from a nearby organ site (eg GI, GU, female reproductive tract).
- Hypoxia and lack of appropriate blood supply limit effective immune response.
- TB and Staphylococcus (skin focus) were previously major pathogens but are less common today.
- Proteus and Escherichia coli are most commonly cultured in retroperitoneal abscess.
- Polymicrobial infections are common.
- Common pathogens (aerobic and anaerobic):
  - Enterobacteriaceae:
    E. coli
    Klebsiella pneumonia
    Proteus sp.
    Pseudomonal aeruginosa (controversial)
  - Anaerobes:
    Peptostreptococcus sp.
    Bacteroides fragilis
    Prevotella sp.
    Clostridium sp.
  - Enterococcus sp.
  - Streptococcus sp.
  - Staphylococcus aureus
- Osmotic forces produce growth of abscess cavity.
- If untreated, bacteremia followed by shock ensues.
- Malignancy frequently violates fascial barriers, whereas abscesses tend to be contained by the fascia.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes, liver disease, renal insufficiency, retroperitoneal hematoma, immune compromise
- GU-specific: Urinary infection, urolithiasis, instrumentation/surgery, malignancy
- GI-specific: Malignancy, surgery, pancreatic pathology

DIAGNOSIS

HISTORY

- Pain, chills, sweats, fever, malaise, nausea/vomiting, altered bowel habits, dysuria, and weight loss

- Recent surgery/trauma
- Recent treatment for UTI
- History of urolithiasis, inflammatory bowel disease, pancreatitis, diverticulitis, appendicitis, osteomyelitis, malignancy, TB
- Associated conditions: Diabetes, renal insufficiency, immunosuppression

PHYSICAL EXAM

- Unlike peritoneal cavity, retroperitoneum is relatively concealed on exam.
- Note temperature, tachycardia, tachypnea:
  - Assess for:

    Tenderness: Usually localized and mild

    Psoas sign: Increased pain on patient raising thigh against examiner's hand; suggests involvement of psoas muscle

    Lower abdominal, groin, and/or upper thigh tenderness due to irritation to retroperitoneal nerves

    CVA tenderness

    Palpable mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Laboratory findings often nonspecific.
- Obtain: WBC count, urinalysis, urine/blood/abscess cultures
- ESR
- Serum glucose level
- ~30% will have microscopic hematuria; pyuria is very common.

Imaging

- CT or MRI cross-sectional imaging is most helpful:
  - MRI:

    Thick purulent collections have high-intensity signal on T1-weighted images.

    May not show calcifications or gas collections
- US: Can show gas/fluid collections
- KUB: May show psoas shadow, loss of real outline, displacement of organs, gas, or urolithiasis
- Gallium67 citrate and Indium111 chloride scanning can be helpful:
  - False-positives: Pyelonephritis, acute tubular necrosis, vasculitis, and neoplasms
- Chest x-ray may show elevation of hemidiaphragm, pleural effusion, secondary pneumonia.

Diagnostic Procedures/Surgery

- CT-, MRI-, or US-guided aspiration and drainage of abscess cavity
- Specimens must be sent for both aerobic and anaerobic cultures.

Pathological Findings

Coagulation necrosis

DIFFERENTIAL DIAGNOSIS

- Malignancy
- Necrotizing fasciitis
- Osteomyelitis
- Perforated viscus
- Perinephric/perirenal abscess
- Psoas abscess
- Pyelonephritis
- Retroperitoneal hematoma
- TB

TREATMENT

- Supportive care
- DVT prophylaxis
- Combination antibiotic therapy with early percutaneous drainage is the standard approach:
  - Some reports of abscess <3 cm treated with antibiotics only. For lesions >3 cm percutaneous drainage is essential.

MEDICATION

- Broad-spectrum antibiotics to empirically cover most likely pathogens (ampicillin, gentamicin, and metronidazole)
- Refine antibiotic coverage based on culture results.
- Duration of treatment is tailored to clinical progress.

SURGERY/OTHER PROCEDURES

- Percutaneous drainage should not be delayed.
- Surgical drainage must be considered if:
  - Safe percutaneous drainage not possible
  - Percutaneous drainage has failed
  - Multiple abscesses
  - Multiloculated abscesses
  - Purulent material too thick to drain

- If patient is persistently febrile after 48–72 hr of appropriate antibiotics
- If primary cause must be addressed surgically (eg, XGP, malignancy, urinary tract stone)

- Surgical approach should be retroperitoneal unless pancreatic pathology is present:
  - Be sure to obtain cultures.
  - Irrigate abscess cavity aggressively.
  - Use drains liberally.

ONGOING CARE

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
- DVT
- GI bleed
- Organ failure
- Pneumonia
- Secondary infections: Osteomyelitis, involvement of psoas muscle, fistulization to the skin

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Reimaging necessary; timing depends on clinical progress
- Drains:
  - Must be monitored carefully and irrigated appropriately
  - Can be removed when:
    Patient is clinically improved
    Drainage stops (<10 mL/d) or become serous
    Abscess cavity involution is documented on imaging

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See Also (Topic, Algorithm, Electronic Media Element)

- Psoas Abscess, Urologic Considerations
- Renal and Perirenal Abscess
- Retroperitoneal Mass and Cysts

CODES

ICD9

567.38 Other retroperitoneal abscess

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle
- DVT: Deep vein thrombosis
- GI: Gastrointestinal
- GU: Genitourinary
- KUB: Kidneys, ureters, bladder
- MRI: Magnetic resonance imaging
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell
- XGP: Xanthogranulomatous pyelonephritis

RETROPERITONEAL FIBROSIS (RPF, ORMOND DISEASE)

Kashif Siddiqi, MD

James A. Brown, MD

BASICS

DESCRIPTION

- RPF is characterized by sclerotic tissue from inflammatory processes causing encasement of the retroperitoneal structures including the ureters, aorta and IVC. The main manifestation is obstructive uropathy.
- Exhibits a perivascular distribution, typically including the periaortic, pericaval, and peri-iliac retroperitoneum.
- Generally classified as either primary (idiopathic) or secondary RPF
- Hallmark is medical deviation of the ureters on imaging with or without hydronephrosis.

EPIDEMIOLOGY

- Unknown, but estimated at 1:200,000–1:500,000/yr
- In Finland, incidence is 0.1:100,000/yr

RISK FACTORS

- Asbestos exposure
- Associated with autoimmune disorders
- Abdominal aortic aneurysm
- Male > Female (2–3:1)
- RPF most common in the 5th–6th decades, but can occur at any age
- Use of implicated medications (see below)

Genetics

Evidence suggests an immunogenetic role with certain HLA haplotypes:

- HLA-DRB1*03 and HLA-B*08

GENERAL PREVENTION

Avoid medication implicated in RPF (see below).

PATHOPHYSIOLOGY

- Most commonly, the retroperitoneal thickening is located between L5–S1, 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 pathogenesis is unclear.

– Mitchinson and Parums classify idiopathic RPF in a range of diseases collectively termed chronic periaortitis.

– Immune-mediated reaction to antigens (ceroid and LDL) within atherosclerotic plaques

– Often have autoantibodies, and thus overlap with many autoimmune disorders

– IgG4-bearing plasma cells may also be involved in 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 methylsergide (Sansert, once widely used for migraine headaches)

Others include LSD, methyldopa, phenacetin, -blockers, amphetamines, hydralazine and analgesics

– Malignancy:

Lymphoma (most common), multiple myeloma, carcinoid, pancreatic tumors, prostate cancer, and sarcoma

Radiotherapy for malignancy such as seminoma, colon or pancreatic cancer

Infections: TB, actinomycosis, histoplasmosis

– Others: Trauma (hemorrhage, urinary extravasation), surgical injury, Crohn disease, inflammatory bowel disease, asbestos exposure, fat necrosis, collagen vascular disease, perianeurysmal inflammation

COMMONLY ASSOCIATED CONDITIONS

- Autoimmune diseases: Ankylosing spondylitis and Wegener granulomatosis
- Multifocal fibrosclerosis: RPF may present as part of a systemic sclerosis:

– Presentation may include sclerosing mediastinitis, sclerosing cholangitis, orbital pseudotumor, and Riedel thyroiditis.

- Membranous glomerulonephritis
- Atherosclerotic disease (abdominal aortic aneurysm)

Pediatric Considerations

- RPF has been reported in children.
- 50% of these are associated with a concomitant immunologic or systemic process.
- Male = Female
- Treatment with combined medical and surgical therapy is usually curative.

DIAGNOSIS

HISTORY

- Constitutional symptoms (fatigue, weight loss, anorexia, low-grade fever]
- Pain (back, flank, abdominal) and duration
- Signs of vascular obstruction:
  - Testicular pain, varicocele, hydrocele, leg edema, deep vein thrombosis, claudication
- GI symptoms such as weight loss, nausea, anorexia, constipation, or vomiting
- Urinary symptoms, including frequency, and dysuria, also oliguria if severe
- Medical history:
  - Malignancies, other autoimmune or collagen vascular diseases, fibrotic processes, inflammatory bowel diseases, asbestos exposure, radiation exposure
  - Medication history, especially ergot alkaloids
- Surgical history:
  - Abdominal, vascular, or endoscopic procedures

PHYSICAL EXAM

- Patient appears pale, ill, and in malaise if significant azotemia is present.
- Low-grade fevers and HTN
- Abdominal exam: Mass, abdominal bruit, CVA tenderness
- Lower extremity edema, varicosities

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- No tests are diagnostic
- Metabolic profile: Electrolyte abnormalities will depend upon the degree of ureteral obstruction.
- ESR and CRP are usually elevated.
- Ferritin and other acute phase reactants are often high.
- Polyclonal hypergammaglobulinemia
- ANA is positive in 60% of patients along with other autoantibodies including anti–smooth muscle antibodies and rheumatoid factor.

Imaging

- Excretory urography:
  - Medial deviation of the ureters with tapering of the middle 3rd of the ureter beginning at the 3rd or 4th lumbar vertebra
  - Varying degrees of hydronephrosis; may see a nonfunctioning kidney.
  - Encasement of ureters may prevent dilation of middle and distal ureteral segments.

- US:
  - More useful for following the response to therapy
- CT:
  - Imaging modality of choice
  - Typically shows a symmetric, geometrically shaped mass encasing the retroperitoneal structures
  - Demonstrates the medial deviation of the ureters and extrinsic compression with hydronephrosis
  - Mass is often isodense to muscle with contrast enhancement.
- MRI:
  - Hypointensity on T1 images but high intensity on T2 weighted images
- PET:
  - Investigational
  - May visualize other disease sites
  - May reveal neoplastic or infectious processes to which the RPF may be secondary

Diagnostic Procedures/Surgery

- Retrograde pyelography 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.

Pathological Findings

- Gross findings:
  - 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 thoracic aorta and other atypical areas
- Microscopic findings:
  - Early findings: Collagen bundles with capillary proliferation and inflammatory cells
  - Later findings: Acellular and avascular mass with sheets of hypocellular collagen
  - Vasculitis of small retroperitoneal vessels with plasma cells staining for IgG4 (rarest 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:
  - Malignant processes; inflammatory myofibroblastic tumors
  - Desmoid-type fibromatosis; associated with Gardner 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
- Unclear if trial of steroids or immediate ureterolysis is optimal therapy

MEDICATION

First Line

- After ureteral obstruction has been relieved, 1st line therapy is generally glucocorticoids (prednisone). No consensus as to duration of therapy:
  - Dose: Prednisone 60 mg every other day for 2 mo, then tapered over 5 mo to 5 mg/d
  - Alternate regimen: 60 mg/d for 6 wk, and tapered over the next 2–3 mo to 10 mg/d for total of 1 yr

Second Line

- In patients with glucocorticoid-resistant RPF or who have recurrent disease, immunosuppressive agents may also be helpful:
  - Prednisone in combination with cyclophosphamide or azathioprine for 6–12 mo
  - Mycophenolate mofetil has also been used in combination with glucocorticoids.

SURGERY/OTHER PROCEDURES

- Relief of ureteral obstruction:
  - Ureteral stents may be helpful during subsequent ureterolysis

    Usually not difficult; often elect to stent both sides even if not bilaterally obstructed to prevent obstruction or provide guide for surgery.

    Percutaneous nephrostomy undertaken only in acutely ill patients; rarely necessary
- Ureterolysis:
  - May be performed via an open approach (transabdominal) or laparoscopically (hand-assisted or standard)
  - Ureters are often wrapped in omentum or intraperitonealized to prevent further fibrous entrapment.

- Other procedures: May require ileal interposition graft, autotransplantation, nephrectomy, or urinary diversion in complicated or severe cases

ADDITIONAL TREATMENT

- Observation:
  - There may be a role in patients on methylsergide after discontinuation of the medication if renal function is not diminished.
  - 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.
  - Tamoxifen has been used with some success.
- Low-protein, sodium-restricted diet for patients with renal insufficiency

ONGOING CARE

PROGNOSIS

Prognosis is excellent with combined medical and surgical therapy.

COMPLICATIONS

- Recurrence of RPF: Typically in 1st yr; usually limited to those treated with medical therapy
- Ureteral injury, requiring further surgical management
- Vascular injury
- Postoperative adhesions due to intraperitoneal procedure

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients can be monitored at regular intervals with symptom check, ESR/CRP levels, creatinine, and degree of hydronephrosis on US.

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- Patients treated with definitive surgical intervention require less frequent follow-up.

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See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult
- Retroperitoneal Hematoma
- Retroperitoneal Mass and Cysts

CODES

ICD9

593.4 Other ureteric obstruction

ABBREVIATIONS

- CRP: C-reactive protein
- CT: Computed tomography
- CVA: Costovertebral angle
- ESR: Erythrocyte sedimentation rate
- HTN: Hypertension
- IVC: Inferior vena cava
- LDL: Low-density lipoprotein
- MRI: Magnetic resonance imaging
- PET: Positron emission tomography
- RPF: Retroperitoneal fibrosis
- TB: Tuberculosis
- US: Ultrasound

RETROPERITONEAL MASSES AND CYSTS

Douglas E. Sutherland, MD

Thomas W. Jarrett, MD

BASICS

DESCRIPTION

- The retroperitoneal space is defined by the following anatomic structures:
  - Diaphragm (superiorly)
  - Posterior parietal peritoneum (anteriorly)
  - Body wall (posteriorly and laterally)
  - Pelvic diaphragm (inferiorly)
- Retroperitoneal lesions can be classified simply:
  - Primary, solid retroperitoneal mass
  - Secondary (metastatic), solid retroperitoneal mass
  - Retroperitoneal cyst
  - Retroperitoneal infection/abscess (see “Retroperitoneal Abscess”)
  - Retroperitoneal fibrosis (see “Retroperitoneal Fibrosis”)
  - Originating from a retroperitoneal organ (such as kidney or adrenal)

EPIDEMIOLOGY

- Metastatic disease is the most common etiology of a solid retroperitoneal mass.
- The majority of primary, solid retroperitoneal tumors are malignant (85%).
- Most cystic lesions within the retroperitoneum are benign; unless the lesion is mostly solid the suspect malignancy.
- Retroperitoneal sarcoma:
  - Accounts for <1% of all adult malignancy, or 9,500 new diagnoses per year:
  - ~2.7 cases per million per year of retroperitoneal sarcoma

RISK FACTORS

- Primary, solid/cystic retroperitoneal mass:
  - Previous radiotherapy (dose dependant)
  - Chemical exposure (vinyl chloride, arsenic)
  - HIV/AIDS
- Primary, cystic retroperitoneal mass:
  - Paracytic infection
  - Embryonic remnants
  - Prior lymphadenectomy

Genetics

Primary, solid/cystic retroperitoneal mass:

- Tuberous sclerosis (TS1, TS2 mutation, tumor suppressor loss)
- Werner syndrome (chromosome 8 alteration, premature aging)
- Li-Fraumeni syndrome (p53 mutation, tumor suppressor loss).
- Neurofibromatosis (NF1, NF2 mutation)

PATHOPHYSIOLOGY

Various, depending on the pathology

COMMONLY ASSOCIATED CONDITIONS

- Previous malignancy
- Inherited disease
- Immunosuppression

DIAGNOSIS

HISTORY

- Age, sex, constitutional symptoms
- History of malignancy, including history of surgical, chemotherapy, or radiation treatment
- Fever, chill, pyrexia, flu-like symptoms
- Night sweats raise suspicion of lymphoma.
- GI complaints: Nausea, vomiting, pain, constipation, increasing abdominal girth
- GU complaints: Flank pain, colic, hematuria
- Neurologic: Back pain, nerve root impingement
- Prior surgical history: Urologic, vascular (eg, iliac bypass), gynecologic
- Medications: Methysergide, methyldopa, LSD

PHYSICAL EXAM

- Palpable abdominal mass: Most common finding.
- Cachexia
- Breast exam
- Testicular exam: Testicular mass or varicocele (gonadal vein impingement).
- Lower extremity pitting edema

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis (infection or lymphoma), leukopenia, anemia
- Serum chemistry: Elevated serum creatinine, azotemia (obstructive uropathy), transaminitis (biliary obstruction), and elevated alkaline phosphatase (bone involvement).
- AFP and -HCG: Testicular tumor markers

- ESR: Elevated in retroperitoneal fibrosis
- Urinalysis: Hematuria, pyuria
- Urine cytology: Evidence of a malignant urothelial source
- Blood and urine culture

Imaging

- CT of the chest, abdomen, and pelvis with IV contrast, including delayed images (CT urogram):
  - Best initial study: Defines primary lesion and may identify the primary malignancy source of metastasis (eg, lung cancer)
  - Differentiates between solid and cystic lesions
  - Dense, fibrotic lesions surrounding the great vessels may indicate lymphoma or fibrosis.
  - Evidence of hydronephrosis, renal obstruction
  - Evidence of aortic aneurysm or vascular source of lesion
- MRI is useful adjunct to CT when a primary retroperitoneal malignancy is suspected to define involvement of adjacent organs and to assess tissue planes.
- MAG3 renal Lasix nuclear scan: Superior to CT for renal function estimate
- Testicular sonogram
- Mammogram
- Bone scan (if AP is elevated, to complete metastatic evaluation)
- Cystogram (if pelvic lipomatosis suspected)

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: Best option if the mass is small and inconveniently located for needle biopsy. Be prepared to complete the resection if sarcoma identified.
- Aspiration of cyst: Fluid for cytology, culture, creatinine
- Angiogram: To delineate relationship of tumor to vascular anatomy or to determine extent of aneurysm

Pathological Findings

- Metastasis pathology is consistent with primary tumor pathology.
- Determination of benign vs. malignant tissue is not always possible, leaving final determination to the surgical pathology.
- Sarcoma: Liposarcoma is most common (35%), followed by leiomyosarcoma (30%), malignant fibrous histiocytoma (20%), rhabdomyosarcoma, and peripheral nerve neoplasm.

- Lymphoma: Diffuse, monomorphous proliferation of lymphocytes
- Fibrosis: Cellular and acellular variants coexist; fibroblast and collagen proliferation

Pediatric Considerations

Rhabdomyosarcoma (33%) and fibrosarcoma (33%) are the 2 most common primary solid tumor histologies in children.

DIFFERENTIAL DIAGNOSIS

- Solid mass:
  - Benign stromal tumor (neural, lipoma, leiomyoma)
  - Fibrosis (Ormond disease)
  - Germ cell tumor (primary)
  - Lymphoma
  - Metastasis
  - Sarcoma
- Cystic mass:
  - Abscess
  - Lymphocele
  - Mesocolic cyst (anterior to the gonadal vessels)
  - Paracytic mass
  - Post-traumatic mass
  - Teratomatous lesion, dermoid cyst
  - Urogenital cyst (persistent Wolffian remnant, posterior to the gonadal vessels)

TREATMENT

- Surgically treated patients typically require long-term critical care postoperatively.
- Bowel preparation prior to surgery may improve perioperative infection rates.

MEDICATION

- Metastatic lesions and lymphoproliferative cancers are best treated with systemic, tumor-specific chemotherapy (in most cases).
- Sarcomas respond variably to chemotherapy, depending on the histology, and generally do not influence survival.
- Infected retroperitoneal cysts are treated with broad-spectrum antibiotics until culture sensitivities are known:
  - Ampicillin 1 g IV q6h: Gram-positive coverage
  - Gentamicin 5–7 mg/kg/d: gram-negative coverage.

SURGERY/OTHER PROCEDURES

- Selective surgical resection of metastatic deposits is reasonable for specific diseases (eg, testicular cancer) or in carefully selected patients with no other evidence of disease.

• Complete surgical resection of retroperitoneal sarcoma remains the best possible option for long-term disease control.

• Resection of adjacent organs (if involved), and generous use of intraoperative frozen sections, should be performed in an effort to obtain negative surgical margins.

• Complete resection of benign retroperitoneal masses generally results in long-term disease-free survival.

• Retroperitoneal cysts are best treated with percutaneous or open surgical drainage, with surgical resection reserved for persistent disease or identification of malignant tissue.

ADDITIONAL TREATMENT

• Retroperitoneal sarcoma is typically radiation-resistant.

• Intraoperative radiotherapy for sarcoma has been shown to improve local control rates, but does not improve survival.

ONGOING CARE

PROGNOSIS

• 5- and 10-yr survival following surgical resection of retroperitoneal sarcoma is 45% and 29%.

• Completely resected, nonmetastatic, and low-grade sarcoma are associated with improved survival.

• Leiomyosarcoma is an independent predictor of poor outcome.

COMPLICATIONS

• Surgical resection of retroperitoneal sarcoma is associated with significant morbidity, including massive hemorrhage, large vessel thrombosis, bowel injury with fistula formation.

• Operative mortality is low (<2%) in high-volume centers.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• 30–60% of patients undergoing surgical resection of the lesion will recur, depending on the tumor histology.

• ~1/3 of recurrences will be local.

• Follow-up includes history, physical exam, and abdominal imaging (CT, MRI) every 3–6 mo following surgery.

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See Also (Topic, Algorithm, Electronic Media Element)

- Retroperitoneal Abscess
- Retroperitoneal Fibrosis
- Retroperitoneal Sarcoma

CODES

ICD9

- 789.39 Abdominal or pelvic swelling, mass, or lump, other specified site
- 567.38 Other retroperitoneal abscess
- 568.89 Other specified disorders of peritoneum

ABBREVIATIONS

- AFP: -Fetoprotein
- -HCG: -human chorionic gonadotropin
- CBC: Complete blood count
- CT: Computed tomography
- ESR: Erythrocyte sedimentation rate
- GI: Gastrointestinal
- GU: Genitourinary
- IV: Intravenous
- LSD: Lysergic acid diethylamide;
- MAG3: Mercaptoacetyltriglycine
- MRI: Magnetic resonance imaging
- US: Ultrasound

RHABDOMYOSARCOMA, PEDIATRIC (SARCOMA BOTRYOIDES)

Shawn E. White, MD
Pasquale Casale, MD

BASICS

DESCRIPTION

- Malignancy arising from embryonal mesenchyme
- Most common soft-tissue sarcoma in pediatric age group
- 15–20% of pediatric rhabdomyosarcoma involve GU system:
  - Bladder
  - Paratesticular
  - Prostate
  - Uterus
  - Vagina
  - Sarcoma botryoides describes a polypoid variant of rhabdomyosarcoma originating in hollow organs (vagina, bladder).

EPIDEMIOLOGY

- 0.5–0.7 cases per million children <15 yr old
- Bimodal distribution:
  - 1st peak: 2–4 yr
  - 2nd peak: 15–19 yr
- 3rd most common tumor in children (behind neuroblastoma and Wilms tumor)

RISK FACTORS

Genetics

- Li-Fraumeni syndrome:
  - Mutation of p53 tumor suppressor gene
  - Higher incidence of rhabdomyosarcoma
- Neurofibromatosis:
  - Higher incidence of rhabdomyosarcoma
- Cytogenetic abnormalities:
  - Alveolar histiologic subtype:
    1;13 translocation (favorable prognosis)
    2;13 translocation (unfavorable prognosis)
  - Embryonal histiologic subtype:

Loss of heterozygosity on chromosome 11

PATHOPHYSIOLOGY

- Rapid growth with local invasion of soft tissues
- Can spread by lymphatic and hematogenous means
- Thought to arise from immature cells that are destined to form striated skeletal muscle:
  - These tumors can 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 depends on histiologic subtype and clinical staging.
- Lungs most common site of distant metastasis

DIAGNOSIS

HISTORY

- Family history of malignancy or genetic syndromes (Li-Fraumeni, neurofibromatosis)
- Bladder/prostate:
  - Urinary frequency
  - Stranguria
  - Urinary retention
  - Hematuria
- Vagina/uterus:
  - Vaginal bleeding
  - Vaginal discharge

PHYSICAL EXAM

- Bladder/prostate:
  - Abdominal mass
  - Bladder distention
  - Firm prostatic mass
- Paratesticular:
  - Unilateral painless scrotal mass
- Vagina/uterus:
  - Vaginal mass (may protrude from introitus)
  - Abdominal mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Basic metabolic panel: BUN/Cr elevated in ureteral obstruction

- CBC: Anemia due to vaginal bleeding or hematuria

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Imaging

- CT/MRI abdomen/pelvis: Evaluate local extent of tumor, pelvic/retroperitoneal lymph nodes, distant metastasis for all primary sites
- CT/x-ray chest: Evaluate for pulmonary metastasis
- Bone scan: Evaluate for osseous metastasis
- US: Characterize paratesticular mass

Diagnostic Procedures/Surgery

- Bone marrow biopsy for evidence of metastasis for all primary sites
- Bladder/prostate:
  - Cystoscopy: Transurethral resection/biopsy for pathologic diagnosis
- Paratesticular:
  - Radical inguinal orchiectomy: Diagnostic and therapeutic
- Vagina/uterus:
  - Cystoscopy/vaginoscopy: Evaluate extent of tumor, biopsy for pathologic diagnosis

Pathological Findings

- Embryonal:
  - Most common subtype
  - Accounts for majority of GU rhabdomyosarcoma
  - Following variants carry excellent prognosis:
    Sarcoma botryoides: Polypoid variant occurring in hollow organs (vagina, bladder)
    Spindle cell/leiomyomatous: Common variant in paratesticular tumors
- Alveolar:
  - Less common in GU system
  - More common in trunk/extremities
  - Higher rate of local recurrence, lymph node spread, and distant metastasis
- Pleomorphic:
  - Undifferentiated/anaplastic variants of embryonal or alveolar
  - Poor prognosis

DIFFERENTIAL DIAGNOSIS

- Bladder/prostate:
  - TCC of bladder
  - Nephrogenic adenoma of bladder
  - Fibroepithelial polyps of prostatic urethra

- Testis:
  - Primary testis tumor
- Vagina/uterus
  - Prolapse of ureterocele, urethra, bladder, vagina

ALERT

- Preoperative staging: IRSG clinical staging based on TNM criteria
- Postoperative grouping: IRSG grouping based on completeness of surgical resection: Helps determine therapy and prognosis

Preoperative Staging for Rhabdomyosarcoma

- T1: Confined to organ of origin, a: 5 cm in size, b: >5 cm in size
- T2: Extension or fixed to surrounding tissue, a: 5 cm in size, b: >5 cm in size
- N0: Regional nodes clinically negative
- N1: Regional nodes clinically positive
- Nx: Unknown
- M0: No distant metastasis
- M1: Metastasis present
- Stage I: Vaginal and paratesticular rhabdomyosarcoma, any T, any N, M0
- Stage II: Bladder/prostate rhabdomyosarcoma, T1a or T2a, N0 or Nx, M0
- Stage III: Bladder/prostate rhabdomyosarcoma, (T1a or T2a) and N1, M0, OR (T1b or T2b), any N, M0
- Stage IV: Any tumor with M1

Postoperative grouping for Rhabdomyosarcoma

- Group 1: Localized disease, completely excised, no microscopic residual
  - a: Confined to site of origin, completely resected
  - b: Infiltrating beyond site of origin, completely resected
- Group 2: Total gross resection
  - a: Gross resection with microscopic local residual
  - b: Regional disease with involved lymph nodes, completely resected with no microscopic residual
  - c: Microscopic local or nodal residual
- Group 3: Incomplete resection or biopsy with gross residual
- Group 4: Distant metastisis

TREATMENT

- All sites of GU rhabdomyosarcoma require multidisciplinary approach to curative therapy including surgical excision, chemotherapy, and radiation therapy.

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MEDICATION

- Bladder/prostate:
  - VA for low-risk
  - VAC for low-risk N1, intermediate-risk, high-risk
  - Irinotecan/topotecan added to regimen for some intermediate-/high-risk tumors
- Paratesticular:

):

VA: Stage 1, <10 yr, no evidence of lymph node involvement on CT

VAC: Administered when any positive lymph nodes after retroperitoneal lymph node dissection

):

- VAC: Primary therapy with repeat biopsy after course completed to assess residual disease

SURGERY/OTHER PROCEDURES

- Bladder/prostate:
  - Partial cystectomy: Primary treatment if tumor at dome/lateral wall with adequate margins
  - Radical cystectomy: Performed after chemotherapy if tumor not amenable to bladder-sparing therapy
  - Urinary diversion: Incontinent conduit can be performed temporarily with staged continent diversion when child matures
  - Radical prostatectomy: Performed for isolated prostatic tumors
- Paratesticular:
  - Radical inguinal orchiectomy

):

All patients >10 yr regardless of CT findings prior to chemotherapy

<10 yr if evidence of lymph node involvement on CT

- Vagina/uterus:
  - Partial vaginectomy: If evidence of residual disease on post-chemotherapy biopsy
  - Complete vaginectomy/hysterectomy: If not amenable to partial resection

ADDITIONAL TREATMENT

- Bladder/prostate:
  - Preoperative: If response to chemotherapy limited
  - Postoperative: If evidence of residual disease

- Paratesticular:
  - If positive lymph node pathology following RPLND
- Vagina/uterus:
  - If residual disease following chemotherapy or surgical resection

ONGOING CARE

PROGNOSIS

- Bladder/prostate:

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Alveolar: 40%

- Management:

50%: Chemotherapy/biopsy

37%: Partial cystectomy

13%: Radical prostatectomy

- Paratesticular:

):

Overall survival: 96%

Prognosis worse (63%) >10 years: Rationale for RPLND in all patients >10 years

- Vagina/uterus:

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COMPLICATIONS

- Bladder/prostate:
  - Complications of bladder preservation/radiation:

Bladder dysfunction/low capacity

Hematuria

Dysuria

  - Complications of radical prostatectomy:

Incontinence

Impotence

- Paratesticular:
  - Complications of RPLND:

Bowel obstruction

Ejaculatory dysfunction

Lower extremity edema

- Vagina/uterus:
  - Complications of vaginal excision/hysterectomy
    Infertility
    Sexual dysfunction

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- CT/MRI for evidence of residual/recurrent disease
- Bladder/prostate and vagina/uterus: Posttreatment biopsy used to guide therapy

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Mass, Differential Diagnosis
- IRS (Intergroup Rhabdomyosarcoma Study Group Clinical Classification)
- Testis, Tumor and Mass, Pediatric, General
- Vaginal Mass, Newborn

CODES

ICD9

- 171.9 Malignant neoplasm of connective and other soft tissue, site unspecified
- 184.9 Malignant neoplasm of female genital organ, site unspecified
- 187.9 Malignant neoplasm of male genital organ, site unspecified

ABBREVIATIONS

- -FTP: -fetoprotein
- -hCG: -human chorionic gonadotropin
- CBC: Complete blood count
- CT: Computed tomography
- GU: Genitourinary
- IRSG: Intergroup Rhabdomyosarcoma Study Group
- RPLND: Retroperitoneal lymph node dissection
- TCC: Transitional cell carcinoma
- US: Ultrasound
- VA: Vincristine, actinomycin D
- VAC: Vincristine, actinomycin D, cyclophosphamide

SACRAL AGENESIS, UROLOGIC CONSIDERATIONS

Shawn E. White, MD

Douglas A. Canning, MD

BASICS

DESCRIPTION

- The partial or complete absence of 2 lower vertebral bodies
- Can be occult or associated with voiding dysfunction

EPIDEMIOLOGY

- 1% of children born to insulin-dependent diabetic mothers (including gestational diabetes).

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- >75% cases detected during infancy

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RISK FACTORS

- Maternal insulin-dependent diabetes (fetal insulin exposure)

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Genetics

- Currarino syndrome (presacral mass, sacral agenesis, anorectal malformations)
- Deletion in chromosome 7 (7q)
- Mutations in HLXB9 gene on chromosome 7 involved in neural plate infolding

GENERAL PREVENTION

Avoid maternal exposure to potentially causative agents.

PATHOPHYSIOLOGY

- Failure of fusion or formation of lower vertebral bodies; caudal regression syndrome
- Spectrum of anomalies including meningocele and anorectal malformations

):

  – Upper motor neuron lesions (35%; detrusor hyperreflexia, detrusor sphincter dyssynergia)
  – Lower motor neuron lesions (40%)
  – No neurologic deficit (25%)

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- Tethered spinal cord
- VATER syndrome

DIAGNOSIS

HISTORY

- UTI in 75% of affected children
- Gestational history
- Drug exposure
- Gestational diabetes
- Toilet training history
- Constipation

PHYSICAL EXAM

- Sacral dermatome sensation is usually intact.
- Lower extremity strength is usually normal.
- High arched feet, claw/hammer toes are possible findings.
- Flat buttocks
- Low-riding, short gluteal cleft
- Palpation of coccyx and sacrum for abnormalities
- Bulbocavernosus reflex: Gently squeeze head of penis or clitoris and observe for anal wink:
  - Present in most UMN lesion
  - Absent in most LMN lesion

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Normal

Imaging

- Lateral x-ray of lower spine:
  - Confirms absence of lower vertebral bodies
  - Eliminates obscured image due to bowel gas on A-P projections
- Prenatal/postnatal US:
  - Defect can be detected after ossification is complete at 18 wk gestation.
  - Can be used to evaluate kidneys and bladder once diagnosis confirmed
- MRI (fetal or postnatal):
  - Confirms diagnosis, often shows sharp cutoff of conus medullaris at T12

Diagnostic Procedures/Surgery

- Video urodynamics/VCUG:

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- Present in 75% of children with UMN lesion
- Present in 40% of children with LMN lesion

DIFFERENTIAL DIAGNOSIS

Part of spectrum of anomalies that include myelomeningocele and other spinal dysraphisms, as well as anorectal malformations.

TREATMENT

- Gastroenterology consultation:
  - Essential to identify and treat fecal incontinence
  - Anorectal manometry may identify abnormalities in anal sphincter
- Orthopedics:
  - Often have normal lower extremity development and function

MEDICATION

- UMN lesions: Anticholinergics:
  - Oxybutynin (Ditropan) (syrup 5 mg/mL):
    <1 yr: Not established
    1–5 yr: 0.2 mg/kg PO b.i.d./q.i.d.
    5–12 yr: 5 mg PO b.i.d.; 15 mg/d max
    >12 yr: Adult dose: 5 mg PO t.i.d.–q.i.d.; XL form, 5 mg/d PO
  - Hyoscyamine
  - Propantheline
- LMN lesions: -agonists (with CIC):
  - Pseudoephedrine:
    <2 yr: 4 mg/kg/d PO divided q6h
    2–5 yr: 15 mg PO q4–6h; 60 mg/d max
    6–12 yr: 30 mg PO q4–6h; 120 mg/d max
    >12 yr: Adults dose: Immediate release: 60 mg PO q4–6h, 240 mg/d max; extended-release 120 mg PO q12h

SURGERY/OTHER PROCEDURES

- UMN lesions:
  - Augmentation cystoplasty may be necessary if anticholinergics fail to allow adequate storage.
- LMN lesions:
  - Endoscopic injections of bulking agents to sphincter if -agonist therapy with CIC not adequate to achieve continence

- Artificial urinary sphincter

- Ureteral reimplantation/endoscopic bulking agents in children with persistent high-grade VUR and/or recurrent UTI

ADDITIONAL TREATMENT

Since the introduction of intermittent catheterization, urinary diversion is uncommon.

ONGOING CARE

PROGNOSIS

Best prognosis for successful toilet training and management of sequelae when defect detected early

COMPLICATIONS

- Renal deterioration/scarring in children with VUR and recurrent UTI
- Social and developmental difficulties associated with fecal/urinary incontinence

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Renal/bladder US may be used to monitor upper urinary tracts

REFERENCES

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Myelodysplasia (Spinal Dysraphism), Urologic Considerations
- Neurogenic Bladder, General
- Spina Bifida/Spina Bifida Occulta, Urologic Considerations
- Tethered Cord

CODES

ICD9

- 593.70 Vesicoureteral reflux unspecified or without reflux nephropathy
- 599.0 Urinary tract infection, site not specified
- 756.13 Absence of vertebra, congenital

ABBREVIATIONS

- CIC: Clean intermittent catheterization
- DSD: Disorders of sexual development
- LMN: Lower motor neuron
- UMN: Upper motor neuron
- US: Ultrasound
- UTI: Urinary tract infection
- VATER: Vertebrae, anus, trachea, esophagus, and renal anomalies
- VCUG: Voiding cystoureterogram
- VUR: Vesicoureteral reflux

SARCOIDOSIS, UROLOGIC CONSIDERATIONS

Bilal Chughtai, MD

Michael Perrotti, MD

BASICS

DESCRIPTION

- A systemic granulomatous disease with unknown etiology; it is characterized by the formation of noncaseating granulomas, primarily in the lungs, but also throughout the rest of the body.
- Hypercalcuria is more common than hypercalcemia. Renal stones secondary to hypercalcuria can be associated in up to 14% of patients. Occasionally, this can be the presenting complaint that leads to the diagnosis of sarcoidosis.
- Other urologic manifestations of sarcoidosis are rare. These include acute interstitial nephritis, neurogenic bladder dysfunction secondary to neurosarcoidosis, bladder sarcoidosis with gross hematuria, and ureteral obstruction due to retroperitoneal adenopathy or fibrosis.

EPIDEMIOLOGY

- In the US, sarcoidosis is 10 times more common in African Americans than in whites (AA: 35–64/100,000; whites: 10–14/100,000).
  - Female > Male
  - Onset is most often at 20–45 yr of age.
  - Prevalence of sarcoidosis is 1–40 cases per 100,000 population.
  - Sarcoidosis affects both men and women, but it seems to be most prevalent among African American women.

RISK FACTORS

- Many organisms have been linked, including Mycoplasma sp., fungi, Histoplasma and Cryptococcus spp.; viruses, and numerous other organisms.
- Environmental exposure to noninfectious agents, such as aluminum, zirconium, talc, pine tree pollen, and clay, have also been implicated.

Genetics

- Familial clustering of cases has been reported. Monozygotic twins who have sarcoidosis are 2–4 times as likely to have the disease as dizygotic twins.
- Most common allele found in sarcoidosis is HLA-B8. Other associated alleles include HLA-A1 and HLA-DR3.

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: Bilateral hilar adenopathy (50%). Less common is bilateral hilar adenopathy and pulmonary infiltrate (25%) and pulmonary infiltrate alone (15%). Other presenting manifestations include cough, wheezing, fever, malaise, fatigue, hepatomegaly, splenomegaly, and uveitis.
- Hypercalcemia:
  - Present in at least 20–30% of patients with sarcoidosis.
  - Sarcoidosis may cause resorptive hypercalciuria and urolithiasis.
  - The sarcoid granuloma produces 1,25(OH)2D3 (calcitriol), causing increased intestinal absorption of calcium, hypercalcemia, and hypercalciuria.
  - 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 hyperoxaluria can be seen.
  - Most sarcoidosis stones are calcium oxylate.
- Glomerular involvement is very rare and may include: Membranous nephropathy, IgA nephropathy, minimal-change disease, proliferative or crescentic glomerulonephritis, and focal glomerulosclerosis.
- Interstitial nephritis with granuloma formation is common in sarcoidosis.
- TINU syndrome is idiopathic; these patients should be evaluated for sarcoidosis and Sjögren syndrome.
- Prostatic involvement has been reported.

ALERT

A diagnosis of sarcoidosis should always be considered when patients present with renal calculi of unknown origin.

COMMONLY ASSOCIATED CONDITIONS

Erythema nodosum

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.

PHYSICAL EXAM

- Cutaneous involvement may be present (lupus pernio; erythema nodosum)
- Wheezing
- Neurologic symptoms
- Adenopathy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Sterile pyuria and mild proteinuria
- Leukopenia and/or thrombocytopenia are common.
- Eosinophilia: 24%
- Anemia: 5%
- Hypercalciuria: 49%
- Hypercalcemia: 13%
- Elevated calcitriol levels
- Serum ACE level is elevated in 60% of patients; therefore, this test is not sensitive in diagnosing sarcoidosis.
- BUN and Cr may be elevated if there is renal involvement.

Imaging

- Chest imaging may demonstrate hilar adenopathy or pulmonary infiltrate.
- Abdominal imaging may show hepatomegaly, retroperitoneal adenopathy, and retroperitoneal fibrosis.
- Stones and nephrocalcinosis secondary to hypercalcemia can be seen on CT.
- In rare cases of urinary involvement, ureterohydronephrosis may be seen from urolithiasis or obstruction.

Diagnostic Procedures/Surgery

- Many physicians prefer a biopsy to confirm the diagnosis of sarcoidosis.
  - Mediastinoscopy is utilized to assess hilar adenopathy.
  - Fiberoptic bronchoscopy with transbronchial biopsy is used for biopsy documentation of pulmonary sarcoidosis.
- Bladder involvement confirmation requires transurethral bladder resection.
- Sarcoidosis can also be differentiated from other diagnoses by the rapid resolution of hypercalcemia with initiation of corticosteroid therapy.

Pathological Findings

Typical sarcoid lesions are characterized by the presence of circumscribed granulomas of epithelioid cells with little or no necrosis (noncaseating granuloma).

DIFFERENTIAL DIAGNOSIS

- Interstitial lung diseases:
  - Medications (nitrofurantoin, methotrexate), idiopathic pulmonary fibrosis, collagen vascular diseases, amyloidosis, hypersensitivity pneumonitis, granulomatous vasculitis, collagen vascular diseases,
  - Other granulomatous diseases: TB, brucellosis, Q fever, biliary cirrhosis, Wegener granulomatosis, Hodgkin disease
- Other skin and arthritic disorders
- Other causes of hypercalcemia/hypercalcuria:
  - PTH-related, malignancy, vitamin D-related, mediations (eg, lithium), endocrine disorders, immobilization
- Causes of interstitial nephritis:
  - Sjögren syndrome
  - Systemic lupus erythematosus
  - Wegener granulomatosis
  - Behçet disease

TREATMENT

- 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 hypercalcuria.

MEDICATION

First Line

- Oral corticosteroids are the treatment of choice for patients with hypercalcemia and systemic involvement.
- Nephropathy due to sarcoidosis appears to respond to steroid therapy.

Second Line

- Inhaled steroids
- Methotrexate
- Chloroquine

SURGERY/OTHER PROCEDURES

- Biopsy is necessary for diagnosis.

- Obstruction may require diversion.
- Surgical management of urolithiasis

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 lithiasis, gross hematuria, ureteral obstruction, neurogenic bladder dysfunction
- Renal failure is rare and is due to hypercalcemic nephropathy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

History, physical exam, chest x-ray, pulmonary function tests, and serum chemistry

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Hypercalcemia, Urologic Considerations
- Urolithiasis, Adult, General

CODES

ICD9

- 135 Sarcoidosis
- 275.40 Unspecified disorder of calcium metabolism
- 592.0 Calculus of kidney

ABBREVIATIONS

- ACE: Angiotensin-converting enzyme
- BUN: Blood urea nitrogen
- Cr: Creatinine
- CT: Computed tomography

- PTH: Parathyroid hormone
- TB: Tuberculosis
- TINU: Tubulointerstitial nephritis and uveitis

SCROTUM AND TESTICLE, MASS

Danielle A. Stackhouse, MD

Judd W. Moul, MD

BASICS

DESCRIPTION

- A mass in the scrotum or testicle can be noted by the patient or during a routine exam.
- Lesions can be in the scrotal wall, testicle, or paratesticular tissues.
- Testicular masses can usually be distinguished from other common intrascrotal masses (hydrocele, varicocele, spermatocele, epididymal cyst, hernia) 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

Depends upon the diagnosis:

- Varicocele: 15–20 % adult males
- Hydrocele: 6% of full-term infants
- Paratesticular tumors: <10% of intrascrotal tumors
- Testicular cancer: Most common solid tumor in men between 18 and 40

RISK FACTORS

- Malignancy: Cryptorchidism, prior testicular neoplasm or hematopoietic malignancy, HIV, 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 testicular cancer

GENERAL PREVENTION

None, but testicular self-exam starting at puberty may impact on testicular cancer outcomes.

PATHOPHYSIOLOGY

- Depends upon the etiology of the mass
- Differential diagnosis can be narrowed based on patients' age and history.

COMMONLY ASSOCIATED CONDITIONS

Inguinal hernia in pediatric hydrocele

ALERT

- Scrotal swelling and testicular masses should be evaluated urgently.
- A solid, firm intratesticular mass must be considered testicular cancer until proven otherwise.
- Patients may present with a complaint of a testicular mass when they have a mass of the paratesticular structures.
- Epididymal lesions, spermatic cord lesions, varicoceles, inguinal hernias, and lesions of the scrotal skin are commonly labeled testicular masses.

DIAGNOSIS

HISTORY

- Age of the patient:
  - Tumor types are age-specific.
  - Torsion usually in the prepubertal age group
- Description of mass:
  - Small discrete masses are more commonly neoplastic or cystic.
  - Diffuse enlargement with tenderness is usually seen in infection, torsion, or trauma.
- Associated pain:
  - Torsion: Sudden, severe, unilateral pain with nausea and vomiting. If torsion is intermittent, pain may wax and wane; may have pain during sleep.
  - Neoplasms rarely cause severe pain and are usually described as a dull ache or fullness.
  - Orchitis pain may gradually increase as the infectious process causes increased inflammation.
  - Referred pain to the scrotum without a mass can be due to renal colic, or nerve root irritation.
- Prior scrotal surgery: Orchidopexy for cryptorchidism; increased risk of cancer; malignancy; postvasectomy granuloma
- History of trauma, surgery, any radiation
- Previous UTI or current lower UTI complaints suggests orchitis ± epididymitis
- Urethral discharge suggests STD-concurrent epididymo-orchitis (Chlamydia and gonorrhea are most common in men <35 yr of age).
- Urethral instrumentation: Ascending infection

- Current illnesses: Mumps, UTI
- Medical problems: Diabetes mellitus, immunodeficiency, 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

PHYSICAL EXAM

- Fever can be a marker of 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:
  - Retroperitoneal lymphadenopathy from metastatic tumors can sometimes be palpated.
  - Palpate for signs of hernia.
- Testes:
  - Evaluate if the mass is testicular or paratesticular.
  - Evaluate for associated pain on palpation.
  - Neoplastic/cystic processes are usually painless.
  - Torsion or epididymoorchitis is exquisitely tender.
  - Phren sign: Scrotal elevation relieves pain in epididymitis, but worsens pain or has no effect in torsion; not reliable.
- Discrete lesion vs. diffuse swelling:
  - Most early-stage neoplasms or cysts are palpable discrete masses.
  - Orchitis and torsion lead to generalized testicular enlargement.
- Position of mass in testicle:
  - May be high riding or in altered position in torsion
  - The bell clapper deformity: In torsion, occurs when the testicle is situated in a horizontally lie with the long axis in the anteroposterior direction.
- Scrotum:
  - Evaluate if the mass is within the testicle, epididymis, spermatic cord, or adherent to the scrotal walls.
  - Edema and erythema: Torsion or orchitis
  - Evaluate for scars or prior cryptorchidism repair.
  - Transilluminate the scrotum to evaluate for hydrocele.
  - Valsalva maneuver to elicit a varicocele

– Cremasteric reflex: Stroke upper thigh and observe ipsilateral testicle/scrotum for contraction:

Usually absent in torsion

- Penis: Ulcers, induration, or discharge can be seen in epididymo-orchitis (STD)
- Epididymis:
  – Normally located posterior relative to the testicle
  – Pain or swelling helps make the diagnosis of epididymo-orchitis. If severe, difficult to demarcate the epididymis and the testicle.
- Extremities:
  – Swelling due to malignant retroperitoneal lymphadenopathy or venous thrombosis.
- Neurologic exam
- Lymphatics:
  – Testicular tumor metastasizes to pelvic and retroperitoneal nodes, not inguinal nodes; tender or enlarged inguinal nodes are associated with infection.
- Rectal exam: Evidence of prostatitis; examine seminal vesicles for fullness.
- Skin: Signs of cellulitis, swelling, discoloration, or breaks in skin:
  – Blue dot sign: Torsion of the appendix testes

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- WBC count to evaluate for infection or leukemia/lymphoma
- HCT to evaluate for anemia associated with malignancy
- Urine analysis and urine culture: May suggest the diagnosis of orchitis or epididymitis
- Hematuria and proteinuria: Viral infection
- Pyuria and bacteriuria: Bacterial infection
- Tumor markers:
  – AFP: Elevated in embryonal cell carcinomas, teratocarcinoma, yolk sac tumors, or combined tumors, but never increased in pure seminomas
  – -hCG: Elevated in all choriocarcinomas and some embryonal cell carcinomas, yolk sac carcinomas, and seminomas
  – LDH: Nonspecific; elevated in metastatic disease
- Urethral swab to rule out gonorrhea/Chlamydia

Imaging

- US (diagnostic procedure of choice):
  – 95% sensitivity for diagnosis of testicular tumors
  – 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-flow Doppler is essential for the differentiation of torsion from epididymo-orchitis:

Decreased blood flow with torsion

Increased blood flow with epididymoorchitis

Will also sometimes show increased vascularity in testicular neoplasms

• MRI: Minor role in testicular masses; can help evaluate intratesticular masses that are difficult to visualize or characterize on US

• Nuclear scintigraphy is most useful for testicular torsion, but is less convenient than US.

Diagnostic Procedures/Surgery

Biopsy is contraindicated if there is suspicion for testicular neoplasm.

Pathological Findings

See specific Section I and II topics.

DIFFERENTIAL DIAGNOSIS

• Adult/pediatric painful mass:
  – Epididymitis/orchitis; bacterial, STD, mumps, TB
  – Fournier gangrene
  – Henoch-Schönlein purpura (usually no mass)
  – Incarcerated/strangulated hernia
  – Postvasectomy syndrome (usually no mass)
  – Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  – Torsion (testicle, testicular, or epididymal appendage)
  – Tumor (infrequent unless traumatized or rapidly growing; see below)
• Adult painless mass:
  – Adenomatoid tumor of testis or epididymis
  – Adrenal rest tumors
  – Adenocarcinoma of the rete testis
  – Chylocele: Usually associated with filariasis
  – Fibrous pseudotumor of the tunica albuginea
  – Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of the cord
  – Lipoma of the cord

– Mesothelioma of tunica vaginalis
– Polyorchidism
– Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma
– Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
– Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcinosis, fat necrosis, malignancy
– Sperm granuloma following vasectomy
– Spermatocele (epididymal cyst)
– Testicular cysts (simple, tunica albuginea, epidermoid)
– Testicular tumor:

Germ cell tumors (95% of testicular malignancies): Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma (1–5%), teratocarcinoma

Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder, and thyroid

Mixed germ cell and stromal tumor (gonadoblastoma)

Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

Leukemia or lymphoma

– Varicocele

• Pediatric painless mass:

– Similar to adult list; most/more common are: Hydrocele, hernia, varicocele, testicular teratoma, adrenal rest tumors, rhabdomyosarcoma

TREATMENT

• Testicular torsion requires immediate exploration and repair to salvage an ischemic testicle:

– 80–100% of testicles salvaged if detorsion occurs within 6 hr of onset.
– 20% salvaged if detorsion occurs after >24 hr from onset.

• Trauma management depends on the severity of the lesion:

– Surgical exploration is warranted if the tunica albuginea is ruptured, significant debridement is required, or uncontrolled bleeding is present.
– Bed rest, scrotal support, ice, analgesics

MEDICATION

- Cause-specific treatment, as well as supportive care, should be applied to cases of orchitis: Bed rest, scrotal support, ice bags, and analgesics
- Broad-spectrum antibiotics should be administered if a bacterial source is suspected.
- A patient's sexual partners should be treated if STD is the cause.

SURGERY/OTHER PROCEDURES

- Testicular neoplasms: Radical orchiectomy with high ligation of the spermatic cord; inguinal incision:
  - Testicular biopsy or orchiectomy 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, testis-sparing surgery for benign lesions such as teratoma, Leydig cell tumor, and epidermoid cyst based on frozen biopsy findings

ADDITIONAL TREATMENT

Some tumors: Seminoma or some sarcomas

ONGOING CARE

PROGNOSIS

- Neoplasms: See tumor types in Section I or II
- Cystic lesions: Simple periodic exam
- Torsion: Evaluation in 6–12 mo to check for testicular atrophy and presence of new masses:
  - Infertility has been noted as a long-term problem.
- Orchitis: If primary cause resolved, no follow-up needed.
  - In prepubertal patients, epididymoorchitis may be due to an underlying urinary tract anomaly, and these patients need structural evaluation of their urinary tracts.
- Trauma: After documentation of adequate healing, no follow-up is required.

COMPLICATIONS

Infertility; complications secondary to radiation or chemotherapy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients should be advised to perform monthly testicular self-exams.
- Patients diagnosed with cancer should have disease-specific follow-up.

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See Also (Topic, Algorithm, Electronic Media Element)

- Paratesticular Tumors, General
- Scrotal and Testicle Trauma
- Scrotum and Testicle Mass Algorithm
- Scrotum Tumors General
- Specific Disease Entities in Section I and II
- Spermatic Cord Mass and Tumors
- Testicle Pain (Orchalgia)
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General
- Torsion, Testis and Testicular Appendages

CODES

ICD9

608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- AFP: -Fetoprotein
- GI: Gastrointestinal
- hCG: Human chorionic gonadotropin
- HCT: Hematocrit
- LDH: Lactate dehydrogenase
- MRI: Magnetic resonance imaging
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection
- WBC: White blood cell

SCROTUM AND TESTICLE, TRAUMA

Paul R. Womble, MD

J. Brantley Thrasher, MD

BASICS

DESCRIPTION

Injury to the scrotum and testicle can occur by the following mechanisms:

- Blunt
- Penetrating
- Avulsion
- Ischemic
- Burn

EPIDEMIOLOGY

- Civilian:
  - <1% of all traumas
  - More common in age 10–30 yr
- Battlefield:
  - 0.6–5% of battlefield injuries
  - More frequently caused by fragmentation devices rather than projectiles
- Burn:
  - <5% of all burn victims

RISK FACTORS

- High-speed trauma
- Contact sports
- Machinists, farm equipment operators
- Bizarre sexual practices

GENERAL PREVENTION

- Protective equipment during contact sports
- Proper safety training for industrial machinery

PATHOPHYSIOLOGY

- Blunt injury:
  - Direct blow, straddle injury, sport-related
- Penetrating injury:
  - GSW, stab wound, animal bite
- Avulsion or ischemic injury:
  - High-speed MVC, industrial injury, self-mutilation, or bizarre sexual practices

- Burn injury:
  - Flame, electrical, or chemical
- Animal or human bite

COMMONLY ASSOCIATED CONDITIONS

- Associated injuries:
  - Testicular
  - Spermatic cord
  - Corpora cavernosa
  - Urethra, corpora spongiosum
  - Femoral artery or vein
  - Pelvic or femoral fracture
- Testicular torsion
- Testicular tumor

DIAGNOSIS

HISTORY

)[C]:

  - Determine type of injury and magnitude of force inflicted.
  - Investigate contamination of objects used in stab injuries.
  - Determine species of animal in bite injuries.

)[C]:

  - Testicular rupture is commonly immediately painful, with acute onset of swelling.
  - Minor trauma is associated with delayed onset of pain, swelling, and discoloration.
  - Tumors typically present with more insidious progression of symptoms.
- Associated abdominal pain, with or without emesis

PHYSICAL EXAM

- Evaluate for other trauma including penile injury.
- Determine location of pain, swelling, and ecchymosis.

)[C]

- Transilluminate any palpable scrotal mass:
  - Hydrocele will transilluminate.
  - Hematocele or tumor will not transilluminate.

ALERT

)[C]:

- RUG, VCUG when patient is stable.
- Alternative: Intraoperative cystoscopy

- Absence of these findings does not exclude urethral injury.
- Evaluate for cremasteric reflex:
  - Absence of reflex is concerning for testicular torsion.
- Assess for inguinal hernia.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:

)[C]

- Urine culture if urine analysis suggests infection
- CBC with differential if the wound appears to be infected
- For delayed presentation with abscess formation, culture abscess contents.

Imaging

Scrotal US, high-resolution

ALERT

- Nontender swelling does not rule out significant injury. US any blunt trauma without a clinical hematocele.

)[B]:

- Operator dependent
- Evaluate the integrity of the tunica albuginea.
- Heterogeneity of the parenchyma with loss of contour is a rupture until proven otherwise.
- Color-flow Doppler US may rule out torsion.
- CT:
  - Follow-up incidental findings with US if exam does not indicate immediate exploration.

Diagnostic Procedures/Surgery

History, physical exam, and imaging will dictate treatment.

DIFFERENTIAL DIAGNOSIS

- Torsion of the testicle or one of its appendages (ie, appendix testis, appendix epididymis, epididymis) resulting in swelling, tenderness
- Epididymitis, epididymo-orchitis, hernia, hydrocele, spermatocele
- Ruptured varicocele resulting in discoloration or tenderness
- Pelvic facture resulting in scrotal swelling or hematoma

Pediatric Considerations

- Painless hematocele after abdominal injury is concerning for ruptured viscera (especially spleen):

– Abdominal blood passed through patent processus vaginalis

• Findings in the evaluation of children with straddle injuries to the external genitalia should raise concern for sexual abuse:

– Presence of other nonurogenital trauma
– Patient <9 mo
– Perianal, rectal injury without history of penetrating trauma
– Findings of more extensive or severe trauma
– Lack of correlation between reported history and physical findings

TREATMENT

• Most cases of trauma to the external genitalia can be managed conservatively.
• Other associated injuries may be more life-threatening.

ALERT

• Tetanus and/or rabies immunization
• Postoperative scrotal edema:
• Elevation of the scrotum while supine
• Scrotal support at all times
• With severe bilateral testicular injury in young patients, consider sperm extraction for cryopreservation, if available.

MEDICATION

• Analgesic of choice:
  – Codeine, hydrocodone, oxycodone, propoxyphene, etc., with or without Tylenol
  – Avoid NSAIDs and aspirin use initially due to bleeding risk.
  – IV narcotic may be necessary for major surgical reconstruction: Morphine, fentanyl, etc.

SURGERY/OTHER PROCEDURES

)[C]:

– Ice, elevation, scrotal support, and analgesics

)[C]

)[C]:

– Irrigation, débridement of devascularized skin
– Meticulous hemostasis
– Noninfected wound:
  Primary closure followed by antibiotic ointment, ice, elevation, and analgesics.
– Infected wound:
  Wet-to-dry dressing changes

Broad-spectrum antibiotics (eg. amoxicillin-clavulanate

)[C]:

– Immediate scrotal exploration
– Debridement of nonviable tissue until bleeding is encountered
– Primary closure of tunica albuginea with a fine, absorbable running suture
– Free graft with tunica vaginalis may be used

)[C]

)[C]

)[C]

– Interrupted closure reduces ischemic injury and allows for drainage.
– Nonabsorbable skin suture may aid in closure of complex wounds.
– Place antibacterial dressing and ointment over incision, supported with fluffed gauze and supportive mesh undergarment.

)[C]:

– Flame or electrical:
Surgical debridement of eschar and devascularized tissue
Split-thickness skin graft for full-thickness
Silver sulfadiazine cream for partial-thickness
– Chemical:
Irrigate with saline if chemical is unknown

ALERT

- Do not irrigate a lye burn with water as this can exacerbate the caustic damage.
  – Alkaline burns: Irrigate with dilute acetic acid
  – Acidic burns: Irrigate with sodium bicarbonate

)[C]:

– Small injuries can be managed as simple lacerations:
Irrigation, debridement, and primary closure
– Complex injuries:
Judicious debridement
Close observation, with wet-to-dry dressing changes
Delayed split-thickness skin graft

)[C]:

– Treat as blunt or penetrating trauma, with addition of broad-spectrum antibiotics
– Dicloxacillin or cephalexin (both 500 mg PO q.i.d.)
– Dog bites: Add penicillin V 500 mg PO q.i.d. for added coverage of Pasteurella multocida)

ONGOING CARE

PROGNOSIS

- Early exploration and repair of testicular injury results in >90% testicular salvage.
- Nonoperative management of testicular rupture will result in ~45% chance of delayed exploration and orchiectomy.

COMPLICATIONS

- Abscess
- Fistula
- Fournier gangrene
- Hematoma
- Infertility or hormonal dysfunction
- Ischemic injury to testicle

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Repeat US for conservatively managed hematoceles or patients with persistent pain

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See Also (Topic, Algorithm, Electronic Media Element)

- Bites to Penis (Animal and Human)
- Burns, External Genitalia and Perineum
- Edema, External Genitalia (Peno-Scrotal Edema)
- Penis, Trauma
- Scrotum and Testicle Trauma Algorithm
- Testicular Mass
- Testis Pain (Orchalgia)
- Torsion, Testis, and Testicular Appendages

CODES

ICD9

- 878.2 Open wound of scrotum and testes, without mention of complication
- 878.3 Open wound of scrotum and testes, complicated
- 959.14 Other injury of external genitals

ABBREVIATIONS

- CBC: Complete blood count
- CT: Computed tomography
- GSW: Gunshot wound
- IV: Intravenous
- MVC: Motor vehicle collision
- NSAID: Nonsteroidal anti-inflammatory drug
- RUG: Retrograde urethrogram
- US: Ultrasound

- VCUG: Voiding cystourethrogram

SCROTUM, SQUAMOUS CELL CARCINOMA

Jeremy A. Davis, MD

J. Brantley Thrasher, MD

BASICS

DESCRIPTION

- A very rare, environmentally induced cancer with high metastatic potential.
- Scrotal cancer is rare, but has historical significance as the 1st reported occupational cancer
- Synonym(s): Potts disease, Chimney sweeps disease, Mule-spinners disease

EPIDEMIOLOGY

- 0.2–0.3 per 100,000 men >35 yr
- Since the early 1900s, <200 cases have been reported in the US.
- 20 times more common in the UK than in the US
- Higher incidence in lower social class
- Urban population with greater incidence than rural
- Lower incidence among Black men
- Most reported in men >50 yr of age
- Very low prevalence given rarity of disease

RISK FACTORS

- Chemical/mechanical irritation:
  - Soot: Chimney sweepers
  - Oil/petroleum: Machine workers (mule-spinners, lathe workers)
- Poor hygiene
- Repeated trauma
- Rarely in patients with a previous scrotal incision/scar
- Psoralen, arsenic, coal tar, or ultraviolet A radiation (PUVA) for treatment of psoriasis
- HPV infection
- Chronic immunosuppression

Genetics

- Oncogene effects of HPV. Association with HPV type 16 and 18
- HPV 16-related mutations of p53 gene and p15INK4B/p16INK4A homozygous deletions have been observed in scrotal cancer patients with no occupational risk factors.

GENERAL PREVENTION

- Improve hygiene
- Decrease exposure to irritants:

- Protective occupational clothing

- Prevention of STDs (HPV)
- Shielding of genitals during UV radiation treatment of psoriasis

PATHOPHYSIOLOGY

- 3’4’-benzpryene is the common carcinogen.
- SCC is a malignant tumor of epidermal keratinocytes.
- Slow growing on anterolateral portion of scrotum
- Starts as a small pimple or nodule; gradually develops ulceration with raised, rolled edges with purulent discharge
- Lesion may persist for 6 months prior to ulcerating.

COMMONLY ASSOCIATED CONDITIONS

- Condylomata
- Psoriasis
- STDs

DIAGNOSIS

HISTORY

- Occupational exposure to chemical or mechanical irritants
- History of STDs: HPV, HIV
- History of trauma or previous incisions/scars
- Change in size of the lesion or ulceration
- Fever
- Nonhealing nodule or ulcer despite self-treatment with ointments
- History of treatment for psoriasis with topical or UV light

PHYSICAL EXAM

Exam of external genitalia, and inguinal and distant lymph nodes:

- Usually a solitary, slow-growing nodule with or without ulceration on anterolateral aspect of scrotum
- 30–60% have palpable inguinal adenopathy at presentation
- 25% have inguinal metastasis at presentation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- WBC count to rule out infectious process
- Urine analysis and urine culture, if indicated

Imaging

- CT may help assess size of nodes, location, and extent of disease, but cannot differentiate inflammation vs. metastasis.

- MRI of the pelvis:
  - Improved accuracy in diagnosis and staging of SCC
  - Can assess infiltrative process vs. inflammatory process
- Lymphangiography is accurate in delineating metastatic vs. inflammatory nodes, but cannot detect micrometastasis.

Diagnostic Procedures/Surgery

Excisional biopsy of primary lesion

Pathological Findings

- SCC:
  - Most are well- or moderately well-differentiated and contain focal areas of keratosis.
  - Surrounding epidermis frequently shows hyperkeratosis, acanthosis, and dyskeratosis.
  - A diffuse lymphocytic infiltrate may be present.
- Staging (TNM classification does not exist):
  - Stage A1: Localized to scrotal wall
  - Stage A2: Locally extensive tumor invading adjacent structures (testis, spermatic cord, penis, pubis, and perineum)
  - Stage B: Metastatic disease involving inguinal lymph nodes only
  - Stage C: Metastatic disease involving pelvic lymph nodes without evidence of distant spread
  - Stage D: Metastatic disease beyond the pelvic lymph nodes involving distant organs

DIFFERENTIAL DIAGNOSIS

- Benign lesions:
  - Condyloma
  - Eczema
  - Hidradenitis suppurativa
  - Folliculitis
  - Nevus
  - Periurethral abscess
  - Psoriasis
  - Sebaceous cysts
  - Syphilis
  - Tuberculous epididymitis with a draining sinus

- Malignant lesions:
  - Basal cell carcinoma
  - Malignant melanoma
  - Paget disease
  - Marjolin ulcer: Cancer arising from any site of chronic inflammation.
  - Kaposi sarcoma: A purple, papular, plaque-like, or ulcerated lesion found on the penis or scrotum
  - Sarcomas: Leiomyosarcoma from the Dartos is most common, although very rare.

TREATMENT

- Management is primarily surgical.
- Local wide excision combines diagnostic and therapeutic procedure.

MEDICATION

- Broad-spectrum antibiotics for 4–6 weeks in patients with lymphadenopathy
- Chemotherapy (single-agent or combination therapy) has not proved successful for primary treatment:
  - Combination chemotherapy:

    Methotrexate, bleomycin, and cisplatin have been used, with subsequent radiotherapy in 1 case report.
- Bleomycin as a single agent has been reported successful in 2 cases.

SURGERY/OTHER PROCEDURES

- Primary lesion:
  - Wide local excision of lesion with a 2-cm margin of skin and dartos
  - Small lesions may be primarily closed.
  - Large lesions may need split-thickness skin grafting, local flaps.
  - If hemiscrotectomy is done, the ipsilateral testis can be transpositioned to the contralateral hemiscrotum or placed in a thigh pouch.
  - Excision of all scrotal contents is rarely indicated except when directly involved by tumor.
- Regional lymph nodes:
  - If palpable adenopathy resolves after an antibiotic course or was never present, then a superficial inguinal lymph node biopsy should be performed:

    Ipsilaterally if lesion is lateral

    Bilaterally if lesion at median raphe
  - If palpable lymphadenopathy persists after a course of antibiotics, then a bilateral superficial inguinal lymph node biopsy should be performed.

– Full ilioinguinal lymphadenectomy should be performed only on the side of the positive biopsy:

If performing a unilateral ilioinguinal lymphadenectomy, a contralateral superficial inguinal lymph node biopsy should also be performed.

If there is a positive frozen section, then perform a bilateral ilioinguinal lymphadenectomy.

- Laser vaporization of primary lesion has been used in patients who refused traditional therapy or who were poor surgical candidates.
- Micrographic surgery has also been used for primary lesions.

ADDITIONAL TREATMENT

Radiotherapy

Has not been effective and is reserved for recurrences and poor surgical candidates

Additional Therapies

Topical 5-FU has not been successful in treating carcinoma in situ of the scrotum.

ONGOING CARE

PROGNOSIS

- Survival at 5 yr:
  - Stage A: 70%–80%
  - Stage B: 40%–50%
  - Stage C: Rare
  - Stage D: Rare
- Local recurrence rates:
  - 21–40%
  - May require additional excision
  - Patients with industrial exposure may be at higher risk for recurrence.

COMPLICATIONS

- Lymphedema/lymphoceles
- Wound infections
- Femoral hernias after ilioinguinal lymphadenectomy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Self-exams for local recurrence of lesion or lymphadenopathy
- Periodic follow-up by physician for monitoring of local recurrence or lymphadenopathy

ADDITIONAL READING

- Arango O, Bielsa O, Lorente JA, et al. Hemiscrotectomy with contralateral testicular transposition for scrotal cancer. J Urol 2002;168:1406–1407.

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• Taniguchi S, Furukawa M, Kutsuna H, et al. Squamous cell carcinoma of the scrotum. Dermatology 1996;193:253–254.

• Waldron HA. A brief history of scrotal cancer. Br J Ind Med 1983;40:390–401.

See Also (Topic, Algorithm, Electronic Media Element)

- Scrotum and Testicle Mass
- Scrotum, Tumors, Benign and Malignant

CODES

ICD9

187.7 Malignant neoplasm of scrotum

ABBREVIATIONS

- 5-FU: 5-Flourouracil
- CT: Computed tomography
- HIV: Human immunodeficiency virus
- HPV: Human papilloma virus
- MRI: Magnetic resonance imaging
- PUVA: Psoralen and ultraviolet A
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- US: Ultrasound
- UV: Ultraviolet
- WBC: White blood cell

SCROTUM, TUMORS, GENERAL

Amit R. Patel, MD
Eric A. Klein, MD

BASICS

DESCRIPTION

- Scrotal wall lesions are usually cutaneous; can be benign (infectious, inflammatory), or malignant.
- Present as macules, papules, nodules, vesicles, pustules, scales, erosions, or ulcers
- The scrotal wall consists of the following layers: Rugous thin skin densely adherent to the Dartos muscle and facia. Deep to this layer is Colles fascia and then the tunica vaginalis.
- The Dartos muscle determines the dynamic size of the scrotum and is responsible for the rugations of the scrotal skin.

EPIDEMIOLOGY

- Psoriasis: 2% of population
- EIC: Common
- EMPD and SCC: Uncommon

RISK FACTORS

- Psoriasis: Trauma, infections, stress, medications
- EIC: Young males
- SCC: Machine operators, lower social class, poor hygiene, HPV, chronic irritation, inflammation

Genetics

- Family history significant of psoriasis
- Oncogene effects of HPV: Increases risk of cancer

GENERAL PREVENTION

- Generally good hygiene
- Early evaluation

PATHOPHYSIOLOGY

- Scrotal skin is more deeply pigmented and contains multiple sebaceous follicles.
- EIC:
  - Formed by cystic enclosure of the epithelium within the dermis and fills with keratin and debris.
  - Implantation of epidermal elements in the dermis
  - Slow growth; may become secondarily infected
  - Foul-smelling cheese-like material may be discharged from lesion.

- Idiopathic scrotal wall calcifications:
  - Unknown etiology. Many be end stage of dystrophic calcification of scrotal epidermoid cysts
- Angiokeratoma: Vascular ectasia of dermal blood vessels.
- EMPD: Multifocal origin, may occur as upward extension of in situ adenocarcinoma.
- SCC: May occur from chronic irritation, inflammation, or virally activated oncogenes

COMMONLY ASSOCIATED CONDITIONS

EMPD: Associated with underlying malignancy in 10–30% of cases; also associated with urethral and bladder malignancy

DIAGNOSIS

HISTORY

- Focus on duration, rate of onset, location, symptoms, family history, allergies, occupation, and previous treatment
- History of psoriasis

PHYSICAL EXAM

- Examine penis and scrotal contentments.
- Palpate scrotal wall. Spread the rugations between gloved fingers to fully view the scrotal wall.
- Examine the intrascrotal contents (testes, epididymis, etc.).
- Examine for inguinal adenopathy.
- Focus on distribution of primary and secondary skin lesions.
- Thorough skin exam
- Any discharge from lesion: Suggests folliculitis or EIC
- Psoriasis: Sharply demarcated erythematous plaque with silvery white scales
- EIC: 0.5–5-mm dermal, subcutaneous nodule
- Angiokeratoma: 1–2-mm red or purple papules; the overlying surface may show scales (hyperkeratosis)
- EMPD: Erythematous plaque, sharp border between normal and affected skin; may be pruritic or painful
- SCC: Usually present with significant growth and ulceration, 50% with palpable adenopathy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- KOH preparations to rule out fungal infection
- Skin biopsy to rule out malignancy

- Urine analysis and urine culture if needed

Imaging

- Scrotal US: Not helpful for cutaneous lesions or for scrotal malignancy
- EMPD: GU tract imaging to rule out associated malignancies.
- CT of abdomen/pelvis for staging SCC
- MRI of pelvis/scrotum can help stage malignancy.

Diagnostic Procedures/Surgery

- Skin biopsy via needle, punch, or excision for smaller lesions
- Local wide excisions combines diagnostic and therapeutic procedure for SCC.
- Cystourethroscopy may be indicated to rule out underlying malignancy for EMPD.

Pathological Findings

- EMPD: Characteristic Paget cells, clear abundant cytoplasm; stains for glandular cytokeratins, epithelial membrane antigen
- Angiokeratoma: Vascular and keratotic elements
- SCC: Most are well differentiated and contain focal areas of keratosis. Surrounding epidermis may demonstrate hyperkeratosis, acanthosis, and dyskeratosis:
  - Staging for SCC:

    Stage A1: Localized to scrotal wall

    Stage A2: Locally extensive tumor invading adjacent structures (testis, spermatic cord, penis, pubis, and perineum)

    Stage B: Metastatic disease involving inguinal lymph nodes only

    Stage C: Metastatic disease involving pelvic lymph nodes without evidence of distant spread

    Stage D: Metastatic disease beyond the pelvic lymph nodes involving distant organs

DIFFERENTIAL DIAGNOSIS

- Primarily differentiate intrascrotal lesion (testicle, epididymis, cord, etc.) from scrotal wall lesion
- Benign scrotal wall lesions:
  - Angiokeratoma of Fordyce (scrotal angiokeratomas)
  - Condyloma
  - Eczema
  - Edema of scrotal wall (idiopathic or secondary to anasarca)
  - EIC
  - Hansen disease (leprosy)

- Hemangioma
- Hidradenitis suppurativa
- Idiopathic scrotal wall calcifications
- Folliculitis
- Fournier gangrene
- Fungal infections (tinea cruris)
- Nevus
- Periurethral abscess
- Psoriasis
- Sebaceous cysts
- Skin tags, external genitalia (acrochordon, pedunculated papilloma)
- Syphilis
- Tuberculous epididymitis with a draining sinus

• Malignant scrotal wall lesions:
- Basal cell carcinoma
- Malignant melanoma
- Paget disease (extramammary)
- Marjolin ulcer: Cancer arising from any site of chronic inflammation.
- Kaposi sarcoma: A purple, papular, plaque-like, or ulcerated lesion found on the penis or scrotum
- Sarcomas: Leiomyosarcoma from the Dartos is most common, although very rare.

TREATMENT

Scrotal malignancy is extremely rare; most scrotal wall lesions are benign.

MEDICATION

First Line

• Psoriasis: Topical corticosteroids, short courses (2 wk)
• EIC: Antibiotic therapy (if ruptured cyst)
• EMPD: 5-Fluorouracil
• SCC: If lymphadenopathy is present, a 6-wk course of broad-spectrum antibiotics may be given.

Second Line

• Psoriasis:
- Topical vitamin D3 analogs, retinoids
- Systemic therapy for severe disease: Methotrexate, cyclosporine, and retinoids

• SCC:

– Chemotherapy (single-agent or combination therapy) has not proved successful for primary treatment of SCC.

SURGERY/OTHER PROCEDURES

- EIC: Incision and drainage
- Angiokeratoma: Usually unnecessary; erbium-YAG, KTP, argon laser photocoagulation can be used in select cases
- Skin tag: Local excision
- EMPD: Treatment of choice:
  - Excision of lesion with margin control
  - Lymphadenectomy may be indicated for dermal involvement and palpable nodes.
- SCC: Wide local excision with negative margins:
  - Negative margins at the skin and Dartos level
  - Primary closure of scrotum if possible
  - Split-thickness skin grafts can be used to assist closure.
  - If hemiscrotectomy is done, the ipsilateral testis can be transpositioned to the contralateral hemiscrotum or placed in a thigh pouch.
- SCC: Regional lymphadenectomy:
  - If palpable lymphadenopathy resolves following antibiotic therapy, or was never present, superficial inguinal lymph node biopsy should be done.
  - If palpable lymphadenopathy persists, then bilateral superficial inguinal lymph node biopsy should be done.
  - Complete the ilioinguinal lymph node dissection if ipsilateral superficial nodes are positive; biopsy contralateral inguinal nodes.
- Literature supports similar treatment for scrotal melanoma or sarcoma.

ADDITIONAL TREATMENT

Radiotherapy

- Psoriasis: Psoralen + UVA:
  - Used to treat nongenital skin lesions
  - Not recommended for scrotal lesions due to increased risk of SCC
- EPMD: Radiation therapy is used with some success.

Additional Therapies

Topical 5-FU has not been successful in treating carcinoma in situ of the scrotum.

ONGOING CARE

PROGNOSIS

SCC survival at 5 yr:

- Stage A1: 75%
- Stage B: 44%
- Stage C: Rare
- Stage D: Rare

COMPLICATIONS

SCC: Local recurrence rates:

- 21–40%
- May require additional excision
- Patients with industrial exposure may be at higher risk for recurrence.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Serial exam by patient and physician, including lymph node exams

ADDITIONAL READING

- Arango O, Bielsa O, Lorent JA, et al. Hemiscrotectomy with contralateral testicular transposition for scrotal cancer. J Urol 2002;168:1406–1407.
- Fitzpatrick TB, Johnson RA, Wolff K. Color Atlas and Synopsis of Clinical Dermatology: Common and Serious Diseases. New York: McGraw-Hill, 2001.
- Froehner M, Lossnitzer A, Manseck A, et al. Favorable long-term outcome in adult genitourinary low-grade sarcoma. Urology 2000;56:373–377.
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- Taniguchi S, Furukawa M, Kutsuna H, et al. Squamous cell carcinoma of the scrotum. Dermatology 1996;193:253–254.
- Waldron HA. A brief history of scrotal cancer. Br J Ind Med 1983;40:390–401.

See Also (Topic, Algorithm, Electronic Media Element)

- Scrotum and Testicle, Mass
- Scrotum, Squamous Cell Carcinoma

CODES

ICD9

- 187.7 Malignant neoplasm of scrotum
- 222.4 Benign neoplasm of scrotum

ABBREVIATIONS

- CT: Computed tomography

- EIC: Epidermoid inclusion cyst
- EMPD: Extramammary Paget disease
- GU: Genitourinary
- HPV: Human papilloma virus
- KOH: Potassium hydroxide
- KTP: Potassium titanyl phosphate
- MRI: Magnetic resonance imaging
- SCC: Squamous cell carcinoma
- US: Ultrasound
- UVA: Ultraviolet A
- YAG: Yttrium aluminum garnet

SEMINAL VESICLE, CYSTS AND MASSES

Steven B. Brandes, MD

BASICS

DESCRIPTION

- SV masses and cysts are uncommon.
- Cysts:
  - Rare; either congenital or acquired
  - Age at diagnosis, 20–50 yr
  - Usually unilateral; size varies considerably from small (5 mm) to huge cysts that fill the pelvis.
- Neoplasms:
  - Primary malignant neoplasms of the SV are exceedingly rare.
  - SV solid mass is more likely from local invasion by another malignancy such as prostate cancer.
  - Up to 12% of prostate cancers invade the SV.

EPIDEMIOLOGY

- Rare; mostly small case series and reports
- Age at peak incidence is 20–30 yr

PATHOPHYSIOLOGY

- 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: Vesiculodeferential artery, a branch of the umbilical artery
- Cystic 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 ureter and/or ipsilateral renal abnormalities:
  - Lesions <5 cm are rarely 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 ureters insert into the SV.
- SV formation occurs at the 12th wk of gestation. Abnormal branching of the ureteral bud from the mesonephric duct can disrupt SV formation and result in an ectopic ureteral orifice:
  - The abnormal ureter and metanephrogenic blastema results in a dysplastic kidney.
- A basement membrane defect that is seen in multiple organs (as in ADPKD) is believed to also effect SV cysts.
- 3 patterns of spread of prostate cancer into SV:
  - Direct spread along the ejaculatory duct
  - Prostatic capsular perforation followed by extension into the periprostatic tissues and the SV
  - Isolated deposits

COMMONLY ASSOCIATED CONDITIONS

- Bladder cancer
- Ectopic ureter
- Ipsilateral renal dysplasia or agenesis
- Prostate cancer
- Rectal cancer

DIAGNOSIS

HISTORY

- Most SV cysts are asymptomatic.
- Typical symptoms, when they occur:
  - Dysuria, irritative voiding
  - Perineal discomfort
  - Recurrent epididymitis
  - Painful ejaculation
  - Hematuria
  - Hematospermia
  - Infertility
- Determine history of other malignancy such as prostate, bladder, or rectal cancer.

ALERT

Normal SVs are not palpable on DRE: A palpable SV is an abnormal SV.

PHYSICAL EXAM

- SV tumors are often palpable and nontender hard areas on DRE, just cranial to the base of the prostate.

- Primary tumors are usually unilateral and not contiguous with the prostate.
- Secondary tumors are usually bilateral and contiguous with a prostate or bladder tumor.
- SV cysts (when large) can usually be palpated on DRE as a ballotable mass.
- Indurated and/or tender epididymis and ductus deferens: Evidence of chronic epididymitis or obstruction

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Low semen volume and lack of fructose and liquefaction implies SV absence or ejaculatory duct occlusion.
- PSA elevation may suggest prostate cancer.

Imaging

- TRUS:
  - 1st-line imaging for suspected SV abnormality or SV mass on DRE
  - SV cystic lesions: Echopenic center with echogenic luminal folds
  - SV tumors: Isoechoic to the prostate, but hyperechoic 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
  - CT cannot distinguish benign from malignant tumors. Obliterated tissue planes suggest a secondary tumor by direct extension.
- MRI:
  - Cannot distinguish benign from malignant tumors
  - SV cyst: T1, low signal intensity; T2, unilocular 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

- Vasovesiculography: Limited value and use today in imaging the SV. Can help determine duct obstruction in azoospermic men; also helps distinguish SV cyst from a Müllerian or other Wolffian duct cyst.
- TRUS-guided needle placement for SV aspiration or biopsy for pathologic diagnosis
- Cystoscopy:
  - Hemi-trigone with absent ipsilateral orifice
  - Intravesical cyst protrusion often noted with congenital SV cysts

Pathological Findings

Most SV masses are benign and rarely neoplastic.

DIFFERENTIAL DIAGNOSIS

- Müllerian duct cysts and ejaculatory duct cysts:
  - Both are midline in location
  - Spermatozoa in the aspirate may differentiate seminal vesicle cysts from Müllerian duct cysts.
- Prostatic cysts
- Diverticulosis of the ampulla of the vas deferens
- Ectopic ureterocele
- SV calcifications/masses can occur from chronic bilharziasis, TB, or old bacterial abscess (commonly from colonic flora):
  - Symptoms may include hematospermia, infertility, and pelvic pain
- SV cysts:
  - Seminal vesiculitis: SV infection is uncommon:
    May occur as a consequence of prostatitis or epididymitis
  - SV abscess: Best imaged on MRI or US.
    Predisposing factors include diabetes or chronic catheterization.
    Patients often have pelvic pain, fullness, and fever.
  - SV calculi: Often present with pain, infection, or hematospermia; usually the result of infection and ejaculatory duct obstruction.
  - Congenital vs. acquired cysts: Congenital cysts are typically associated with ipsilateral ectopic ureter and/or ipsilateral renal dysplasia.
- Benign SV tumors:
  - Papillary adenoma or cystadenoma: Middle-aged men; mimics a simple cyst in presentation and on imaging
  - Amyloid: Subendothelial deposits of amyloid:
    Usually presents in the elderly
    Often concomitant 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 phyllodes tumor, benign mesenchymoma, adenomyosis, and mesonephric hamartoma
- Malignant SV tumors:
  - Most SV neoplasms are from secondary invasion from prostate, bladder, or rectal cancer, or lymphoma:

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 CEA elevated.

Stains positive for CA125 and negative for PSA

– Primary sarcoma:

Extremely rare aggressive tumor; usually diagnosed late in disease course

Variants: Leiomyosarcoma, angiosarcoma, and müllerian adenosarcoma

TREATMENT

• Asymptomatic cystic lesions do not require any specific intervention. Imaging of the urinary tract may reveal renal agenesis.

• Solid lesions require biopsy.

• Adjuvant therapy has no demonstrated efficacy in primary malignancy of the SV.

MEDICATION

Seminal vesiculitis is treated with standard antibiotic regimens used to treat prostatitis (eg, ciprofloxacin, ofloxacin, etc.)

SURGERY/OTHER PROCEDURES

• Symptomatic cysts:

– For small cysts, percutaneous transperineal or TRUS-guided aspiration/drainage (cysts typically recur)

– Marsupialization (unroof into the prostate/bladder by TUR or TUI)

– Laparoscopic or robotic-assisted laparoscopic excision. Laparoscopy has good efficacy with minimized morbidity.

– Open surgical excision (transperineal, coccygeal or vesical, or retroperitoneal) is rarely performed today.

– If associated with a congenital ectopic ureter and dysplastic kidney: An ipsilateral nephroureterectomy, along with the SV, should be performed.

– SV duct stones: Lithopaxy 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/or MRI

– Enlarging asymptomatic benign tumors are treated with simple seminal vesiculectomy.

– Historically, small benign tumors were excised transperineally or retrovesically, and large tumors, transvesically or transcoccygeally.

– 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.

– SV invasion by another malignancy: Directed at the primary tumor type

ADDITIONAL TREATMENT

May have utility in management of other secondary malignancies such as prostate cancer

ONGOING CARE

PROGNOSIS

Primary SV malignancies typically present and are diagnosed late.

COMPLICATIONS

ED can occur after SV excision since the neurovascular bundle lies lateral to the tip of the SV.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Asymptomatic benign tumors: Close follow-up with DRE and TRUS. After radical surgery for malignancy, no clear follow-up consensus exists.

ADDITIONAL READING

- Cherullo EE, Meraney AM, Bernstein LH, et al. Laparoscopic management of congenital seminal vesical cysts associated with ipsilateral renal agenesis. J Urol 2002;167:1263–1267.
- Van den Ouden D, Blom JH, Bangma C, et al. Diagnosis and management of seminal vesical cysts associated with ipsilateral renal agenesis: A pooled analysis of 52 cases. Eur Urol 1998;33:433–440.

See Also (Topic, Algorithm, Electronic Media Element)

- Prostate Nodule
- Renal Dysplasia, Hypodysplasia and Hypoplasia
- Renal Ectopia
- Seminal Vesicle, Amyloidosis
- Seminal Vesicle, Carcinoma
- Seminal Vesiculitis (Pyospermia)

CODES

ICD9

- 608.0 Seminal vesiculitis

- 608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- ADPKD: Autosomal dominant polycystic kidney disease
- CEA: Carcinoembryonic antigen
- CT: Computed tomography
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- MRI: Magnetic resonance imaging
- PAP: Pancreatitis-associated protein
- PSA: Prostate-specific antigen
- SV: Seminal vesicle
- TB: Tuberculosis
- TRUS: Transrectal ultrasound
- US: Ultrasound

SEXUAL ABUSE, PEDIATRIC

Monica M. Metzdorf, MD
Julia S. Barthold, MD

BASICS

DESCRIPTION

- Sexual activity involving a child or a minor
- Spectrum includes intercourse, fondling, pornography, and exhibitionism

EPIDEMIOLOGY

Common problem:

- ~1% of children sexually abused each year
- 12–25% of girls and 8–10% of boys have been sexually abused by age 18

RISK FACTORS

- Occurs in all socioeconomic levels
- Increased risk with:
  - Parents who were abused
  - Poverty
  - Drug or alcohol abuse
  - Teen parents
  - Parental violence
  - Mental illness
  - Multiple child caretakers

GENERAL PREVENTION

- Education
- Social services

PATHOPHYSIOLOGY

American Academy of Pediatrics definition:

- Child sexual abuse is the engaging of a child in sexual activities that the child cannot comprehend, for which the child is developmentally unprepared and cannot give informed consent, and that violate the social taboos of society.
- Children cannot consent to any sexual activity, but note that the legal age of consent may vary on a state-by-state basis.

COMMONLY ASSOCIATED CONDITIONS

- Physical abuse
- Emotional abuse

DIAGNOSIS

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
- Presenting symptoms may be general and nonspecific:
  - Sleep disturbances
  - Abdominal pain, enuresis, encopresis
- Consider evaluation by trained forensic interviewer.
- Avoid leading questions or showing strong emotions/shock: Use “tell me more” or “and then what happened approach?”
- Parent/caregiver should be interviewed separately to avoid influences/distraction.
- Questions asked and verbatim answers in quotation marks should be documented as accurately as possible.

ALERT

Findings in the evaluation of children with straddle injuries to the external genitalia should raise concern for sexual abuse:

- Presence of other nonurogenital trauma
- Patient <9 mo
- Perianal, rectal, injury without history of penetrating trauma
- Findings of more extensive or severe trauma
- Lack of correlation between reported history and physical findings

PHYSICAL EXAM

- 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 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.
- 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 detailed 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.
- Concerning findings on exam:
  - Abrasions or bruising of genitalia
  - Acute or healed tear in posterior aspect of hymen
  - A markedly decreased amount of hymenal tissue
  - Injury or scarring of posterior fourchette, fossa navicularis, or hymen
  - Anal bruising or lacerations

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Culture for gonorrhea and Chlamydia.
- Vesicles should be tested for HSV.
- All postmenarchal 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 (if prenatal transmission excluded for the STDs) makes sexual abuse a near medical certainty.

Imaging

None needed unless physical abuse is suspected

Diagnostic Procedures/Surgery

Consider exam under anesthesia.

DIFFERENTIAL DIAGNOSIS

- Accidental trauma (straddle injuries, toilet-lid injury to penis, masturbation injuries)
- Anal fissure
- Hemangioma
- Hematochezia
- Henoch-Schönlein purpura
- Lichen planus
- Nonspecific vaginitis
- Normal anatomic variants (perihymenal bands, prominent linea vestibularis)
- Physical abuse
- Poor hygiene
- Urethral prolapse

- Vaginitis
- Vaginal foreign body

TREATMENT

- Mental health evaluation is essential
- Acute evaluation and treatment of injuries

MEDICATION

Varies with presentation:

- Pain medication as appropriate
- PEP for prevention of pregnancy and STDs should be offered to adolescents.
- PEP generally not indicated for prepubertal children

SURGERY/OTHER PROCEDURES

- Consider exam under anesthesia
- Depends upon findings/injuries

ADDITIONAL TREATMENT

Possible pregnancy should be discussed with the pubertal child

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
  - Suicidal behaviors
  - Self-injury
- Pregnancy
- STDs

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up exams for healing of injuries
- Evaluation for development of STDs
- Emotional support/therapy

ADDITIONAL READING

- Adams J, et al. Guidelines for medical care of children who may have been sexually abused. J Pediat Adolesc Gynecol 2007;20(3):163–172.
- American Academy of Pediatrics. Guidelines for the evaluation of sexual abuse of children: Subject review. American Academy of Pediatrics Committee on Child Abuse and Neglect. Pediatrics 1999;103(1):186–191.
- Bernard D, et al. The evaluation of suspected pediatric sexual abuse. Clin Pediat Emerg Med 2006;7:161–169.
- Kellogg N, et al. The evaluation of sexual abuse in children; American Academy of Pediatrics Clinical report. Pediatrics 2005;116(2):506–512.

See Also (Topic, Algorithm, Electronic Media Element)

Scrotum and Testicle, Trauma

CODES

ICD9

995.53 Child sexual abuse

ABBREVIATIONS

- DRE: Digital rectal exam
- HIV: Human immunodeficiency virus
- HSV: Herpes simplex virus
- PEP: Postexposure prophylaxis
- STD: Sexually transmitted disease

SEXUAL DYSFUNCTION, FEMALE

Anil A. Thomas, MD
Sandip P. Vasavada, MD

BASICS

DESCRIPTION

- A disorder of sexual functioning involving sexual desire, orgasm, arousal, or sexual pain that results in significant personal distress
- Includes:
  - Hypoactive sexual desire disorder
  - Sexual aversion disorder
  - Female arousal disorder
  - Female orgasmic disorder
  - Dyspareunia
  - Vaginismus
  - DSM-IV defines FOD (formerly, inhibited female orgasm) as persistent or recurrent delay in, or absence of, orgasm following a normal sexual excitement phase.

EPIDEMIOLOGY

20–50% of adult women

RISK FACTORS

- Age
- Cardiovascular disease
- Depression, alcoholism, or drug abuse
- Diabetes mellitus
- Hyperlipidemia
- HTN
- Menopause
- Pelvic trauma, radiation, or surgery
- SCI

GENERAL PREVENTION

- Lifestyle modification to reduce cardiovascular disease or psychosocial stressors
- Improvements in surgical technique during pelvic surgery have lessened damage to nerves important in sexual arousal.

PATHOPHYSIOLOGY

- Multifactorial etiology
- Vascular causes: Vascular insufficiency often secondary to atherosclerosis, causes diminished genital blood flow leading to vaginal and clitoral smooth muscle fibrosis.

- Hormonal influences: Estrogen plays a significant role in regulating sexual function and maintains the vaginal mucosal epithelium and lubrication. Testosterone is the predominant female androgen that also supports sexual arousal and libido. Low estrogen or testosterone levels are associated with sexual dysfunction.
- Neurogenic causes: SCI or disruption of the sacral reflex arcs interfere with vaginal sensation or the ability to reach orgasm.
- Psychogenic causes: Emotional issues or psychological stressors such as depression, fatigue, or sexual abuse can negatively affect the female sexual response.
- Iatrogenic:
  - Various medications such as antidepressants can decrease sexual desire and function.
  - Prior pelvic surgery such as hysterectomy or cystectomy can disrupt the autonomic pelvic nerve plexus, thus contributing to sexual dysfunction.

COMMONLY ASSOCIATED CONDITIONS

- Depression
- Urinary incontinence
- Interstitial cystitis
- Menopause
- Multiple sclerosis

DIAGNOSIS

HISTORY

- Age: Higher prevalence of sexual dysfunction in older women:
  - Physical and psychological factors associated with aging affect sexual desire and response.
  - Decreased estrogen and testosterone after menopause decreases libido and promotes vaginal dryness and atrophy.
- Self-administered, validated questionnaires such as the FSFI are useful objective tools to assess sexual function.
- Childbirth: Short-term sexual dysfunction is common postpartum (22–86%), with loss of desire and dyspareunia.
- Past medical history:
  - HTN, hyperlipidemia, or diabetes mellitus.
  - Thyroid disorders can also affect sexual function.
  - Previous history of endometriosis, infections, or tumors should also be elucidated.
- Past surgical history: Previous pelvic trauma, pelvic surgery, or radiation

- Medications:
  - Antidepressants such as SSRIs or tricyclics can decrease libido.
  - Oral contraceptives and tamoxifen can interfere with testosterone binding.
  - Spironolactone or ketoconazole have antiandrogen properties.
  - Antihypertensives and chemotherapeutic agents can also contribute to female sexual dysfunction.
- Social history: Alcohol or drug abuse; pertinent psychosocial factors or interpersonal relationships are also important

PHYSICAL EXAM

A thorough physical and pelvic exam:

- Assess for vaginal atrophy and genital/perineal sensation.
- If neurologic signs are present, a more detailed neurologic assessment is then warranted.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Basic chemistry panel, CBC, TSH, and lipid profile to help identify chronic medical conditions, renal failure, diabetes, or hyperlipidemia
- Hormonal profile:
  - Serum total and free testosterone
  - Estradiol level
  - LH, FSH, prolactin
  - SHBG

Imaging

Vaginal plethysmography or duplex US can be used to measure genital blood flow.

Diagnostic Procedures/Surgery

Genital vibratory sensation threshold testing, genital temperature sensation, and the bulbocavernous reflex can be evaluated to help rule out associated neurologic dysfunction.

DIFFERENTIAL DIAGNOSIS

- Psychological disorders related to anxiety or depression
- Chronic pelvic pain syndrome or interstitial cystitis

TREATMENT

- Attempt to identify a correctable cause.
- Exercise and pelvic floor training can improve sexual function.
- Treat prolapse and incontinence in affected patients, as female sexual dysfunction may be in part related to inhibition due to leakage during sexual relations.

MEDICATION

- HRT is the mainstay of treatment in postmenopausal or oophorectomized women.
- Oral estrogen or topical vaginal estrogen may improve libido and ameliorate symptoms of dryness or irritation.
- 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.

SURGERY/OTHER PROCEDURES

InterStim therapy is currently under investigation to treat sexual arousal disorders.

ADDITIONAL TREATMENT

- Eros Clitoral 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 the treatment of female sexual dysfunction:
  - PDE5 inhibitors are thought to enhance vaginal lubrication and engorgement in postmenopausal women; however, the benefit is not well established.
  - -Adrenergic antagonists such as phentolamine and yohimbine produce vasodilation of the smooth muscle, increasing genital blood flow and lubrication.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Education, sex therapy, psychotherapy, and cognitive behavioral therapy are also important in the multidisciplinary management of sexual dysfunction.
- 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 regarding its risks and benefits.

ADDITIONAL READING

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR, 4th ed., Text Revision. Washington DC: American Psychiatric Association; 2000.
- Basson R, Berman J, Burnett A, et al. Report of the international consensus development conference on female sexual dysfunction: Definitions and classifications. J Urol 2000;163:888–893.

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• Berman LA, McLean KA. Female sexual dysfunction: effective treatment strategies for all ages. In: Culligan PJ, Goldberg RP, eds. Urogynecology in Primary Care, 1st ed. London: Springer London, 2007.

• Mayer ME, Bauer RM, Schorsch I, et al. Female sexual dysfunction: What's new? Curr Opin Obstet Gynecol 2007;19:536–540.

See Also (Topic, Algorithm, Electronic Media Element)

- Dyspareunia
- Female Hypoactive Sexual Desire Disorder
- Pelvic Pain, Female
- Vaginal Atrophy, Urologic Considerations

CODES

ICD9

- 302.70 Psychosexual dysfunction, unspecified
- 302.71 Hypoactive sexual desire disorder
- 302.72 Psychosexual dysfunction with inhibited sexual excitement

ABBREVIATIONS

- CBC: Complete blood count
- DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
- FDA: Food and Drug Administration
- FOD: Female orgasmic disorder
- FSH: Follicle-stimulating hormone
- FSFI: Female Sexual Function Index
- HTN: Hypertension
- HRT: Hormone replacement therapy
- LH: Luteinizing hormone
- PDE5: Phosphodiesterase type 5
- SCI: Spinal cord injury
- SHBG: Sex hormone-binding globulin
- SSRI: Selective seratonin reuptake inhibitor
- TSH: Thyroid-stimulating hormone
- US: Ultrasound

SEXUALLY TRANSMITTED DISEASES (STD), GENERAL

J. Nathaniel Hamilton, MD
Matthew R. Eskridge, MD

BASICS

DESCRIPTION

A disease with a predominantly sexual mode of transmission; however, intercourse is not always necessary for transmission

EPIDEMIOLOGY

- 15–19 million new US cases annually
- 65 million in America with incurable viral STDs:
  - 1 in 4 females between the ages of 14–19 affected with an STD
  - 50% of all cases reportable disease to CDC are STDs.

RISK FACTORS

Female gender, multiple sex partners, infected partner, low socio-economic status, unprotected intercourse, age 18–28, history of previous STD or current STD

GENERAL PREVENTION

- Abstinence
- Long-term, mutually monogamous relationship with both partners tested and negative for STD
- Male and female condoms
- Diaphragms can reduce cervical Chlamydia, gonorrhea, and trichomoniasis; not HIV
- Multivalent vaccination against HPV

PATHOPHYSIOLOGY

- Ulcerative lesions (HSV, types 1 and 2):
  - Type 2: 85–90% of genital cases
  - Type 1: 10–15% usually oral to genital contact
  - Initial infection: Painful ulcers of genitals or anus and painful inguinal adenopathy bilaterally
  - Classic lesion is vesicles on an erythematous base that does not follow nerve distribution
  - Can present with flu-like prodrome
- Ulcerative lesions (chancroid; Haemophilus ducreyi):
  - More common in men (3:1); painful ulcer with friable base and purulent discharge
  - Tender unilateral adenopathy and suppurative with fistula formation to the skin
- Ulcerative lesions (syphilis; spirochete Treponema pallidum):

– Primary syphilis presents with a single painless ulcer that can remain for 4–6 wk:

Can have bilateral nontender inguinal lymphadenopathy

– If untreated, 2–4 mo after primary infection secondary syphilis ensues.

– Secondary syphilis: Maculopapular rash on body and arms; generalized nontender lymphadenopathy:

Rash: Palms of hands and soles of feet

– If untreated, ~1/3 of patients will progress to tertiary syphilis, which can take months to years.

Tertiary syphilis can affect any organ and can lead to aortitis, eye involvement, meningitis, spinal column (tabes dorsalis), and skin gumma formation.

- Ulcerative lesions (granuloma inguinale; Donovanosis):
  - Klebsiella granulomatis
  - Painless ulcerative lesions without lymphadenopathy; tend to be hypervascular
- Ulcerative lesions (LGV; caused by C. trachomatis serovars L1, L2, or L3):
  - Can present with a transient genital ulcer
  - Usually has tender inguinal/femoral lymphadenopathy, typically unilateral
  - If not treated promptly, LGV can lead to an invasive systemic infection, lead to secondary bacterial infection in the lesion, and form stricture or fistulas.
- Urethritis and cervicitis (Chlamydia trachomatis):
  - Most common STD
  - Asymptomatic infection is common:

    Annual screening of all sexually active women aged 25 yr is recommended

    ~1/2 of men have symptoms

    Lower urinary tract symptoms of urethritis, epididymitis (most common cause in young males), or prostatitis

    Can have a clear or white urethral discharge
  - 25% of women are symptomatic, and can have a mucopurulent cervical discharge.
  - 40% of untreated women will develop PID:

    Ascending reproductive tract infection that can damage reproductive structures with chronic inflammation and scar tissue formation which may lead to infertility, chronic pelvic pain, ectopic pregnancy, or abscess
- Urethritis and cervicitis (gonorrhea; Neisseria gonorrhoeae):
  - Men will have lower urinary tract symptoms of urethritis, epididymitis, proctitis, or prostatitis.
  - Mucopurulent discharge

– Women are usually asymptomatic but can have vaginal or pelvic discomfort or dysuria.

– Asymptomatic infection is common:

Annual screening of all sexually active women aged 25 yr is recommended.

- Vaginal discharge (trichomoniasis):
  - Infection with protozoan Trichomonas vaginalis
  - Men may have urethritis but are often asymptomatic.
  - Women may have symptoms with a diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation; can be asymptomatic.
- Other: Genital warts (condylomata acuminata caused by HPV):
  - Virus spread by direct skin-to-skin contact
  - 30 subtypes known to affect genital region but 6, 11 tend to cause genital warts and 16, 18, 31, 33, and 35 are high risk for cellular dysplasia and increase cancer risk.
  - Most infections are asymptomatic and resolve spontaneously.
- Other: Pubic lice (Phthirus pubis; crab louse):
  - Itching at infection site or patients notice lice or nits (eggs); maculopapular rash may be present
- Other: Scabies (Sarcoptes scabiei):
  - Mite infestation; severe itching at night

COMMONLY ASSOCIATED CONDITIONS

- Co-infection with 1 other STD
- Genital (cervical, vulvar, penile) and anal carcinoma
- HIV
- PID (see above)
- Reiter syndrome.
- Septic arthritis: Disseminated gonococcal infection

DIAGNOSIS

HISTORY

- Symptoms, duration, onset, quality, severity, related conditions:
  - Lesions on genitals or perineal area
  - Urethral discharge, dysuria, dyspareunia, rectal discomfort or pelvic pain
- Screen for other high-risk behaviors such as drug use and binge drinking
- Specific sexual history:
  - Ask questions in nonjudgmental manner
  - History of STD

- Type and number of partners
- Use of protection

Pediatric Considerations

When considering the diagnosis of an STD in a child, rule out sexual abuse.

PHYSICAL EXAM

- Fever and skin exam for rash
- Abdominal tenderness, rebound, or guarding
- Inguinal adenopathy
- Examine the genitalia for ulceration, vesicles, urethral discharge
- Anal region for lesions such as warts
- Pelvic exam for uterine tenderness or cervicitis
- Neurologic exam for tertiary syphilis (tabes dorsalis, Argyll-Robertson pupil, etc.)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- HSV:
  - Growth of HSV in culture with serologic subtyping is gold standard.
  - PCR assays for HSV DNA are available though not FDA approved for genital HSV.
  - Cytologic detection (Tzanck smear) is not very sensitive and should not be relied upon.
- Chancroid:
  - H. ducreyi can be grown on culture, although sensitivity is <80%.
  - PCR is available, but not FDA approved.
- Syphilis:
  - Definitive diagnosis is based on darkfield microscopy of lesion exudate or DFA.
  - Presumptive diagnosis is based on serology:

    RPR

    Sensitivity is ~80% in primary syphilis, 100% in secondary, and over 95% in tertiary syphilis.

    Reflects disease activity; should be negative after 1 yr of treatment

    If positive, confirm by Treponemal testing:

    FTA-ABS and TP-PA; positive for life after initial infection
- Granuloma inguinale:
  - Difficult to culture; requires visualization of dark-staining Donovan bodies in sample
- Lymphogranuloma venereum:

– Swabbing of lesions or aspiration of nodes can be cultured for C. trachomatis or have direct immunofluorescence

- Chlamydia:
  – Urine or cervical, vaginal, urethral, or anal swab specimens:
    Cultured for C. trachomatis
    Direct immunofluorescence
    For urine, NAATs are the most sensitive tests and are FDA approved.
- Gonorrhea:
  – Culture and sensitivity of urethral or endocervical swab (in females)
  – NAAT can be performed on urine.
- Trichomoniasis:
  – Wet prep for flagellated protozoans
  – In men, wet preparation is not sensitive; therefore culture of urethral swab, urine, or semen is required for diagnosis.
- Genital warts: Detection of viral nucleic acid or capsid protein on cellular analysis
- Pubic lice: Seen on low-power microscopy

Diagnostic Procedures/Surgery

HPV: Aceto-white test for occult disease:

- Application of 3–5% acetic acid usually turns HPV-infected genital mucosal tissue to a whitish color.
- Sensitivity and specificity has not been determined; some question utility.

Pathological Findings

See “Lab” section.

DIFFERENTIAL DIAGNOSIS

- STD genital ulcer mnemonic CHISEL:
  – Chancroid (painful)
  – Herpes genitalis (painful)
  – Inguinale (granuloma inguinale)
  – Syphilis (early not painful)
  – Eruption secondary to drugs
  – Lymphogranuloma venereum
- Other causes of genital ulcers:
  – Behçet disease
  – Excoriations
  – Fixed drug eruption

- Genital trauma
- Pyoderma
- Scabies (Sarcoptes scabiei)
- Yeast

- Other nonulcerative STDs:
  - PID: C. trachomatis, N. gonorrhea, Mycoplasma hominis, facultative or anaerobic organisms
  - Syphilis (secondary/tertiary)
  - HIV
  - Hepatitis B and C
- STD with urethral discharge:
  - Gonorrhea
  - Nongonococcal urethritis: C. trachomatis (35–45%), Ureaplasma urealyticum (15–25%), Trichomonas vaginalis

TREATMENT

- Screen for coinfection (including HIV).
- Screen for disease in sexual partners.
- Educate for prevention of transmission.
- Pre-exposure vaccination (HPV)

MEDICATION

First Line

- HSV: Acyclovir 400 mg PO t.i.d. for 7–10 days, or famciclovir 250 mg PO t.i.d. for 7–10 days, or valacyclovir 1 g PO b.i.d. for 7–10 days
- Chancroid: Azithromycin 1 g PO in 1 dose or ceftriaxone 250 mg IM in 1 dose
- Syphilis:
  - Primary: Benzthiazide penicillin G 2.4 million units IM in 1 dose
  - Latent: Repeat benzthiazide penicillin G 2.4 million units IM weekly for 4 weeks
  - Tertiary: Aqueous crystalline penicillin G, 3–4 million units IV q4h for 10–14 days
- Granuloma inguinale: Doxycycline 100 mg PO b.i.d. for 21 days or until all lesions are healed
- Lymphogranuloma venereum: Doxycycline 100 mg PO b.i.d. for 21 days
- Chlamydia: Azithromycin 1 g PO in 1 dose or doxycycline 100 mg PO b.i.d. for 7 days
- Gonorrhea: Ceftriaxone 125 mg IM in 1 dose, or cefixime 400 mg PO in 1 dose; also treat for Chlamydia
- Trichomoniasis: Metronidazole 2 g PO in 1 dose

- Genital warts:
  - Observation usually successful
  - Podofilox 0.5% solution or gel (lesion <10 cm) q12h for 3 days then off for 4 days; cycle may be repeated 4 times
- Pubic lice: Permethrin cream (5%) to affected areas and washed off within 10 min

Second Line

Please refer to the CDC's published Sexually Transmitted Diseases Treatment Guidelines 2006 with updates at http://www.cdc.gov/std/treatment/2006/toc.htm

SURGERY/OTHER PROCEDURES

PID may require surgical intervention.

ONGOING CARE

PROGNOSIS

Most STDs have excellent prognosis with appropriate and timely treatment:

- There is a high risk for reinfection

COMPLICATIONS

- Cancer of genital tract or anus, PID, infertility
- Neurologic disease

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Compliance is often an issue.
- Periodic follow-up is recommended.

ADDITIONAL READING

Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006. MMWR 2006;55 (No. RR-11). Available at http://www.cdc.gov

See Also (Topic, Algorithm, Electronic Media Element)

Sections I and II individual topics

CODES

ICD9

- 042 Human immunodeficiency virus (HIV) disease
- 054.10 Genital herpes, unspecified
- 078.19 Other specified viral warts

ABBREVIATIONS

- CDC: Centers for Disease Control and Prevention
- DFA: Direct fluorescent antibody
- FDA: Food and Drug Administration

- FTA-ABS: Fluorescent treponemal antibody absorbed
- HIV: Human immunodeficiency virus
- HPV: Human papilloma virus
- HSV: Herpes simplex virus
- IV: Intravenous
- LGV: Lymphogranuloma venereum
- NAATs: Nucleic acid amplification tests
- PCR: Polymerase chain reaction
- PID: Pelvic inflammatory disease
- RPR: Rapid plasma reagin
- STD: Sexually transmitted disease
- TP-PA: T. pallidum particle agglutination

SICKLE CELL DISEASE, UROLOGIC CONSIDERATIONS

Benjamin R. Lee, MD
Gordon L. Fifer, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- SC disease is a chronic hemoglobinopathy transmitted genetically and marked by severe chronic hemolytic anemia and periodic acute painful episodes.
- The heterozygote is termed sickle cell trait and usually has no symptoms.
- Major GU complications can include priapism and a spectrum of renal disorders from hematuria and decreased renal concentrating ability through renal medullary carcinoma and renal failure.

EPIDEMIOLOGY

- 1:500 African American births and 1:1,000 Hispanic American births
- 2 million Americans, or 1 in 12 African Americans, carry the sickle cell trait.
- ~4,000–5,000 pregnancies are at risk of SC disease.
- Life expectancy: Men, 42 yr; women, 48 yr
- Prevalence estimated at 8% of African Americans
- 8–10% of African Americans have SC trait.
- 25–30% of Western Africans have SC trait

RISK FACTORS

Family history of disease

Genetics

- Autosomal codominant inheritance pattern
- Allele is on chromosome 11.
- Several haplotypes; allelic with -thalassemia
- SC disease: Inheritance of 2 alleles, all RBCs contain HbS
- SC trait: From 1 allele, 40% of Hb is HbS

GENERAL PREVENTION

Avoid situations that precipitate sickling episodes (dehydration, hypoxia, cold, infections, fever, acidosis).

PATHOPHYSIOLOGY

- Sickling of RBCs caused by HbS in ischemic state leading to vaso-occlusive state and causing most complications of SC disease:
  - Substitution of valine for glutamate at 6th amino acid position

– HbS tetramer: The deoxygenated state polymerizes into double-stranded filaments and bundles.
– Chronic anemia is the hallmark of the disease; RBC mean lifespan: 17 days
– SC trait (heterozygote) usually asymptomatic

- Decreased renal concentrating ability is common and results in polyuria and nocturia.
- Hematuria is due to chronic papillary infarctions:
  – Predominantly left-sided
- Renal infarction due to ischemia; may present with nausea, vomiting, abdominal and flank pain, and HTN
- Renal papillary necrosis due to ischemia; may cause secondary infection or obstruction
- Progressive renal failure and proteinuria due to glomerular injury; renal failure in ~10%
- Renal medullary carcinoma:
  – An aggressive malignancy
  – Almost exclusively found in young African American patients with SC trait, or SC disease

COMMONLY ASSOCIATED CONDITIONS

- Acute papillary necrosis
- Anemia
- Hepatitis C and HIV (increased risk for these and other transfusion-associated infections)
- Priapism
- Renal medullary carcinoma

DIAGNOSIS

HISTORY

- Prior episodes of SC complications and outcomes
- Timing of sexual maturation
- Determine time length of any priapism episodes.
- Painful crisis brought on by cold or dehydration

PHYSICAL EXAM

- HTN is unusual.
- Look for staging of sexual maturation.
- Palpate testes in men to check for atrophy.
- In cases of priapism, examine the glans to determine bi- or tri-corporal involvement.
- Splenic sequestration causes painful enlargement of the spleen.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Degree of anemia
- Peripheral blood smear: Presence of sickled or deformed RBCs with high reticulocyte count
- Hb electrophoresis: Types and percentages of Hb present
- SC prep: Rapid determination of SC disease vs. trait vs. normal
- Urine analysis: Hematuria, proteinuria, or infection
- Urine culture: Infection if indicated by urine analysis or symptoms
- Creatinine
- Monitor for renal insufficiency, and calculate GFR as needed. The creatinine clearance may overestimate the GFR.
- Hyperphosphatemia may be present
- ABG on corporal blood aspirates in priapism setting to assess high- vs. low-flow state:
  - pH <7.10 (acidotic) suggests a low-flow state.

Imaging

- CT urogram as indicated for hematuria:
  - May not be useful in progressive renal insufficiency (poor concentrating ability limits visualization)
  - Papillary necrosis may be present.
- Renal medullary carcinoma may present as a centrally located infiltrative lesion invading the renal sinus with peripheral caliectasis.
- US: Noninvasive; look for renal source of hematuria if renal insufficiency precludes contrast use.

Diagnostic Procedures/Surgery

- Cystoscopy: As needed for hematuria
- Retrograde pyelograms: Upper-tract sources of bleeding if IVP limited or suspect papillary necrosis
- Ureteroscopy: For hematuria as indicated
- Renal biopsy: As needed for specific glomerulopathies
- Impotence evaluation by nocturnal penile tumescence testing is rarely useful as an additive beyond the information gained by history and physical exam.

Pathological Findings

- Peripheral blood smear: Presence of sickled or deformed RBCs
- Hb electrophoresis: Types and percentage of Hb present
- Renal biopsy:

– Early: Glomerular hypertrophy, hemosiderin deposits, focal areas of hemorrhage or necrosis

– Late: Interstitial inflammation, edema, fibrosis, tubular atrophy, and papillary infarcts

DIFFERENTIAL DIAGNOSIS

- Other SC diseases: SC trait, sickle- thalassemia, etc.
- Hematuria (see Section I topic)
- Papillary necrosis (see Section I topic)
- Priapism (see Section I topic)

TREATMENT

For acute SC crisis:

- Oxygenation, nasal canula
- Aggressive hydration: Counters dehydration, increases perfusion, and improves blood rheology
- Metabolic alkalinization limits further sickling
- Pain control
- Narcotics for pain: Risk of addiction is negligible in the acute setting; PCA for inpatients

MEDICATION

- Simple transfusion:
  - Increases proportion of RBCs with normal Hb to decrease SC sludging
  - Indications: Acutely (priapism, life-threatening hemorrhage) and preoperatively if indicated by procedure
- Exchange transfusion:
  - Indications as for simple transfusion
  - Used when needed to remove RBCs and replace with transfused blood products if simple transfusion fails
  - Risk of cerebrovascular accidents with increased hematocrit, causing a relative hyperviscosity (ASPEN syndrome)
- Antibiotics:
  - As needed for infections
- Hematuria:
  - Diuresis with IV hydration is standard.
  - Alkalization decreases sickling and hematuria.
  - Aminocaproic acid is used to induce thrombosis and control persistent and threatening hematuria, but can cause clot formation in the urinary tract.

– Persistent or life-threatening hematuria may rarely necessitate nephrectomy.
– High-dose urea in selected cases

- Priapism (see Section I):

– Prompt corporal irrigation is important to induce detumescence and remove old clotted blood.
– Use -adrenergic agents for corporal injection to decrease inflow to corpora, aiding in detumescence.
– Impotence due to fibrosis as a complication can be managed by implantation of penile prosthesis after the process stabilizes for 6 mo.

- Delayed sexual maturation:

– Gonadotropic supplementation by testosterone used, as needed, to induce sexual characteristics; may improve fertility in select patients.

SURGERY/OTHER PROCEDURES

May be needed for priapism or urinary tract obstruction due to sloughed papilla

ADDITIONAL TREATMENT

- Hydroxyurea
- Bone marrow transplants
- Folic acid and penicillin in pediatrics
- Genetic counseling

ONGOING CARE

PROGNOSIS

Several factors aside from genetic inheritance determine prognosis, including frequency, severity, and nature of specific complications.

ALERT

- Risk of hyperkalemia with -blockers, captopril, or K-sparing diuretics

COMPLICATIONS

- Nephropathy:

– Renal insufficiency
– Vaso-occlusion in renal medulla secondary to hypertonicity, inducing HbS sickling
– Progressive cortical infarction leads to CRF; average age of onset is 23 yr
– Hyposthenuria: Inability to maximally concentrate urine in the face of dehydration or vasopressin
– Usually associated with renal insufficiency; able to dilute urine
– Associated impairment of K excretion
– Renal biopsy: Focal and segmental glomerulosclerosis, membranous glomerulopathy, or MPGN

– Proteinuria can progress to full-blown nephrotic syndrome.

- Hematuria:
  – Microscopic or gross hematuria; mechanism unknown. Source rarely identified; ? due to papillary necrosis
  – Usually unilateral (left-sided)
  – Male > Female
  – Usually remits with conservative measures (eg, bedrest, hydration) but recurrence noted in ~50% of cases
- Papillary necrosis:
  – Due to medullary ischemia from sickling in vasa recta
  – Radiologic diagnosis with contrast can be difficult due to poor concentrating ability of kidneys from renal insufficiency.
  – Can be cause of hematuria; essential to rule out this entity in settings of hematuria in sickle patients.
  – Can obstruct if sloughed papillae block the UPJ
- Priapism:
  – Affects ~66% of SC disease patients
  – 2 age peaks; onset usually after puberty
    5–13 yr, then at 21–29 yr
    Initiating factors: Nocturnal penile tumescence and sexual arousal
    Typically, bicorporal involvement
    Pathophysiology: Engorgement and sludging of the corpora, with no outflow and low-flow state
    Major risk is fibrosis and subsequent impotence; children have greater chance of recovery and subsequent erectile function.
- Impotence:
  – Fibrosis as result of recurrent episodes of priapism
- Retarded sexual maturation:
  – Primary hypogonadism, due to testicular ischemia or infarction, hypopituitarism, or hypothalamic insufficiency
  – Correlates with severity of sickle disease
- Infertility:
  – Complication of hypogonadism and direct testicular insult by ischemia and infarction
- UTI:

- Usually Escherichia coli, or other gram-negative bacteria
- Can lead to more serious infections or bacteremia

• RTA:
- Incomplete distal RTA (type IV) from progressive medullary infarction
- Inability to lower urine pH to <5
- Can develop hyperchloremic metabolic acidosis in SC disease and renal insufficiency
- Not associated with nephrolithiasis

• 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 RECOMMENDATIONS

Patient Monitoring

Renal function over time

ADDITIONAL READING

• Advances in clinical research in sickle cell disease. Br J Haematol 2008;141(3):346–356.

• Health-related quality of life in sickle cell disease. Pediatr Blood Cancer 2008;51(1):5–9.

• National Institutes of Health Consensus Development Conference statement. Ann Intern Med 2008;148(12):932–938.

See Also (Topic, Algorithm, Electronic Media Element)

• Papillary Necrosis, Renal

• Priapism

• Renal Medullary Carcinoma (Renomedullary Interstitial Cell Tumor)

CODES

ICD9

• 282.5 Sickle-cell trait

• 282.60 Sickle-cell disease, unspecified

ABBREVIATIONS

• ABG: Arterial blood gas

• ASPEN: Association of sickle cell disease, priapism, exchange transfusion, and neurologic events

- CBC: Complete blood count
- CRF: Chronic renal failure
- CT: Computed tomography
- GFR: Glomerular filtration rate
- GU: Genitourinary
- Hb: Hemoglobin
- HIV: Human immunodeficiency virus
- HTN: Hypertension
- IV: Intravenous
- IVP: Intravenous pyelogram
- K: Potassium
- MPGN: Membranoproliferative glomerulonephritis
- PCA: Patient-controlled analgesia
- RBC: Red blood cell
- RTA: Renal tubular acidosis
- SC: Sickle cell
- UPJ: Ureteral pelvic junction
- US: Ultrasound
- UTI: Urinary tract infection

SPERMATIC CORD MASS AND TUMORS

Cory A. Chevalier, BS, MSII
Gabriel P. Haas, MD

BASICS

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 vas deferens, pampiniform plexus, lymphatics, nerves, investing layer of fascia, and cremaster muscle.
- Considered paratesticular tissue
- Masses or swelling can be cystic or solid:
  - Most cystic (70–75%)
  - Most benign (75–80%)
  - Usually asymptomatic
  - Most solid spermatic cord masses are benign.

EPIDEMIOLOGY

See “Pathophysiology.”

RISK FACTORS

Prematurity may increase risk of congenital hernia and hydrocele or undescended testicle.

PATHOPHYSIOLOGY

- Cord mass can arise from cord contents or from structures above or below the cord.
- Generally nonacute
- Malignant tumors rare; most are sarcoma
- Varicocele:
  - Enlarged, tortuous spermatic vein above the testis; almost always occurs on the left side
  - Asymptomatic, often found on routine exam
  - Grade I: Palpable with Valsalva
  - Grade II: Palpable without Valsalva
  - Grade III: Visible
  - May cause infertility; likely increasing scrotal temperature, inhibiting spermatogenesis
- Hydrocele:
  - Incomplete obliteration of processus vaginalis can result in collection of fluid between the tunica vaginalis and the testis.

– Usually manifested as painless groin mass contiguous with the cord structures.
– Communicating hydrocele with hernia
– Congenital; seen in early adolescence
– Persistence of processus vaginalis allows peritoneal fluid to freely communicate with the scrotal limits; inguinal hernia results if communication with peritoneal cavity is large; narrow communicating channel results in hydrocele.
– May have associated inguinal hernia (usually children)

- Spermatic cord hydrocele:
  – Loculated fluid collection along the spermatic cord, separated from and located above the testicle and the epididymis
  – Rare congenital anomaly that results from an abnormal closure of the processus vaginalis; 2 types recognized:

Encysted hydrocele of the cord: The fluid collection does not communicate with the peritoneum or the tunica vaginalis.

Funicular hydrocele of the cord: A fluid collection along the cord, communicating with the peritoneum at the internal ring

- Spermatocele:
  – Cloudy fluid and sperm-filled cyst arising from epididymal tubules; usually at head of epididymis
  – Usually asymptomatic; incidental finding
- Inguinal hernia in adults:
  – Late-onset communicating hernia in adults
  – Direct through floor of inguinal canal
  – Indirect presents as mass in inguinal cord or extends through external ring into scrotum
- Lipoma of the cord:
  – Benign; most common tumor of the cord and paratesticular tissues
  – From adipose tissue of the cord; fat collections around hernia sac not true lipomas
- Adenomatoid tumor:
  – Benign neoplasms; most common epididymal tumor; no reliable echo pattern for diagnosis and can involve the spermatic cord
- Sarcomas:
  – Rare lesions of spermatic cord, epididymis, and paratesticular soft tissue, from muscle, adipose, or connective tissue
  – Incidence peaks: Adolescence and >40.

- Rhabdomyosarcoma and leiomyosarcoma most common

- Other malignant tumors of spermatic cord:
  - Melanoma and metastatic cancers are rare.
- TB of spermatic cord:
  - Rare; 70% of cases have history of TB; usually in young, sexually active males
  - Presents as TB epididymitis; difficult to differentiate from acute epididymo-orchitis
  - Usually secondary to infection of epididymis via direct extension
- Sarcoidosis:
  - Systemic granulomatous disease; increased intestinal adsorption of calcium; hypercalcemia and hypercalciuria
- Funiculitis:
  - Inflammation of spermatic cord secondary to severe epididymitis or due to trauma
- Filarial hydroceles:
  - Caused by Wuchereria bancrofti; often have a thickened spermatic cord and epididymis
- Undescended testicle
- Retractile testicle

COMMONLY ASSOCIATED CONDITIONS

- Renal tumor invading renal vein or retroperitoneal mass compressing right gonadal vein with acute onset of right varicocele
- TB with spermatic cord involvement
- Filariasis

DIAGNOSIS

HISTORY

- Patients present with symptomatic (pain) or asymptomatic mass with or without swelling:
  - Rule out torsion of cord if pain is acute.
  - Most masses are painless at onset.
  - Pain may be associated with malignant or inflammatory lesion or expanding cystic lesion (size related to discomfort).
  - Presence or absence of pain does not differentiate benign or malignant mass.
  - Sudden-onset is nonspecific; most masses have history of several years; acute onset of pain if rapid increase in size (uncommon).
  - Slow size increase can cause heavy dragging sensation or dull ache.
  - Scrotal elevation may provide relief.

– Sarcomas often reoccur after surgery.

- Alleviating factors:

– Recumbant position may resolve mass and pain in varicocele and communicating hydrocele.

- History of cryptorchidism

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 thumb and 1st 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 palpitation.
- 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.
- Valsalva maneuver performed with patient in supine and prone positions for varicocele or hernia:

– Varicocele best palpated with Valsalva in standing position as a painless or tender mass of veins (bag of worms); may compress in supine position, resulting in missed cases

– Usually palpable posterior to and above the testicle

– Crucial to assess testicular volume and consistency in boys with varicocele

– The ipsilateral testis may be atrophic.

– Palpation can determine superior and inferior extent of mass (unlike inguinal hernia).

– Can mimic solid mass

- Communicating hydrocele:

– Enlarges when upright and with activities that increase intra-abdominal pressure.

– Supine position drains fluid into peritoneal cavity and decreases size.

– Bowel sounds over mass if associated with hernia; small intestine, omentum, bladder, or genital contents may be found in hernia sac:

Proximal limit not palpable since contents extend through inguinal ring

- Adult inguinal hernia:

– May be direct or indirect, reducible or incarcerated

– Superior extent of the mass not palpable
– May have bowel sounds over the mass
– Attempt to reduce hernia with gentle pressure in supine or Trendelenburg position.
– After reduction, insert finger through external ring into inguinal canal.
– Cough or Valsalva maneuver produces impulse, caused by abdominal contents felt at fingertip.

- Lipoma of the cord is palpated as smooth, firm mass in inguinal canal or upper scrotum:
  – Nontender; does not transilluminate
  – Usually incidental finding during inguinal procedures; may be overlooked in laparoscopic hernia repair
  – Can be sole cause of hernia symptoms
  – Occasional source of groin pain with no physical findings
- Adenomatoid tumors found on routine exam:
  – Painless, well-circumscribed, hard; nearly 1/2 at the head of the epididymis
- Sarcomas present as firm to hard mass, occasionally tender:
  – May be distinct and well-circumscribed or invade surrounding tissues
  – Explore all solid masses for malignancy:
    No signs or symptoms distinguish between benign or malignant solid mass.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Urine analysis to rule out epididymitis

Imaging

- Scrotal US: Solid vs. cystic mass
- Cannot differentiate benign or malignant mass
- Bowel can usually be identified in a hernia sac.
- Duplex Doppler for low-grade varicocele

Diagnostic Procedures/Surgery

Solid masses: Biopsy with surgical exposure

Pathological Findings

Distinguish leiomyosarcoma from leiomyoma based on occasional or absent mitotic figures and uniform cellular arrangement.

DIFFERENTIAL DIAGNOSIS

- Adenomatoid tumor of the cord
- Epidermoid cyst

- Epididymitis/epididymo-orchitis
- Fibrous pseudotumor
- Filarial hydroceles
- Funiculitis
- Hernia
- Hemangioma
- Hydrocele/hydrocele of the cord
- Inguinal lymphadenopathy
- Leiomyoma
- Malignant tumor: Liposarcoma, rhabdomyosarcoma, leiomyosarcoma, malignant fibrous histiocytoma
- Mesothelioma
- Metastatic: Melanoma and others
- Polyorchidism
- Sarcoid
- Sperm granuloma
- Spermatocele
- Testis tumor
- TB of the cord (tuberculoma)
- Undescended/retractile testicle
- Varicocele
- Vasitis and vasitis nodosa (usually associated with epididymitis)

ALERT

Torsion of the cord or incarcerated/strangulated hernia are surgical emergencies.

TREATMENT

- Distinguish testis and epididymis (physical exam, transillumination, scrotal US)
- Most cystic masses do not need treatment.
- Investigate pain as presenting feature; sarcoma is often misdiagnosed as inflammatory lesion.

MEDICATION

Anti-TB drug therapy for 6–9 mo for TB (tuberculoma) in spermatic cord

SURGERY/OTHER PROCEDURES

- Spermatocele: Excision if painful or continued enlargement
- Hydrocelectomy (only if large or symptomatic):
  - In children, repair hydrocele by age 2 if it does not resolve; usually associated with indirect hernia.

– Communicating hydrocele often spontaneously resolves in most children within 1st yr.

- Inguinal hernia (adults): Herniorrhaphy
- Communicating hydrocele with hernia:
  - Explore through inguinal incision.
  - Exploration of asymptomatic contralateral inguinal canal in children with inguinal hernia or communicating hydrocele is controversial.
  - Preserve testicular artery and vas deferens.
- Varicocele:
  - Varicocelectomy may relieve pain and improve fertility.
  - Standard testis volume measurements are mainstay of assessing need for surgical management of varicocele.
- Explore solid masses for malignancy:
  - Inguinal incision; testis is delivered
  - Early control of cord at internal ring
  - Biopsy to confirm diagnosis
- TB of cord: Excision of the mass
- Sarcoma: Radical orchiectomy with high ligation of the cord (wide resection margins if possible); possible flaps to reconstruct large anatomic defects

ADDITIONAL TREATMENT

Retroperitoneal lymphadenectomy with adjuvant radiation or chemotherapy for malignant tumor

ONGOING CARE

PROGNOSIS

Excellent for benign lesions

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- None for benign masses
- Liposarcoma and sarcoma has high local recurrence; closely monitor (exam, imaging)

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

Specific Section I and II topics

CODES

ICD9

- 187.6 Malignant neoplasm of spermatic cord
- 222.8 Benign neoplasm of other specified sites of male genital organs
- 456.4 Scrotal varices

ABBREVIATIONS

- TB: Tuberculosis
- US: Ultrasound

SPERMATOCELE

Irvin H. Hirsch, MD
Leonard G. Gomella, MD

BASICS

DESCRIPTION

- 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.
- 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:
  - 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

- Peak incidence in 4th–5th decades
- Rare in children
- No racial or ethnic predilection
- Reported in 30–70% of postpubertal males undergoing high-resolution scrotal US

RISK FACTORS

- DES exposure in utero
- Inflammation
- Not clearly related to prior vasectomy, prior epididymitis, or herniorrhaphy
- Trauma
- VHL syndrome

Genetics

VHL syndrome:

- Mutations of the VHL suppressor gene on 3p.
- Increased incidence of epididymal cysts and papillary cystadenomas of the epididymis

PATHOPHYSIOLOGY

- Main concern is usually that of confusion with a true testicular mass.

- Precise mechanism is unknown.
- Most are idiopathic.
- Trauma and inflammation may result in obstructed efferent ductules or epididymal tubules, resulting in a dilated spermatocele.
- No effect on fertility
- Most 1 cm in size

COMMONLY ASSOCIATED CONDITIONS

Epididymal obstruction may rarely be present.

DIAGNOSIS

HISTORY

- Typical presentation is a painless, asymptomatic, intra-scrotal mass found on testicular self-exam or on routine office exam.
- Occasionally may present with orchalgia or scrotal heaviness.
- No associated urinary symptoms

PHYSICAL EXAM

- Palpation shows a smooth, soft, spherical nontender mass at the head (caput) of the epididymis.
- Lies just superior and posterior to the testis but is distinct from testis.
- Cystic mass is usually demonstrated on scrotal transillumination.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis
- Urine culture
- Serum AFP, hCG, LDH to rule out testis tumor

Imaging

Scrotal US is diagnostic:

- Lesion is hypoechoic with posterior acoustic enhancement.
- May have internal echoes
- MRI if US is indeterminate

Diagnostic Procedures/Surgery

Needle aspiration for diagnosis is not usually indicated. If indicated, a 30-gauge needle can be used to aspirate the cyst fluid.

Pathological Findings

- Clear or opaque fluid-filled mass
- Fluid contains spermatozoa, lymphocytes, and cellular debris

- Fibromuscular wall lined by cuboidal epithelium

DIFFERENTIAL DIAGNOSIS

- Adenomatoid tumor of the epididymis:
  - Most common solid tumor of the epididymis
- Ectopic tissues:
  - Adrenal cortical rests
  - Spleno-gonadal fusion
- Epidermoid cyst
- Epididymal calcinosis
- Epididymitis:
  - Acute; very tender on exam
  - Chronic; may have secondary calcification
- Fibroma of epididymis
- Fibrous pseudotumor
- Funiculitis
- Hernia
- Hydrocele
- Hydrocele of the cord
- Leiomyoma
- Malignant epididymal tumor:
  - Primary (very rare): Liposarcoma, rhabdomyosarcoma, leiomyosarcoma, adenocarcinoma, lymphoma
  - Metastatic: Prostate, kidney, stomach most common
- Papillary cystadenoma:
  - 1/3 of all epididymal tumors
  - 2/3 associated with VHL syndrome
  - On US, most common appearance is 15–20-mm solid mass with small cystic components.
- Polyorchidism
- Sarcoid
- Sperm granuloma:
  - Seen in 40% post vasectomy or 2.5% idiopathic in general population
  - Granulomatous lesion with few giant cells
  - Consequence of extravasation of spermatozoa generally post vasectomy (of vasectomized men and of general population)

- Testis tumor
- TB of the epididymis
- Varicocele
- Vasitis and vasitis nodosa (usually associated with epididymitis)
- Young syndrome (obstructive azoospermia, sinusitis, bronchiectasis)

TREATMENT

- Most do not require treatment unless symptomatic.
- Supportive care is usually sufficient:
  - Scrotal supporter
  - Heat
  - NSAIDs
  - Continued testicular self-exam

MEDICATION

Oral analgesics or NSAIDs

SURGERY/OTHER PROCEDURES

- Spermatocelectomy is elective and indicated for progressive enlargement or persistent pain.
- Performed by magnified or microsurgical dissection of cyst from epididymal bed to preserve arterial supply and avoid injury to the epididymal tubules and resultant epididymal obstruction
- Ligation of spermatocele at its stalk
- Surgery should be deferred in men seeking fertility since the spermatocelectomy can occasionally cause epididymal obstruction.

ADDITIONAL TREATMENT

- Trans-scrotal cyst aspiration with or without sclerotherapy:
  - Agents used have included tetracycline, fibrin glue, phenol, 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.

ONGOING CARE

PROGNOSIS

- Most require no intervention and do not lead to epididymal obstruction.
- Recurrence rate is low postoperatively.

COMPLICATIONS

- Orchalgia
- Concern for cancer
- Postoperative spermatocelectomy:
  - Regrowth of spermatocele
  - Vascular injury 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 RECOMMENDATIONS

Patient Monitoring

- Periodic scrotal exam
- Subsequent scrotal US if symptoms recur

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Paratesticular Tumors, General
- Spermatic Cord Mass and Tumors

CODES

ICD9

608.1 Spermatocele

ABBREVIATIONS

- AFP: -Fetoprotein
- DES: Diethylstilbestrol
- hCG: Human chorionic gonadotropin
- ICSI: Intracytoplasmic sperm injection
- IVF: In vitro fertilization
- LDH: Lactate dehydrogenase
- MRI: Magnetic resonance imaging

- NSAID: Nonsteroidal anti-inflammatory drug
- TB: Tuberculosis
- US: Ultrasound
- VHL: von Hippel-Lindau

SPINAL CORD INJURY (SCI), UROLOGIC CONSIDERATIONS

Patrick J. Shenot, MD

BASICS

DESCRIPTION

SCI alters lower urinary tract function based on level and completeness of injury. Bladder and sphincter dysfunction is a significant cause of morbidity in SCI.

EPIDEMIOLOGY

- Incidence: 32 new injuries per 1,000,000 population in the US
- Prevalence: 906 per 1,000,000 population
- 85% of injuries: At/above T12
- 55% in quadriplegia, 45% in paraplegia
- 54% of injuries neurologically incomplete, 46% complete

RISK FACTORS

- Male: Males account for nearly 80% of SCI patients
- Young adult: Most common at ages 16–30

GENERAL PREVENTION

- Drive safely, prevent falls.
- Prevention of secondary complications of SCI including:
  - Infections
  - Incontinence
  - Skin breakdown
  - Urolithiasis

PATHOPHYSIOLOGY

- NDO:
  - Uncontrolled reflex bladder contraction
  - Collateral sprouting of new neural pathways
  - Loss of inhibitory impulses from cortical centers; primitive reflex pathways
- DSD:
  - Abnormal reflexive sphincter contraction during involuntary detrusor contraction
  - Functional bladder outflow obstruction, elevated intravesical pressure
  - Secondary damage: Pressure, infection, urolithiasis
  - Detrusor overactivity must be present for DSD. NDO may occur without DSD.
  - 10–20% of patients have internal (bladder neck) sphincter dyssynergia with external sphincter dyssynergia

  - Elevated intravesical pressure >40 cm H2O responsible for sequelae of NDO-DSD
- Detrusor areflexia:
  - Interruption of sacral reflex arc; no detrusor contraction
  - Low-pressure storage (volumes up to 500 mL)
  - Adrenergic overgrowth: Decreased bladder compliance, elevated storage pressure

COMMONLY ASSOCIATED CONDITIONS

Multiple etiologies for SCI:

- Arachnoiditis, arteriovenous malformation, congenital malformation (myelodysplasia)
- Guillain-Barré, herniated intervertebral disc, cord infarct
- Plaques of multiple sclerosis, spinal stenosis
- Transverse myelitis, trauma, tumor

DIAGNOSIS

HISTORY

- Neurologic disease: Onset, duration
- Voiding symptoms:
  - Irritative or obstructive
  - Incontinence: Urge, stress
- Method of urinary management:
  - Condom catheter urinary collection
  - Intermittent self-catheterization
  - Indwelling urethral or suprapubic catheter
  - Credé, Valsalva voiding
- UTI:
  - Severity of infection: Febrile, hospitalization, IV antibiotics required
  - Frequency of recurrence
- Urolithiasis episodes, surgical intervention, calculus composition
- AD: Associated with urination

PHYSICAL EXAM

- Fever: Parenchymal UTI source:
  - Men: Prostate, testes/epididymis, renal
  - Women: Renal
- HTN: AD with manipulation of the GI/GU systems
- Generalized edema: Severe renal insufficiency
- Palpable flank mass: Hydronephrosis
- Flank tenderness: Ureteral obstruction, pyelonephritis

- Abdominal mass: Distended bladder, urinary retention
- Incontinence of urine:
  - Spontaneously
  - Stress maneuvers: Marshall test
  - Abdominal/pelvic palpation/compression
- Testicular mass:
  - Epididymo-orchitis/epididymitis; secondary abscess
- Prostate mass/nodule: Focal prostatitis
- Neurologic:
  - Sacral root
  - Perianal sensation
  - Anal tone, sphincter control
  - Bulbocavernosus reflex: Contraction of anal sphincter with stimulation of glans penis/clitoris

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood studies:
  - Serum chemistry: Renal function, creatinine
  - CBC: Elevated WBC, secondary anemia due to decreased renal function or chronic infection
- Urine analysis:
  - Proteinuria: Renal dysfunction
  - Pyuria, nitrite, leukocyte esterase: Acute or chronic infection
  - Hematuria: Infection or lithiasis

Imaging

- Renal US: To screen for calculus, hydronephrosis, or mass
- ExU:
  - Delayed excretion of contrast with high urinary storage pressures
  - Hydroureteronephrosis:
    Marked elevation of intravesical pressure (ie, NDO/DSD) or calculi
- VCUG:
  - Bladder thickening, trabeculation, diverticulum, incomplete emptying
  - Ureter: Vesicoureteral reflux, hydroureter, hydroureteronephrosis
  - Urethra: Usually normal; rule out stricture:
    NDO + DSD: Prostatic urethra dilated; membranous urethra persistently narrow, stenotic, nonrelaxing

- Nuclear medicine renal scan:
  - Sequential studies detect deterioration of renal function.
  - Furosemide wash-out analysis (1 mg/kg IV) determines obstruction: Half-life >20 minutes

Diagnostic Procedures/Surgery

Urodynamics: Essential to determine effective urologic management for all patients with neurogenic lower urinary tract dysfunction

Pathological Findings

Bladder wall thickening and fibrosis common

TREATMENT

- Urodynamics are essential to determine lower urinary tract function/dysfunction and to plan urologic management.
- Control intravesical pressure: Protects upper tracts
- Spontaneous voiding with continence is possible with NDO controlled medically.
- Urinary drainage: Intermittent catheterization or external collection appliance
- Indwelling catheterization: Avoid due to complications (UTI, erosion, calculi, etc.).
- Intermittent self-catheterization: Most effective treatment; requires low storage pressure:
  - Urinary tract colonized; treat only symptomatic UTI.
  - If unable to self-catheterize urethra: Consider continent catheterizable stoma.
  - Males unable to self-catheterize:

    Condom catheter

    Outlet obstruction (BPH, DSD, etc.) requires medical or surgical treatment.

    Ileal conduit bladder chimney if patient cannot maintain appliance
  - Females unable to catheterize urethra or stoma: Incontinent ileal bladder chimney urostomy
  - Incontinence or elevated intravesical pressure due to poor compliance or hyperreflexia:

    Reduce storage pressure: Continence between catheterizations preserves upper urinary tracts.

    Augmentation cystoplasty if anticholinergic therapy is ineffective.
- Lower urinary tracts that cannot be reconstructed require cystectomy and urinary diversion:
  - Incontinent urostomy
  - Continent urinary reservoir

MEDICATION

First Line

- Anticholinergics to improve urinary storage pressure/decrease involuntary contraction:
  - Oxybutynin 5 mg PO t.i.d.–q.i.d.
  - Hyoscyamine 0.125 mg PO q.i.d.
  - Tolterodine LA 4 mg/d PO
- -Adrenergic blockers: Decrease internal sphincter function, lower voiding pressure; ineffective for DSD. May help control symptoms of autonomic dysreflexia:
  - Doxazosin 2–8 mg/d PO
  - Terazosin 2–5 mg PO once or twice daily
  - Tamsulosin 0.4 mg/d PO

Second Line

)[C]

SURGERY/OTHER PROCEDURES

- Endoscopic sphincter ablation or stenting:

)[A]

- Augmentation cystoplasty using an intestinal segment to enlarge the bladder, increasing bladder volume and decreased pressure:
  - Intermittent catheterization for urinary drainage
  - Limited dexterity mandates construction of a continent catheterizable stoma for the urinary reservoir, especially in females.
- Ileovesicostomy (bladder chimney):
  - Useful for those unable to perform self-catheterization (ie, quadriplegia)
- Cystectomy with continent urinary reservoir
- Ileal or colon pouch; continent catheterizable stoma (appendix or tapered ileum) on abdomen
- Cystectomy with ileal urostomy

ADDITIONAL TREATMENT

- Vanilloid agents such as capsaicin and resiniferatoxin suppress uninhibited involuntary detrusor contraction.
- Sacral nerve root stimulation:
  - Deafferentation with dorsal rhizotomy abolishes spontaneous detrusor contraction, improving urinary storage.
  - Nerve root stimulation allows control over detrusor contraction.

ONGOING CARE

PROGNOSIS

Proper urologic management greatly improves both life expectancy and quality of life in SCI individuals.

COMPLICATIONS

- Bladder wall thickening, detrusor hypertrophy, diverticula:
  - Bladder wall fibrosis, decreased compliance, vesicoureteral reflux: All associated with chronic catheter
- Recurrent UTI:
  - Males febrile with parenchymal involvement; abscess formation possible
  - Prostatitis, epididymo-orchitis, pyelonephritis
  - Female febrile UTI: Pyelonephritis
- Urolithiasis:
  - Urinary stasis
  - Chronic infection (urea-splitting organisms)
  - Bladder calculi with chronic indwelling catheter
- Urinary retention
- Hydroureteronephrosis:
  - Intravesical pressure >40 cm H2O impairs ureteral urine flow.
  - Ureteral dilatation impairs the ureterovesical junction to prevent reflux.
- Neoplastic transformation: Associated with chronic catheter:
  - Chronic inflammation: Squamous metaplasia in 80%, squamous cell carcinoma in 5%
- Urethral erosion, fistula with chronic catheterization

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

):

- Videourodynamic testing: Consider if elevated filling pressures, poor bladder compliance, or reflex voiding. Assure low intravesical pressure.
- Upper tract imaging (US, ExU) to rule out upper tract changes (calculi, hydronephrosis)
- Serum chemistry to confirm normal renal function and electrolyte balance

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ADDITIONAL READING

• Consortium for Spinal Cord Medicine. Bladder management for adults with spinal cord injury: A clinical practice guideline for health care providers. Available at http://www.pva.org/site/DocServer/Bladder.WEB.pdf?docID=1101. Accessed August 8, 2009.

• Watanabe T, Rivas DA, Chancellor MB. Urodynamics of spinal cord injury. Urol Clin North Am 1996;23:459–473.

See Also (Topic, Algorithm, Electronic Media Element)

- Detrusor-Sphincter Dyssynergia (DSD)
- Neurogenic Bladder, General
- Urodynamics, Indications and Normal Values

CODES

ICD9

- 344.00 Quadriplegia, unspecified
- 344.1 Paraplegia
- 952.9 Unspecified site of spinal cord injury without spinal bone injury

ABBREVIATIONS

- AD: Autonomic dysreflexia
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- DSD: Detrusor sphincter dyssynergia
- ExU: Excretory urography
- GI: Gastrointestinal
- GU: Genitourinary
- HTN: Hypertension
- IV: Intravenous
- NDO: Neurogenic detrusor overactivity
- SCI: Spinal cord injury
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- WBC: White blood cell

STROKE (CVA), UROLOGIC CONSIDERATIONS

Douglas F. Milam, MD

BASICS

DESCRIPTION

- Cerebrovascular accidents (CVAs or strokes) can cause transient or permanent urinary tract dysfunction.
- Brain injury may cause transient UR. Within a few weeks, however, the retention usually resolves without need of surgical intervention.
- Patients often then develop bladder overactivity leading to urinary urgency and urge incontinence.
- Resolution of urinary symptoms is proportional to the extent of resolution of other sequelae of stroke. Patients who resolve cognitive and motor deficits usually resolve their urinary symptoms as well.

EPIDEMIOLOGY

- 270 per 100,000 individuals in the US population experience CVA or about 800,000 per year
- Mean age is about 72 yr.
- 2.6% of noninstitutionalized adults have history of stroke.
- UI and UR typically develop in the recovery period.

GENERAL PREVENTION

Providers should be aware of the possibility of acute UR in the early phase of CVA. Bladder overactivity usually begins within days to weeks and may persist depending on the degree of resolution of other CVA sequelae. Unlike MS or spinal cord injury, CVA does not cause urinary sphincter dyssynergia. Bladder overactivity is the rule, but decreased bladder compliance and increased bladder storage pressure is extremely uncommon.

PATHOPHYSIOLOGY

- Acute UR: Detrusor areflexia, presumably from cerebral shock:
  - UR usually resolves in days to weeks
- UI is multifactorial, and depends on the location of the CVA
- Common urodynamic findings with CVA:
  - Normal bladder and normal sphincter
  - Bladder overactivity and a normal sphincter
  - DSD is rare after a CVA.
  - Diminished bladder contractility (often due to preexisting conditions)

COMMONLY ASSOCIATED CONDITIONS

BPH:

– Men with CVA and urinary symptoms should undergo urodynamic testing to ascertain whether the symptoms are due to CVA or to bladder outlet obstruction from prostatism.

DIAGNOSIS

- Acute UR after CVA:
  - Due to cerebral shock
  - Factors contributing to UR include impaired consciousness, restricted mobility, inability to communicate, acute overdistention of bladder
- UI occurs in 38–60% in initial recovery period:
  - Frequency, urgency, and urge incontinence most common urologic symptoms
  - Factors contributing to UI include severe motor deficits, altered mental status, dysphagia, preexisting lower urinary tract pathology
  - Poor prognostic indicator of recovery and survival

HISTORY

- Symptoms suggestive of a reversible cause of UI:
  - Acute change in mental status
  - Dysuria, fevers, and chills suggest UTI
- Previous urologic complaints, symptoms, or UI:
  - Suggest underlying/preexisting condition
  - Medication history, such as those used to treat BPH or an overactive bladder

PHYSICAL EXAM

- Assess the abdomen for bladder distention.
- Neurologic exam
- Assess the prostate for size and consistency.
- Pelvic exam in women
- Assess the chest for signs of congestive failure.
- Assess the lower extremities for edema:
  - Fluid retention may result in postural diuresis and UI at night

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis, BUN, and creatinine
- Urine culture (if suspect UTI)

Imaging

IVP, CT scan, or US scan of abdomen and pelvis:

- Rule out bladder or kidney stones or cancer (if suspected)

- KUB to rule out impaction of stones (if suspected)

Diagnostic Procedures/Surgery

- Check PVR urine if suspect incomplete emptying
- Urodynamics for more accurate assessment of LUT function:
  - Indications: Confirm presence/etiology of LUT dysfunction; failure of conservative measures; surgical planning
  - Urodynamic testing done by a urologic specialist is the principal method of separating lower urinary tract symptoms due to bladder outlet obstruction (BPH) from those produced by CVA
- Voiding diary:
  - Assesses day-to-day function
  - Functional bladder capacity; fluid intake; time and frequency of incontinence; situation in which UI occurs; diurnal variation in urine output

TREATMENT

- Initial goals:
  - Adequate bladder drainage by CIC or Foley catheter until patient resumes voiding
  - Prevent acute complications; see above
- Long-term goals:
  - Attain adequate bladder drainage and maintain urinary continence
  - Prevent complications, minimize risk of infection, maintain renal function
- UR or PVRs elevated (>200 mL):
  - CIC is the best treatment
  - Indwelling Foley or SP tubes are discouraged
  - SP tube is a last resort due to complications (eg, stones, UTI, etc.)
- If frequency, urgency, UI due to bladder overactivity:
  - Time voiding, prompted voiding, bladder training, and behavior modification are the 1st line of management.
  - Fluid restriction as needed (based on the voiding diary)
  - Improve access to a bathroom to allow the patient to reach the bathroom when urgency episodes occur; provide a commode, urinal, or assistance.
  - Condom catheter: Undesirable; risk of UTI and penile skin breakdown

MEDICATION

First Line

- Anticholinergic/antimuscarinics may be used as needed in an attempt to decrease the frequency and force of involuntary bladder contractions:

– There are many medication choices. Individual response is idiosyncratic, so several medications often have to be tried before finding the optimal:

Oxybutynin 5 mg b.i.d./t.i.d.
Oxybutynin XL 10–15 mg/d
Tolterodine 2–4 mg/d
Trospium XR 60 mg/d
Solifenacin 5–10 mg/d
Hyoscyamine XR 0.375 mg b.i.d.
Transdermal oxybutynin patch 3.9 mg/d

• Changes in sensorium are uncommon, but judicial use is recommended in the elderly and those with severe CVA deficits.

Second Line

• Botulism toxin injection has been used in the CVA population:
  – Decreases the force and frequency of involuntary bladder contraction
  – Office-based therapy performed under local anesthesia—well tolerated
  – Cystoscopic injection of 50–300 units of botulism toxin into 10–25 sites within the bladder muscle
  – Treatment effect lasts 4–8 mo
  – Occasionally patients develop temporary total urinary retention and require 4-times daily intermittent self-catheterization. All patients receiving this therapy need to understand this possibility.
  – Due to the temporary nature of the effect, botulism toxin injection is not a particularly good long-term therapy.

SURGERY/OTHER PROCEDURES

• Sacral neuromodulation (InterStim) has been used for treatment of involuntary bladder contraction in this population.
• The therapy is less effective in the CVA population than when used for idiosyncratic urinary urgency and urge incontinence.
• If bladder outlet obstruction is identified by urodynamic testing in a man with urgency or urge incontinence, it may be addressed by TURP or other BPH therapy:
  – TURP without proven BOO leads to 25% incidence of incontinence.
  – TURP with proven BPH confers a 5% risk.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

• Continence pads should be used as an aid, not as a substitute for other measures.
• Biofeedback and electrical stimulation have unproved efficacy in this setting.

ONGOING CARE

PROGNOSIS

- Resolution of urinary symptoms due to CVA are directly proportional to the degree of resolution of other CVA symptoms.
- Symptoms that do not resolve within 6–12 mo are usually lifelong.

COMPLICATIONS

- Early: If bladder drainage is not provided during the acute retention phase:
  - Acute overdistention injury, UTI, acute renal failure, incontinence
- Late: If lower urinary tract dysfunction is not addressed:
  - UI, skin breakdown, UTI, diminished quality of life, and rarely renal insufficiency

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients performing CIC or with indwelling catheters should be followed at least biannually:
  - Yearly: BUN, creatinine, renal US. Those with indwelling catheters should also have yearly KUB x-ray to evaluate for bladder or upper urinary tract stones.
- Bladder overactivity only with adequate bladder emptying and no UTIs can be followed yearly.

PATIENT EDUCATION

Patients should be counseled that, in the majority, UR will resolve and UI can be controlled with medication.

ADDITIONAL READING

- Brittain KR, Peet SM, Castleden CM. Stroke and incontinence. Review. Stroke 1998;29(2):524–528.
- Pettersen R, Stien R, Wyller TB. Post-stroke urinary incontinence with impaired awareness of the need to void: Clinical and urodynamic features. BJU Intl 2007;99(5):1073–1077.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Outlet Obstruction (BOO)
- Detrusor Overactivity
- Incontinence, Urinary, Adult Male
- Incontinence, Urinary, Adult Female
- Neurogenic Bladder, General
- Urodynamics, Indications and Normal Values

CODES

ICD9

- 434.91 Cerebral artery occlusion, unspecified with cerebral infarction
- 596.51 Hypertonicity of bladder
- 788.20 Retention of urine, unspecified

ABBREVIATIONS

- BOO: Bladder outlet obstruction
- BPH: Benign prostatic hypertrophy
- BUN: Blood urea nitrogen
- CIC: Clean intermittent catheterization
- CT: Computed tomography
- CVA: Cerebrovascular accident
- DSD: Detrusor-sphincter dyssynergia
- IVP: Intravenous pyelogram
- KUB: Kidneys, ureters, bladder
- LUT: Lower urinary tract
- MS: Multiple sclerosis
- PVR: Post-void residual
- SP: Suprapubic
- TURP: Transurethral resection of prostate
- UDS: Urodynamic studies
- UI: Urinary incontinence
- UR: Urinary retention
- US: Ultrasound
- UTI: Urinary tract infection

SUPRAPUBIC PAIN

Benjamin R. Lee, MD
Gordon L. Fifer, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- Pain in midline of lower abdomen, immediately above the pubic symphysis, most often due to GU disease, occasionally GI, gynecologic causes, and other rare conditions.
- Suprapubic region is sometimes referred in anatomic texts as the hypogastrium.

RISK FACTORS

- Recurrent infections
- BPH
- May cause acute urinary retention
- Urolithiasis
- Immunocompromised patients
- Increased susceptibility to infections
- Radiation treatment for malignancy

PATHOPHYSIOLOGY

- Various reproductive, GI, urologic, and neuromuscular disorders may cause pain in this area.
- Acute suprapubic pain: Most often caused by pathology of pelvic organs:
  - Visceral pain from the pelvic organs is poorly localized until the process involves the peritoneum
- CPPS or NIH Type III B prostatitis is unexplained pelvic pain involving the groin, genitalia, or perineum and may be associated with voiding symptoms occurring in the absence of pyuria or bacteruria.
- This was previously described by some as prostatodynia, and the use of this term is currently discouraged.
- Many believe that the symptoms of CPPS in men closely relate to the similar symptom complex in women with interstitial cystitis.
- GU tract pain is usually associated with inflammation or obstruction.
- Inflammatory pain is typically more severe if it involves organ parenchyma.
- Constant suprapubic pain unrelated to urinary retention is rarely of genitourinary origin.
- Tumors from GU tract malignancies generally do not produce pain unless causing obstruction or extend into adjacent nerves. Pain is usually a late manifestation.

- Prostatitis:
  - If acute (NIH I), usually secondary to inflammation with secondary edema and distention of prostatic capsule
  - Symptoms are localized primarily in perineum, but frequently pain is referred to suprapubic area.
  - Severe edema may produce acute urinary retention.
- Vesical:
  - Usually produced by overdistention of bladder secondary to acute urinary obstruction or inflammation
  - Chronic, slowly progressing urinary retention usually asymptomatic despite large residual volumes.
- Inflammation of bladder usually produces intermittent suprapubic discomfort:
  - Bacterial and interstitial cystitis is most severe when bladder full; symptoms improve when bladder is relieved of distension.
  - Sharp and stabbing pain is present at the end of micturition.
  - Pain can be referred to distal urethra and is associated with irritative voiding symptoms (urgency, frequency).
  - Spasms from overactive bladder
- Urethra:
  - Urethral strictures
  - Infection, trauma
  - Can cause acute urinary retention

COMMONLY ASSOCIATED CONDITIONS

- Urinary retention
- Urethral strictures

DIAGNOSIS

HISTORY

- Constant suprapubic pain unrelated to urinary retention is seldom of urologic origin.
- Acute urinary retention:
  - Marked edema and distention of prostatic capsule (prostatitis, cancer)
  - Urethral stricture
  - BPH
  - Distal ureteral calculi
  - Neurogenic bladder
- Irritative urinary symptoms (frequency, dysuria, nocturia, and urgency):

  - Infection of urinary tract or soft tissue
  - Interstitial cystitis
  - Prostatodynia
  - Urolithiasis
  - Foreign body:
    Stents, catheters
- Hematospermia
- Painful ejaculation
- Trauma
- Radiation treatment for cancer
- History of diarrhea or bowel disease
- Last menstrual period
- History of STD

PHYSICAL EXAM

- Rectal exam:
  - Tender, swollen, and/or boggy prostate during palpation
  - Bacterial, nonbacterial, and granulomatous prostatitis
  - Firm and indurated prostate; warm to the touch: Bacterial prostatitis
  - Evidence of masses or blood with GI tract disease
- Abdominal exam:
  - Abdominal distention
  - Bowel sounds
  - Acute retention due to dilated bladder
  - Rebound tenderness
  - Suprapubic tenderness to palpation:
    Urinary obstruction
    Inflammation and infection
- Pelvic exam:
  - Chandelier sign (tenderness with movement of the cervix) with PID
  - Cervical discharge
  - Evidence of masses

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Leukocytosis with left-shift; nonspecific infection and inflammation
- Urine analysis and culture:

- Pyuria, nitrite, and bacteria with infection
- pH, crystals/calcium, uric acid, oxalate, citrate, 24-hr excretion with urolithiasis

- Urine cytology for malignancy
- Pregnancy testing in females

Imaging

- Plain films: Little value in inflammatory disease; important in evaluation of urolithiasis, tumors, and foreign bodies
- Retrograde urethrogram:
  - Evaluation of urethral strictures
- CT:
  - Staging for GU tumors
  - Evaluation of calculi
  - No role in uncomplicated infections of GU tract
- US bladder (residual urine, stone, etc.)
- Pelvic US for gynecologic causes
- Transvaginal US best for uterine or ovarian evaluation

Diagnostic Procedures/Surgery

- Mears-Stamey 4-glass test for prostatitis evaluation
- Cystoscopy:
  - Contraindicated during acute bacterial prostatitis
  - Interstitial cystitis:
    Perform under anesthesia to allow sufficient distention of the bladder.
    1st therapeutic modality
  - Evaluate bladder calculi for outlet obstruction
    Assess mucosa for lesions and areas of inflammation.
- Urodynamics:
  - Assess bladder capacity in interstitial cystitis.
  - Evaluate neurogenic bladder.
- Ureteroscopy:
  - Visualize upper tract, remove calculi.

Pathological Findings

Based on specific entity

DIFFERENTIAL DIAGNOSIS

- Acute appendicitis
- Bladder perforation

- Bowel perforation
- Diverticulitis
- Inflammatory bowel disease
- Interstitial cystitis
- Malignancy (bladder, prostate, gynecologic)
- Mesenteric adenitis
- Prostatitis:
  - Acute, bacterial (NIH I)
  - Asymptomatic inflammatory (NIH IV)
  - Chronic, bacterial (NIH II)
  - Chronic, nonbacterial, inflammatory/noninflammatory (NIH III A)
- Sexual abuse
- Trauma
- Urinary retention
- UTI
- Urolithiasis/nephrolithiasis/bladder calculi
- Gynecologic/pregnancy-related:
  - Abruptio placentae
  - Ectopic pregnancy
  - Endometriosis
  - Incomplete abortion
  - Miscarriage
  - Mittelschmerz
  - Ovarian cyst (hemorrhagic or ruptured)
  - Ovarian torsion
  - PID
  - Pelvic neoplasm
  - Preterm labor
  - Primary dysmenorrhea
  - Rupture corpus luteum cyst
  - Septic abortion
  - Threatened abortion
  - Uterine fibroids
  - Uterine rupture
- Neurologic disorders:

  - Neuralgia/cutaneous nerve entrapment (surgical scar in the lower part of the abdomen; usually iliohypogastric, ilioinguinal nerves)
  - Shingles (herpes zoster infection)
  - Degenerative joint disease
  - Disk herniation
  - Spondylosis
  - Abdominal epilepsy
  - Abdominal migraine
  - Neoplasia of spinal cord or sacral nerve
- Musculoskeletal disorders:
  - Abdominal wall myofascial pain (trigger points)
  - Chronic coccygeal pain
  - Fibromyalgia
  - Hernias (eg, obturator, sciatic, inguinal, femoral, spigelian, umbilical)
  - Muscular strains and sprains
  - Osteitis pubis
  - Rectus tendon strain
- Psychologic and other disorders:
  - Personality disorders
  - Depression
  - Sleep disorders
  - Sexual and/or physical abuse

TREATMENT

- The focus of this discussion is on pathologic processes in the genitourinary system.
- Prostatitis:
  - Urine analysis and culture should be performed if signs or symptoms should recur.
- Bladder calculi:
  - Evaluate with urodynamics for bladder outlet obstruction
- Bladder cancer:
  - Urine cytology, cystoscopy, and CT urogram
- Acute bacterial cystitis:
  - Routine urine analysis and culture
- Urethral stricture:
  - Not considered corrected until stable for at least 1 yr post treatment
  - Urinary flow rates and urethrograms during followup

MEDICATION

- Acute bacterial cystitis:
  - A 3-day course of antibiotic has shown to be as effective as 7–14 day course, with fewer side effects in women.
  - Men with uncomplicated cystitis should be treated with a 7-day course of antibiotic.
- Retention: Urethral catheterization
- Prostatitis, acute:
  - Fluoroquinolones or trimethoprim/sulfamethoxazole until culture and sensitivities available
- BPH:
  - Transurethral catheterization to relieve acute obstruction; if unable to perform, then suprapubic catheter should be placed

SURGERY/OTHER PROCEDURES

- BPH:
  - Transurethral resection of prostate or other ablative procedure (laser, microwave)
  - Urodynamics to assess detrusor contraction
- Interstitial cystitis:
  - Hydrodistention under anesthesia
  - Patient education and empowerment
  - Amitriptyline
  - Antihistamines
  - Intravesical lavage with DMSO
  - Sacral neuromodulation
- Bladder calculi:
  - Remove transurethrally with Holmium laser
  - Open cystolithotomy rarely needed
- Bladder cancer:
  - Superficial tumors:
    TURBT
    Intravesical BCG
  - Invasive tumors: Cystectomy
- Urethral stricture: Urethral dilation, urethrotomy

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Saw palmetto for BPH

ONGOING CARE

PROGNOSIS

Good prognosis with treatment of a clearly identified problem

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Assessment of postobstructive diuresis following relief of obstruction includes measurement of serum electrolytes

ADDITIONAL READING

- Edwards JL. Diagnosis and management of benign prostatic hyperplasia. Am Fam Physician 2008;77(10):140310.
- Selius BA, Subedi R. Urinary retention in adults: Diagnosis and initial management. Am Fam Physician 2008;77(5):64350.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Calculi
- Cystitis, General
- Interstitial Cystitis (IC)
- Osteitis Pubis
- Prostate, Benign Hyperplasia/Hypertrophy (BPH)
- Prostatitis, General
- Stamey Test (Meares-Stamey Test)
- Urethra Stricture, Male; Female
- Urinary Retention, General

CODES

ICD9

789.09 Abdominal pain, other specified site

ABBREVIATIONS

- BCG: Bacillus Calmette Guérin
- BPH: Benign prostatic hypertrophy
- CBC: Complete blood count
- CT: Computed tomography
- CPPS: Chronic pelvic pain syndrome
- DMSO: Dimethylsulfoxide
- GI: Gastrointestinal
- GU: Genitourinary
- PID: Pelvic inflammatory disease
- STD: Sexually transmitted disease

- TURBT: Transurethral resection of bladder tumor
- US: Ultrasound

SYPHILIS

Michael A. Pontari, MD

BASICS

DESCRIPTION

- STD caused by Treponema pallidum, a spirochete
- May also be transmitted by infected blood products and transplacentally
- Characterized by primary, secondary, latent, and tertiary stages
- Manifestations range from simple genital ulcer disease to systemic disease with life-threatening sequelae.

EPIDEMIOLOGY

- From 2000–2004, an increase occurred in number of reported cases of primary and secondary syphilis by 33% from 5,979–7,980.
- Increase in cases driven by 80% increase in number of cases in males:
  - Current male-to-female ratio for cases of syphilis has increased from 1.5 to 5.9.

RISK FACTORS

- Commercial sex workers
- Inmates in adult correctional facilities
- MSM
- Persons with HIV

Pregnancy Considerations

For PCN-allergic patient, doxycycline is contraindicated for uses in pregnancy. Need de-sensitization to PCN and then treat with PCN.

GENERAL PREVENTION

Safe sex practices

PATHOPHYSIOLOGY

- Incubation period is 10–90 days (mean 21):
  - Spread is by contact with infected lesions or body fluids, in utero or through blood transfusions
- Primary syphilis:
  - Regional lymphadenopathy
  - Chancre: Painless shallow ulcer with firm raised borders; on glans or penis in men; vulva or cervix in females
  - Painless papule ulcerates
- Untreated leads to secondary syphilis in 4–10 wk, then becomes latent
- Secondary syphilis:

- Nonspecific symptoms: Malaise, fatigue, headache, fever, sore throat
- Generalized lymphadenopathy
- Papulosquamous dermatosis:
  Pale, red discrete round lesions
  Scaling over surface
  Nickels and dimes
  Papules <1 cm called dimes, typically 5–10 mm
  Plaques >1 cm called nickels
  Symmetric palms, soles, and trunk
- Condyloma lata: Papules coalesce and develop into large, flat, highly contagious lesions involving moist areas such as the genitalia.
- Systemic manifestations can include hepatitis, periostitis, nephropathy, ocular symptoms (uveitis, iritis).

• Latent syphilis: Seroreactivity with no clinical evidence of disease:
  - Defined as early (<1 yr) or late (>1 yr)

• Latent progresses to tertiary in 1/3 of cases (up to 20 yr after exposure), regresses in 1/3 with negative serology, remains latent in 1/3.

• Tertiary:
  - 50% have only parenchymal gummas; 25% involves CNS, 25% cardiac.
  - Other areas involved include skin and skeletal systems.

• Congenital syphilis:
  - Syphilis acquired in utero and manifested by any of several characteristic tooth (Hutchinson teeth) or bone malformations and by active mucocutaneous syphilis at birth or shortly thereafter
  - Ocular and neurologic changes may also occur.

COMMONLY ASSOCIATED CONDITIONS

• HIV: HIV testing should be performed on all patients with an initial diagnosis of syphilis:
  - Presence of chancres increases risk of HIV acquisition by 2–5 times.

• Should also screen all initial diagnoses of syphilis for hepatitis B and C, gonorrhea, and chlamydial infection.

DIAGNOSIS

HISTORY

• Development of genital lesions
• History of other STDs
• History of genital trauma

- Medications: Rule out fixed drug eruption
- New recent sexual contacts, use of condoms, high-risk behaviors
- Dysuria, urethral discharge to suggest urethritis, other STD
- ROS: Constitutional symptoms, CNS findings including headache or weakness, cardiac involvement with DOE

PHYSICAL EXAM

- Primary syphilis:
  - Painless chancre on glans, corona, or perineal area in men, and labia or anal area in women.
  - Often associated with bilateral nontender inguinal adenopathy.
  - Since both lesion and adenopathy heal without treatment and are painless, may have primary syphilis without findings on exam.
- Latent syphilis: Seropositive but no clinical findings
- Secondary syphilis:
  - Maculopapular rash seen on trunk and arms, generalized nontender adenopathy
  - Can develop papular lesions on palms and soles, which may become necrotic and pustular due to endarteritis; in intertriginous areas these enlarge and erode to become condyloma lata (very infectious).
- Tertiary syphilis:
  - Can affect any organ system but especially cardiac, skeletal, skin, and CNS.
  - Cardiac exam: Aortitis
  - Neuro exam: Meningitis, tabes dorsalis (sensory deficits)
  - Eye exam: Uveitis/optic neuritis/iritis
  - Skin: Gummas

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Dark-field microscopy and DFA:
  - From primary and secondary lesions
  - Dark-field not widely available but DFA is available through commercial labs.
  - Best when lesion easily identified
- Serum tests: Nontreponemal, most common method of screening:
  - RPR
  - VDRL: Now almost exclusively used as CNS fluid test
  - Positive nontreponemal tests must be confirmed by treponemal serologic test.
  - Nontreponemal tests correlate with disease activity.

- Serum tests—treponemal:
  - FTA-ABS or microhemagglutination assay for antibodies to T. pallidum
  - Positive treponemal tests usually positive for lifetime, but does do not correlate with disease activity.
  - False-positives seen in pregnancy, IV drug users, SLE, or systemic viral infections.

Diagnostic Procedures/Surgery

- Lumbar puncture in patients with high clinical suspicion for neurosyphilis:
  - HIV patient with syphilis for >1 yr and serum nontreponemal test titer of >1:32
  - CSF VDRL: Highly specific
  - Retest if CSF VDRL negative
  - Treponemal-specific CSF tests (eg, TPHA): High false-positive rate
  - Consider TPHA index: This compares CSF to serum titer
  - Spirochete DNA PCR from CSF sample has higher specificity than TPHA but not widely available.
- Biopsy penile lesion to rule out squamous cell carcinoma or other STD.

Pathological Findings

Gumma, a characteristic lesion of tertiary syphilis, may form in any organ or tissue:

- Central area of coagulative necrosis, surrounded by epithelioid cells, occasional giant cells, and a perimeter of fibrous tissue
- Small vessels surrounding the gumma: Thick walls and narrow lumens
- Common sites in syphilis include the skin, liver, testis

DIFFERENTIAL DIAGNOSIS

- Chancroid: Painful ulcer and tender lymphadenopathy
- Fixed drug eruption: Occurs after use of 1 particular medication
- Granuloma inguinale: Tender, velvety looking lesions
- Herpes simplex: Group of vesicles on erythematous base that does not follow a neural distribution
- LGV from Chlamydia: Painless ulcer that heals in 1–4 wk but has tender inguinal adenopathy.
- Squamous cell carcinoma

TREATMENT

The presentation of syphilis varies extensively; a high degree of suspicion is needed for prompt diagnosis and treatment.

MEDICATION

- Primary, secondary, and early latent: Benzathine penicillin G 2.4 million units IM in 1 dose:

– PCN-allergic: Doxycycline 100 mg PO b.i.d. for 2 wk or ceftriaxone 1 g/d IM or IV for 8–10 days

- Late or indeterminate latent or tertiary (except neurologic):
  - Benzathine penicillin 2.4 million units IM once per week for 3 wk.
  - PCN-allergic: Use doxycycline for 4 wk
- Neurosyphilis: Aqueous crystalline penicillin G 2.4 million units IV q4h for 10 days

ADDITIONAL TREATMENT

Postexposure prophylaxis:

- Ceftriaxone 250 mg IM AND
- Doxycycline

100 mg for 14 days OR

- Azithromycin (Zithromax) 1 g PO in 1 dose

ONGOING CARE

PROGNOSIS

Rate of treatment failure ranges from 4–21%.

COMPLICATIONS

Jarisch-Herxheimer reaction: Headache, myalgia, fever, tachycardia, and tachypnea starting in 1st 24 hr after treatment with PCN. Manage with bed rest and NSAIDs.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients should be followed with nontreponemal antibody titers at 6 and 12 mo. If no 4-fold decrease in titers occurs, check for neurosyphilis.
- Neurosyphilis: Repeat CSF exam every 6 mo until normal result is achieved.

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See Also (Topic, Algorithm, Electronic Media Element)

- Sexually Transmitted Diseases (STD), General
- Penis, Lesion, General

CODES

ICD9

- 091.0 Genital syphilis (primary)

- 091.9 Unspecified secondary syphilis
- 095.8 Other specified forms of late symptomatic syphilis

ABBREVIATIONS

- CNS: Central nervous system
- CSF: Cerebrospinal fluid
- DFA: Direct fluorescent antibody
- DOE: Dyspnea on exertion
- FTA-ABS: Fluorescent treponemal antibody absorption
- HIV: Human immunodeficiency virus
- IM: Intramuscularly
- LGV: Lymphogranuloma venereum
- MSM: Men having sex with men
- NSAID: Nonsteroidal anti-inflammatory drug
- PCN: Penicillin
- PCR: Polymerase chain reaction
- ROS: Review of systems
- RPR: Rapid plasma reagin
- SLE: Systemic lupus erythematosus
- STD: Sexually transmitted disease
- TPHA: Treponema pallidum hemagglutination test
- VDRL: Venereal disease research laboratory

TESTIS, CANCER, GENERAL

Brett S. Carver, MD
Joel Sheinfeld, MD

BASICS

DESCRIPTION

- Testicular cancer is a malignancy of germ cell origin originating in the testis; it accounts for >95% of testicular malignancies.
- Testis cancer is the most common malignancy in males 15–35 yr.
- Patients with testicular cancer may present with a testicular mass, gynecomastia, infertility, abdominal mass, or symptoms related to metastatic disease such as back pain, or cough.

EPIDEMIOLOGY

- In the US, ~8,090 new cases of testicular cancer were diagnosed, and 380 men died of this disease in 2008.
- GCT of the testis occurs predominantly in Caucasian males.

RISK FACTORS

Cryptorchidism, Klinefelter syndrome, family history, testicular atrophy, infertility, marijuana use

Genetics

Identification of isochromosome 12p amplification

PATHOPHYSIOLOGY

- GCTs of the testis can be divided into 2 major subgroups: Seminoma and nonseminoma.
- Seminoma: 50% of all testicular cancers and most frequently appears in the 4th decade of life:
  - ~10–15% of seminomas will produce hCG.
- Remainder of GCTs are comprised of nonseminomatous histology (embryonal cell carcinoma, yolk sac tumor, choriocarcinoma, and teratoma):
  - ~50–70% of nonseminomas will produce AFP and/or hCG.
- Most nonseminomatous tumors are mixed germ cell tumors, composed of 2 cell types, of which seminoma may be a component; however, the definition of a pure seminoma excludes the presence of any nonseminomatous elements or an elevated serum AFP.

COMMONLY ASSOCIATED CONDITIONS

- Infertility
- Cryptorchidism

- Gynecomastia

ALERT

Testicular cancer must always be considered in males presenting with a testicular mass or swelling.

DIAGNOSIS

HISTORY

- Ask about history of undescended testicle, family history of testis cancer.
- 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:
  - Mass in the left neck
  - Pulmonary complaints such as hemoptysis or dyspnea
  - Abdominal mass
  - Back pain that can often be disabling
  - In 5% of patients, gynecomastia 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 emphasizing palpation of the cervical lymph nodes (lymphadenopathy), breasts (gynecomastia), abdomen (retroperitoneal masses/lymphadenopathy, liver masses), and contralateral testis (bilateral testicular tumors).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Serum tumor markers (AFP, hCG, LDH) should be obtained prior to and following radical orchiectomy:

- The serum tumor markers are necessary for diagnosis, staging, and risk classification.
- Whereas normal postorchiectomy serum tumor markers do not preclude the finding of metastatic disease, an elevation of either AFP or hCG does signify the presence of metastasis.

Imaging

- Testicular US: Imaging modality of choice with a >95% sensitivity and specificity in identifying intratesticular lesions.
- Testicular US often reveals a solid hypoechoic mass present within the testis.

- Image contralateral testis: 2% of patients will have bilateral testicular cancers.
- The initial staging evaluation should include a CT of the chest, abdomen, and pelvis. CT is the most effective radiographic technique for identifying metastatic disease both above and below the diaphragm. The CT scan shows no evidence of metastases in ~70% of patients with seminoma and 30% of patients with nonseminoma.

Diagnostic Procedures/Surgery

A radical orchiectomy 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.

Pathological Findings

- Histologic findings of seminoma, embryonal carcinoma, choriocarcinoma, yolk sac tumor, teratoma
- Pathologic documentation of lymphovascular invasion
- Pathologic and clinical staging follows the TNM classification and risk assessment if performed using the IGCCCG risk classification.

DIFFERENTIAL DIAGNOSIS

- Adult/pediatric painful mass:
  - Epididymitis/orchitis; bacterial, STD, mumps, TB
  - Incarcerated/strangulated hernia
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  - Torsion (testicle, testicular or epididymal appendage)
  - Tumor (pain infrequent unless traumatized or rapidly growing; see below)
- Adult painless mass:
  - Adenomatoid tumor of testis or epididymis
  - Adrenal rest tumors
  - Adenocarcinoma of the rete testis
  - Chylocele: Usually associated with filariasis
  - Fibrous pseudotumor of the tunica albuginea
  - Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of the cord
  - Lipoma of the cord
  - Mesothelioma of tunica vaginalis
  - Polyorchidism
  - Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma

– Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)

– Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcinosis, fat necrosis, malignancy

– Sperm granuloma following vasectomy

– Spermatocele (epididymal cyst)

– Testicular cysts (simple, tunica albuginea, epidermoid)

– Testicular tumor:

GCTs (95% of testicular malignancies): Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma (1–5%), teratocarcinoma

Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder and thyroid.

Mixed germ cell and stromal tumor (gonadoblastoma)

Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

Leukemia or lymphoma

– Varicocele

• Pediatric painless mass:

– Similar to adult list; Most/more common are: Hydrocele, hernia, varicocele, testicular teratoma, adrenal rest tumors, rhabdomyosarcoma

TREATMENT

• All patients with a testicular mass should be evaluated thoroughly for testicular cancer.

• 18–33% of patients with testicular cancer were initially treated for epididymitis, resulting in a delay in diagnosis and management.

• Radical orchiectomy should be performed for diagnosis and treatment of the primary tumor.

• Primary therapy is based on:

– Histology (seminoma vs. NSGCT)

– Clinical TNM stage (see Section VII)

– IGCCCG classification is useful in advanced GCT (good, intermediate, or poor risk).

• General treatment options (see specific types elsewhere in book) after orchiectomy and staging (serum):

- Seminoma:
  - Stage I: Surveillance, radiation to para-aortic nodes, single-agent chemo
  - Stage IIA: RT
  - Stage IIB/IIC: Chemotherapy
  - Stage III chemotherapy; with brain mets brain RT ±excision
- NSCGT:
  - Stage I: Surveillance, RPLND, chemo
  - Stage IB: Consider 2 cycles chemo
  - Stage IS: Full-cycle chemo
  - Stage IIA: RPLND or 2 cycles using 2-drug chemotherapy
  - Stage IIB/IIC: 2 or 3 cycles of 3-drug chemo; RPLND with residual mass
  - Stage III: 3 cycles using 3-drug chemo; RPLND with residual mass

MEDICATION

First Line

Chemotherapy:

- Regardless of histology, patients with advanced GCTs (cIIB–cIII) and those with persistently elevated tumor markers following radical orchiectomy (CIS), are initially treated with platinum-based chemo according to the IGCCCG risk stratification.
- Good-Risk: BEP q 21 days × 3 cycles
  - Bleomycin 30 U IV weekly
  - Etoposide 100 mg/m2 IV × 5 days
  - Cisplatin 20 mg/m2 IV × 5 days

OR

EP q 21 days × 4 cycles

  - Etoposide 100 mg/m2 IV × 5 days
  - Cisplatin 20 mg/m2 IV × 5 days

- Intermediate/high risk: BEP q 21 days × 4 cycles
  - Bleomycin 30 U IV weekly
  - Etoposide 100 mg/m2 IV × 5 days
  - Cisplatin 20 mg/m2 IV × 5 days

OR

VIP q 21 days × 4 cycles

  - Etoposide 75 mg/m2 IV × 5 days
  - Ifosfamide 1.2 g/m2 IV × 5 days
  - Cisplatin 20 mg/m2 IV × 5 days

Second Line

- ~30–40% of patients with poor risk disease fail to achieve a durable response to conventional chemotherapy.
- 2nd-line chemotherapy is reserved for patients with advanced testicular cancer in whom serum tumor markers do not normalize following initial chemotherapy regimen: VeIP, TIP, or VIP: For those who did not receive etoposide as initial therapy

SURGERY/OTHER PROCEDURES

- Radical orchiectomy with high ligation of the cord
- In the US, the preferred management for patients at high risk for relapse in the retroperitoneum (ie, predominant embryonal carcinoma, lymphovascular invasion, or extension into the tunica or scrotum), is primary RPLND if serum tumor markers have normalized.
- PC-RPLND and resection of residual masses are an integral in the management of advanced nonseminoma:
  - Following induction chemotherapy, ~40% of patients undergoing RPLND will have teratoma in their retroperitoneum, and an additional 10–15% will have viable GCT.

ADDITIONAL TREATMENT

Radiotherapy

In US, RT to the retroperitoneum remains the treatment of choice for stage I and IIa seminoma. Highly selected patients may undergo surveillance with CT every 4–6 mo.

Additional Therapies

- Pretreat with Mesna to reduce incidence of ifosfamide hemorrhagic cystitis
- CEB: As for BEP but carboplatin substituted for cisplatinum
- High-dose chemo with HDT is used in relapsed disease.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Counsel concerning fertility and sperm banking before definitive therapy.

ONGOING CARE

PROGNOSIS

- Dependent on initial clinical stage, risk stratification, and histology
- Multidisciplinary approach GCTs of the testis has resulted in survival rates of >90%.

COMPLICATIONS

- Radical orchiectomy: Wound infection, scrotal hematoma, and retroperitoneal hematoma
- RPLND: Wound infection, pancreatitis, venous thrombosis, chylous ascites, anejaculation, and small bowel obstruction
- Chemotherapy: Neutropenia, GI symptoms, alopecia, pulmonary fibrosis, secondary cancer and cardiovascular events

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Following treatment, patients should be followed with history and physical exam, serum tumor markers, chest x-ray, and periodic CT imaging of the chest, abdomen, and pelvis for life. Follow-up protocols should be followed according to guidelines established by the NCCN (www.nccn.org).

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- TNM Classification
- Specific Tumor Type

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

ABBREVIATIONS

- AFP: -Fetoprotein
- BEP: Bleomycin, etoposide (VP-16), cisplatin
- CEB: Bleomycin, etoposide (VP-16), carboplatin
- CIS: Carcinoma in situ
- CT: Computed tomography
- GCT: Germ cell tumor
- GI: Gastrointestinal
- hCG: Human chorionic gonadotropin
- HDT: Hematopoietic stem cell rescue
- IGCCCG: International Germ Cell Cancer Collaborative Group
- IV: Intravenous
- LDH: Lactate dehydrogenase

- NCCN: National Comprehensive Cancer Network
- NSGCT: Nonseminomatous germ cell tumor
- PC-RPLND: Post-chemotherapy retroperitoneal lymph node dissection
- RPLND: Retroperitoneal lymph node dissection
- RT: Radiation therapy
- STD: Sexually transmitted disease
- TIP: Paclitaxel, ifosfamidel, and cisplatin
- US: Ultrasound
- VeIP: Vinblastine, ifosfamide, and cisplatin
- VIP: Etoposide (VP-16), ifosfamide, and cisplatin

TESTIS, CHORIOCARCINOMA

Paul L. Crispen, MD

Michael L. Blute, MD

BASICS

DESCRIPTION

- A histologic type of GCT of the testis; it is considered the most aggressive form.
- Tumors are composed of syncytiotrophoblastic, cytotrophoblastic, and other trophoblastic cells.
- Pure choriocarcinomas are commonly associated with metastatic disease and high levels of -hCG at the time of presentation.

EPIDEMIOLOGY

- Testicular cancer is the most common malignancy in males 20–35 yr.
- An estimated 8,090 cases of testicular cancer diagnosed in 2008.
- <1% pure choriocarcinoma
- 10% of tumors with mixed GCT will contain elements of choriocarcinoma.
- Almost never seen in prepubertal males

RISK FACTORS

- Cryptorchidism. The risk of malignancy is not decreased with orchiopexy.
- Testicular atrophy
- In utero hormonal exposure to exogenous estrogens

Genetics

~5% of patients with testis cancer will have a family history of testis cancer, most commonly among brothers.

PATHOPHYSIOLOGY

- 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 predictable. 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 hr.
- Elevated serum levels of -hCG are also noted in 40–60% of embryonal carcinomas and 5–10% of pure seminomas.

COMMONLY ASSOCIATED CONDITIONS

Gynecomastia, cryptorchidism

DIAGNOSIS

HISTORY

- Onset and duration of symptoms
- Past medical history focusing on history of cryptorchidism
- Thorough review of symptoms may reveal signs of metastatic disease.
- Social history focusing on fertility
- Painless testicular enlargement; acute pain is the presenting symptom in ~10% of patients.
- Metastatic disease may be associated with abdominal, flank, or back pain. Disease outside of the abdomen may be associated with shortness of breath from pleural effusions or neurologic symptoms from CNS involvement.

PHYSICAL EXAM

- Thorough exam of both gonads
- Careful palpation of surrounding spermatic cord structures on involved side to evaluate extent of disease
- Transillumination of scrotal contents if hydrocele is associated or suspected.
- Exam for metastatic disease including inguinal, abdominal, thoracic, neurologic exams.
- Gynecomastia can be noted in ~5% of patients with GCT:
  - -hCG can stimulate estrogen production from Leydig cells, leading to breast enlargement and tenderness. However, gynecomastia is not always associated with elevated -hCG.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Tumor markers (-hCG, LDH, AFP) should be drawn prior to orchiectomy.
- Elevated -hCG can also be seen in marijuana smokers, hypogonadotropic patients and other malignancies including liver, pancreas, stomach, bladder, breast, lung, and kidney.
- Some assays for -hCG are cross-reactive with LH, which can lead to false-positive elevations.
- Karyotype for isochromosome 12p I(12p). I(12p) is noted to be present in 80% of GCT. This cytogenetic marker can be used in cases in which the origin of a tumor is in question, as can be the case with extragonadal GCT.
- Macroscopically, tumors are often hemorrhagic with areas of necrosis, and can be associated with areas of fibrosis and tumor regression.

- Hemorrhage is usually central with viable tumor located peripherally.

Imaging

- Testicular US
- Chest x-ray
- CT of abdomen and pelvis
- CT or MRI of head if CNS involvement is suspected
- PET scans are of limited utility in the evaluation of NSGCT.

Diagnostic Procedures/Surgery

Radical orchiectomy (inguinal approach)

Pathological Findings

- Cut surface may demonstrate multiple areas of hemorrhage and necrosis.
- Pathology evaluation may demonstrate a burned-out primary tumor with only residual scarring.
- Mix of mononuclear cells with lightly staining cytoplasm (cytotrophoblasts) combined with multinucleated cells with smudged/degenerating nuclei and densely eosinophilic cytoplasm (syncytiotrophoblasts)
- Multiple fields need to be examined to clearly identify the cytotrophoblasts.
- Area surrounding tumor is often hemorrhagic.
- Syncytiotrophoblasts stain strongly with HCG.

TREATMENT

- Treatment options are based on clinical staging.
- Clinical staging following removal of the primary tumor is similar to all GCT and is based on physical exam, radiographic studies, serum tumor markers, and histologic tumor features according the TNMS staging system.

MEDICATION

First Line

)[B]

)[A]

- See Section I: “Testis Cancer, General” for specific chemotherapy regimens.

Second Line

)[B]:

- Standard dose 3-agent combinations based on ifosfamide and cisplatin.
- High-dose chemotherapy with autologous stem-cell support

SURGERY/OTHER PROCEDURES

- Radical orchiectomy (inguinal approach)

)[B]

)[A]

ADDITIONAL TREATMENT

Radiotherapy

As with other NSGCTs, choriocarcinomas are less sensitive to radiation than seminomas.

Additional Therapies

)[B]

- Patient education:
  - Monthly self-exams
  - Fertility counseling, especially for patients undergoing chemotherapy or RPLND
  - Offer sperm banking in patients undergoing systemic therapy.

ONGOING CARE

PROGNOSIS

)[B]:

- Good prognosis: Testis or retroperitoneal primary, no nonpulmonary visceral metastases, AFP <1,000, -hCG <5,000, and LDH <1.5 for upper limit of normal
- Intermediate prognosis: Testis or retroperitoneal primary, no nonpulmonary visceral metastases, AFP 1000–10,000, -hCG 5,000–50,000, or LDH 1.5–10 for upper limit of normal
- Poor prognosis: Mediastinal primary, nonpulmonary visceral metastases, AFP >10,000, -hCG >50,000, or LDH >10 for upper limit of normal

COMPLICATIONS

- Delay in diagnosis is common; however, the efficacy of contemporary chemotherapeutic regimens decreases the impact of delayed treatment in the majority of patients.

)

- Increased cardiac toxicity and secondary malignancies have been noted in patients receiving chemotherapy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Although late relapses do occur, the majority of recurrences occur within the 1st 2 yr following treatment. More frequent imaging is recommended for patients undergoing surveillance of stage 1 disease:

- Serial exams of contralateral testis
- Serial imaging of chest, abdomen, pelvis at 3–4-mo intervals for 1st 2 yr, at 6-mo intervals during years 3–5, and annually thereafter
- Measurements of serum tumor markers should be performed at the time of imaging.

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- TNM Classification

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ABBREVIATIONS

- AFP: -Fetoprotein
- BEP: Bleomycin, etoposide, and cisplatinum
- CNS: Central nervous system
- CT: Computed tomography
- GCT: Germ cell tumor
- hCG: Human chorionic gonadotropin
- IGCCC: International germ cell consensus classification
- LDH: Lactase dehydrogenase
- LH: Luteinizing hormone
- MRI: Magnetic resonance imaging
- NSGCT: Nonseminomatous germ cell tumor
- PET: Positron emission tomography
- RPLND: Retroperitoneal lymph node dissection
- TNM: Tumor, node, metastatic disease
- US: Ultrasound

TESTIS, EMBRYONAL CARCINOMA

Avi C. Weiss, MD

J. Nathaniel Hamilton, MD

BASICS

DESCRIPTION

- Most common histologic subtype of NSGCT
- Pure form of embryonal cell carcinoma is present in only 2% of all germ cell tumors.

EPIDEMIOLOGY

- Annual age-adjusted incidence rate among American men for all testicular cancers is 3.7 per 100,000.
  - 0.9 per 100,000 among African American men
  - 6.4 per 100,000 in Denmark
- 6900 new cases of GCT per year in US: ~1,100 mixed germ cell tumors containing embryonal carcinoma, 200 pure embryonal carcinoma (2)
- Highest among men of 20–40 yr
- 2nd most common germ cell tumor following seminoma
- Present in 40% of mixed germ cell tumors:
  - Pure embryonal carcinoma represents 3–4% of all germ cell tumors
- Slightly more common in right testicle; bilateral in 2–3% of cases.

RISK FACTORS

- Cryptorchidism (3–14 times increased risk of all GCTs); also increased risk in contralateral gonad
- Testicular atrophy (mumps-associated) or nonspecific
- Estrogen exposure (conflicting data)
- Pollutants with estrogenic or antiandrogenic activity (conflicting results)
- Infertility (more likely an associated finding than a cause)

Genetics

- No evidence of familial disease
- 2–3% bilateral, suggesting predisposition

GENERAL PREVENTION

- Testicular self-exam
- Self-exam of contralateral testes in posttreatment patients

PATHOPHYSIOLOGY

- Pure embryonal carcinoma represents 3–4% of all germ cell tumors. Present in 40% of mixed germ cell tumors.

- Histology of metastasis may be different from that of primary tumor, often teratoma.
- More aggressive than other germ cell tumors, this subtype is most associated with relapse (35–40%).
- Predictable lymphatic spread:
  - 1st site is retroperitoneum:

    Left-sided tumors spread to preaortic and para-aortic lymph nodes; left-to-right spread is rare.

    Right-sided tumors spread to precaval, interaortocaval, and then may spread to preaortic and para-aortic nodes.
  - 2nd most common site is lungs
- Carcinoma in situ: 50% progress to invasive disease at 5 yr.
- Other germ cell tumors:
  - Seminoma: 40% of tumors (typical 85%, anaplastic 5–10%, spermatocytic 5–10%)
  - Mixed GCT (40%)
  - Teratoma: 3% in adults, yolk sac tumor (far more common in children), choriocarcinoma 1–2%

COMMONLY ASSOCIATED CONDITIONS

- Infertility
- Cryptorchidism
- Seminoma

DIAGNOSIS

HISTORY

- Signs and symptoms:
  - Painless mass (50–60%)
  - Testicular pain or dull ache (30–40%)
  - Symptomatic metastases (10%) such as cough, dyspnea, supraclavicular nodal mass, anorexia, abdominal mass, back pain
  - Gynecomastia (5%)
  - Trauma (4%)
  - Infertility
- History of undescended testis found in 10% of patients
- Previous testicular malignancy: ~5% will develop another tumor.
- Mumps

PHYSICAL EXAM

- Thorough exam of both gonads

- Careful palpation of surrounding spermatic cord structures on involved side to evaluate extent of disease
- Transillumination of scrotal contents if hydrocele is associated or suspected
- Exam for metastatic disease including inguinal, abdominal, thoracic, neurologic exams.
- Gynecomastia can be noted in ~5% of patients with GCT.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- AFP produced by fetal gut, liver, and yolk sac:
  - Half-life of ~5 days. Elevated in 80% of embryonal carcinoma, also yolk sac and teratoma. Absent in pure seminoma and choriocarcinoma.
- b-hCG normally secreted by placental syncytiotrophoblasts.
  - Half-life of ~24–36 hr. Consists of - and -chains: -Chain analogous to LH and TSH.
  - Elevated in 60% of all NSGCT, 30% of seminomas and all choriocarcinomas.
- LDH most useful when other markers are negative. Relates to tumor bulk.

Imaging

- Scrotal US: Considered by some an extension of physical exam
- CT of abdomen and pelvis: For retroperitoneal disease and visceral metastasis
- Chest x-ray: For lung and mediastinal disease
- Head CT only if symptomatic

Diagnostic Procedures/Surgery

- Lymphangiography: Not routine. Has been replaced by CT
- MRI: In selected cases

Pathological Findings

- Gross: Variegated, grayish white, fleshy tumor, often with areas of necrosis or hemorrhage and a poorly defined capsule
- Microscopic: Epithelioid cells arranged in glands or tubules, indistinct cell borders, pale or vacuolated cytoplasm, rounded nuclei with coarse chromatin and large nucleoli; pleomorphism, mitotic figures, and giant cells are common.

DIFFERENTIAL DIAGNOSIS

See Section I: “Testis Cancer, General.”

ALERT

Encourage patient to bank sperm prior to undergoing treatment, because of the increased risk of infertility following any treatment.

TREATMENT

- See Section VII for TNM stage grouping:

– Stage I: Radical inguinal orchiectomy for diagnosis and primary treatment PLUS observation OR RPLND OR chemotherapy (2 cycles BEP)

– Stage IIa and IIb: Radical inguinal orchiectomy for diagnosis and primary treatment PLUS RPLND OR 2–4 cycles of chemotherapy (BEP). 2/3 have complete response.

– Stage IIc or Stage III: Radical inguinal orchiectomy for diagnosis and primary treatment PLUS chemotherapy (3–4 cycles BEP). 70% have complete response.

- Salvage protocols:

– Post-chemo RPLND if tumor makers negative and still evidence of retroperitoneal disease

– Post-RPLND chemotherapy if markers persistently elevated OR positive nodal disease on pathology

– Salvage chemotherapy ± bone marrow transplant for advanced disease after chemotherapy

MEDICATION

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First Line

- BEP or EP regimens
- See Section I: “Testis Tumor, General” for specific chemotherapy regimens

Second Line

VIP: Salvage protocol. Vinblastine, ifosfamide, cisplatinum. Pretreat with Mesna to reduce incidence of hemorrhagic cystitis

SURGERY/OTHER PROCEDURES

- Considered a preferred 1st-line therapy for testicular cancer

)[A]:

– For all stages of testis cancer

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ADDITIONAL TREATMENT

May be a role in palliative care but not primary in this tumor type

ONGOING CARE

PROGNOSIS

- Stage I: >30% relapse with observation alone
- Stage II and III: >60% have complete response to primary treatment

COMPLICATIONS

- 50% of men are subfertile at time of diagnosis. Recommend banking sperm before treatment.

- RPLND:
  - Loss of ejaculation (10%) with sympathetic-nerve sparing procedure.
  - Also surgical complications:
    Damage to small bowel or great vessels, ileus, lymphocele, ileus.
    ARDS in patients who have previously been treated with bleomycin (post-chemo RPLND)
- Chemotherapy:
  - Bleomycin:
    Pulmonary fibrosis
    ARDS
  - Etoposide:
    Myelosuppression
    Alopecia
    Secondary leukemia
  - Cisplatin:
    Renal insufficiency
    Nausea
    Vomiting
    Neuropathy
  - Ifosfamide: Hemorrhagic cystitis
  - Vinblastine: Neuromuscular toxicity

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- If primary surveillance, >30% will suffer recurrence, the vast majority within 1st 2 yr. Follow-up protocols vary, an example is listed here:
  - Year 1: Tumor markers and chest x-ray every month; abdominal CT every 2 mo
  - Year 2: Tumor markers and chest x-ray every 2 mo; abdominal CT every 4 mo
  - Years 3–5: Tumor markers and chest x-ray every 6 mo; abdominal CT every 6 mo
  - After year 5: Tumor markers and chest x-ray once a year
- If status is post-RPLND without evidence of disease, follow-up protocols vary, an example is listed here:
  - Year 1: Tumor markers and chest x-ray every month
  - Year 2: Tumor markers and chest x-ray every 2 mo
  - Abdominal CT every 6 mo for 1st 2 yr
  - Years 3–5: Tumor markers and chest x-ray every 6 mo, abdominal CT every year.

- After year 5: Tumor markers and chest x-ray once a year

ALERT

- Patient reliability is a large factor. If follow-up is not guaranteed, strong recommendations for 2 cycles of BEP prior to initiating surveillance.
- Always examine contralateral testis on follow-up exam.

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- TNM Classification

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

ABBREVIATIONS

- AFP: -Fetoprotein
- ARDS: Acute respiratory distress syndrome
- BEP: Bleomycin, etoposide, cisplatinum
- CEB: Carboplatin, etoposide, bleomycin
- CT: Computed tomography
- EP: Etoposide, cisplatinum
- GCT: Germ cell tumor
- hCG: Human chorionic gonadotropin
- LDH: Lactate dehydrogenase
- LH: Luteinizing hormone
- MRI: Magnetic resonance imaging
- NSGCT: Nonseminomatous germ cell tumor

- RPLND: Retroperitoneal lymph node dissection
- TSH: Thyroid-stimulating hormone
- US: Ultrasound
- VIP: Vinblastine, ifosfamide, cisplatinum

TESTIS, ENDODERMAL SINUS TUMOR (YOLK SAC TUMOR)

Matthew D. Katz, MD
Adam S. Kibel, MD

BASICS

DESCRIPTION

- Endodermal sinus tumor is a type of NSGCT of the testis.
- Bimodal age distribution: Infants and young boys; postpubertal males
- TNM classification for postpubertal males is identical to other testis tumors and listed in Section VII.
- Prepubertal staging is based on the Children's Oncology Group Staging for GCT:
  - Stage I: Tumor limited to testis and completely resected. If scrotal orchiectomy done, completed cord resection must have negative margins. Normal tumor markers. If patient has radiographic evidence of RP nodes >2 cm and normal or unknown markers at diagnosis, must have ipsilateral RP node sampling to confirm stage I
  - Stage II: Microscopic residual disease in scrotum/cord. Marker elevation after appropriate T1/2. Tumor rupture or scrotal biopsy orchiectomy
  - Stage II: RP node involvement. Lymph nodes >4 cm by CT. Lymph nodes >2 cm and <4 cm need biopsy to document metastatic disease
  - Stage IV: Distant metastatic deposits
- Synonym(s): Yolk sac tumor (YST), endodermal sinus tumor (EST), adenocarcinoma of the infantile testis, juvenile embryonal carcinoma, orchioblastoma, and Teilum tumor

EPIDEMIOLOGY

- Most common testicular tumor in infants and children <2 yr
- Most common malignant prepubertal testicular tumor
- 2nd most common prepubertal testicular tumor of germ cell origin (teratoma most common)
- Incidence of testicular tumors is 0.05–1 per 100,000:
  - In boys <2 yr, 40–60% are YST
- In boys <2 yr old, 98% of cases involving malignant GCT are pure YST
- In contrast, 60% of postpubertal malignant GCTs contain mixed histology

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RISK FACTORS

Genetics

- Gains of chromosome 1q and 3 in children <4 yr
- Deletion of short arm of chromosome 1 (1p36 80–100% of time) in pre-/postpubertal men

PATHOPHYSIOLOGY

- 80–90% of tumors present as stage I.
- YST cause elevation in AFP, typically >100 ng/mL.
- YST does not produce hCG.

COMMONLY ASSOCIATED CONDITIONS

- In infants, often presents with associated hydrocele (25% of time), or history of trauma leads to incidental finding.
- Elevated AFP >90% of cases

DIAGNOSIS

HISTORY

- Most common finding in a child is painless testicular mass.
- History of trauma may lead to incidental diagnosis.
- Acute abdominal pain with torsion of an abdominal undescended testis containing tumor
- General symptoms such as weight loss, fatigue, loss of appetite

PHYSICAL EXAM

- Scrotal exam includes palpating testis, epididymis, and spermatic cord to localize the tumor.
- Transilluminate the scrotum to check for hydrocele.
- Check for tenderness.
- Examine contralateral testis.
- Evaluate for abdominal mass or tenderness.
- Evaluate for any general lymphadenopathy from neck down.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis, which may help diagnose infection with the presence of bacteria or WBCs.
- AFP, -hCG, and LDH; LDH is a nonspecific tumor burden marker.
- AFP:
  - Normal adult levels of <10 mg/mL are not reached until the age of 8 mo, and elevation does not always represent the presence of malignant tumor or persistent disease.

– Half-life of AFP is 5–7 days

- -hCG (half-life of 24 hr) is rarely elevated in prepubertal tumors.
- LFTs and alkaline phosphatase may be elevated with advanced disease.

Imaging

- Scrotal US routinely performed:

– Very important especially when physical exam is hindered by presence of hydrocele.

– On US, presence of cystic lesion with onion-skin appearance and normal AFP is consistent with epidermoid cyst.

- CT of abdomen and pelvic and/or chest x-ray/chest CT to evaluate for retroperitoneal lymphadenopathy, liver, or pulmonary involvement

Diagnostic Procedures/Surgery

- Generally none
- Biopsy is not advised, but if performed and reveals YST, child is automatically a stage II.
- Inguinal completion orchiectomy with removal of remaining cord structure should be done, but hemiscrotectomy is not required.

Pathological Findings

- Most variable histologic findings of all GCTs
- Grossly tumor is firm and yellow-white.
- Microscopic appearance is sometimes referred to as honeycomb or chicken wire.
- Many other patterns are recognized (reticular, papillary, glandular, solid, hepatoid).
- Characteristic histologic finding is Schiller-Duval bodies:

– The large, irregularly shaped nuclei contain 1 prominent nucleoli and variable amounts of chromatin.

- Embryoid bodies, a common finding in yolk sac tumors, resemble 1–2-wk-old embryos.
- Eosinophilic inclusions are common.
- Positive staining for AFP

DIFFERENTIAL DIAGNOSIS

See Section I: “Testis Cancer, General.”

TREATMENT

- If cystic lesion is identified on scrotal US in child and no elevation in AFP, surgeon can plan on testis-sparing procedure.
- If child has stage II and is then confirmed to have +lymph nodes, then should be treated as if stage III with systemic chemotherapy.

MEDICATION

First Line

- See Section I: “Testis Cancer, General” for specific chemotherapy regimens
- Pediatric:
  - Combination chemotherapy for stage III/IV with BEP
  - Significant risk of ototoxicity and nephrotoxicity with cisplatin

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- Adult:
  - Combination chemotherapy with 3 cycles of BEP or 4 cycles of EP for advanced stage and persistent tumor marker elevation, as with other GCTs

Second Line

- Children with persistent RP masses after 1st-line chemo or persistent elevation of tumor markers should undergo lymph node sampling at 12 wk to establish diagnosis.
- If viable tumor found, alternative chemotherapy regimen is started.
- Adults with persistent RP masses after 3 cycles of BEP and normalization of markers should undergo full bilateral RPLND.
- Adults with persistent RP masses and marker elevation should receive salvage chemotherapy with ifosfamide.

SURGERY/OTHER PROCEDURES

- Pediatric:
  - Inguinal radical orchiectomy with high cord ligation (curative for most children with stage I)
  - Partial orchiectomy in selected cases with compromised contralateral testis and peripheral tumor
  - Routine RPLND or adjuvant chemotherapy is not indicated for stage I.
  - Stage II should undergo radiographic imaging to evaluate for RP nodes and if >2 cm or persistent elevation of tumor markers should undergo RP lymph node sampling to confirm diagnosis
  - For residual mass following chemo without tumor marker elevation, proceed with RPLND (exceedingly rare event and very little data available)
- Adult:
  - Inguinal radical orchiectomy with high cord ligation as for any GCT
  - Indications for RPLND are the same as for other NSGCT.
  - Poor surveillance candidates with negative markers and post chemotherapy masses

ADDITIONAL TREATMENT

Surveillance for stage I (see “Patient Monitoring”)

ONGOING CARE

PROGNOSIS

- Radical inguinal orchiectomy is curative for most stage I disease.
- Stage I:
  - 5-yr survival: 100% with relapse rate of 15–22%
- Stage II:
  - 6-yr EFS and OS with BEP was 100%
- Stage III:
  - 6-yr EFS with BEP was 100% (children <15 yr) vs. 83.3% (children >15 yr) and OS of 100% for both age groups
- Stage IV:

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- Adult YST clinical behavior similar to all other NSGCTs

COMPLICATIONS

- RPLND:
  - Loss of ejaculation (10%) with sympathetic nerve–sparing procedure
  - Damage to small bowel or great vessels, ileus, lymphocele, ileus
  - ARDS in patients who have previously been treated with bleomycin (post-chemo RPLND)
- Chemotherapy:
  - Bleomycin: Pulmonary fibrosis, ARDS
  - Etoposide: Myelosuppression, alopecia, secondary leukemia
  - Cisplatin: Renal insufficiency, nausea, vomiting, neuropathy
  - Ifosfamide: Hemorrhagic cystitis
  - Vinblastine: Neuromuscular toxicity

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Recommended follow-up for boys with stage I disease is chest x-ray, CT, or MRI of abdomen/pelvis for initial staging; if negative, then proceed with tumor markers every 3 mo for 2 yr.
- Adult YST follow-up is identical to all other GCTs (see Section I: “Testis Cancer, Embryonal”).

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See Also (Topic, Algorithm, Electronic Media Element)

- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General
- TNM Classification

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

ABBREVIATIONS

- AAP: American Academy of Pediatrics
- AFP: -Fetoprotein
- ARDS: Acute respiratory distress syndrome
- BEP: Bleomycin, etoposicle, cisplatin
- CT: Computed tomography
- EFS: Event-free survival
- EP: Etoposide, cisplatinum
- EST: Endodermal sinus tumor
- GCT: Germ cell tumor

- hCG: Human chorionic gonadotropin
- LDH: Lactase dehydrogenase
- LFT: Liver function test
- MRI: Magnetic resonance imaging
- NSGCT: Nonseminomatous germ cell tumor
- OS: Overall survival
- RP: Retroperitoneal
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound
- WBC: White blood cell
- YST: Yolk sac tumor

TESTES, LEYDIG CELL TUMOR

Timothy R. Yoost, MD
Gary W. Bong, MD

BASICS

DESCRIPTION

- Leydig cell (interstitial cell) tumors (sex cord stromal tumors) make up ~90% of non-GCTs of the testis.
- The majority of testicular neoplasms are derived from germ cells.
- 4–10% of testicular tumors are from non-germ cells. Non-GCTs tend to develop over a long period of time.
- These tumors are usually benign. However, 10% of Leydig cell tumors are malignant variants that occur in adults only.

EPIDEMIOLOGY

- 3% of testicular neoplasms are Leydig cell tumors.
- 3% of these occur bilaterally.
- It is the single most common type of interstitial testis tumor.
- Occurs from 2–90 yr.
- Most common at 30–60 yr.

Pediatric Considerations

20% are found in pediatric patients, and present commonly at 5–10 yr.

RISK FACTORS

- Reported almost exclusively in white males.
- No association with cryptorchidism.

Genetics

- Questionable association with Klinefelter syndrome
- Have been described in the ovarian stroma of females; unlike their male counterparts, however, ovarian Leydig cell tumors are usually malignant.

PATHOPHYSIOLOGY

- Leydig cells primarily produce testosterone and some estrogens.
- Exact cause of Leydig cell tumor is unknown.
- LHRH hyperstimulation may be 1 possible cause.
- Leydig cell tumors can produce other hormones (estrogen, progesterone):
  - Estrogen excess and feminizing syndromes may be due to peripheral aromatization of testosterone or from the estrogen production by the tumor itself.
  - Criterion of malignant Leydig tumor is the documentation of metastasis.

– About 20% of adults have endocrine manifestations.

• Leydig endocrine function is independent of the hypothalamus-pituitary-gonadal axis and should not respond to ACTH or dexamethasone suppression testing.

• Leydig cell tumors described in female ovaries are almost always malignant.

• Leydig cell hyperplasia is a diffuse process that may form multiple nodules in the testicle and is distinct from Leydig cell tumor. These nodules are not usually palpable and are detected by imaging studies:

– Associated with elevated human chorionic somatrophin levels

– Seen in cases of testicular atrophy, Klinefelter, adrenogenital, and Nelson syndromes

– Are multifocal and hyperplastic

– Do not contain Reinke crystals.

COMMONLY ASSOCIATED CONDITIONS

• Associated with unilateral renal agenesis
• Infertility
• ED in adults
• Precocious puberty in children

DIAGNOSIS

HISTORY

• Symptoms of orchitis and epididymitis

• History of undescended testis (5–10% of cases) but not apparently related to development of Leydig cell tumor

• Past trauma
• Pain, weight loss, malaise
• Breast enlargement or soreness
• ED
• Decreased libido
• Precocious puberty in children

PHYSICAL EXAM

• Palpable, painless testicular mass: 80–90% of cases
• Gynecomastia
• Feminine hair distribution in adult
• Groin, flank, or abdominal mass
• In children, asymmetric testicular enlargement in the absence of mass

Pediatric Considerations

Virilizing effects in children, such as pubic or axillary hair, should raise the possibility of a Leydig cell tumor.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- -hCG, AFP, LDH, cell count, urine analysis chemistries, and CBC are minimal recommended laboratories for any suspected testicular neoplasms:
  - Routine testis tumor markers should be normal
- FSH, LH, and serum testosterone are useful to differentiate primary from secondary testis effect.
- Urinary 17-ketosteroids
- Serum and urinary estradiol
- If there is concern for metastasis, consider obtaining LFTs.
- Steroid secretion pattern is variable.
- No specific diagnostic tests exist.
- Testosterone is usually elevated.
- Serum estradiol may also be elevated.

Imaging

- Testicular US:
  - Solid hypoechoic mass
- CT of abdomen and chest to evaluate lymphatic spread if malignant tumor
- MRI may have limited role in identifying occult tumors.

Diagnostic Procedures/Surgery

- Selective venous sampling of gonadal vein:
  - Detects excess hormone production
- MRI is not frequently used; however, may detect some tumors undetected by US

Pathological Findings

- Solid, well-circumscribed tumor
- Yellow to gray nodular appearance
- 0.5–10.0 cm in size
- Crystals of Reinke:
  - Pathognomonic for Leydig cell tumor
  - Intracytoplasmic, eosinophilic, rod-shaped structure
  - 30–40% of specimens
- Von Hanseman cells:
  - Cells with abundant granular eosinophilic cytoplasm

  - 60% secrete testosterone and/or corticosteroids.
  - 50% secrete estrogen.

DIFFERENTIAL DIAGNOSIS

- Testicular Masses (see Section I: “Testis Cancer, General”)
- Adrenogenital syndrome/congenital adrenal hyperplasia
- Klinefelter syndrome
- Leydig cell hyperplasia
- Metastatic tumor to testis
- Paraneoplastic syndromes may mimic gynecomastia secondary to Leydig cell tumors.

TREATMENT

- Management is primarily surgical.
- Radical orchiectomy is the gold standard.
- Conservative management in younger patients with testis-sparing surgery
- Metastatic disease:
  - 10% of cases
  - Persistent estrogen levels in serum of micrometastatic disease
  - Responds poorly to radiation and chemotherapy, yet preferred if RPLND is positive
  - Median survival: 2–4 yr

MEDICATION

None

SURGERY/OTHER PROCEDURES

- Radical inguinal orchiectomy:
  - Definitive method of diagnosis and treatment for stages I, II neoplasm
- RPLND if suspicion of malignancy by CT criteria
- Enucleation of mass with testis-sparing surgery:
  - Inguinal exploration as for radical orchiectomy with use of intraoperative US and frozen section confirmation of benign Leydig cell tumor
  - May have a role in children and younger adults to preserve fertility.

ADDITIONAL TREATMENT

Radiotherapy

Responds poorly to radiation

Additional Therapies

- Responds poorly to chemotherapy, but is indicated when there in recurrence/persistence following RPLND.
- Limited response to palliation with mitotane

ONGOING CARE

PROGNOSIS

Benign/local disease in the majority of patients portends a good prognosis.

COMPLICATIONS

May have residual gynecomastia after removal of testis tumor.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up visits should include careful exam of the remaining testis, the abdomen, and regional lymph nodes.
- RPLND patients should be followed every 3 mo for 2 yr, then every 6 mo for 3 yr, then yearly.
- Tumor markers, serum testosterone, and 17-estradiol should be checked at routine visits.
- CT imaging of the lung and abdomen may be indicated.
- CBC, electrolytes, and endocrine levels should be performed at routine visits.

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See Also (Topic, Algorithm, Electronic Media Element)

- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- TNM Classification

CODES

ICD9

- 186.9 Malignant neoplasm of other and unspecified testis
- 222.0 Benign neoplasm of testis
- 236.4 Neoplasm of uncertain behavior of testis

ABBREVIATIONS

- ACTH: Adrenocorticotropic hormone

- AFP: -Fetoprotein
- CBC: Complete blood count
- CT: Computed tomography
- ED: Erectile dysfunction
- FSH: Follicle-stimulating hormone
- GCT: Germ cell tumor
- hCG: Human chorionic gonadotropin
- LDH: Lactate dehydrogenase
- LFT: Liver function test
- LH: Luteinizing hormone
- LHRH: Luteinizing hormone-releasing hormone
- MRI: Magnetic resonance imaging
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound

TESTIS, NONSEMINOMATOUS GERM CELL TUMORS (NSGCT), GENERAL

Cory Hugen, MD

Marcus L. Quek, MD

BASICS

DESCRIPTION

- Malignant neoplasm 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)
- This section provides an overview of NSCGT. Details on each subtype can be found in their respective chapters.

EPIDEMIOLOGY

- US, ~8,090 new cases of testicular cancer; 380 men died of this disease in 2008.
- GCTs of the testis occurs predominantly in Caucasian males.
- Most common solid neoplasm in men 20–34 yr old.
- Ages 15–39: 48 per 100,000
- Prevalence of 184,074 cases

RISK FACTORS

- Age: Choriocarcinoma, embryonal, and teratoma most common in 20–30s. Yolk sac most common in infants and children.
- Cryptorchidism: 7–10% occurs in patients with a history of undescended testicle, ipsilateral side. ~5% of patients develop a testicular malignancy in the normal contralateral testicle.
- Race: Caucasian men have 3 times the incidence of black men.
- Microlithiasis: Controversial risk factor.

Genetics

- Identification of isochromosome 12p amplification
- 2–3% incidence of bilateral testis tumors may suggest a congenital predisposition.

GENERAL PREVENTION

- No proven preventative methods
- Monthly testicular self-exams are recommended

PATHOPHYSIOLOGY

- ITGCN or CIS is believed to be the precursor lesion of all GCTs, excluding spermatocytic seminoma.

- GCTs typically have predictive spread via the retroperitoneal lymph nodes, except for choriocarcinoma:
  - Left-sided tumors typically spread to paraaortic lymph nodes.
  - Right-sided tumors typically spread to interaortocaval lymph nodes. May have right-to-left spread.
  - Subsequent drainage through cisterna chyli, thoracic duct, and supraclavicular nodes (usually left), or retrograde to iliac and inguinal nodes
- Nearly 60% of NSGCT contain >1 of the following histologic subtypes in varying amounts (known as mixed GCTs)
- Choriocarcinoma:
  - Rare in its pure form but present in nearly 40% of mixed tumors.
  - Often presents as a small primary tumor.
  - -hCG elevated in all cases; AFP normal.
  - Distinctive predilection for hematogenous route of metastasis (lung, brain)
- Embryonal cell carcinoma:
  - Present in 40% of mixed GCTs.
  - Only 3% are pure embryonal type.
  - Not associated with any particular serum tumor maker pattern.
  - >40% embryonal component in primary tumor puts patient at high risk for relapse.
- Teratoma:
  - Composed of 2 germ cell layers: Endoderm, mesoderm, and ectoderm.
  - Benign lesions when occurring in prepubertal boys; malignant lesions after puberty.
  - Mature teratoma: Tumors with completely differentiated cell types and somatic tissue.
  - Immature teratoma contains cells with incompletely differentiated cells.
  - Areas may undergo malignant transformation depending on which layer transforms (ie, endoderm to adenocarcinoma).
  - Chemotherapy and radiation-resistant tumors
- Yolk sac (endodermal sinus):
  - Most common testicular tumor in prepubertal boys
  - Elevated AFP is distinguishing serum tumor marker.
  - Absence of yolk sac elements in mixed GCT is a positive predictor of relapse.

COMMONLY ASSOCIATED CONDITIONS

- Infertility

- Cryptorchidism

DIAGNOSIS

HISTORY

- Classically presents as painless mass or swelling of 1 testicle.
- Delay in presentation is common because of embarrassment.
- Nearly 10% of patients present with symptoms secondary to metastatic disease, such as cough, vomiting, back pain (50% have metastatic disease at presentation).

PHYSICAL EXAM

- Scrotal exam including both testes, epididymis, and cord structures
- Abdominal exam with particular attention to presence of palpable lymphadenopathy and viscera
- Supraclavicular nodes, neck mass
- Gynecomastia is a rare finding (~5%).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- -hCG: Produced by syncytiotrophoblasts with half-life of 24–36 hr
- AFP: Produced by the epithelial lining of endodermal sinus with half-life of 5–7 days
- LDH: Helpful in assessing tumor burden; can be helpful with surveillance and recurrence
- Markers should be drawn at regular intervals prior to and during treatment and follow-up.
- Other markers with limited current clinical use include PLAP, CD30, and GGTP.

Imaging

- Scrotal US:
  - Tumors tend to be hypoechoic. Blood flow is often seen within tumor. Assess the contralateral testis for any abnormalities.
- MRI has a limited role in detection of intratesticular masses.

Diagnostic Procedures/Surgery

- In addition to scrotal US, abdominal/pelvic CT, and chest x-ray or chest CT should be routinely performed as part of the metastatic workup.
- No role for percutaneous biopsy (unless dealing with an extragonadal GCT).

Pathological Findings

- Choriocarcinoma:
  - Must have both syncytiotrophoblasts and cytotrophoblasts to make diagnosis
- Embryonal:

- Distinct cell arrangements.
- Vascular invasion often present

- Teratoma:
  - At least 2 germ cell layers present
  - Can be in different stages of development
- Yolk sac:
  - Schiller-Duval bodies often seen on histology

DIFFERENTIAL DIAGNOSIS

See Section I: “Testis Cancer, General.”

ALERT

Encourage patient to bank sperm prior to undergoing treatment because increased risk of infertility follows any treatment.

TREATMENT

- Radical inguinal orchiectomy is considered standard of care.
- Additional therapy for NSGCT depends on staging. Commonly used staging system is the TNM staging and Group Staging by the American Joint Committee on Cancer:
  - Patients are often divided into low- and high-stage disease along with good, intermediate, and poor risk based on IGCCC system
- Treatment algorithms have been devised based on this staging.
- Risk factors for relapse: T2 disease, + lymphovascular invasion, >40% embryonal component, absence of yolk sac
- Stage I disease treatment options:
  - Surveillance: Appropriate for reliable patients with no risk factors:
    25–30% relapse rate
    Close follow-up with imaging (CT, CXR), tumor markers, and physical exam.
  - RPLND: Modified unilateral template/nerve-sparing; 70–75% will be pN0:
    Cures 95% if nodes negative, 5% relapse; may cure low-volume nodal disease
  - Chemotherapy: 2 cycles of BEP; 95% survival.
- Stage IIa/IIb:
  - Controversy exists regarding most effective treatment regimen.
  - Options include RPNLD with modified bilateral template, RPNLD + adjuvant chemotherapy, or primary chemotherapy
  - If RPNLD performed and no tumor found, observe patient.
  - If RPNLD performed and tumor found, adjuvant 2-cycle chemotherapy.
  - If RPNLD performed and high-volume disease or tumor left behind, adjuvant 3-cycle chemotherapy.

- Stage IIC or III:
  - Chemotherapy is initial treatment. Either 3 or 4 cycles depending on risk.
  - Complete responses are observed.
  - Partial responses with residual retroperitoneal masses undergo full bilateral RPN-LD (nerve-sparing if applicable). Pathologic follow-up:

Residual masses: Fibrosis in 40%, teratoma in 40%, and viable malignancy in 20%

Malignancy present and post resection tumor markers elevated or tumor left behind, salvage chemotherapy

Malignancy present and post resection tumor markers normal and no tumor left behind, 2 cycles of chemotherapy can be given

Teratoma/fibrosis observe only

  - If no response to primary chemotherapy, consider salvage chemotherapy (ifosfamide, vinblastine, cisplatin), bone marrow transplant.

MEDICATION

See Section I: “Testis Cancer, General” for specific chemotherapy regimens

SURGERY/OTHER PROCEDURES

- Radical inguinal orchiectomy is considered standard of care:
  - Repeat tumor markers according to half-life of each and compare to preoperative values.
  - Use tumor markers, histologic subtype, pathologic staging, and metastatic workup to determine additional therapy as outlined below.
- Testicular-sparing surgery can be selectively considered in patients with bilateral testicular tumors or solitary testicle.
- RPLND:
  - For low-stage disease, a modified nerve-sparing template used.
  - Right-sided tumor: The limits include the right common iliac artery medially and inferiorly up to bifurcation. Dissection continues along the aorta up to the inferior mesenteric artery. Superior to the IMA, the dissection carried out to the left ureter. Superior limit is the renal hilum bilaterally. On the right side, lateral limit is the ureter and the gonadal vessels and stump of the spermatic cord is included in the specimen.
  - Left-sided tumor: Limits include the left common iliac artery medially and inferiorly up to bifurcation. Dissection continues along the aorta to the inferior mesenteric artery. Superior to the IMA, the dissection is carried out to the lateral edge of the inferior vena cava. The superior limit of the dissection is the renal hilum bilaterally. On the left side, the dissection limit laterally is the ureter and gonadal vessels. Stump of the spermatic cord is included in the spe-

cimen.

ADDITIONAL TREATMENT

Radiotherapy

Unlike stage I seminomas, retroperitoneal radiation is usually not given for NSGCT.

Additional Therapies

Surveillance in stage I NSGCTs that do not contain any teratomatous elements, have no lymphovascular invasion, and have no embryonal cell carcinoma in the primary specimens. In addition, patients must be reliable.

ONGOING CARE

PROGNOSIS

Has been divided into good, intermediate, and poor prognosis based on stage and risk factors: Good: Testis/retroperitoneal primary tumor, absence of nonpulmonary metastasis, slightly elevated tumor markers; 92% 5-yr survival rate:

– Intermediate: Same as Good prognosis but tumor markers are more elevated; 80% 5-yr survival rate

– Poor: Mediastinal primary tumor, nonpulmonary visceral metastasis, elevated tumor markers; 48% 5-yr survival rate

COMPLICATIONS

- RPNLD:
  - Ejaculatory dysfunction. Rate can be markedly decreased with nerve-sparing modified templates.
  - Mortality rate 1%, morbidity 5–25% (atelectasis, ileus, lymphocele, pancreatitis, chylous ascites)
  - Late bowel obstruction (1–2%)
- Surveillance: Risk of recurrence as well as potential risk of secondary malignancy due to cumulative radiation exposure from CT imaging
- Chemotherapy:
  - Bleomycin: Pulmonary toxicity causing pulmonary fibrosis; can be life-threatening
  - Cisplatin: Nephrotoxicity, ototoxicity, peripheral neuropathy
  - Vascular toxicity, metabolic syndrome
  - Secondary malignancy, especially leukemias, skin malignancies, lymphomas
  - Infertility (50% will have normal sperm counts 2 yr after chemotherapy, 25% will remain azoospermic)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Monitoring patients with NSGCT takes place at every stage of disease and includes radiographic assessments (CXR, CT), blood tests (tumor markers, liver function studies), and physical exam.
- Numerous surveillance and observation protocols have been published and are available elsewhere.
- Frequency of follow-up may be tailored depending on therapy, stage, and risk.

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Scrotum and Testicle, Mass
- Specific Tumor Type
- Testis Cancer, General
- Testis Cancer, Nonseminomatous Germ Cell Tumor Algorithm
- Testis, Tumor and Mass, Adult, General
- TNM Classification

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

ABBREVIATIONS

- AFP: -Fetoprotein
- BEP: Bleomycin, etoposide, cisplatin
- CIS: Carcinoma in situ
- CT: Computed tomography
- CXR: Chest x-ray
- GCT: Germ cell tumor
- GGTP: -Glutamyl transpeptidase
- hCG: Human chorionic gonadotropin

- IMA: Inferior mesenteric artery
- ITGCN: Intratubular germ cell neoplasia
- MRI: Magnetic resonance imaging
- NSGCT: Nonseminomatous germ cell tumor
- PLAP: Placental alkaline phosphatase
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound

TESTIS, PAIN (ORCHALGIA)

Ashley E. Ross, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- Testis or scrotal pain that is intermittent or constant, may be unilateral, bilateral, or bilaterally alternating and lasts >3 mo
- A chronic condition that should be differentiated from acute pain associated with torsion, trauma, or epididymo-orchitis
- Can remain localized to scrotum or radiate to groin, perineum, back, or legs
- Dysuria or suprapubic pain alone is excluded from the definition
- Etiology and treatment in many cases is poorly understood.
- Synonym(s): Orchalgia, idiopathic testicular pain, orchiodynia, chronic scrotal pain syndrome

EPIDEMIOLOGY

- Majority of patients present at around 35–40.
- May be increased in men with psychological disturbance.
- The prevalence of neurogenic-origin pain in the general population may be ~1%.
- Prevalence of chronic testicular pain is characterized for postvasectomy pain syndrome, where it is ~15–19%

RISK FACTORS

- Organic risk factors:
  - Previous trauma or operation:
    - Postvasectomy pain syndrome
    - Post hernia repair orchalgia
  - Mass lesions in scrotum:
    - Testicular tumors
    - Varicocele
    - Hydrocele
    - Cystic lesions: Epididymal cysts, spermatoceles
  - Infection:
    - Chronic epididymitis
  - Neuropathic conditions:
    - Diabetic neuropathy
    - Withdrawal from imipramine

- Psychological risk factors:
  - Men with genital pain without organic findings have a high incidence of life stress and psychological disturbance.
  - 1/3 of patients are socially isolated and many experience an important emotional loss at time of onset of pain.

GENERAL PREVENTION

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PATHOPHYSIOLOGY

- Testicular innervation:
  - Testes bring their sympathetic nerve supply with them on their descent from T10–12 segments. These nerves accompany the internal spermatic vessels. After penetrating the tunica albuginea, they are distributed to the interior of the testes between the seminiferous tubules. The main function of these nerves is to supply arteries and stimulate smooth muscles of the tunica albuginea.
  - The testis shares innervations with the epididymis.
  - Epididymis and vas deferens also have distinct sympathetic fibers from those to the testis, arising from the sympathetic outflow of T10–L1. They supply smooth muscles of vas deferens and epididymis but afferent nociceptive fibers also travel in them.
  - The parietal and visceral layers of the tunica vaginalis and cremaster receive afferent innervations at L1–L2 carried by the genital branch of the genitofemoral nerve.
- Etiology of pain in many cases is idiopathic.
- Injury may cause neural plasticity:
  - Disease or injury results in changes at all levels of the nervous system, so that pain messages are amplified.
  - Sprouting between axons may occur after injury, such that light touch is felt as pain.
- Vasectomy may result in chronic congestive epididymitis with distention of epididymis causing pain in some men; post vasectomy sperm granulomas, with inflammatory response to sperm, may cause pain in some men.
- Referred pain:
  - Any organ sharing same nerve pathway with scrotal contents can refer pain to scrotum.
  - Ureter, hip, intervertebral disc prolapse, entrapment neuropathies of ilioinguinal or genitofemoral nerves

COMMONLY ASSOCIATED CONDITIONS

- Often idiopathic (~25%)
- Can be associated with:
  - Hydrocele
  - Herniated intervertebral disc
  - Infection
  - Intermittent torsion
  - Spermatocele
  - Trauma
  - Previous surgery (vasectomy, herniorrhaphy)
  - Tumor
  - Varicocele
  - Vasculitis (polyarteritis nodosa)

DIAGNOSIS

HISTORY

- Patients have often consulted multiple physicians and other urologists.
- Frequently patients have undergone a variety of previous treatments (antibiotics, anti-inflammatory drugs) for various diagnoses with little or no relief.
- Ask about onset, location, duration, quality, exacerbating activities (exercise, sexual intercourse, or ejaculation), palliative activities
- Social history:
  - Social support
  - Satisfaction with relationships
  - Current stressors
- Assessment of sexual function including sources of guilt
- Assessment of mood and anxiety
- History of previous scrotal/inguinal surgeries

PHYSICAL EXAM

- Penis, scrotum, testis, epididymides, spermatic cords for evidence of mass
- Inguinal areas for presence of an inguinal hernia
- DRE to evaluate the prostate and rectum
- Exam often does not reveal abnormality

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and urine culture
- Semen culture (for chronic epididymitis)

- Microscopic exam of expressed prostatic secretion or urine voided after prostatic massage (VB3) (see Section II: “Stamey Test”)

Imaging

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- Evaluate scrotal contents, particularly to rule out tumor

Diagnostic Procedures/Surgery

Cystoscopy and urodynamics have been performed in men with orchalgia and usually are of limited value.

DIFFERENTIAL DIAGNOSIS

- Chronic bacterial (NIH II):
  - Chronic pelvic pain syndrome
- Epididymo-orchitis:
  - Hydrocele, spermatocele, varicocele
  - Infection
  - Inguinal hernia
  - Previous operation (vasectomy, inguinal herniorrhaphy)
- Prostatitis, chronic nonbacterial, noninflammatory (NIH CP/CPPS III B)
- Prostatitis, chronic, nonbacterial, inflammatory (NIH CP/CPPS III A):
  - Referred pain (nerve root irritation)
  - Testicular torsion
  - Trauma
  - Tumor
- Urethritis

TREATMENT

Scrotal support, limited activity, sitz baths

MEDICATION

First Line

- NSAIDs: Variable and temporary relief
- Antibiotics: Often used, rarely beneficial

Second Line

- Gabapentin, nortriptyline (and other tricyclic antidepressants), carbamazepine:

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- -Adrenergic antagonists (tamsulosin, etc.):
  - Given under the premise that drugs that modify the activity of prostatic smooth muscle should also affect the vas.

SURGERY/OTHER PROCEDURES

- Minimally invasive treatment options:
  - Needle aspiration/enucleation of cystic lesions
  - Local anesthetic infiltration of spermatic cord with or without methylprednisolone
  - Local anesthetic infiltration of the pelvic plexus under TRUS guidance
- Surgery should be avoided if possible.
- Denervation of spermatic cord (via division of ilioinguinal nerve and its branches and vas):

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  - Denervation can be performed microscopically or laparoscopically.
- Epididymectomy:
  - Poor results
- Orchiectomy:
  - Last resort; many will have persistent pain
  - Inguinal approach may be superior to scrotal
- Surgery may be more successful in relieving scrotal pain if it is directed at correction of a readily identifiable intrascrotal lesion:

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ADDITIONAL TREATMENT

- Pulsed radiofrequency of nerves:

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- TENS

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Multidisciplinary approach:

- Mental health professional conducts a formalized psychological evaluation
- Ongoing psychotherapy as needed
- Biofeedback
- Pelvic muscle exercises

ONGOING CARE

PROGNOSIS

Depends on etiology

COMPLICATIONS

- Interference with daily activities
- Surgical therapies can result in testicular loss, infertility, and undesired fertility.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Urology follow-up every 2–3 mo

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See Also (Topic, Algorithm, Electronic Media Element)

- Postvasectomy Syndrome
- Prostatitis, Chronic Nonbacterial, Noninflammatory (NIH CP/CPPS III B)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Scrotum and Testicle, Mass
- Testis, Tumor and Mass, Adult, General

CODES

ICD9

608.9 Unspecified disorder of male genital organs

ABBREVIATIONS

- DRE: Digital rectal exam
- NSAID: Nonsteroidal anti-inflammatory drug
- TENS: Transcutaneous electrical stimulation
- TRUS: Transurethral ultrasound
- US: Ultrasound

TESTIS, SEMINOMA

Danielle A. Stackhouse, MD
Judd W. Moul, MD

BASICS

DESCRIPTION

- GCT of the testicle composed of cells that are considered the malignant counterpart of gonocytes
- These tumors are generally very sensitive to both chemotherapy and radiation therapy.
- GCTs account for 95% of testicular cancer and are broadly classified as seminoma or NSGCT.
  - Seminoma accounts for 50% of GCTs
  - Represents 20% of mixed GCTs (combinations of seminomatous and NSGCT)
- Histologic subtypes:
  - Classic seminoma (peak age 35–39)
  - Spermatocytic seminoma typically found in men >50–60
  - Anaplastic seminoma is no longer recognized as distinct entity.

EPIDEMIOLOGY

- Peak incidence among men aged 20–40
- 4–5 times more common among white than African American men.
- Patients who have had 1 seminoma are at an increased risk of developing a contralateral seminoma.

RISK FACTORS

- Cryptorchidism; 3–14 times the normal incidence
- HIV infection
- Gonadal dysgenesis with Y chromosome
- Testicular feminization >30 yr of age

Genetics

- Genetic changes in the form of amplifications and deletions are observed mainly in the 12p11.2–p12.1 chromosomal regions.
- A gain of 12p sequences is associated with invasive growth of both seminomas and NSGCTs.
- In contrast, spermatocytic seminoma shows a gain of chromosome 9, whereas most infantile yolk sac tumors and teratomas show no chromosomal changes.
- P53 mutations are also seen with seminoma.

PATHOPHYSIOLOGY

- The slow growth characteristics of most seminomas result in them most commonly being diagnosed at an early stage (85% stage I).
- Right-sided tumors tend to spread in the following sequence: Interaortocaval nodes, precaval zone, and paraaortic nodes.
- Left-sided tumors spread in the following order: The paraaortic, preaortic, and renal hilar nodes. Interaortocaval nodes are involved with typically higher-stage disease.
- Rarely presents as an extragonadal GCT in a site remote from the testicle.
- Hematogenous dissemination is much less common than in NSGCT.
- -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 therapy.

COMMONLY ASSOCIATED CONDITIONS

Increased risk in patients with cryptorchidism; risk is >35 times the general population

DIAGNOSIS

HISTORY

- Painless mass or swelling in the testes
- History of undescended testicle or inguinal surgical procedure as a child

PHYSICAL EXAM

- Palpate the testes bilaterally.
- Transilluminate the mass.
- Examine the groin for evidence of surgical scar (prior orchiopexy).
- 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

Lab

- CBC and chemistry
- -hCG and AFP to rule out NSGCT:
  - Seminoma with never have elevated AFP.
  - 10–20% may have elevated -hCG.
- Placental alkaline phosphatase: Pulmonary and renal function tests for patients who may receive chemotherapy

Imaging

- Scrotal US: Often diagnostic, characterizes solid vs. cystic lesions, flow
- Chest x-ray: To rule out metastatic lesions
- CT of chest, abdomen and pelvis to evaluate for lymphatic spread:
  - Studies suggest that in seminoma patients treated for retroperitoneal adenopathy, up to 50% will resolve on subsequent imaging.
  - Bipedal lymphangiography was once the standard of care to identify retroperitoneal nodes to direct radiation planning. It is no longer routinely used.
  - PET: Limited role in patients with postchemotherapy residual masses to determine the presence of viable tumor.

Diagnostic Procedures/Surgery

Biopsy not indicated. The diagnostic procedure of choice is the radical orchiectomy.

Pathological Findings

- Classical seminoma (most common):
  - Large cells or uniform size with clear cytoplasm and distinct cell borders
  - Stains positive for PLAP
- Spermatocytic seminoma (up to 4%):
  - Cells of varying size that resemble maturing spermatogonia (peak age >50)
  - Does not stain for PLAP
- Anaplastic seminoma is no longer considered a distinct subtype of seminoma:
  - Same histology as classic seminoma, with high mitotic activity and unchanged prognosis using current treatment standards
  - Histologically, must differentiate from lymphoma and embryonal carcinoma

DIFFERENTIAL DIAGNOSIS

- Adult/pediatric painful mass:
  - Epididymitis/orchitis; bacterial, STD, mumps, TB
  - Incarcerated/strangulated hernia
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  - Torsion (testicle, testicular, or epididymal appendage)
  - Tumor (pain infrequent unless traumatized or rapidly growing; see below)
- Adult painless mass:
  - Adenomatoid tumor of testis or epididymis
  - Adrenal rest tumors
  - Adenocarcinoma of the rete testis
  - Chylocele: Usually associated with filariasis

– Fibrous pseudotumor of the tunica albuginea

– Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of the cord

– Lipoma of the cord

– Mesothelioma of tunica vaginalis

– Polyorchidism

– Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma

– Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)

– Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcinosis, fat necrosis, malignancy

– Sperm granuloma following vasectomy

– Spermatocele (epididymal cyst)

– Testicular cysts (simple, tunica albuginea, epidermoid)

– Testicular tumor:

GCTs (95% of testicular malignancies): Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma (1–5%), teratocarcinoma

Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder, and thyroid.

Mixed germ cell and stromal tumor (gonadoblastoma)

Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

Leukemia or lymphoma

– Varicocele

• Pediatric painless mass:

– Similar to adult list; most/more common are: Hydrocele, hernia, varicocele, testicular teratoma, adrenal rest tumors, rhabdomyosarcoma

TREATMENT

• Stage I: Radical orchiectomy and adjuvant RT in low stage most common treatment:

– Close surveillance with CT scanning in lieu of RT for low-stage seminoma is gaining acceptance.

• Stage II:

– Nonbulky retroperitoneal nodes: RT 35 Gy or chemotherapy

– Bulky lymphadenopathy (>5–7 cm nodes) or higher visceral metastasis (retroperitoneal adenopathy) and is treated with standard platinum-based chemotherapy (BEP/EP).

MEDICATION

- See Section I: “Testis Tumor, General” for specific chemotherapy regimens
- Chemotherapy:

– Carboplatin 1 or 2 cycles as adjuvant to stage I seminoma in place of RT or observation

– Bulky disease: Standard NSGCT chemotherapy regimens:

BEP, 3 cycles OR

4 cycles of EP

SURGERY/OTHER PROCEDURES

- Radical inguinal orchiectomy
- RPLND is not usually performed for seminoma.

ADDITIONAL TREATMENT

Radiotherapy

- Subdiaphragmatic radiation is traditional method: 35 Gy to the para-aortic and ipsilateral iliac lymph nodes following radical orchiectomy (hockey stick template).
- Newer techniques limit radiation to paraortic region with contralateral testicular shielding.
- Generally radiation doses in the adjuvant setting are in the range of 25 Gy.
- In the setting of bulky disease, the total dose is 35 Gy.
- Prophylactic mediastinal RT has generally been abandoned due to side-effect profile (cardiovascular) and failure to significantly improve outcomes. It also interferes with ability to administer salvage chemotherapy.

Additional Therapies

Active surveillance for low-risk, early disease:

- Avoids unnecessary treatment and related side effects
- CT every 4–6 mo; can reduce interval after ~5 yr
- Should be discouraged if the following risk factors are present that increase the recurrence risk: Tumor >4 cm, invasion of the rete testis, anaplastic features, small vessel invasion

COMPLEMENTARY AND ALTERNATIVE MEDICINE

The role of salvage chemotherapy, surgical removal, or RT of persistent masses detected by CT continues to be controversial.

ONGOING CARE

PROGNOSIS

- Elevation of LDH, hCG, or both and number of metastatic sites are the most important prognostic factors in patients with GCTs
- ~75% have localized disease (stage I) at diagnosis. ~15% have metastatic disease to the regional lymph nodes, and 5–10% have involvement of regional nodes or visceral metastases.
- All stages have at least a 90% cure rate:
  - Stage I: 98–100%
  - Stage II (B1/B2 nonbulky): 98–100%
  - Stage II (B3 bulky) and stage III: >90% complete response to chemotherapy and 86% durable response rate to chemotherapy
- Response rates to chemotherapy seem to be slightly better without prior radiation.

COMPLICATIONS

- Infertility, GI complications, and possible induction of secondary malignancies is a concern following adjuvant RT.
- Involvement of retroperitoneal lymph nodes may produce backache.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Surveillance protocols mandate careful long-term follow-up, which is complicated by the fact that there is no reliable serum tumor marker to follow.
- CXR and clinical exams at 1 mo, every 3 mo for 2 yr, then every 6 mo until 5 yr post diagnosis
- Pelvic CT scans should be performed in patients treated with para-aortic RT at 1, 2, and 5 yr post treatment or every 6 mo in patients with metastatic disease until abnormalities stabilized

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis Cancer, Seminoma Algorithm
- Testis, Tumor and Mass, Adult, General
- TNM Classification
- Specific Testicular Tumor Type

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

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- CXR: Chest x-ray
- EP: Etoposide, cisplatin
- GCTs: Germ cell tumors
- GI: Gastrointestinal
- hCG: Human chorionic gonadotropin
- HIV: Human immunodeficiency virus
- LDH: Lactate dehydrogenase
- NSGCT: Nonseminomatous germ cell tumor
- PET: Positron emission tomography
- PLAP: Placental-like alkaline phosphatase
- RPLND: Retroperitoneal lymph node dissection
- RT: Radiation therapy
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

TESTIS, SERTOLI CELL TUMOR

David A. Hatch, MD

BASICS

DESCRIPTION

- Sertoli cell tumor is a sex cord stromal tumor of the testis.
- A rare tumor, 90% are benign.
- Can present as a mass in the testicle or due to hormonal effects.
- Sex cord stromal tumors account for <5% of all testicular tumors and include:
  - Sertoli cell tumor
  - Leydig cell tumor
  - Granulosa cell tumor

EPIDEMIOLOGY

- <1/1,000,000
- 1/3 occur in prepubertal males.

PATHOPHYSIOLOGY

- The normal function of the Sertoli cell is to support spermatogenesis:
  - Also called a sustentacular or nurse cell.
- Sertoli cell tumor may secrete estrogens and/or testosterone:
  - Estrogen may cause gynecomastia.
  - Testosterone may cause precocious puberty.
  - 1/3 are hormonally active.
  - 10% malignant
- No reported malignancy in prepubertal males
- Can be found in the ovary
- Identification of metastases only certain criteria for malignancy:
  - Lymphatics
  - Lung
  - Bone

COMMONLY ASSOCIATED CONDITIONS

- Gynecomastia in 33%
- Precocious puberty (rare)
- Carney syndrome:
  - Leydig cell tumors
  - Pituitary tumors
  - Pigmented nodular hyperplasia of the adrenal cortex

  - Cardiac myxomas
  - Spotty pigmentation of skin
- Tuberous sclerosis
- Peutz-Jeghers syndrome

Pediatric Considerations

Isolated gynecomastia may be the 1st sign of a Sertoli cell tumor in a child. With a Leydig cell tumor, the child will not develop gynecomastia without accompanying virilization.

DIAGNOSIS

HISTORY

- Painless or painful testis mass
- Gynecomastia
- Feminization or breast pain
- Precocious puberty
- History of dysplastic syndromes:
  - Carney syndrome, tuberous sclerosis

PHYSICAL EXAM

- Testis mass
- Bilateral masses:
  - Suggests large-cell calcifying Sertoli cell type, or adrenal rests in males with congenital adrenal hyperplasia
- Palpate for evidence of gynecomastia
- Feminization, hair patterns with estrogen excess
- Precocious puberty

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Sex steroids, when elevated, may be useful in following disease for progression:
  - Androgen
  - Estrogen
  - Progesterone
- AFP is usually negative.
- -hCG is usually negative.
- Placental alkaline phosphatase is usually negative.

Imaging

- Testis US:
  - Usually a solid, well-circumscribed mass

- Occasionally cysts are seen.
- Calcifications with shadowing suggest large-cell calcifying type.

- CT pelvis and abdomen to detect metastases
- Chest x-ray to detect metastases
- Bone scan to detect metastases

Diagnostic Procedures/Surgery

- Excisional biopsy usually by radical nephrectomy
- 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.

Pathological Findings

- Gross: Gray-white to creamy yellow homogenous, encapsulated tumor
- Histology:
  - Stromal epithelial cells resembling Sertoli cells
  - Call-Exner-like bodies sometimes seen
  - Pattern is variable and may include small cysts
  - Extracapsular invasion is suggestive of, but not diagnostic for malignancy.
- Histologic subtypes:
  - Sertoli cell tumor:
    Sometime referred to as NOS
    40% occur in prepubertal males
    Low malignant potential
    Highly variable histology, often making diagnosis difficult
  - Large-cell calcifying Sertoli cell tumor:
    Most occur in males <20 yr
    Up to 1/2 are bilateral
    Can be very large
    Low malignant potential
    Variety of patterns, sometimes with tubule formation; abundant, eosinophilic cytoplasm
    Fibrosis is seen in the surrounding stroma
    Areas of calcification are prominent
  - Sclerosing Sertoli cell tumor:
    Only adult males
    Usually small

Dense fibrous stroma surrounding scattered small tubules, cords of cells, and individual cells with small nuclei and scant cytoplasm

- Sertoli cell nodules:
  - Hyperplastic foci found almost exclusively in undescended testicles
  - Contain laminated calcifications also called tubular adenoma of Pick
  - Relationship to malignancy is not clear.
- Mixed Sertoli-Leydig cell tumor is more commonly seen in the ovary and produces excess testosterone. Rare reports in the testicle.

DIFFERENTIAL DIAGNOSIS

- Adult/pediatric painful mass:
  - Epididymitis/orchitis; bacterial, STD, mumps, TB
  - Fournier gangrene
  - Henoch-Schönlein purpura (usually no mass)
  - Incarcerated/strangulated hernia
  - Post vasectomy syndrome (usually no mass)
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  - Torsion (testicle, testicular, or epididymal appendage)
  - Tumor (infrequent unless traumatized or rapidly growing; see below)
- Adult painless mass:
  - Adenomatoid tumor of testis or epididymis
  - Adrenal rest tumors
  - Adenocarcinoma of the rete testis
  - Chylocele: Usually associated with filariasis
  - Fibrous pseudotumor of the tunica albuginea
  - Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of the cord
  - Lipoma of the cord
  - Mesothelioma of tunica vaginalis
  - Polyorchidism
  - Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma
  - Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
  - Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcinosis, fat necrosis, malignancy

– Sperm granuloma following vasectomy
– Spermatocele (epididymal cyst)
– Testicular cysts (simple, tunica albuginea, epidermoid)
– Testicular tumor:

Germ cell tumors (95% of testicular malignancies): Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma (1–5%), teratocarcinoma

Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder, and thyroid

Mixed germ cell and stromal tumor (gonadoblastoma)

Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

Leukemia or lymphoma

– Varicocele

• Pediatric painless mass:

– Similar to adult list; most/more common are: Hydrocele, hernia, varicocele, testicular teratoma, adrenal rest tumors, rhabdomyosarcoma

Pediatric Considerations

• Sertoli cell tumors are rare in children, but they make up 1/3 of all Sertoli cell tumors.
• Boys with Sertoli cell tumor may have gynecomastia, or less commonly, precocious puberty.
• Sertoli cell tumors in prepubertal males are benign.

TREATMENT

Radical inguinal orchiectomy is the primary procedure of choice as these rare tumors are usually thought to be a more common malignancy of the testicle.

MEDICATION

• Platinum-based chemotherapy
• Used in metastatic disease, but unproven benefit

SURGERY/OTHER PROCEDURES

• Radical orchiectomy
• In prepubertal boys, testis-sparing local excision has been reported (none are malignant) after frozen section biopsy confirms the diagnosis.
• RPLND: Reported, but unproven efficacy

ADDITIONAL TREATMENT

Used in metastatic disease, but unproven benefit

ONGOING CARE

PROGNOSIS

- Benign, completely excised: Excellent
- Malignant: Poor

COMPLICATIONS

- Recurrence: Rare
- Metastases: Uncommon
- Men with sex cord stromal tumors are at increased risk for hypogonadism following orchiectomy.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Benign tumors: Periodic scrotal exam
- Malignant tumors: Imaging of metastases

ADDITIONAL READING

- Giglio M, et al. Testicular Sertoli cell tumours and relative sub-types. Analysis of clinical and prognostic features. Urol Int 2003;70:205–210.
- Richie JP, Steele GS. Neoplasms of the testis. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007.

See Also (Topic, Algorithm, Electronic Media Element)

- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General

CODES

ICD9

222.0 Benign neoplasm of testis

ABBREVIATIONS

- AFP: -Fetoprotein
- CT: Computed tomography
- -hCG: -human chorionic gonadotropin
- GI: Gastrointestinal
- hCG: Human chorionic gonadotropin
- NOS: Not otherwise specified
- RPLND: Retroperitoneal lymph node dissection

- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

TESTIS, TERATOMA, MATURE AND IMMATURE

Brett S. Carver, MD
Joel Sheinfeld, MD

BASICS

DESCRIPTION

- Teratoma is a neoplasm of germ cell origin forming somatic-type tissue in various stages of maturation and differentiation; part of the nonseminomatous category of testicular cancers.
- Testicular teratomas in prepubertal boys have not been reported to metastasize.
- Testicular teratomas in adults are associated with clinical metastases in ~60% of cases, demonstrating the diverse nature of teratoma.

EPIDEMIOLOGY

- Incidence of testicular tumors in children ranges from 0.5–2.0 cases per 100,000 boys.
- It is projected that, in the US, ~8,090 new cases of testicular cancer would be diagnosed and 380 adult men would die of this disease in 2008.
- While teratomatous elements are found in 55–80% of primary NSGCTs in adults, only 2–6% of cases are comprised of pure teratoma.
- Most pure teratomas present in boys <4 yr of age.

RISK FACTORS

Risk factors associated with the development of testicular cancer include:

- Cryptorchidism
- Family history
- Infertility
- Testicular atrophy

Genetics

Identification of isochromosome 12p amplification

PATHOPHYSIOLOGY

- Teratoma is a neoplasm of germ cell origin that is composed of several types of tissue representing different germinal layers (endoderm, mesoderm, ectoderm), forming somatic-type tissue in various stages of maturation and differentiation.
- Infantile teratomas follow a benign course, and genetic studies (karyotyping and comparative genomic hybridization) tumors have failed to demonstrate chromosomal changes in these tumors.
- In contrast, teratomas in adult testes are hypotriploid and have genetic changes similar to those seen in other components of germ cell tumors.

COMMONLY ASSOCIATED CONDITIONS

- Germ cell tumors of the testis:
  - Yolk sac for pre-pubertal males
  - Seminoma or nonseminoma for adult males.
- Infertility
- Cryptorchidism

DIAGNOSIS

HISTORY

- Family history of testicular neoplasm or history of undescended testicle.
- 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.
- For adult males with teratoma, at initial presentation, symptoms manifesting secondary to metastatic disease occur in ~20% of patients.

PHYSICAL EXAM

- The most common finding on physical exam is a solid intratesticular mass or swelling.
- Patients should undergo a complete physical exam, emphasizing palpation of the cervical lymph nodes (lymphadenopathy), breasts (gynecomastia), abdomen (retroperitoneal masses/lymphadenopathy, liver masses), and the contralateral testis (bilateral testicular tumors).

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and urine culture as part of the workup for a testicular mass
- Serum tumor markers (AFP, hCG, LDH) should be obtained prior to and following radical orchiectomy.
- Pure teratomas do not produce either AFP or hCG as serum tumor markers:
  - Elevation suggests the presence of other testicular cancer elements

Imaging

- Testicular US is the initial imaging modality of choice with a >95% sensitivity and specificity in identifying intratesticular lesions:
  - Testicular US often reveals a solid or cystic hypoechoic mass present within the testis.
  - Additionally, hyperechoic areas of calcification are often imaged within the tumor.
- For adult males, a CT of the chest, abdomen, and pelvis should be performed to evaluate for metastatic disease.

Diagnostic Procedures/Surgery

A radical orchiectomy 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.

Pathological Findings

- Gross exam:
  - Teratomas are usually nodular and firm with a variably cystic and solid cut surface.
  - The cysts may be filled with keratinous material or clear serous or mucoid fluid. The solid areas may contain translucent, gray-white nodules representing cartilage. Hair or melanin-containing tissue may also be rarely seen.
  - Areas of immature tissue are mostly solid and may have an encephaloid, hemorrhagic, or necrotic appearance.
- Mature teratomatous lesions contain well-differentiated tissues resembling normal postnatal tissue and typically include structures derived from the 3 germ layers:
  - Tissue of ectodermal origin: Nests of squamous epithelium with or without cyst formation and keratinization.
  - Neural tissue may be seen as foci of neuroglia.
  - Structures of endodermal origin are represented by glandular epithelium of enteric- or respiratory-type.
  - Mesodermal elements are represented by cartilage, bone, adipose tissue, fibrous tissue, and, most commonly, muscle.
- Immature teratoma:
  - Fetal-type tissue; also consists of ectodermal, endodermal, and/or mesodermal elements
  - It usually occurs as islands of immature neuroepithelium resembling that of the developing embryonic neural tube.
  - Immature tissue may also have an organoid arrangement with blastomatous and primitive tubular structures resembling that of the developing kidney or lung.
  - Embryonic skeletal muscle, cartilage, and nonspecific cellular stroma may also be encountered.
  - Mature cystic teratomas (dermoid cysts) are rare in the testis but common in the ovary.
  - Teratoma with malignant transformation can have elements of somatic tissue such as adenocarcinoma or SCC and are highly metastatic. Chemotherapy is often tailored to the somatic tissue histology.

– Teratocarcinoma occurs when teratoma coexists with embryonal carcinoma; this term has been replaced by the term malignant mixed germ cell tumor.

DIFFERENTIAL DIAGNOSIS

- Adult/pediatric painful mass:
  - Epididymitis/orchitis; bacterial, STD, mumps, TB
  - Incarcerated/strangulated hernia
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  - Torsion (testicle, testicular, or epididymal appendage)
  - Tumor (pain infrequent unless traumatized or rapidly growing; see below)
- Adult painless mass:
  - Adenomatoid tumor of testis or epididymis
  - Adrenal rest tumors
  - Adenocarcinoma of the rete testis
  - Chylocele: Usually associated with filariasis
  - Fibrous pseudotumor of the tunica albuginea
  - Hydrocele, primary or due to trauma, torsion, tumor, epididymitis; hydrocele of the cord
  - Lipoma of the cord
  - Mesothelioma of tunica vaginalis
  - Polyorchidism
  - Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma
  - Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
  - Scrotal wall: Sebaceous and inclusion cysts, idiopathic calcinosis, fat necrosis, malignancy
  - Sperm granuloma following vasectomy
  - Spermatocele (epididymal cyst)
  - Testicular cysts (simple, tunica albuginea, epidermoid)
  - Testicular tumor:

    Germ cell tumors (95% of testicular malignancies): Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma (1–5%), teratocarcinoma

    Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

    Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder and thyroid.

Mixed germ cell and stromal tumor (gonadoblastoma)

Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

Leukemia or lymphoma

– Varicocele

• Pediatric painless mass:

– Similar to adult list; most common are hydrocele, hernia, varicocele, testicular teratoma, adrenal rest tumors, rhabdomyosarcoma

ALERT

~18–33% of patients with testicular cancer were initially treated for epididymitis by their physician, resulting in a delay in diagnosis and appropriate management of testicular cancer.

TREATMENT

• From a treatment standpoint, mature and immature teratoma are considered to be the same.

• Radical orchiectomy should be performed for diagnosis and treatment of the primary tumor.

• 2/3 of patients with NSGCTs, including those with pure testicular teratomas, will present with advanced metastatic disease:

– These patients are managed initially with chemotherapy according to the IGCCG risk criteria, followed by PC-RPLND.

– The post-chemotherapy histologic findings in the retroperitoneal specimen reveal fibrosis, teratoma, and viable GCT, in 44%, 50%, and 6% of patients, respectively.

MEDICATION

• See Section I: “Testis Cancer, General” for specific chemotherapy regimens

• None (see “Testis Cancer” for associated metastatic germ cell tumor)

SURGERY/OTHER PROCEDURES

• Radical orchiectomy with high ligation of the cord

• Although pure testicular teratomas have a benign clinical course in prepubertal children, in adults, metastases have been reported in 29–76% of cases at initial presentation:

– Retroperitoneal metastases have been identified in ~20% of patients with clinical stage I pure testicular teratoma treated with primary RPLND.

ADDITIONAL TREATMENT

Surveillance, employed in other low-stage NSGCTs, is usually contraindicated in teratoma.

ONGOING CARE

PROGNOSIS

- The prognosis of prepubertal teratoma is excellent with a 100% survival rate following radical orchiectomy.
- The prognosis of adult teratoma is excellent and parallels the prognosis of NSGCTs. The multidisciplinary approach to the management of germ cell tumors of the testis has resulted in survival rates of >90% overall.

COMPLICATIONS

- The complications of radical orchiectomy include wound infection, scrotal hematoma, and retroperitoneal hematoma.
- The complications of RPLND include wound infection, pancreatitis, venous thrombosis, chylous ascites, anejaculation, and small bowel obstruction.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow with history and physical exam; adult patients should also have serum tumor markers, chest x-ray, and periodic CT imaging of the chest, abdomen, and pelvis for life.
- Follow-up protocols should be followed according to guidelines established by the NCCN.

ADDITIONAL READING

- Carver BS, Al-Ahmadie H, Sheinfeld J. Adult and pediatric teratoma. Urol Clin North Am 2007;34(2):245–251.
- National Comprehensive Cancer Network. Available at www.NCCN.org

See Also (Topic, Algorithm, Electronic Media Element)

- IGCCG System
- Scrotum and Testicle, Mass
- Testis Cancer, General
- Testis, Tumor and Mass, Adult, General

CODES

ICD9

186.9 Malignant neoplasm of other and unspecified testis

ABBREVIATIONS

- AFP: -Fetoprotein
- CT: Computed tomography
- GCT: Germ cell tumor
- GI: Gastrointestinal

- hCG: Human chorionic gonadotropin
- IGCCG: International Germ Cell Collaborative Group
- LDH: Lactate dehydrogenase
- NCCN: National Comprehensive Cancer Network
- NSGCT: Nonseminoma germ cell tumor
- PC-RPLND: Post-chemotherapy retroperitoneal lymph node dissection
- RPLND: Retroperitoneal lymph node dissection
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

TESTIS, TUMOR AND MASS, ADULT, GENERAL

David F. Penson, MD, MPH

BASICS

DESCRIPTION

- Testicular cancer is the most common malignancy in men age 15–35.
- Mortality from this malignancy has dropped from >50% in the 1970s to under 5% today, due to improved imaging, better tumor markers, and multidrug chemotherapy regimens.
- Testicular tumors are 95% germ cell tumors, although tumors occasionally arise from other cell lines in the testis (sex cord/stromal).

EPIDEMIOLOGY

- ~8,090 new cases of testicular cancer will be diagnosed in the US in 2008, and 380 men will die of this disease.
- From 2001–2005 in the US:
  - The median age at diagnosis was 34
  - Age distribution at diagnosis

5.8% <20 yr
13.3% 45–54 yr
46.3% 20–34 yrs
3.3% 55–64 yrs
29.2% 35–44 yr
1.8% >65 yr

– Age-adjusted incidence rate was 5.4/100,000 men per year:

White men: 6.3/100,000
Black men: 1.4/100,000
Asian men: 1.7/100,000
Hispanic men: 3.9/100,000
More common on right (53%), 2–3% bilateral

On January 1, 2005, in the US, there were 184,074 men alive with history of testicular cancer.

RISK FACTORS

- History of cryptorchidism:
  - 7–10% of cases; 4–14 times more likely to develop testicular cancer
  - Seminoma is most common tumor type
  - Orchiopexy does not reduce risk, although it facilitates self-exam

- Hormonal exposure:
  - Exposure to DES in utero increases the relative risk of testicular cancer roughly 3–5%

Genetics

- Isochromosome 12p amplification
- Twin studies are negative, but 2–3% incidence of bilateral tumors implies genetic factors.

GENERAL PREVENTION

Testicular self-exam should be performed monthly for earlier diagnosis.

PATHOPHYSIOLOGY

- Germ cell tumors (seminoma, embryonal cell carcinoma, teratoma, choriocarcinoma, and yolk sac tumor) comprise 90–95% of testicular tumors.
  - Mixed germ cell tumors common (60% of all)
- Seminoma: 35–65% of germ cell tumors; classified into 3 subtypes:
  - Typical (classic) seminoma: 82–85% of seminomas; most commonly men in 30s; less common in men in 40s–50s

    Syncytiotrophoblast in 10–15% of typical seminomas and makes to -hCG.
  - Anaplastic seminoma:

    Designation not widely used; considered an aggressive classic seminoma
  - Spermatocytic seminoma:

    2–12%; roughly 1/2 in men >50 yr

    Lower malignant potential
- Embryonal cell carcinoma:
  - Occurs in 40% of germ cell tumors
- Choriocarcinoma
  - Rarely found in pure form; pure form is often advanced, with a small primary tumor.
  - Prognosis for pure choriocarcinoma is poor.
- Yolk sac tumor:
  - 92% stain for AFP
- Non-germ cell tumors (5–7%):
  - Leydig cell tumors: 2–3% of tumors; not associated with cryptorchidism;10% malignant
  - Sertoli cell tumors:

    1% of testicular tumors; 90% benign

- Gonadoblastoma:

  Quite rare; most in men <30

COMMONLY ASSOCIATED CONDITIONS

- Cryptorchidism
- Karyotype abnormalities in gonadoblastoma

DIAGNOSIS

HISTORY

- Local symptoms:
  - Change in testicular size or texture
  - Testicular pain
- Systemic symptoms:
  - Weight loss
  - Abdominal pain/discomfort
  - Fevers
  - Gynecomastia or other changes in secondary sex characteristics
- History of cryptorchidism
- History of infertility
- Prior orchiopexy

PHYSICAL EXAM

- Check all lymph nodes, including supraclavicular nodes.
- Abdominal exam for masses
- Examine for gynecomastia (in 5% of cases).
- Testicular exam: Examine both testes:
  - Any firm or hard area in the testis should be considered cancer; determine if mass is distinct from epididymis.
  - Note consistency of testis, whether it is fixed to scrotum, and size of lesion
  - Palpate for hydrocele, hernia.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Tumor markers obtained prior to orchiectomy:
  - 1 or both markers elevated in 85–90% of NSGCT
- -hCG:
  - Half-life: 24–36 hr
  - Elevated in 40–60% with testis cancer; 100% of choriocarcinomas;10–15% pure seminomas

- 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.
- Serum and urine estrogens may be elevated in Leydig cell tumors

Imaging

- Scrotal US:
  - Diagnostic imaging mainstay for identifying testicular tumors
  - Any hypoechoic lesion within the testicular parenchyma should be considered cancer.
  - 80% of testicular tumors are hypoechoic.
- Abdominal CT:
  - Critical for staging of testicular tumors
  - Should be performed prior to orchiectomy if possible, as postoperative retroperitoneal hematoma can distort imaging.
  - Accuracy is 70–90%, depending upon stage.
  - Cannot detect micrometastasis in normal-sized lymph nodes
- Plain chest x-ray:
  - Needed for staging of chest for metastases
  - If abnormal, chest CT is obtained.

Diagnostic Procedures/Surgery

- Radical inguinal orchiectomy:
  - Important for determining pathology of primary tumor. Therapeutic in that chemotherapy does not penetrate testis well.
- Transscrotal testicular biopsy or orchiectomy should NOT be performed.

Pathological Findings

- Typical/classic seminoma: Islands or sheets of relatively large cells with clear cytoplasm and densely staining nuclei:
  - Anaplastic seminoma: Increased mitotic activity; now a subtype of classic seminoma
- Spermatocytic seminoma: Cells vary in size and have deeply pigmented cytoplasm and rounded nuclei that contain characteristic filamentous chromatin. The cells closely resemble different phases of maturing spermatogonia.
- Embryonal cell carcinoma: Distinctly malignant epithelioid cells arranged in glands or tubules. Cell borders are indistinct, cytoplasm pale or vacuolated, and nuclei rounded with

coarse chromatin and 1 large nucleoli. Mitotic figures, giant cells commonly seen.

- Choriocarcinoma: 2 distinct cell types must be demonstrated to satisfy the histologic diagnosis of choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts.
- Yolk sac tumor: Epithelioid cells form glandular and ductal structures arranged in columns, papillary projections, or solid islands within a primitive stroma. Tumor cells have poorly defined cell borders and vacuolated cytoplasm with glycogen and fat.
  - Embryoid bodies, resemble 1–2-wk-old embryos.
- Leydig cell tumors: Uniform, closely packed cells with round, slightly eccentric nuclei and eosinophilic granular cytoplasm with lipoid vacuoles, brownish pigmentation, and occasional inclusions known as Reinke crystals.
- Sertoli cell tumors: Epithelial elements resembling Sertoli cells and varying stroma.
- Gonadoblastoma: Must have 3 elements: Sertoli cells, interstitial tissue, and germ cells.
  - 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

These are testicular masses only. For a complete listing of intrascrotal and testicular masses see Section I: “Scrotum and Testicle Mass”:

- Epididymitis/orchitis; bacterial, STD, mumps, TB
- Incarcerated/strangulated hernia
- Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
- Torsion (testicle or appendages)
- Adenomatoid tumor of testis or epididymis
- Adrenal rest tumors
- Adenocarcinoma of the rete testis
- Fibrous pseudotumor of the tunica albuginea
- Mesothelioma of tunica vaginalis
- Paratesticular sarcomas: Rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma
- Cysts (simple, tunica albuginea, epidermoid)
- Testicular tumor:
  - Germ cell tumors: Seminoma, embryonal cell carcinoma, choriocarcinoma, yolk sac carcinoma teratoma, teratocarcinoma
  - Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors
  - Metastatic tumors: Prostate, lung, and GI tract; rare kidney, malignant melanoma, pancreas, bladder and thyroid

– Mixed germ cell and stromal tumor (gonadoblastoma)

– Angioma, fibroma, leiomyoma, hamartoma, carcinoid, mesothelioma, and neurofibroma

– Malignant fibrous histiocytoma (most common soft-tissue sarcoma in late adult life)

– Leukemia or lymphoma

TREATMENT

- Radical inguinal orchiectomy is considered standard of care.
- Additional therapy for NSGCT depends on staging. Commonly used staging system is the TNM staging and Group Staging by the AJCC.
- Surveillance, with serial imaging and tumor markers, is appropriate in certain low-risk patients:
  - Stage I seminoma
  - Stage I NSGCT: No teratomatous elements, no lymphovascular invasion, and no embryonal cell carcinoma in the primary specimens. Patients must be reliable.

MEDICATION

First Line

- Treatment depends upon primary cell type of tumor and stage at presentation.
- Cisplatin-based chemotherapy is the 1st-line regimen for treating testicular cancer:
  - Commonly used for stage IIc and higher seminoma; numerous regimens used.
  - 2 cycles of BEP in stage I NSGCT
  - 3 cycles of BEP commonly used for stage IIa, IIb; good risk stage IIc and III disease
  - Poor-risk stage IIc and II disease: 4 cycles of BEP have been used:

Some centers have replaced etoposide with ifosfamide and some use advocated 4 cycles of vinblastine, ifosfamide, and cisplatin.

Second Line

High-dose chemotherapy with autologous bone marrow transplantation in patients with residual disease and or recurrent disease

SURGERY/OTHER PROCEDURES

- Radical orchiectomy:
  - Inguinal approach is used to prevent violation of tissue planes
  - May be adequate treatment for stage I seminoma and certain stage I NSGCTs
- RPLND:
  - Indicated in patients with stage I and IIa NSGCT, particularly those with teratoma in the primary specimen

– With residual mass after chemotherapy
– Nerve-sparing approach will preserve antegrade ejaculation in 90% of patients.
– For low-stage disease, a modified nerve-sparing template is normally used.
– For RPLND description, see Section I: “Testis Cancer, Nonseminomatous Germ Cell Tumors”

ADDITIONAL TREATMENT

Radiotherapy

- Commonly used in stage I and IIa seminomas
- External beam radiation to retroperitoneal and ipsilateral ilioinguinal lymph nodes
- Contralateral inguinal region is included if history of inguinal or scrotal procedures

Additional Therapies

Patients should consider sperm banking.

ONGOING CARE

PROGNOSIS

Depending upon stage and cell type of primary tumor, prognosis is excellent, with 95% of patients experiencing a long-term cure.

COMPLICATIONS

- Infertility
- RPLND: Retrograde ejaculation, ileus, atelectasis, chylous ascites, chylothorax, pneumonitis, lymphocele, pancreatitis, and vascular or bowel injury
- Increased risk of secondary malignancies in patients undergoing chemotherapy or radiation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- In patients who underwent RPLND:
  – Serial monitoring with chest x-ray, physical exam, and tumor markers. Retroperitoneal recurrence 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 RPLND:
  – 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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- IGCCC System
- Scrotum and Testicle Mass
- Testis Cancer, General
- Testis Tumor and Mass, Adult, General
- TNM Classification
- Specific Testicular Tumor Type

CODES

ICD9

- 186.9 Malignant neoplasm of other and unspecified testis
- 608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- AFP: -Fetoprotein
- AJCC: American Joint Committee on Cancer
- BCG: -Human chorionic gonadotropin
- BEP: Bleomycin, etoposide, and cisplatin chemotherapy
- CT: Computed tomography
- DES: Diethylstilbestrol
- GI: Gastrointestinal
- NSGCT: Nonseminomatous germ cell tumor
- PAS: Periodic acid-Schiff
- RPLND: Retroperitoneal lymph node dissection
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

TESTIS, TUMOR AND MASS, PEDIATRIC, GENERAL

Douglas E. Coplen, MD

BASICS

DESCRIPTION

- Painless scrotal mass sometimes replacing the entire testicle in a male <18 yr of age.
- In contrast to adults, testicular tumors in children are much more often benign.
- Must differentiate true testicular tumor or mass from masses in the scrotal wall and paratesticular tissues.
- The most common causes of painless scrotal swelling in a child include hernias and hydrocele, with lesions such as varicocele, scrotal wall swelling (insect bite or nephrotic syndrome), and testicular neoplasms less common.

EPIDEMIOLOGY

- 0.5–2 per 100,000 children/yr
- Peak age of incidence is 2 yr
- Lower incidence of germ cell tumors when compared to adults
- 25–30% of pediatric tumors are malignant.
- Rare in black and Asian children
- Accounts for 2% of pediatric tumors
- Testicular tumors in children:
  - Teratoma: 40–50%
  - Epidermoid cyst: 10–15%
  - Yolk sac tumor: 25–35%
  - Gonadal stromal tumors: 10–15%
  - Gonadoblastoma: 1–2%
  - Leukemia: 1–2%
  - Cystic dysplasia: <1%

RISK FACTORS

- Cryptorchidism a risk for postpubertal germ cell tumors.
- Congenital adrenal hyperplasia and intratesticular adrenal rests

Genetics

- Gonadoblastoma is associated with gonadal dysgenesis and a 45XO/46XY karyotype.
- Yolk sac tumors: Abnormalities: 1p, 6q, and 3p
- Large-cell calcifying Leydig tumor is associated with Peutz-Jeghers syndrome and Carney complex.
- No clear genetic etiology exists for teratoma, Leydig cell tumor, and granulosa cell tumor.

GENERAL PREVENTION

- Orchidopexy does not eliminate the risk of developing testicular cancer in cryptorchidism. Studies suggest it may reduce the risk.
- Early orchidopexy to place the testicle in a scrotal position permits earlier detection of testicular masses. Other benefits include improved fertility and a reduced risk of torsion.

PATHOPHYSIOLOGY

- Teratoma: Monodermal (epidermoid cyst) or multiple histologic types present (nerve, cartilage, intestinal epithelium, etc.)
  - Not associated with an elevated AFP
  - Metastasis not reported before puberty
  - Testis sparing enucleation via an inguinal incision is possible.
- Germ cell tumor:
  - Seminomas and mixed germ cell tumors rare in prepubertal children.
  - Yolk sac (endodermal sinus tumor; 82%):

    AFP elevated in 80% of yolk sac, and normally elevated in a neonate. Its half-life is 5–7 days. Persistent elevation after orchiectomy implies metastatic disease.

    Metastatic spread is hematogenous.

    Yolk sac elements stain positive for AFP

    b-hCG produced by syncytiotrophoblast is rarely elevated in yolk sac tumors.
- Gonadal stromal tumors:
  - Leydig cell tumors:

    Peak age of 4–5 yr; increased testosterone production with normal LH

    Differential diagnosis includes pituitary lesions, Leydig cell hyperplasia, CAH based on hormonal production

    Reinke 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 are not hormonally active

    Gynecomastia when hormonally active

    Retroperitoneal spread rarely reported
  - Granulosa-cell tumor:

    Rarely metastasizes
  - Testis tumor of adrenogenital syndrome:

    Benign, suppressible with glucocorticoids

– Gonadoblastoma:
Most common tumor in DSD (intersex)
Germ cell component is prone to malignant degeneration
– Lymphoma, leukemia
– Cystic dysplasia of the testis:
Irregular cysts in rete testis; associated with renal agenesis and multicystic dysplasia

- Intergroup staging system:

– Stage 1: Limited to testis, markers normalize in the half-life. Normal markers at diagnosis require normal imaging and a negative ipsilateral retroperitoneal node dissection.
– Stage 2: Transscrotal orchiectomy or tumor rupture during orchiectomy, persistent elevated markers, residual disease in scrotum or <5 cm from testicular cord margin
– Stage 3: Nodes >4 cm, no visceral or distant disease. Nodes >2 and <4 cm require biopsy.
– Stage 4: Distant metastases

COMMONLY ASSOCIATED CONDITIONS

- Precocious puberty
- Undescended testicle

DIAGNOSIS

HISTORY

- Asymptomatic scrotal mass or asymmetry noted by parents
- Acute pain or fever with hemorrhage, trauma, rapid growth of the tumor, infection
- Precocious sexual development
- Breast tenderness with gynecomastia
- Undescended testicle or hernia repair

PHYSICAL EXAM

- Scrotal asymmetry
- Abnormality intratesticular vs. intrascrotal
- 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

Lab

- Serum markers AFP and -hCG:

– Obtain prior to orchiectomy in all patients with a testicular mass

– Marked AFP elevations present in newborn; detectable is normal up to 8 mo of age

• Serum testosterone, LH, and FSH levels if a gonadal stromal tumor is suspected; testosterone is elevated and gonadotropins are suppressed in Leydig cell tumor.

• Estrogen and progesterone: Elevated with gynecomastia

Imaging

• Scrotal US:

– Differentiate intratesticular vs. extratesticular

– Extratesticular/paratesticular usually benign (except rhabdomyosarcoma)

– Does not differentiate benign from malignant except classic epidermoid cyst (round with layers, onion peel appearance)

– Paratesticular rhabdomyosarcoma:

Hypervascular solid extratesticular mass on US

Often large; testicle not seen on US

– Indeterminate lesions on US that resemble testicular neoplasm include tubular ectasia of the rete testis, inflammation, infarction, fibrosis, and traumatic hematoma.

• Chest x-ray: Evaluate for yolk sac tumors mets

• Abdominal and pelvic CT:

– Obtained after histology confirms malignancy

– Evaluate retroperitoneum for lymph node metastases and liver for metastases

• Bone scan indicated by symptoms

• MRI may have utility in the evaluation of indeterminate lesions seen on US.

Diagnostic Procedures/Surgery

Inguinal exploration with enucleation with frozen section and/or radical inguinal orchiectomy is the gold standard approach to diagnosis.

Pathological Findings

• Typical seminoma: Islands or sheets of relatively large cells with clear cytoplasm and densely staining nuclei.

• Embryonal cell carcinoma: Malignant epithelioid cells arranged in glands or tubules. Cell borders indistinct, cytoplasm pale or vacuolated, and nuclei rounded with coarse chromatin. Pleomorphism, mitotic figures, and giant cells are commonly seen.

• Choriocarcinoma: 2 distinct cell types must be demonstrated to satisfy the histologic diagnosis of choriocarcinoma: Syncytiotrophoblasts and cytotrophoblasts. The syncytiotrophoblasts may be large, multinucleated cells containing abundant, often vacuolated, eosinophilic cytoplasm and large, hyperchromatic, irregular nuclei:

– Cytotrophoblasts are closely packed, uniform cells with a distinct cell border, clear cytoplasm, and single nucleus.

• Yolk sac tumor: Epithelioid 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. The large, irregular nuclei contain 1 prominent nucleoli and variable chromatin. Embryoid bodies (common) resemble 1–2-wk-old embryos.

• Leydig cell tumors: Uniform, closely packed cells with round, slightly eccentric nuclei and eosinophilic granular cytoplasm with lipoid vacuoles, brownish pigmentation, and inclusions known as Reinke crystals.

• Sertoli cell tumors: Epithelial elements resembling Sertoli cells and varying stroma.

• Gonadoblastoma: Must have 3 elements: Sertoli cells, interstitial tissue, and germ cells:

– 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:
  – Epididymitis/orchitis; bacterial, mumps
  – Fournier gangrene
  – Henoch-Schönlein purpura (usually no mass)
  – Incarcerated/strangulated hernia
  – Testis trauma: Contusion, rupture; hematocele
  – Torsion (testicle, testicular, or epididymal appendage); more common after puberty
  – Tumor (infrequent unless traumatized or rapidly growing; see below)
• Painless mass (**most common in children)
  – Adenomatoid tumor of testis or epididymis
  – Adrenal rest tumors**
  – Cystic dysplasia of the testis
  – Chylocele: Usually associated with filariasis
  – Fibrous pseudotumor of the tunica albuginea
  – Hydrocele, primary** or due to trauma, torsion, tumor, epididymitis; hydrocele of cord
  – Hernia
  – Lipoma of the cord
  – Polyorchidism

– Paratesticular rhabdomyosarcoma (**bimodal age 3–4 and teens)
– Scrotal edema (insect bite, nephrotic syndrome, acute idiopathic scrotal edema)
– Spermatocele (epididymal cyst): Uncommon
– Testicular cysts (simple, tunica albuginea, epidermoid)
– Testicular tumor:

Germ cell tumors: Yolk sac carcinoma**, teratoma** seminoma, embryonal cell carcinoma, choriocarcinoma

Gonadal stromal tumors: Leydig tumor, Sertoli cell, granulosa cell tumors

Metastatic tumors: Unusual in childhood

Mixed germ cell and stromal tumor (gonadoblastoma)

Hamartoma, carcinoid, and neurofibroma

Testis tumor of adrenogenital syndrome

Leukemia or lymphoma

– Varicocele: Fullness and not a firm mass; changes with position

TREATMENT

• Testis preservation with benign lesions most common in children as opposed to adults.

• Prepubertal testicular teratomas, and Leydig and Sertoli cell tumors are benign; orchiectomy or testicular-sparing surgery is curative and no additional therapy is indicated in benign lesions.

• Yolk sac tumor or other malignant tumor; radical orchiectomy and observation if low stage

MEDICATION

• Chemotherapy for all yolk sac tumor stage II or greater or other germ cell tumor
– Platinum-based as for other nonseminomas (cisplatin, etoposide, and bleomycin); see Section I: “Testis, Cancer General”

• Rhabdomyosarcoma: Adriamycin and dactinomycin chemotherapy

SURGERY/OTHER PROCEDURES

• Inguinal exploration and exposure in all patients
• Radical inguinal orchiectomy with solid tumor:
– Consider enucleation and frozen section for epidermoid cyst or mixed echogenicity suspicious for teratoma.

• Retroperitoneal lymph node dissection:
– Postchemotherapy with residual mass
– Rarely indicated since 90% of yolk sac tumors are stage 1 at presentation
– Older children with cord rhabdomyosarcoma

ADDITIONAL TREATMENT

Utilized for testicular recurrence of leukemia

ONGOING CARE

PROGNOSIS

Prepubertal teratoma is uniformly benign:

- 90% of yolk sac tumors are stage I at presentation
- 85% 6-yr survival in stage 4 patients with yolk sac tumor

COMPLICATIONS

Related to surgery and chemotherapy

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Depends on stage of disease and the pathologic diagnosis
- Routine follow-up is not required for teratoma.
- Stage 1 yolk sac tumor:
  - Monthly AFP for 1 yr
  - CT abdomen every 3 mo for 1 yr and every 6 mo for 2 yr if AFP is initially negative

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Rhabdomyosarcoma, Pediatric
- Scrotum And Testicle, Mass
- Specific Testis Tumor Type in Section I
- Testis, Cancer, General
- Testis, Leukemia of
- TNM Classification
- Torsion, Testis and Testicular Appendages

CODES

ICD9

  - 186.9 Malignant neoplasm of the testis
  - 608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- AFP: -Fetoprotein
- CAH: Congenital adrenal hyperplasia
- CT: Computed tomography
- DSD: Disorders of sexual differentiation
- FSH: Follicle-stimulating hormone
- hCG: Human chorionic gonadotropin
- LH: Luteinizing hormone
- MRI: Magnetic resonance imaging
- PAS: Periodic acid-Schiff
- US: Ultrasound

TESTOSTERONE DECREASED (HYPOGONADISM)

Wilmer B. Roberts, MD, PhD

Arthur L. Burnett, MD

BASICS

DESCRIPTION

- Inadequate levels of the primary androgenic hormone in the male
- T is essential for:
  - Normal sexual function, growth, and development of male sexual organs, maintenance of male secondary sexual characteristics
- Normal levels and function result in:
  - Enhanced libido, increased energy, increased production of RBCs and protection against osteoporosis
- Prepubertal hypogonadism:
  - Small testes, phallus, and prostate
  - Scant pubic and axillary hair
  - Disproportionately long arms and legs (from delayed epiphyseal closure)
  - Reduced male musculature, gynecomastia, persistent high-pitched voice
- Postpubertal hypogonadism:
  - Progressive decrease in muscle mass, increase in visceral fat mass
  - Hypercholesterolemia, loss of libido, ED, oligospermia, or azoospermia
  - Occasionally, menopausal-type hot flushes (with acute onset of hypogonadism), poor ability to concentrate
  - Osteoporosis and increased risk of fractures

EPIDEMIOLOGY

- 20% of men in the 7th decade of life
- 30% in the 8th decade of life

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- Testosterone levels decrease 0.8–1.6% per year in men aged 40–70

RISK FACTORS

- Testicular trauma/orchiectomy
- Medications:
  - Decreased production of T: Dopamine antagonists, corticosteroids, ethanol, ketoconazole, GnRH analogues, metoclopramide
  - Decreased conversion of T to DHT: 5-reductase inhibitors
  - Androgen receptor blockade: Flutamide, spironolactone, cyproterone, cimetidine

- Infections (mumps orchitis, HIV)
- Medical conditions:
  - Hemochromatosis: Iron toxicity to pituitary gonadotrophs, autoimmune diseases, ESRD/uremia, histiocytosis X, pituitary apoplexy, myotonic dystrophy

Genetics

Klinefelter syndrome

PATHOPHYSIOLOGY

Normal hypothalamic-pituitary-testicular axis:

- GnRH neurons originate in the olfactory placode and migrate through the cribriform plate of the ethmoid to localize in the hypothalamus.
- Hypothalamus secretes GnRH, which stimulates the pituitary to secrete LH and FSH.

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- LH stimulates Leydig cells within the testes to produce T. Feedback inhibition by T on the hypothalamus and pituitary maintains hormonal balance.
- FSH stimulates Sertoli cells to:
  - Support spermatogenesis
  - Secrete inhibin, which provides feedback on the pituitary

COMMONLY ASSOCIATED CONDITIONS

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DIAGNOSIS

HISTORY

- Developmental: Assess the following
  - Testicular descent, delayed puberty, decreased sexual function/libido, loss of body hair or decreased frequency of shaving
- Sexual:
  - Libido, frequency of intercourse, prior fertility assessments
- School performance:
  - Learning disabilities (suggestive of Klinefelter syndrome)
- Chronic medical illnesses or infections:
  - Mumps, sinopulmonary symptoms, STDs/GU infections
- Surgical procedures involving the inguinal/scrotal region:
  - Vasectomy, orchiectomy, herniorrhaphy
- Drugs/environmental exposures:
  - Ethanol frequency, anabolic steroid use, chemo/radiation therapy, pesticide exposure, drugs causing hyperprolactinemia, hormonal modulators

• Assess for symptoms of anterior pituitary hormone deficiency or excess along with any possible mass effects (headache, visual disturbance, bitemporal visual field loss, cranial nerve palsies, cerebrospinal fluid rhinorrhea).

PHYSICAL EXAM

• Assess height and eunuchoidal proportions:
  – Arm span >2 cm > height; heel–pubis >2 cm > pubis–crown normal
• Secondary sexual characteristics, gynecomastia, bone age determination (according to the Greulich and Pyle atlas)
• External genitalia:
  – Testis volume:
    Measure with a Prader orchidometer (normal adult 15–25 mL)
    <6 mL is characteristic of prepubertal hypogonadism
    Soft and atrophic but normal sized suggestive of postpubertal hypogonadism
  – Small, firm testes suggestive of Klinefelter syndrome
  – Assess for ambiguity of genitalia/hypospadias/micropenis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

If an isolated serum T is low, measure an early morning total serum T, bioavailable T (useful in equivocal cases), and LH:

• If the morning T is low, check serum prolactin:
  – Prolactin elevated: Obtain MRI and consult with an endocrinologist
  – Prolactin normal/low:
    LH elevated: Primary hypogonadism
    LH normal/low: Obtain serum FSH and evaluate causes of secondary hypogonadism in consultation with an endocrinologist

Imaging

MRI if lab analysis suggests presence of pituitary tumor

Diagnostic Procedures/Surgery

See “Lab.”

Pathological Findings

Atrophic testes in primary hypogonadism

DIFFERENTIAL DIAGNOSIS

• Hypergonadotropic hypogonadism (primary testicular failure); inadequate production of T despite adequate/elevated levels of LH/FSH:
  – Klinefelter syndrome (most common); congenital XXY karyotype (1 in 576 male births)

Small, fibrotic testes (<6 mL) associated with gynecomastia

– Impaired secretion of T and spermatogenesis:

Cryptorchidism, varicocele, bilateral anorchia

– Gonadal failure following chemotherapy or radiotherapy

– Inactivating mutations of GnRH or gonadotropin receptor

• Hypogonadotropic hypogonadism (secondary hypogonadism): Inadequate stimulation of production of testicular androgen/spermatogenesis (low FSH/LH associated with low T)

– Kallmann syndrome: Abnormal migration of the GnRH neurons; associated with anosmia and small testes:

Adrenal hypoplasia congenita: Constitutional delay of growth and puberty

Chronic illness (celiac disease, Crohn disease, sickle cell anemia, cystic fibrosis, diabetes mellitus)

Malnutrition, hyperprolactinemia, hypothyroidism

Hypopituitarism: Congenital vs. acquired (radiotherapy, CNS malignancy, infection, trauma)

– Isolated gonadotropin deficiency:

Congenital: Kallmann syndrome; mutation in Dax-1

Acquired: Intracranial neoplasm (craniopharyngiomas, germinomas, gliomas and prolactinomas)

– Syndromes with hypogonadotropism: Laurence-Moon Biedl syndrome; Bardet-Biedl subgroup; Prader-Willi, Alstrom, Rud, Bloom syndromes; mutation in leptin

TREATMENT

• Should be guided by the intent/desires of the patient.

• Avoid testosterone-replacement therapy in a man with infertility seeking to regain fertility.

• Hypogonadotropic hypogonadism:

– Treat the underlying cause.

– T-replacement therapy may still be required.

• Hyperprolactinemia:

– Discontinue offending medications.

– Dopamine agonists (bromocriptine)

• If fertility is not desired, T replacement therapy may be instituted:

• Obtain baseline DRE, CBC, lipid profile, and PSA because T replacement may be associated with lipid abnormalities, polycythemia, azoospermia, sleep apnea, and possible prostatic changes.

MEDICATION

First Line

- Transdermal systems: Associated with local skin irritation and greater expense:
  - Scrotal patch: Testoderm (6 mg): Need hairless scrotal area; associated with elevated DHT
  - Nonscrotal: Androderm patch (2.5/5 mg/d), AndroGel (5–10 g/d), and Testoderm TTS (10–15 mg/d)
- Parenteral preparations:
  - Testosterone undecanoate (Nebido):
    More stable levels
    1,000 mg every 12–14 wk
- Transmucosal buccal preparation (Striant):
  - 30 mg b.i.d.
  - Common side-effect profile similar to other non-PO formulations
- Rarer side effects include cholestatic jaundice syndrome, liver carcinoma, neoplasm of liver, peliosis hepatis.

Second Line

- Parenteral preparations:
  - Testosterone cypionate and testosterone enanthate:
    Least expensive, but associated with peaks and troughs
    200–400 mg every 3–4 wk
- PO preparations: Methyltestosterone and fluoxymesterone:
  - Not recommended because can cause liver toxicity

SURGERY/OTHER PROCEDURES

For pituitary adenoma:

- Transsphenoidal resection

ADDITIONAL TREATMENT

Radiotherapy

Pituitary microadenoma:

- Transsphenoidal resection ± radiation therapy

Additional Therapies

If hypogonadotropic:

- May provide GnRH/gonadotropins to stimulate testicular production of androgen

ONGOING CARE

PROGNOSIS

Can restore T levels to the normal range by adjusting dosage of medication and improve symptoms of hypogonadism

COMPLICATIONS

- Gynecomastia
- Hepatotoxicity
- Theoretical risk of progression of prostate cancer:
  - Unsubstantiated by recent studies

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Every 3 mo (CBC, PSA, DRE) after treatment initiation and then annually for response to treatment and adverse effects

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Hyperprolactinemia, Urologic Considerations
- Kallmann Syndrome
- Klinefelter Syndrome
- Laurence-Moon-Bardet-Biedel Syndrome
- Prader-Willi Syndrome
- Testosterone (Free and Total) Laboratory Testing

CODES

ICD9

257.2 Other testicular hypofunction

ABBREVIATIONS

- CBC: Complete blood count
- CNS: Central nervous system
- DHT: Dihydrotestosterone
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- ESRD: End-stage renal disease
- FSH: Follicle-stimulating hormone
- GnRH: Gonadotropin releasing hormone
- GU: Genitourinary
- HIV: Human immunodeficiency virus
- LH: Leuteinizing hormone
- MRI: Magnetic resonance imaging
- PSA: Prostate-specific antigen
- RBC: Red blood cell
- STD: Sexually transmitted disease
- T: Testosterone

TORSION, TESTIS AND TESTICULAR APPENDAGES

Monica M. Metzdorf, MD

Julia S. Barthold, MD

BASICS

DESCRIPTION

Acute scrotal pain, sometimes with redness or swelling, associated with vascular compromise to the testicle or 1 of its appendages:

- Testicular torsion: Usually severe pain with nausea/vomiting, exquisitely tender to palpation
- Torsion of appendix testis or epididymis: Pain usually not as severe, onset more gradual, not usually with nausea/vomiting
- Occurs primarily in children
- Bimodal distribution: Neonatal and puberty

EPIDEMIOLOGY

- 1:4,000 males <25 yr
- Most cases of testis torsion occur at 12–18 yr
- Bimodal age presentation of testicular torsion:
  - Extravaginal torsion in perinatal period
  - Intravaginal torsion peaks in puberty (but can be seen at any age).
  - Torsion of appendix testis/epididymis is usually prepubertal.

RISK FACTORS

- Cryptorchidism for intravaginal torsion
- With intravaginal torsion, increased risk of torsion of contralateral testis

Genetics

- Unknown
- Case reports of familial testicular torsion:
  - Possibly autosomal or X-linked recessive

GENERAL PREVENTION

- In cases of surgically treated torsion, the other testicle should undergo orchidopexy.
- Any identified appendices should be ablated during scrotal exploration for possible torsion.

PATHOPHYSIOLOGY

- Intravaginal testicular torsion:
  - Testis and spermatic cord twist within the tunica vaginalis due to improper fixation of the testis (Bell-clapper deformity).

– There is inadequate fixation of the testis to the tunica vaginalis via the gubernaculum.

– Testis lies transversely within scrotum; the tunica vaginalis extends up over the spermatic cord. Instead of being fixed, the testis is suspended within the tunica vaginalis by the spermatic cord.

– Torsion results in compromised venous outflow, then arterial inflow, leading to ischemia and infarction.

– 10–15% males have bell-clapper deformity

- Extravaginal torsion:

– Poor fixation of the spermatic cord within the inguinal canal and scrotum, allowing entire cord and tunica vaginalis to twist

- Torsion of appendix:
  - Appendage present in about 92% of males
  - Appendix testis is müllerian remnant.
  - Appendix epididymis is wolffian remnant.
  - Both are pedunculated, predisposing to torsion.
  - Testicular appendage more likely to undergo torsion than epididymis
- Intermittent testicular torsion:

– Acute, intermittent sharp testicular pain and scrotal swelling, usually with quick resolution (seconds to minutes).

– May be accompanied by nausea and vomiting.

– May awaken at night from sleep and characterized by long symptom-free periods.

– Often normal exam after episode. Requires high degree of suspicion and follow-up evaluation.

COMMONLY ASSOCIATED CONDITIONS

- Bell clapper deformity
- Cryptorchidism (neonatal torsion)

ALERT

- Extravaginal torsion is a surgical emergency; patient can lose testis with >6 hr of ischemia.
- Do not delay surgery on the basis of assumed nonviability of the testis.

DIAGNOSIS

HISTORY

- Intravaginal testicular torsion:
  - Peri-pubertal period

– Rapid onset of severe pain, usually <12 hr
– Nausea and vomiting more common (this will be variable between studies)
– May be intermittent, with history of multiple occurrences including waking up at night with testicular pain that resolves (intermittent torsion)

- Extravaginal testicular torsion:
  – Neonatal period most common
  – Infants may not manifest any symptoms beyond fussiness and/or restlessness.
  – Painless
  – Testis usually necrotic at birth; salvage rare
- Torsion of appendix:
  – Usually more gradual onset, aching pain, worse with activity
  – Systemic symptoms of nausea/vomiting usually absent

PHYSICAL EXAM

- Intravaginal testicular torsion:
  – Abnormal (transverse) lie of testicle; may lie in a higher position due to cord shortening
  – Loss of cremasteric reflex (normal reflex elevation of the testis in response to stroking of the upper inner thigh due to contraction of cremaster muscle)
  – Swelling; exquisitely tender to palpation
  – Loss of epididymal-testicular landmarks
  – Scrotum may be edematous
  – Prehn sign: Elevation of the scrotal contents relieves the pain with epididymitis and aggravates or has no effect on the pain in testicular torsion. Not considered reliable to base diagnosis.
- Extravaginal testicular torsion:
  – Newborn with firm, nontender discolored scrotum
- Torsion of appendix:
  – Normal testicular position
  – Cremasteric reflexes often preserved
  – Reactive hydrocele
  – May be focally tender at superior pole
  – May see bluish discoloration (blue dot sign)
  – Swelling, erythema common
  – Localized mass often palpable

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis to rule out infection, hematuria
- Culture if suspicious for infection

Imaging

Scrotal US with Doppler flow including waveforms:

- Shows decreased or absent flow in testicular torsion
- Changes in echotexture c/w necrosis (in advanced torsion) or calcification (in prenatal torsion).
- May see actual twist in cord in testicular torsion
- Reactive hyperemia of testis/epididymis common in torsion of appendix with or without hypoechoic area at superior pole.
- Nuclear scan of the scrotum can also demonstrate decreased flow, but is less commonly used today with the ready access of Doppler US units.

Pathological Findings

May see testicular necrosis in prolonged torsion

Geriatric Considerations

Rare in older adults and elderly patients but has been reported and should be in differential of acute testicular pain.

DIFFERENTIAL DIAGNOSIS

- Testicular torsion, torsion of the appendix testis, and epididymitis are the most common causes of acute scrotal pain in children.
- Pediatric painful scrotum:
  - Epididymitis/orchitis; bacterial, STD, mumps, TB
  - Fournier gangrene
  - Henoch-Schönlein purpura (usually no mass)
  - Incarcerated/strangulated hernia
  - Referred testicular pain from nerve root irritation; retrocecal appendicitis, urolithiasis
  - Testicular trauma: Usually blunt; contusion, rupture; usually associated hematocele
  - Torsion (testicle, testicular or epididymal appendage)
  - Torsion, intermittent
  - Tumor (infrequent unless traumatized or rapidly growing)

TREATMENT

- Testicular torsion requires immediate exploration and repair to salvage an ischemic testicle:

  - 80–100% of testicles are salvaged if detorsion occurs within 6 hr of onset.
  - 20% are salvaged if detorsion occurs after >24 hr from onset.
- Intravaginal testicular torsion:
  - May attempt manual detorsion, but treatment is primarily surgical
- Extravaginal testicular torsion:
  - Affected testis is almost always nonsalvageable and often does not require emergent exploration; will eventually atrophy.
- Torsion of appendix testis or epididymis:
  - Anti-inflammatory medication
  - Limited activity until no sign of inflammation
  - Scrotal exploration if diagnosis uncertain
- Intermittent torsion:
  - Consider elective orchidopexy if diagnosis is certain.

MEDICATION

- None for extravaginal or intravaginal torsion
- NSAIDs in appendix torsion

SURGERY/OTHER PROCEDURES

- Intravaginal testicular torsion:
  - Open detorsion and scrotal fixation of affected testis (vs. orchiectomy if nonviable) and fixation of contralateral testis.
- Extravaginal testicular torsion:
  - Surgery is controversial; some suggest urgent orchiectomy with fixation of contralateral testis to avoid asynchronous torsion and anorchia.
- Torsion of appendix:
  - Surgical intervention is usually unnecessary; if persistent pain or inflammation, surgical removal of necrotic appendage
- Orchidopexy procedure:
  - Usually midline incision through raphe
  - Enter compartment and evaluate testicle
  - Untwist testicle and evaluate viability by observing restoration of flow.
  - Pexy viable testicle through tunica albuginea to tunica vaginalis by 3–4 nonabsorbable sutures. Enter the other hemiscrotum and perform orchidopexy on contralateral testis.
  - With an obviously necrotic, nonviable testis, orchiectomy is usually performed (delayed placement of testicular prosthesis should be considered).

ADDITIONAL TREATMENT

Manual detorsion of testicle:

- Most effective acutely before extensive swelling develops
- Not considered a routine procedure; usually requires some sedation or analgesia and an experienced urologist.
- Reasonable option in surgical delay
- Traditionally, the testis is thought to undergo medial torsion and the testis is rotated outward toward the thigh to untwist it. However, in up to 33% of cases, the torsion can be caused by lateral twisting, requiring a medial rotation maneuver to allow detorsion.
- Regardless, surgical correction and orchidopexy is required for definitive repair

ONGOING CARE

PROGNOSIS

- Intravaginal testicular torsion:
  - Testicular salvage is directly related to time of onset of symptoms with only 20% salvage after 12 hr and virtually no salvage after 24 hr.
  - Usually, treatment within 6-hr window is optimal.
- Extravaginal testicular torsion:
  - Rarely is affected testis salvageable.
  - Asynchronous torsion reported; risk of fixation of contralateral testis vs. anesthetic risks
- Torsion of appendix:
  - Atrophy of appendage and resolution of symptoms with supportive care
  - No known adverse affects on testis

COMPLICATIONS

Testicular torsion:

- Ischemia, infarction, hemorrhage, reactive hydrocele, loss of testicle
- Fertility issues (controversial)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Vigilance of contralateral testis; scrotal protection in contact sports
- Monitor testes for atrophy and/or appropriate growth/pubertal development.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Scrotum, Tumors, Benign and Malignant
- Testis, Tumor and Mass, Adult, General
- Testis, Tumor and Mass, Pediatric, General

CODES

ICD9

- 608.20 Torsion of testis, unspecified
- 608.21 Extravaginal torsion of spermatic cord
- 608.22 Intravaginal torsion of spermatic cord

ABBREVIATIONS

- NSAID: Nonsteroidal anti-inflammatory drug
- STD: Sexually transmitted disease
- TB: Tuberculosis
- US: Ultrasound

TRANSPLANT REJECTION, RENAL

Jason C. Hedges, MD, PhD
Michael J. Conlin, MD

BASICS

DESCRIPTION

- Renal transplant rejection refers to a transplanted kidney's functional and structural demise due to immune responses by the recipient.
- 3 types of renal allograft rejection are described:
  - Hyperacute (minutes to weeks following transplantation)
  - Acute (weeks to months following transplantation)
  - Chronic (months to years following transplantation). Also sometimes referred to as transplant nephropathy or chronic renal allograft nephropathy.
- Likelihood of rejection (from most to least likely):
  - Cadaver transplant
  - Living, nonrelated transplant
  - Living, related transplant

EPIDEMIOLOGY

15% rejection rate in 1st yr for those rejection-free at discharge

RISK FACTORS

- Failure of immune suppression, resulting in T-cell stimulation against donor antigens
- Prior rejection episodes: Development of HLA antibodies
- Delayed initial graft function

Genetics

Increased level of graft survival with increased degree of HLA cross-matching

GENERAL PREVENTION

- Algorithm-driven immunosuppression protocols based on donor and recipient histocompatibility and risk factors
- Compliance with immunosuppressive medications
- Minimizing sensitizing events (eg blood transfusions)

PATHOPHYSIOLOGY

- Hyperacute: Mediated by preformed cytotoxic antibodies against graft (develop after prior transfusion, transplantation, childbirth)
- Acute: Mediated by mononuclear cell infiltration and vasculitis (T-cell recognition and activation by foreign antigen presented by MHC proteins of presenting cells):
  - Most of these occur in the 1st 6 mo after transplantation

- Chronic: Interstitial fibrosis, vascular changes, minimal mononuclear cell infiltration
- Banff grading system (see Section II) of the severity of chronic renal graft nephropathy. This system uses renal biopsy specimen and grades severity based on interstitial fibrosis and the degree of atrophy and loss of tubules:
  - Grade I: Mild fibrosis of the interstitium (affecting 6–25% of the cortical area) and mild atrophy of the tubules (eg, up to 25% of the area of the cortical area) either with or without specific glomerular or vascular findings suggestive of chronic allograft nephropathy
  - Grade II: Moderate interstitial fibrosis (affecting 25–50% of the cortical area) and moderate tubular atrophy (eg, 26–50% of the area of the cortical area) with or without specific changes as in Grade I
  - Grade III: Severe interstitial fibrosis (affecting >50% of the cortical area) and tubular atrophy (eg, >50% of the cortical area) with or without specific changes as in Grade I

COMMONLY ASSOCIATED CONDITIONS

Coexisting medical conditions that cause initial renal failure such as diabetes mellitus, etc.

DIAGNOSIS

HISTORY

Suspect diagnosis of rejection if:

- Pain or swelling over graft site
- Oliguria
- Fluid retention/weight gain
- Increased BP

)[A]

PHYSICAL EXAM

Tenderness/erythema at site of graft:

- May not be prominent with current immunosuppressive regimens

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Rising BUN/creatinine:
  - Note: Baseline may be elevated; a creatinine rise >25% over 1–2 days suggests rejection.
- Urine analysis with culture:
  - Rule out pyelonephritis.
- CsA levels:
  - Suspect CsA toxicity if abnormal levels
  - Trough 12–18 hr after oral dose, 12 hr after IV dose

  - Reference range: 150–400 ng/mL
  - Urinary cytology or urinary PCR for BK virus

Imaging

- Renal scan: Decreased renal blood flow/glomerular filtration rate:
  - Progressively worsens on serial examinations; stabilizes in ATN
- Renal US:
  - Rule out obstructive uropathy.
  - Assess for diminished vascular flow.
  - Detect graft swelling (graft may be small/atrophic in chronic rejection).

Diagnostic Procedures/Surgery

Needle biopsy of transplant kidney (confirmation of rejection):

- Repeat biopsies may be required.
- Subendothelial vascular mononuclear cell infiltrates are characteristic.

Pathological Findings

- Acute:
  - Subendothelial vascular mononuclear cell infiltrates are characteristic
  - Vasculitis
  - Tubulitis
- Chronic:
  - Interstitial fibrosis
  - Tubular atrophy
  - Arteriolar hyalinosis

DIFFERENTIAL DIAGNOSIS

- ATN
- Cyclosporin A (CsA) toxicity
- Obstructive uropathy:
  - Extrinsic compression
  - Ureteroneocystostomy stenosis
  - Ureteral stricture usually due to ischemia
- Pyelonephrosis
- Renal artery stenosis (chronic)
- PVAN:
  - 1–10% of patients with kidney transplant
  - Most due to the BK virus
- Technical complications in early posttransplant setting:

– Arterial or venous thrombus, arterial stenosis, urinary obstruction
– Recurrence of original disease causing the renal failure (eg, glomerulonephritis)
– Noncompliance with antirejection medications

TREATMENT

• Attempt to reverse rejection through medical therapy; graft removal may be necessary.

)[A]:

– Can result in DIC if transplanted kidney not removed promptly

• Acute rejection: Initial high-dose steroids
• Chronic rejection: No effective therapy. Avoid excessive immunosuppression.

MEDICATION

First Line

Acute rejection:

• Pulse-dose steroids (protocols may vary between institutions)
• Solu-Medrol 500 mg/d IV for 3 days; then prednisone taper

Second Line

)[A]:

– ATG (polyclonal antithymocyte antibodies) at 15–30 mg/kg/d for 10 days

Must institute CMV prophylaxis with ganciclovir; follow WBC with differential and platelets

Continue immunosuppression with CsA and steroids.

– OKT3 (monoclonal anti-CD3 antibodies) at 5 mg/d for 10–14 days

Must institute CMV prophylaxis with ganciclovir and follow biweekly CD3 levels

Continue immunosuppression with CsA.

Significant 1st-dose reactions are possible.

– PE: Must have a clear chest x-ray <24 hr prior to dosing OKT3
– Fever, chills: Steroids, Benadryl, acetaminophen prophylaxis

SURGERY/OTHER PROCEDURES

Allograft nephrectomy:

• Remove a symptomatic, irreversibly rejected kidney transplant.
• Remove an asymptomatic, chronically rejected kidney to withdraw immunosuppression and prevent further development of anti-HLA antibodies.

ADDITIONAL TREATMENT

• Data suggest that cyclosporine and or tacrolimus may cause long-tern renal damage, and reduction in lowest effective dose or complete elimination is recommended in selected cases.

- Maintain target BP at <130/80 to limit chronic renal damage.
- Treat hyperlipidemia.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Low-dose aspirin, fish oils, and other regimens are under study in chronic rejection.

ONGOING CARE

PROGNOSIS

The number of episodes of acute rejection reduces allograft survival at 2 yr:

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COMPLICATIONS

Rejection can result in graft loss, HTN, recurrent renal insufficiency

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Determination of adequate immunosuppression and CsA levels

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ADDITIONAL READING

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CODES

ICD9

996.81 Complications of transplanted kidney

ABBREVIATIONS

- ATG: Antithymocyte globulin
- ATN: Acute tubular necrosis
- BP: Blood pressure
- CMV: Cytomegalovirus
- CsA: Cyclosporin A
- DIC: Disseminated intravascular coagulation
- HLA: Histocompatibility locus antigen
- HTN: Hypertension
- IV: Intravenous
- OKT3: A monoclonural antibody
- PCR: Polymerase chain reaction
- PE: Pulmonary embolism
- PVAN: Polyomavirus-associated nephropathy
- US: Ultrasound
- WBC: White blood cell

TUBERCULOSIS, GENITOURINARY

Benjamin R. Lee, MD
Gordon L. Fifer, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- Genitourinary TB refers to urinary and GU infection with Mycobacterium TB. Common GU sites include the kidney, ureter, bladder, prostate, and testis/epididymis.
- Over the last 35 yr, major changes have occurred in approach to GU TB. As a result, morbidity and mortality associated with the disease have been greatly reduced.

EPIDEMIOLOGY

- Predominate age group: 20–40 yr
- Male > Female (2:1)
- During past 10–15 yr, an increase in cases has been secondary to spread of disease from other parts of the world and the AIDS epidemic.
- 139 per 100,000 population, globally.
- 0.5 million cases of multidrug-resistant TB (2006)
- 90% of global TB cases and deaths occur in developing world.
- GU tract is 2nd most common site after lungs for tuberculous infection.
- True prevalence is underestimated. Tubercle bacilli found in 7–29% of urine in patients with extrarenal TB.
- 14.4 million global cases of TB in 2006

RISK FACTORS

HIV/AIDS

GENERAL PREVENTION

- Diagnose and treat patients with TB before development of active disease.
- Take careful precautions with patients hospitalized with TB.
- Test annually with PPD if at high risk for exposure.

PATHOPHYSIOLOGY

- Hematogenous spread to kidneys from pulmonary disease
- M. tuberculosis infections acquired by inhalation of aerosolized droplet nuclei (1–5 m), which reach pulmonary alveoli
- Invasion of GU organs by ascent (prostate to bladder) or descent (kidney to bladder, prostate to epididymis)
- Kidney and prostate are primary sites of TB infection in the GU tract.

- Tuberculomas develop in glomerular capillaries as result of hematogenous seeding from lungs.
- Renal TB may take years to develop in patients with normal immune system.
- Normal renal parenchyma is slowly replaced by caseous material; calcium is laid down as part of the reparative process.
- Perinephric abscess is rare but may develop.
- Large calcifications in the prostate should suggest TB.
- Ureters undergo fibrosis, shortening, and straightening in 50% with renal TB.
- Involvement of testis is unusual but prostatic ducts and seminal vesicle involvement is common.
- Prostate may feel hard and nodular.
- BCG therapy for bladder cancer can cause disseminated disease mimicking TB, granulomatous prostatitis.
- Secondary amyloidosis can be found; often resulting in proteinuria and nephrotic syndrome.
- Anti-TB medications can damage the kidney (eg, rifampin can cause tubular and glomerular injury with interstitial nephritis and occasional acute renal failure. May also cause glycosuria, polyuria due to nephrogenic diabetes mellitus)

COMMONLY ASSOCIATED CONDITIONS

- Chronic TB infection
- Immunocompromised states (eg, AIDS)
- Malnutrition
- Poor living conditions/poverty

DIAGNOSIS

HISTORY

- Initial symptoms may be minimal, even in presence of extensive disease. No classical clinical picture, most symptoms are of bladder/lower urinary origin.
- History or exposure to TB; Determine last PPD testing 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 TB. Common to see recurrent UTIs with Escherichia coli
- Dysuria from seeding of the bladder with TB

- Chronic cystitis unresponsive to therapy

PHYSICAL EXAM

- Suprapubic pain when disease is extensive
- Painful swollen testis
- Chronic draining scrotal sinuses should be considered TB until proven otherwise.
- Nontender, enlarged epididymis with beaded or thickened vas deferens
- Nodular, indurated prostate and thickened seminal vesicles on rectal exam mimic neoplasm.
- Upper abdominal bruit may be indication of advanced renal disease.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Routine urine analysis, standard culture:
  - Sterile pyuria classic finding; typically >20 WBC/HPF.
  - 20% of patients will also have bacterial cystitis or urinary tract infection with E. coli.
- Specific staining of urine for acid-fast bacteria and mycobacterial culture is gold standard:
  - Caution, in that nonpathogenic mycobacteria can also stain positive; culture more useful.
  - Ziehl-Neelsen or Kinyoun acid fast stain; more rapid fluorochrome (fluorescence microscopy) procedure
  - 1st morning 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.
  - Acid-fast stains from 24-hr urine specimen are positive in 60% of cases.
  - High index of suspicion for persistent pyuria without bacteria on repeated cultures (stain with methylene blue)
  - PCR assay may identify organisms
- CBC, electrolytes, ESR: Measure monthly as indicator of response to therapy
- 88% have positive skin tests of PPD
- Heavy proteinuria in a patient with TB suggests secondary involvement of the kidney with amyloid.

Imaging

- Chest x-ray: Abnormal in 75%
- KUB:
  - Enlargement of 1 kidney

  - Punctuate calcifications in renal parenchyma
  - Large calcified structures in prostate
  - Renal stones in 10%
  - Obliteration of psoas shadow due to perinephric abscess
- Excretory urogram:
  - Considered a mandatory study; moth-eaten appearance in ulcerated calyces
  - Dilation of upper tract secondary to ureteral stricture
  - Obliteration of calyces
  - Loss of kidney function due to complete occlusion or renal destruction
- Retrograde pyelography with selective culture for TB; assessment of ureteral stricture
- CT is an option if IVP contraindicated:
  - Useful in delineating disease in seminal vesicles; limited value in early management

Diagnostic Procedures/Surgery

- Tuberculin skin test:
  - Induration >10 mm in diameter is considered positive reaction.
  - >5 mm in high-risk patient
  - Positive reaction indicates exposure, not necessarily active disease.
  - May be negative in a patient with miliary TB, AIDS, or advanced age
  - Negative tuberculin skin test makes diagnosis of TB unlikely.
  - Must not have had BCG vaccine or therapy in the past
- Cystoscopy:
  - TB appears as a patchy erythematous ulceration with exudate.
  - Demonstrates extent of disease
  - Biopsy for tissue confirmation
  - TB may mimic TCC or CIS.

Pathological Findings

Tubercles replaced by caseating necrosis

DIFFERENTIAL DIAGNOSIS

- Amicrobic cystitis
- BCG sepsis/BCG ossis
- Chronic nonspecific cystitis or pyelonephritis
- Disseminated coccidioidomycosis
- Granulomatous prostatitis; prostate cancer
- Medullary sponge kidney

- Necrotizing papillitis
- Nonspecific epididymitis
- Renal stones or nephrocalcinosis
- Urinary bilharziasis (schistosomiasis)

TREATMENT

- Treat active disease promptly in an outpatient setting:
  - Supervision to ensure compliance and to monitor for complications from chemotherapy
  - It is no longer necessary to manage in an inpatient setting unless compliance is an issue.
- Drain abscesses.

MEDICATION

First Line

Antituberculous drugs are isoniazid, rifampin, streptomycin, pyrazinamide, and ethambutol:

- Patient with uncomplicated TB infection:
  - Isoniazid (300 mg/d), rifampin (450–600 mg/d), and pyrazinamide (25 mg/kg/d) 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.
- 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 is increasing and necessitates tight therapy control, expanded antibiotic regimen of 4 of the following: Ethionamide, prothionamide, quinolones, clarithromycin, cycloserine, kanamycin, viomycin, capreomycin, thiacetazone, and para-amino-salicylate
- Steroids:
  - No role in initial therapy
  - For acute TB cystitis or stricture at distal ureter: Prednisone 20 mg PO t.i.d.

SURGERY/OTHER PROCEDURES

- Nephrectomy:
  - Symptomatic (HTN, obstruction, pyelonephritis) nonfunctioning kidney with extensive disease
  - Coexistent renal cell carcinoma

- Perform 4–6 wk after start of antituberculous drugs

- Epididymectomy:
  - Indicated for caseating abscess unresponsive to chemotherapy
- Ureteral strictures:
  - Stenting vs. reconstruction
- Bladder augmentation:
  - Small capacity, fibrotic bladder.
- Surgery not necessary for TB abscesses:
  - Treat medically, reserve surgery for treatment failure

ADDITIONAL TREATMENT

People who have TB that cannot be spread to others (latent TB) also receive treatment to prevent infection from becoming active.

ONGOING CARE

PROGNOSIS

- Prognosis for recovery is good for most patients.
- Key to success is early diagnosis of the disease followed by careful program of medication.

COMPLICATIONS

- Ureteral TB:
  - Stricture formation
  - Hydronephrosis
  - Complete nonfunctioning of an affected kidney (autonephrectomy) described
- Renal TB:
  - Obliteration of the renal and psoas shadow on plain radiographs
  - A perinephric abscess may cause an enlarging mass in the flank.
- Genital TB:
  - Sterility a consequence
  - An abscess of the epididymis may erode through the scrotal wall or testis, creating a sinus tract and drainage.
- Bladder TB:
  - Stenosis of ureterovesical junction
  - Fibrosis and contraction of bladder
- Nephrotoxicity induced by antimicrobial agents (especially rifampin)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Completion of TB regimens long-term is essential.
- Strictures can evolve after organism is eradicated.
- Follow regularly after completion of therapy as stricturing can continue:
  - 3,6,9,12 mo with urine culture and TB staining and excretory urography.
  - Need long-term imaging follow-up of calcifications if present.

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See Also (Topic, Algorithm, Electronic Media Element)

- BCG Sepsis/BCGossis
- Prostatitis, Granulomatous
- Prostatitis, Tuberculous
- Tuberculosis, Bladder and Urethra
- Tuberculosis, Male External Genitalia

CODES

ICD9

- 016.30 Tuberculosis of other urinary organs, unspecified examination
- 016.50 Tuberculosis of other male genital organs, unspecified examination

ABBREVIATIONS

- AIDS: Acquired immunodeficiency syndrome
- BCG: Bacille Calmette-Guérin
- CBC: Complete blood count
- CIS: Carcinoma in situ
- CT: Computed tomography
- ESR: Erthrocyte sedimentation rate
- GU: Genitourinary
- HPF: High-power field
- HTN: Hypertension
- IVP: Intravenous pyelogram

- KUB: Kidneys, ureters, bladder
- PCR: Polymerase chain reaction
- PPD: Purified protein derivative
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- UTI: Urinary tract infection

TUNICA ALBUGINEA/PARATESTICULAR TUMORS AND CYSTS

Eric C. Umbreit, MD

Michael L. Blute, MD

BASICS

DESCRIPTION

- Intrascrotal paratesticular and distal spermatic cord masses and cysts are rare and involve the testicular tunica, epididymis, or cord structures.
- 90% of paratesticular tumors originate from the spermatic cord.
- Most common tumors are adenomatoid tumors, whereas rhabdomyosarcomas are the most aggressive.

EPIDEMIOLOGY

- Paratesticular rhabdomyosarcoma:
  - 2 incidence peaks at 2–6 yr and 15–19 yr

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- Adenomatoid tumors:
  - Most common tumor of paratesticular tissues, accounting for 30%
  - Occurs predominantly during the 3rd and 4th decade of life
- Rhabdomyosarcoma:
  - Affects primarily children and adolescents
  - In children and adolescents, paratesticular tumors account for 6% of all rhabdomyosarcoma.
  - Most common during the 1st 2 decades of life; median age of diagnosis is 5 yr
  - Accounts for 25% of adult paratesticular tumors
  - Represents <1% of adult malignancies

RISK FACTORS

Patients with von Hippel-Lindau syndrome have a higher incidence of epididymal cystadenomas.

Genetics

Rhabdomyosarcoma, embryonal subtype, frequently has monosomy of chromosome 11.

GENERAL PREVENTION

It is recommended that males perform self-exams of the testicles and cord structures monthly for early detection of intrascrotal masses.

PATHOPHYSIOLOGY

Rhabdomyosarcoma:

- Originates from primitive embryonal mesenchyme of striated skeletal muscle
- Rapid progression with invasion of local tissues
- Primary metastatic sites include retroperitoneal lymph nodes, lung, liver, bone, and bone marrow

COMMONLY ASSOCIATED CONDITIONS

- Von Hippel-Lindau syndrome (epididymal cystadenomas)
- Li-Fraumeni syndrome (rhabdomyosarcoma)

DIAGNOSIS

HISTORY

- Incidentally detected or enlarging scrotal mass that may or may not be distinct from the testicle:
  - Tumors may present within inguinal region.
  - Usually painless
- Discuss recent voiding history:
  - LUTS may suggest epididymitis or orchitis.
- Acute pain may suggest vascular compromise or infection, torsion, epididymitis, or orchitis.
- Document recent scrotal trauma and history of scrotal surgery.

PHYSICAL EXAM

- Full genital exam bilaterally:
  - Palpate testes, epididymis, and spermatic cords.
- Palpate external inguinal ring and evaluate for hernia.
- Transillumination of any scrotal mass:
  - Transillumination suggests hydrocele or, less commonly, a tunical cyst
  - May still be associated with tumor
- Adenomatoid tumors are anatomically restricted to the area of the epididymis, testicular tunicae and spermatic cord:
  - Slightly higher incidence in lower pole of testis
  - Usually small, solid, asymptomatic masses found on routine exam
- Rhabdomyosarcoma usually presents as a large intrascrotal mass that borders the testis and epididymis:
  - Tends to be firm and distinguishable from the adjacent compressed testicle.
- Spermatocele is smooth, spherical, and usually located at head of epididymis. May be large and will transilluminate.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis with microscopy
- Urine Gram stain and culture
- CBC to evaluate for leukocytosis
- AFP, LDH, -hCG if any concern for germ cell tumor

Imaging

ALERT

A scrotal US is a vital part of the workup for any scrotal process, pathology, or mass.

- Scrotal US:
  - Evaluates for intra- and extratesticular lesions or masses
  - Evaluates vascular flow to both the testicular parenchyma and mass
  - Solid masses require exploration by a surgeon.
  - Simple cystic lesions are less worrisome and almost always benign.
- CT of abdomen and pelvis and chest x-ray to evaluate for metastatic disease in patients with malignant pathology.

Diagnostic Procedures/Surgery

ALERT

Percutaneous biopsies should not be performed and are strongly contraindicated due to the documented risk of seeding in the scrotal wall with malignancy.

Pathological Findings

- Adenomatoid tumors:
  - Always benign
  - Range, 0.5–5 cm in diameter
  - Usually attached to the testicular tunicae, although origin of tumor is unknown
  - Common feature is the presence of vacuoles in epithelial cells
  - Typically well-differentiated
- Rhabdomyosarcoma:
  - Malignant tumor
  - Grossly, appears circumscribed, but microscopic margin often extends beyond surgical margin
  - 80% are embryonal cell tumors, which are a favorable histology
  - Marked variability in microscopic features between tumors
  - Electron microscopy may reveal cytoplasmic myofilaments and Z bands.

DIFFERENTIAL DIAGNOSIS

- Adenomatoid tumors
- Cystadenoma:
  - Benign epithelial hyperplasia of epididymis
  - 1/3 of cases are bilateral and associated with von Hippel-Lindau disease
  - Young adults with minimal to no discomfort
- Epidermoid cysts
- Epididymitis
- Fibrosarcoma
- Hematocele
- Hydrocele
- Inguinal hernia
- Leiomyoma
- Leiomyosarcoma
- Lipoma
- Liposarcoma
- Malignant lymphoma
- Mesothelioma:
  - Asbestos exposure
  - Usually present with an associated hydrocele
- Metastatic carcinoma
- Ovarian-type epithelial tumor
- Papillary mesothelioma:
  - Recurrent hydroceles
  - Not associated with asbestos
- Postoperative changes (sperm granuloma after vasectomy, scarring, etc.)
- Rhabdomyosarcoma
- Spermatocele (epididymal cyst):
  - Adolescent, found on routine exam
  - Increased incidence in von Hippel-Lindau syndrome
- Testicular germ cell tumor
- Testicular torsion
- Traumatic injury
- Tunica albuginea cysts
- Variocele

TREATMENT

• Rhabdomyosarcoma requires chest x-ray, CT of the abdomen and pelvis with and without contrast after radical orchiectomy:
  – Clinical staging of retroperitoneal lymph nodes
  – ~80% are localized to the scrotum
• Benign tumors and cysts: No additional therapy is needed

MEDICATION

Rhabdomyosarcoma:

)[B] initiated after radical orchiectomy

SURGERY/OTHER PROCEDURES

ALERT

)[B]

• Rhabdomyosarcoma:
  – Primary metastatic spread via lymphatic drainage along testicular vessels
  – Hemiscrotectomy is recommended in cases with scrotal wall involvement
  – Some authors recommend routine RPNLD, but controversial
  – Understaging with future relapses is a concern when staged by CT alone
• Benign lesions:
  – Although a transscrotal approach could be utilized, the malignant potential of the tumor or cyst is often not known. Thus excision via an inguinal incision is advised.

ADDITIONAL TREATMENT

Radiation therapy in rhabdomyosarcoma:

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ONGOING CARE

PROGNOSIS

• Benign lesions: Recurrence is rare and based upon surgical technique.
• Rhabdomyosarcoma in children:
  – Overall, 5-yr survival rate of 92–95%
  – Event-free survival of 82%
  – Stage III has 35% survival and stage IV has a 5.2% survival despite combined therapy
  – Tumors >5 cm in diameter and/or patients >10 yr are independent poor prognostic variables

)[B]

• Rhabdomyosarcoma in adults:

- Overall, 5-yr survival rate of 40%

COMPLICATIONS

- Hypogonadism and/or infertility following surgery and chemotherapy
- Hemorrhagic cystitis secondary to chemotherapy with cyclophosphamide
- Retrograde ejaculation if RPLND is nonnerve sparing.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Importance of testicular self-exam monthly
- Educate patient on signs and symptoms of recurrent malignant tumor.
- Serial US for equivocal lesions, especially in the epididymis or lesions on the tunica <5 mm
- Rhabdomyosarcoma:
  - Routine guidelines are not established for rhabdomyosarcoma and postoperative surveillance will be provider-dependent
  - These patients should be followed closely by a urologist

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See Also (Topic, Algorithm, Electronic Media Element)

- Epididymis, Mass (Epididymal Tumor and Cysts)
- Rhabdomyosarcoma, Pediatric (Sarcoma Botryoides)
- Scrotum and Testicle, Mass
- Spermatic Cord Mass and Tumors
- Spermatocele

CODES

ICD9

- 187.6 Malignant neoplasm of spermatic cord
- 222.8 Benign neoplasm of other specified sites of male genital organs
- 608.89 Other specified disorders of male genital organs

ABBREVIATIONS

- AFP: -Fetoprotein
- -hCG: -human chorionic gonadotropin
- CBC: Complete blood count
- CT: Computed tomography
- GU: Genitourinary
- hCG: Human chorionic gonadotropin
- LDH: Lactase dehydrogenase
- LUTS: Lower urinary tract symptoms
- RPLND: Retroperitoneal lymph node dissection
- US: Ultrasound

TRANSURETHRAL RESECTION (TUR) SYNDROME

Christopher L. Amling, MD
Sean J. Clark, MD
Stephen B. Riggs, MD

BASICS

DESCRIPTION

- TUR syndrome is associated with TURP and is characterized by confusion, HTN, bradycardia, and visual disturbances.
- Symptoms are caused by hypervolemia, dilutional hyponatremia, and solute effects from irrigant absorption during resection.
- Irrigants are electrolyte-free to facilitate loop electrocautery, so by default they are hypo-osmotic.
- While traditionally associated with prostate resection, it can also be seen in TURBT and has also been described for procedures such as hysteroscopy.
- Synonym(s): TURP syndrome

EPIDEMIOLOGY

- Can occur as early as 15 min into resection or up to 24 hr after a transurethral resection procedure

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- The declining use of TURP to treat obstructing prostate tissue has led to a reduction in the incidence of this syndrome.

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.

GENERAL PREVENTION

- Using irrigants such as glycine, sorbitol, and mannitol solutions reduces the hemolytic effects associated with sterile water irrigation.
- Intravesical pressure can be reduced by using continuous-flow equipment, draining 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 may be best to abandon procedure after achieving hemostasis to prevent excessive fluid absorption.

- Appropriate selection of patients for TURP is based on gland size:
  - Limit resection time to <60–90 min.
  - Consider open prostatectomy for adenoma >100 g.
- Bipolar resectoscopes to perform TURP allows for saline irrigation:
  - Reduces the hypoosmotic effect of the absorbed fluid
  - Increases volume effects of absorbed fluid

Geriatric Considerations

Patients with depressed cardiac function are at risk for PE and respiratory failure due to TUR-associated hypervolemia.

PATHOPHYSIOLOGY

- Irrigants used are osmotically active.
- Osmolarity of TUR irrigant solutions:
  - Normal serum: 280–310 mOsm/L
  - 5% mannitol: 275 mOsm/L
  - 1.5% glycine: 200 mOsm/L
  - 2.7% sorbitol/0.5% mannitol: 178 mOsm/L
  - 3% sorbitol: 165 mOsm/L
- Irrigant is absorbed by venous sinuses opened during resection or by slow absorption from the periprostatic and perivesical spaces in case of capsular perforation.
- As osmotically active solute enters the intravascular space, the plasma sodium concentration drops, leading to hypoosmolality.
- Volume effects:
  - Increase in intravascular volume initially leads to hypervolemia, HTN, and reflex bradycardia; later hypotension can occur.
  - Volume overload of the left ventricle may also lead to PE and respiratory failure.

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- Solute effects:
  - Hyponatremia:

    Caused by loading the intravascular space with nonelectrolyte solution

    Contributes to CNS disturbances

    If serum sodium levels rapidly decrease to <120 mEq/L, negative inotropic effects are manifested as hypotension and ECG changes of widened QRS complexes, ventricular ectopy, ST-segment depression, or T-wave inversions
  - Hypo-osmolality:

    Blood–brain barrier is essentially impermeable to sodium, but water crosses freely.

Osmotic gradient causes uptake of water by CNS tissue.

Resulting cerebral edema can exacerbate HTN and bradycardia via the Cushing reflex.

– Hypo-osmolar plasma results in RBCs taking on water, causing hemolysis.
– Renal failure secondary to hypotension and hemoglobinemia
– Hyperglycemia:

Glycine is a GABA-like inhibitory neurotransmitter.

Serum levels of glycine 17 times that of normal adults have been recorded in patients after TURP using glycine irrigant.

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Glycine can cause visual disturbances and even transient blindness independent of hyponatremic or hypo-osmolar effects.

Glycine may also have direct toxic effects on the kidney, possibly via metabolism to oxalate.

– Hyperammonemia:
– Glycine is metabolized by the liver and kidneys to 2 potential toxins, glyoxylic acid and ammonia.
– Elevated serum ammonia may contribute to CNS derangement.

Sodium Concentration
Symptoms
130–135 mEq/L
Asymptomatic
120–130 mEq/L
Restlessness, confusion
115–120 mEq/L
Nausea
<115 mEq/L
Seizures, coma

COMMONLY ASSOCIATED CONDITIONS

- BPH
- Bladder tumors

DIAGNOSIS

HISTORY

- Patient may complain of any of the following, but there is no classic presentation:
  – Chest pain

  - Confusion
  - Headache
  - Itching
  - Lethargy
  - Nausea and vomiting
  - Shortness of breath
- During procedure: HTN and brachycardia may be a prodrome to rapid reduction in BP

PHYSICAL EXAM

- Nonspecific physical findings, although skin may be clammy
- Neurologic exam will reveal altered sensorium and confusion, but no focal signs

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum sodium <125 mEq/L
- Serum ammonia and glycine may be elevated if glycine solution is used
- Determine measured and calculated plasma osmolality:
  - Posm = 2 × plasma Na + (glucose)/18 + BUN/2.8
  - The difference between measured osmolality and calculated osmolality is known as the osmolality gap.
  - Normal osmolality gap: <5–10 mOsm/kg
  - Clinically significant gap is usually >14 and may be due to the presence of substances such as ethanol, ethylene glycol, or in this case irrigating solutions.
  - Osmolality gap can be >30–60 mOsm/kg following transurethral resection due to the accumulation of glycine or sorbitol.

Imaging

Cystogram or CT cystogram in cases where perforation may be cause of excess fluid absorption

Diagnostic Procedures/Surgery

ECG changes as noted above

DIFFERENTIAL DIAGNOSIS

- Cerebrovascular accident
- Myocardial infarction
- Narcotic overdose
- PE
- Seizure

ALERT

A patient who is slow to awaken from anesthesia or complains of visual disturbances should be considered to have the TUR syndrome following TURP.

TREATMENT

- Glycine is no longer recommended as an irrigation fluid.
- No specific therapy is necessary in the absence of symptomatology.
- In the setting of normal renal function, patient can normally correct mild hyponatremia.
- Hemodynamic and cardiopulmonary support should be provided as needed.
- Vasoactive agents may be required to increase systemic vascular resistance in case of severe hypotension and circulatory collapse.

MEDICATION

First Line

Furosemide:

- Indicated to treat PE and hypervolemia when diuresis does not occur spontaneously
- Furosemide: 20–100 mg IV
- Water diuresis outpaces sodium diuresis, correcting both hypervolemia and hyponatremia.
- Routine use to counteract fluid absorption is not supported by the literature.

Second Line

Hypertonic saline:

- Indicated for serum Na <120 mEq/L or multiple symptoms
- Na deficit is calculated: (pre-op Na – post-op Na) for TBW
- TBW in males = 0.6 for weight in kg
- Determine amount of 3% hypertonic saline (513 mEq/L) needed to correct deficit
- Increasing serum Na by 0.5–1 mEq/L/hr is considered a safe rate to avoid central pontine myelinolysis.
- In case of cerebral edema, more rapid correction is indicated, as the risk of brainstem herniation exceeds that of osmotic demyelination.

ALERT

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SURGERY/OTHER PROCEDURES

Very rarely, decompression of a large retroperitoneal or pelvic irrigant collection is indicated in order to prevent further absorption of hypo-osmolar fluid.

ADDITIONAL TREATMENT

1% ethanol in the irrigant has been used to detect fluid absorption by a breathalyzer, allowing an estimate of the volume of excess fluid that has been absorbed.

ONGOING CARE

PROGNOSIS

- When recognized and treated early, prognosis is favorable.
- Mortality 0.2–0.8%
- If therapy is delayed and hyponatremia is severe, significant morbidity and mortality can occur.

COMPLICATIONS

- Cardiopulmonary collapse
- Central pontine myelinolysis
- Cerebral edema and brainstem herniation
- Seizures
- Transient blindness

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Hemodynamic monitoring and close attention to serum electrolytes, especially sodium, is essential during and after procedure.
- Serial neurologic exams including mental status exams should be performed until symptoms improve.

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostate, Benign Hyperplasia/Hypertrophy
- Hyponatremia, Urologic Considerations

CODES

ICD9

- 276.1 Hyposmolality and/or hyponatremia
- 276.6 Fluid overload disorder

ABBREVIATIONS

- BP: Blood pressure
- BPH: Benign prostatic hyperplasia
- BUN: Blood urea nitrogen
- CNS: Central nervous system
- CT: Computed tomography
- ECG: Electrocardiogram
- GABA: -Aminobutyric acid
- HTN: Hypertension
- IV: Intravenous
- PE: Pulmonary embolism
- RBC: Red blood cell
- TBW: Total body water
- TUR: Transurethral resection
- TURBT: Transurethral resection of bladder tumors

- TURP: Transurethral resection of prostate

UMBILICAL ABNORMALITY (DRAINAGE AND MASSES)

Florian R. Schroeck, MD
Judd W. Moul, MD
Perry R. Weiner, DO

BASICS

DESCRIPTION

- The umbilicus is the site of a large number of well-recognized and more unusual congenital anomalies.
- Most present during the neonatal period or early infancy.
- Accurate diagnosis is imperative: It varies from trivial to life-threatening (peritonitis):
  - Common abnormalities early in life include granulomas, infection, and other anomalies such as remnants (urachal, omphalomesenteric duct) or hernia.
  - Conditions typically presenting later in life include urachal carcinoma, urachal bladder diverticulum, and urachal cyst.

EPIDEMIOLOGY

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- Single umbilical artery: 1/100 live births
- Microscopic urachal remnants are common, appearing in 3% of autopsy specimens; almost always asymptomatic.

RISK FACTORS

- Babies with significant urethral obstruction (ie, posterior urethral valves) generally have no urachal problems.
- Bladder outlet obstruction causes anatomic persistence of the urachus:
  - 15% of patients with urachal problems have bladder outlet obstruction; most prune-belly/triad syndrome

Genetics

Not generally associated with any single syndrome, many patients with urachal problems are found to have coexisting congenital abnormalities of other systems.

PATHOPHYSIOLOGY

- The primitive umbilical cord develops with the anterior abdominal wall during the 2nd and 3rd wk of gestation:
  - At ~4–5 wk, the umbilical cord contains the following structures:

    Omphalomesenteric duct (vitelline duct) develops from the yolk sac (connects to gut).

The allantois becomes the urachus connecting to the developing bladder.

2 arteries and 1 vein

Surrounded by a gelatinous substance known as Wharton jelly.

– In normal fetal development, the omphalomesenteric duct and the urachus involute.

– At birth the normal contents of umbilicus: 2 arteries and 1 vein supported by primitive mesenchymal tissue (Wharton jelly) with outer covering of amnion.

– Within 1 wk of birth, the cord stump separates leaving the umbilicus or navel.

• Faulty embryologic involution of the connections (omphalomesenteric duct or urachus) results in umbilical abnormalities; patent urachus, urachal sinus or cys.

• A single umbilical artery (most common abnormality of cord) may be associated with a higher risk of multisystem congenital anomalies:

– Found in 0.2–0.6 live births. Up to 30% will have significant anomalies.

– Urologic considerations include:

Vesical-ureteral reflux

Renal abnormalities (renal cystic dysplasia)

Potter sequence

• Umbilical polyp consists of a firm mass histologically containing urinary or intestinal epithelium.

• Umbilical granuloma is a moist appearing, pink, pedunculated, friable lesion. Consists of granulation tissue that can be up to 10 mm in length; overgrowth of tissue at the base of the separated cord stump.

• Persistent urachal tissue at the dome of the bladder can degenerate in adults to mucin-producing adenocarcinoma.

COMMONLY ASSOCIATED CONDITIONS

• Bladder outlet obstruction (eg, posterior urethral valves)

• Prune belly/triad syndrome

DIAGNOSIS

HISTORY

• Timing of detection of anomaly:

– Most umbilical disorders found antenatally or at birth

– Fistulas can occur later, often associated with inflammatory processes (Crohn) or surgery/percutaneous procedures.

• Delayed cord stump separation in a newborn suggests infection or umbilical cord anomaly

- Silver nitrate therapy fails:
  - Think umbilical polyp/sinus tract.
- Discharge appears enteric in nature:
  - Suggests persistence of entire vitelline duct
- Discharge appears urine-like:
  - Suggests persistence of patent urachus
- Association with menses suggests endometriosis.
- Medical history of malignancy or inflammatory bowel disease
- Patent urachus: Clear fluid draining from the umbilicus in the newborn period, often exaggerated with crying or straining
- Urachal sinus: May present in infancy or later with umbilical drainage or nonspecific periumbilical erythema
- Symptomatic urachal diverticula of the bladder: UTI is the most common presentation.

PHYSICAL EXAM

- Signs range from silent process to acute abdomen.
- Clinically: Local swelling, redness, inflammation, umbilical discharge or bleeding
- Caution: An enlarged or edematous umbilical cord could represent normal cord slough.
- Urachal cyst: Most commonly presents in an older child with signs of suppuration ("calor, rubor, dolor") in the lower abdominal wall. Occasionally, a urachal cyst will present as an asymptomatic midline lower abdominal mass or tenderness.
- Urachal sinus may have wetness or purulence or malodorous discharge.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Check any discharging fluid for creatinine to determine if the discharge is urine (patent urachus).
- Culture any discharge.

Imaging

- High-resolution US suggested as best tool for initial assessment:
  - Accurately determines anatomy of umbilical structures; with compression, look for small bowel communications/bands.
  - 62% of bladder US demonstrate a urachal remnant over the dome of the bladder.
  - In newborns with single umbilical artery, recommended to screen for congenital abnormalities.
- Fistulography: Contrast injected into sinus/tract; unreliable, may miss communicating cysts, may have difficulty cannulating tract:

– Note: Urachal sinuses head inferiorly; vitelline duct remnants extend inward toward the peritoneum.

• VCUG: Evaluates for urachal remnant/sinus, and associated bladder outlet obstruction (unlikely that urinary obstruction is directly related to patent urachus)

DIFFERENTIAL DIAGNOSIS

• Embryonic:

– Urachal remnants: Most common; comprise spectrum of anomalies:

Patent urachus (rare, 3 in 1 million): Un-obliterated urachus draining urine from the bladder to the umbilicus

Urachal sinus: Urachus obliterated at the bladder level, but open sinus remains at the umbilicus. Drainage often is the result of episodic infections of the sinus

Urachal cyst: Urachus obliterated proximally and distally, but unobliterated fluid-filled cyst remains in between

Infected urachal cysts found in all ages

Urachal diverticulum of the bladder: May result from drainage of a urachal cyst to the bladder.

– Vitelline duct remnant (omphalomesenteric duct):

Connects fetal midgut to yolk sac

Umbilical sinus, vitelline cyst, or Meckel (8%–10% of Meckel have umbilical anomaly)

– Arterial umbilical remnants

• Acquired anomalies:

– Umbilical hernia:

Defect of umbilical ring with sac, which includes inner lining of peritoneum (often adherent to undersurface of umbilical skin)

More common in females and blacks

80% close spontaneously (if <2 cm). Lesions >2 cm typically do not close and need surgical repair after 3–4 yr of observation (rarely associated with incarceration).

– Omphalitis: Infection of umbilical stump; carries mortality of up to 15%

– Umbilical polyp: Excrescence of vitelline duct mucosa retained in umbilicus:

Resembles granuloma, but does not disappear with silver nitrate

Caution: May be associated with persistent vitelline duct or umbilical sinus

– Endometriosis: Pain and hemorrhagic umbilical discharge during menses

– Umbilical granuloma: After umbilical cord separation, a small granuloma can develop.

– Others: Dermoid cyst, sebum cyst, spontaneous umbilical fistula from Crohn disease/TB/perforated appendix, umbilical hernia, urachal carcinoma, skin cancers such as basal cell or SCC

– Sister Mary Joseph nodule (adults): Umbilical metastasis of primary tumors (if primary is known, usually from genital or GI tract)

TREATMENT

- In the newborn, granuloma is most common cause of persistent drainage.
- Most symptomatic lesions are treated with surgical excision.

MEDICATION

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SURGERY/OTHER PROCEDURES

- Umbilical polyp: If not associated with persistent vitelline duct or umbilical sinus, locally excise.
- Surgical exploration: Inject methylene blue into tract/sinus:
  - Infraumbilical incision down to fascia
  - If there is no dye or tract below the fascia, close; otherwise, open the fascia along the linea alba and resect.
- Umbilical sinus:
  - Simple sinus tract: Excise
  - Patent vitelline duct (enteric contents per umbilicus); needs prompt laparotomy and duct excision to avoid intussusception/volvulus
  - Patent urachus: Resect entire duct via infra-umbilical incision (in newborns), or transverse mid-hypogastric incision in older children; remove cuff of bladder with specimen
  - Infected urachus with abscess formation: Initial drainage under antibiotic therapy; complete excision after infection has subsided

ONGOING CARE

PROGNOSIS

Varies based on lesion

COMPLICATIONS

Vary based on lesion/treatment

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See Also (Topic, Algorithm, Electronic Media Element)

- Urachal Abnormalities
- Omphalocele
- Urachal Carcinoma

CODES

ICD9

- 686.1 Pyogenic granuloma of skin and subcutaneous tissue
- 753.7 Congenital anomalies of urachus
- 771.4 Omphalitis of the newborn

ABBREVIATIONS

- GI: Gastrointestinal
- TB: Tuberculosis
- SCC: Squamous cell carcinoma
- UTI: Urinary tract infection
- US: Ultrasound
- VCUG: Voiding cystourethrogram

UNDESCENDED TESTES (CRYPTORCHIDISM)

Shawn E. White, MD

Pasquale Casale, MD

BASICS

DESCRIPTION

- Cryptorchidism (undescended testes) is defined as congenital maldescent of testis (unilateral or bilateral) into the normal dependent scrotal position.
- Most cryptorchid testes are undescended in that they have stopped before the normal scrotal position. The testicle is not able to be manipulated into the scrotum by several months of age.
- Occasionally, a cryptorchid testicle has descended through the inguinal ring but lies in an aberrant ectopic position (eg, suprapubically, femoral canal, perineum, or contralateral scrotum)
- Classified as:
  - Intra-abdominal (proximal to internal ring) (10–20%)
  - Intracanalicular: Within inguinal canal
  - Extracanalicular: Above scrotum
  - Ectopic: Through canal but in an aberrant location
- Synonym(s): Empty scrotum

EPIDEMIOLOGY

- 3–5% in full-term boys
- Reported up to 30% in premature boys (<37 wk)
- 10% bilateral; slightly more on left side
- ~1.0% by 1 yr of age, remaining constant throughout adulthood

RISK FACTORS

- Prematurity/low birth weight
- Family history
- Other possible associations:
  - Maternal factors (age, complicated birth, cesarean section, preeclampsia)
  - Asian ethnicity

Genetics

- Multifactorial:

):

6.9-fold if brother affected

4.6-fold if father affected

- Association with other abnormalities (eg, hypospadias) has 12–25% incidence of chromosomal anomaly
- Isolated cryptorchidism has 3–4% incidence of chromosomal anomaly.

PATHOPHYSIOLOGY

- Testicular descent is usually complete by week 32 of gestation.
- Endocrine factors:
  - Estrogen (DES): Prenatal exposure impairs descent
  - Androgens (testosterone/DHT): Deficiency of synthesis or action impair descent into scrotum
  - Calcitonin gene-related peptide: Produced by genitofemoral nerve may play role in descent
- Anatomic factors:
  - Gubernaculum: Anchors testis near inguinal canal during cranial migration of kidney
  - Patent processus vaginalis: Allows migration of testis into scrotum
  - Intra-abdominal pressure: Conditions with lower pressures (prune belly, cloacal exstrophy, etc.) have higher incidence of cryptorchidism
  - Epididymis: Abnormalities found in 90% of boys with cryptorchidism
- Up to 90% of undescended testes have an associated patent processus vaginalis.
- Many UDTs will descend spontaneously by 6 mo.
- By 24 mo of age, up to 40% of UDT have no spermatogonia. Increased temperature of the UDT may be the cause of impaired spermatogenesis.
- A retractile testicle is thought to be caused by an overactive cremasteric reflex.

COMMONLY ASSOCIATED CONDITIONS

- Unilateral: Commonly isolated finding
- Bilateral: More likely to be associated with other conditions/complexes:
  - DSD, especially in presence of hypospadias
  - Prune-belly syndrome, bladder exstrophy, pituitary disorders, trisomy 13 and 18, Kallmann, Noonan, Prader-Willi, Laurence-Moon-Biedl, and multiple other syndromes

ALERT

In patients with bilateral UDTs, congenital adrenal hyperplasia and intersex disorders must be excluded in phenotypic male infants. Congenital adrenal hyperplasia is potentially life-threatening.

DIAGNOSIS

HISTORY

- Maternal and gestational history (steroid, estrogen exposure)
- Neonatal physical exam
- Medical/surgical history
- Family history of cryptorchidism

PHYSICAL EXAM

- Complete physical exam for characteristics of congenital syndromes
- Scrotal exam: 80% cryptorchid testes palpable on exam, 20% nonpalpable:
  - Assess for development of hemiscrotum
  - Exam includes most common sites of ectopic testes:

Superficial pouch between external oblique fascia and Scarpa fascia (Denis-Browne pouch)

Transverse scrotal position

Femoral canal

Perineum

Prepenile area

  - Nonpalpable testes may be detected by placing patient supine and milking testis inferiorly along path of descent after wetting hands with warm water.
- Penile exam: Inspect for hypospadias, micropenis, ambiguous phallus
- Evidence of inguinal hernia

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Unilateral: None indicated
- Bilateral: FH, LSH, testosterone may aid in verifying presence of testes:
  - Elevated FSH in prepubescent boy usually indicates anorchia.
  - Normal gonadotropin levels: hCG stimulation test may aid in establishing diagnosis; surgical exploration indicated regardless:

Testosterone production in response to hCG injection indicates presence of functional Leydig cells.

Imaging

)[B]:

- May be occasionally used to evaluate the UDT in very obese children where an adequate exam cannot be performed for the presence of a uterus in a phenotypic male with bilateral cryptorchidism

Diagnostic Procedures/Surgery

- Surgical exploration: Open or laparoscopic often done at time of definitive surgical treatment

• Diagnostic laparoscopy: Aids in diagnosis of intra-abdominal, intracanalicular (cord structures entering internal inguinal ring), absent testes (blind-ending cord structures)

Pathological Findings

• Leydig cell hypoplasia
• Sertoli cell degeneration
• Defective maturation of fetal gonocytes to adult dark (Ad) spermatogonia
• Reduced total germ cell counts

DIFFERENTIAL DIAGNOSIS

• Monorchia/anorchia: Unilateral or bilateral absence of testes
• Ectopic testis: Descended but in abnormal location; most located in the superficial inguinal pouch
• Retractile testis: Can be brought into scrotum to normal dependent position but retracts toward inguinal canal by very active cremasteric reflex
• Ascending testicle: A testicle that is noted to be in normal position early in life and then becomes acquired undescended:
  – May be due to a short spermatic cord or tethering of the testicle as the child grows due to scarring or other anatomic anatomy
  – Some cases may be due to an ectopic testicle that becomes fixed in position as the child grows.

TREATMENT

• Must differentiate UDT from retractile, ascending, or absent testicle.
• Definitive surgical therapy is recommended between 6 mo and 1 yr of age for best outcomes.
• In the setting of unilateral postpubertal cryptorchidism, the decision between orchiopexy vs. orchiectomy is not standardized:
  – Factors to consider in decision include:
    Condition of the health of contralateral testicle
    Fertility and plans for subsequent paternity
    With a normal contralateral testis, orchiectomy may be preferred to eliminate the risk of malignancy or torsion.
    The UDT should be definitively salvaged only if the contralateral testis is absent or abnormal (only source of sperm or testosterone production).

MEDICATION

• Exogenous hCG (IM injection):
  – Mechanism: Stimulates Leydig cell production of testosterone (similar to LH).

– May aid in palpation of UDT

– Many dosing schemes described; typically, 1,500–2,500 units hCG twice a week for 4 wk

– Side effects of hCG therapy; penile and testicular enlargement, growth of pubic hair, and aggressive behavior during treatment

- GnRH agonists (intranasal spray): Approved in Europe only:

– Mechanism: Stimulates pituitary release of LH/FSH which increase gonadal testosterone production

– Efficacy: Overall success rates for hormonal therapy ~20%, higher success rates reported for testes below external inguinal ring

– Side effects: Increased scrotal rugae, pigmentation, pubic hair, penile growth

SURGERY/OTHER PROCEDURES

- Standard orchiopexy (gold standard):

– General steps:

Mobilization of spermatic cord and testis

Ligation of patent processus vaginalis

Dissection of internal spermatic fascial layers to provide adequate added length of spermatic cord

Fixation of testis in superficial sub-Dartos pouch created in ipsilateral hemiscrotum

)[A]

- Fowler-Stephens orchiopexy:

– Indication: Inability to sufficiently mobilize spermatic cord to reach a dependent scrotal position using standard dissection

– Technique: Ligation of testicular artery and vein to allow greater mobilization of spermatic cord (deferential artery and cremasteric arteries provide collateral blood supply to testis)

)[A]

- Laparoscopic orchiopexy:

– Standard and Fowler-Stephens can be performed laparoscopically

– Advantages: Improved visualization and ease of dissection for high inguinal and intra-abdominal testes

- Additional operative techniques:

– Prentiss maneuver: Passage of testis directly through the abdominal wall medially near the pubic tubercle, dividing the inferior epigastrics to provide shorter distance to a dependent scrotal position

– Microvascular autotransplantation: Microvascular anastomosis of testicular vessels performed for intra-abdominal testes instead of ligation as in Fowler-Stephens

ONGOING CARE

PROGNOSIS

- Fertility:

)

  - Ectopic testes may have impaired spermatogenesis.
  - Histopathology:

    Failure of formation of Ad spermatogonia from fetal gonocytes at 2–3 mo of age

    Failure of formation of primary spermatocytes from Ad spermatogonia at 4–5 yr of age

- Malignancy:
  - Relative risk: ~40 times greater in men with history of cryptorchidism regardless of whether orchiopexy is performed or not
  - Incidence: 10% of testicular tumors arise from a cryptorchid testis. Ectopic tests less likely to undergo malignant transformation
  - Pathology: Most common tumor is seminoma

COMPLICATIONS

- Torsion of UDT 10 times higher than normal testes
- Canalicular and ectopic UDT are at risk for trauma
- Surgical complications of orchiopexy:
  - Hematoma
  - Ilioinguinal nerve injury
  - Testicular atrophy (compromised blood supply)
  - Testicular retraction
  - Testicular torsion
  - Vas deferens injury

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Testicular self-exam:
  - Facilitated by dependent scrotal position after successful orchiopexy
  - Recommended in all patients given higher risk of developing testicular malignancy
- Periodic physician exam of retractile testicle to verify that it can be manipulated into the scrotum and in not a missed ectopic testicle

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See Also (Topic, Algorithm, Electronic Media Element)

- Disorders of Sexual Development (DSD)
- Testis Cancer, General

CODES

ICD9

752.51 Undescended testis

ABBREVIATIONS

- Ad: Type of spermatogonia
- DES: Diethylstilbestrol
- DHT: Dihydrotestosterone
- DSD: Disorders of sexual development
- FH: Follicular hormone
- GnRH: Gonadotropin-releasing hormone
- hCG: Human chorionic gonadotropin
- LH: Luteinizing hormone
- LSH: Lutein stimulating hormone
- UDT: Undescended testis

URACHAL CARCINOMA

David S. Sharp, MD

Robert R. Bahnson, MD

BASICS

DESCRIPTION

- Rare tumor
- Commonly adenocarcinoma, but cell type may be urothelial, squamous, or mesenchymal
- May arise anywhere between umbilicus and dome of bladder
- Prognosis generally poor, usually due to delayed diagnosis
- Cure attainable in appropriately resected localized disease
- Traditional TNM bladder staging does not apply to these tumors, as they do not originate from the bladder epithelium:

) staging systems

EPIDEMIOLOGY

- Annual incidence ~1 in 5 million
- 0.35–0.7% of bladder cancers and 10–35% of bladder adenocarcinomas
- Most common in 4th and 5th decades
- Males predominate: ~60%
- No reliable data reported

RISK FACTORS

- Due to rarity, not well known
- Adenomatous hyperplasia, cysts, or calculi may be risk factors.

Genetics

Carcinogenic pathways and genetic defects are unknown.

PATHOPHYSIOLOGY

- Urachus derived from glandular epithelium embryonically connecting bladder to allantois:
  - Becomes median umbilical ligament
  - Urachal remnants may occur along umbilical ligament, in dome of bladder, or rarely in posterior or anterior wall of bladder
- Urachus has intramucosal, intramuscular, and supravesical segments containing epithelium of urothelium, submucosal connective tissue, and outer smooth muscle. Lesions can arise in all 3 of these layers.
- Focal glandular metaplasia may give rise to intestinal-type tumors, or alternatively tumors may arise from enteric rests.

- Invades locally into muscularis propria and perivesical fat with demarcation between tumor and bladder epithelium
- Tumor may extend into space of Retzius, anterior abdominal wall, or umbilicus, and may extend through peritoneum, leading to peritoneal implants.
- Metastases to iliac and inguinal lymph nodes, lung, liver, and/or bone

COMMONLY ASSOCIATED CONDITIONS

Urachal cyst

DIAGNOSIS

HISTORY

- Many tumors are primarily extravesical and may be asymptomatic until tumor grows large enough to invade bladder or adjacent structure to cause symptoms.
- Hematuria is the most common presenting symptom.
- Other symptoms may include mucoid discharge per urethra or skin, irritative voiding symptoms, or palpable abdominal mass.
- May be discovered incidentally on imaging
- Pneumaturia may suggest a enterovesical fistula and be due to benign inflammatory condition or intestinal primary malignancy.
- A mass that changes in size and intermittently shrinks may be consistent with a draining urachal cyst.

PHYSICAL EXAM

- Palpable abdominal mass likely indicates more advanced disease.
- Evaluate if mass is mobile or fixed to help discern resectability.
- Evaluate for ascites indicative of peritoneal involvement.
- A thorough pelvic exam with bimanual vaginal and/or rectal exam is necessary for staging and to exclude gynecologic or rectal primaries.
- Evaluate for signs of anemia, infection, metastatic disease, or cachexia as well as to assess comorbidities and anesthetic risk.
- Evidence of umbilical discharge is more likely with infected urachal sinus.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis: Urine culture to evaluate for infection
- Urine cytology: Urothelial carcinoma may be less likely urachal primary
- Hematology and chemistry panels as routine cancer and preoperative evaluation

)[C]

Imaging

- Abdominal US may be used as part of initial evaluation:
  - Evaluate for hydronephrosis.
  - Characterize mass as cystic, solid, or mixed.
- Excretory urography may be used to evaluate hematuria and may reveal bladder mass or ureteral obstruction.
- CT or MRI of abdomen and pelvis with PO and IV contrast is mainstay of evaluation for both diagnosis and staging evaluation:
  - Typical CT finding is calcified midline supravesical mass that is mixed cystic and solid. This is highly suspicious though not pathognomonic.
  - Mass may also be intravesical at bladder dome.
  - CT may also suggest peritoneal carcinomatosis or pseudomyxoma peritonei.
- Chest x-ray or CT chest for staging
- May consider bone scan if advanced disease, bony symptoms present, or elevated alkaline phosphatase
- FDG-PET has been used to evaluate for metastases, though its sensitivity is unknown.

Diagnostic Procedures/Surgery

- Cystoscopy and transurethral biopsy with exam under anesthesia:
  - Evaluate location of tumor and rule out multifocal urothelial carcinoma.
  - Tumor may be submucosal and neither visible endoscopically nor amenable to transurethral biopsy.
  - Tumor may be papillary, polypoid, or fungating.
  - Biopsy of tumor and adjacent normal bladder epithelium is recommended.
- Percutaneous biopsy may be performed if lesion is extravesical, though a concern exists (via case reports in other tumors) of tumor seeding of biopsy tract.

Pathological Findings

- A majority of cases (>80%) are adenocarcinomas with enteric features, with or without mucin production, sometimes with signet ring pattern.
- Other urachal cell types reported:
  - Typical urothelial carcinoma
  - SCC
  - Mesenchymal tumors or sarcomas
- Pathologic criteria for diagnosis are controversial but include:
  - Location of tumor in bladder dome or in midline
  - Demarcation between tumor and normal surface epithelium (although in some cases where urachal remnants can be identified, tumor can be found to extend into the bladder epithelium)

- Supportive criteria, although not required include:
  - Presence of urachal remnants in tumor
  - Enteric-type pathology
  - Absence of urothelial dysplasia
  - Absence of cystitis cystica or cystitis glandularis transitioning to the tumor
  - Absence of primary adenocarcinoma of another organ

DIFFERENTIAL DIAGNOSIS

- Solitary primary bladder malignancy of any histologic cell type at bladder dome
- Secondary malignancy invading into bladder:
  - Colorectal primary
  - Ovarian, endometrial, cervical, or prostatic primary
- Benign lesion of urachus:
  - Urachal cyst
  - Urachal diverticulum
  - Urachal sinus

ALERT

For any solitary lesion at the bladder dome, regardless of histology, recommendation is to treat as if it is a urachal carcinoma. It is imperative that diagnosis is entertained preoperatively. Final pathology may or may not confirm urachal origin.

TREATMENT

- Usually presents with locally advanced disease
- A localized tumor requires prompt resection; transurethral surgery alone is inadequate.
- A metastatic tumor requires chemotherapy and perhaps focal radiation.

MEDICATION

First Line

- Currently, no definitive role for neoadjuvant or adjuvant chemotherapy in this tumor

)[B]

)[C]

Second Line

Different multiagent as well as single-agent regimens and targeted therapies are being utilized, but little data exist to support a recommendation.

SURGERY/OTHER PROCEDURES

- For resectable disease, surgery is treatment of choice.

)[C]

- No data show that radical cystectomy offers superior survival to extended partial cystectomy for this tumor.

)[C]

)[C]

- Case reports of laparoscopic and robotic surgeries have been published, although follow-up is <1 yr.

ADDITIONAL TREATMENT

Radiation therapy:

- Not well studied as primary therapy
- May play a role in palliation, salvage therapy, and local control in setting of metastatic disease

ONGOING CARE

PROGNOSIS

- 5-yr overall survival rates depending on series are 27–80%

)[B]

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- Outcomes after minimally invasive treatments are not known.

COMPLICATIONS

- DVT or PE
- Development of recurrence or metastatic disease
- Hemorrhage
- Infection
- Loco-regional organ involvement and injury
- Lymphocele
- Urine leak

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Periodic evaluation every 3–6 mo or longer:

- General physical assessment
- Metastatic survey
- Pelvic and abdominal imaging with CT or MRI to assess local and distant recurrence
- If bladder is preserved, screen for local recurrence:
  - Urine analysis and cytology
  - Cystoscopy

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Exstrophy
- Umbilical Abnormalities, Urologic Considerations
- Urachal Abnormalities

CODES

ICD9

188.7 Malignant neoplasm of urachus

ABBREVIATIONS

- CT: Computed tomography
- DVT: Deep vein thrombosis
- FDG-PET: Positron emission tomography with 18Ffluorodeoxyglucose
- Gem-FLP: Gemcitabine, 5-fluorouracil, leucovorin, cisplatin
- ITP: Ifosfamide, paclitaxel, cisplatin
- IV: Intravenous
- MRI: Magnetic resonance imaging
- PE: Pulmonary embolism
- SCC: Squamous cell carcinoma
- US: Ultrasound

URETER AND RENAL PELVIC TUMORS, GENERAL

Benjamin R. Lee, MD
Mathew C. Raynor, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- Tumors of the ureter and renal pelvis are uncommon.
- Tumors in this location are most often malignant and account for 5% of all urothelial tumors; most commonly TCC.

EPIDEMIOLOGY

- Male > Female (2:1)
- Whites > Blacks (2:1)
- Rare <40 yr, peak incidence 6th–7th decade
- Balkan nephropathy: Endemic to Bulgaria, Greece, Romania, and Yugoslavia:
  - Associated with upper tract urothelial tumors.
  - Tumors are often multiple, bilateral, and indolent. Renal-sparing surgery is indicated where possible.
- 5-yr survival rate:
  - Stage I, 80%
  - Stage II, 50%
  - Stages III–IV, <10%
- Ureteric TCC is 1 per 1,000–3,600; these account for 1 in every 25 upper-tract tumors
- Primary renal pelvis neoplasms <10% of all renal tumors
- Bladder tumors 50 times more common than renal pelvis tumors

RISK FACTORS

- Urothelial carcinoma:
  - Smoking: Risk from 2.6–8.0; risk increases with higher dose and duration of tobacco use.
  - History of bladder cancer: 2–25% of patients with bladder cancer can develop upper-tract TCC
  - Occupational exposure: Similar to bladder cancer; ~20% of TCCs, with disease latency of 30–50 yr. Most chemicals are aromatic amines (aniline dyes [color fabrics]), 2-naphthylamine, 4-aminobiphenyl, 4-nitrobiphenyt, 4,4-diaminobiphenyl, 2-amino-1-naphthol, soot from coal, combustion gas, and aliphatic hydrocarbons.
  - High-risk occupations: Autoworkers, leather workers, painters, truck drivers, metal workers, machinists, dry cleaners, dental technicians, beauticians, and physicians:

Relative risk of disease following exposure: 4.0–5.5

– Coffee: Minor contribution, with relative risk of 1.3

– Analgesic abuse: All components implicated; highest risk with phenacetin abuse; latency of 25 yr (dose of 10–15 g over 10 yr); tend to be women who present with high-stage tumors. Relative risk: 2.4 for men and 4.2 for women

• Infectious agents: Chronic bacterial infection with calculi and obstruction; increased risk of SCC

• Cyclophosphamide: Hemorrhagic cystitis and carcinoma; 9 times increased risk of carcinoma after exposure; latency of 6–13 yr

Genetics

• Most have no family history of disease

• Certain familial cancer syndromes show an increased incidence of TCC (Lynch type II).

• Familial clustering exists; difficult to determine if related to environmental factors.

• Data are inconclusive on a direct genetic relationship.

• Low-grade superficial TCC: Loss of p15 and p16 (chromosome 9p)

• High-grade TCC: Loss of p53 (chromosome 17p)

• Amplification and overexpression of normal genes that code for growth factors or their receptors

– EGF-R (on chromosome 7): Trisomy 7 associated with TCC

– Erb-2 mutations associated with TCC

GENERAL PREVENTION

• Smoking cessation

• Avoid or limit chronic analgesia use.

• Avoid occupational exposure to implicated toxins.

PATHOPHYSIOLOGY

• >90% upper tract urothelial tumors are TCC:

– ~70% ureteral TCC occur in distal ureter, 25% mid ureter, 5% proximal ureter.

– Tumors of the ureter tend to be less invasive and smaller than those of the renal pelvis.

– Up to 50% of ureteral TCCs are multicentric.

• SCC: 7%; associated with long-term infection, inflammation, and calculi

• Rare malignant tumors include adenocarcinoma, sarcoma, and carcinosarcoma.

• Rare benign tumors include inverted papilloma and fibroepithelial polyp.

COMMONLY ASSOCIATED CONDITIONS

Urothelial carcinoma of the bladder

DIAGNOSIS

HISTORY

- Age and sex of patient: Uncommon before the age of 40, peak incidence in mid-60s
- Hematuria: Most common presenting symptom (75% of patients)
- Dull flank pain due to the gradual distention of collecting system (30% of patients)
- Tobacco use: Occupational exposure (up to 20% of TCCs)
- History of analgesia abuse in past: Dose-related effect; phenacetin is most common
- History of recurrent infections and staghorn calculi: SCC
- Asymptomatic: Incidental diagnosis in 10–15%
- Rarely, patients present with signs of advanced disease (abdominal or flank mass, anorexia, weight loss, etc.).

PHYSICAL EXAM

Usually normal; flank or abdominal mass with advanced disease

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis: Hematuria (gross or microscopic)
- Cytopathology:
  - Voided specimen: Low sensitivity for upper tract TCC; ureteral catheterization specimens are more sensitive.
  - Accuracy increases with increasing grade of tumor.

Imaging

- IVP:
  - 50–75%: Radiolucent filling defect; is irregular and continuous with the wall
  - 10–30% show obstruction or nonvisualization of the collecting system, which indicates more invasive disease.
  - Examine the contralateral kidney for lesion and function.
- Retrograde urography: Better visualization than IVP (>75% accuracy)
- Antegrade pyelography:
  - Used only if not possible to visualize collecting system via retrograde approach. Risk of seeding of tumor cells along the tract is small.
- CT urogram: Now primary imaging study useful for both diagnosis and staging of tumors
- MRI: Useful for staging

Diagnostic Procedures/Surgery

- Ureteroscopy and nephroscopy:

– Diagnostic accuracy of 58–83%. Not accurate for staging TCCs due to difficulty in determining the depth of invasion, particularly renal pelvic TCC

- Brush biopsy:
  – High positive predictive value, overall accuracy of 78%; significant risk of bleeding and ureteral perforation
- Selective cytology barbotage useful to localize tumor

Pathological Findings

- Urothelial carcinoma: Papillary (exophytic) predominate:
  – Slender stalks or endophytic (flat)
  – Invasive or noninvasive
- SCC is characterized by sheets of cells with well-defined cell borders, deeply eosinophilic cytoplasm, and focal keratin pearl formation.

DIFFERENTIAL DIAGNOSIS

- Malignant filling defect of ureter and renal pelvis:
  – TCC:
    The most common malignant cause of upper urinary tract filling defects
  – SCC
  – Rare malignant tumors: Adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  – RCC:
    Usually found in conjunction with renal mass on US or CT; has been reported without associated renal mass as a filing defect in the collecting system
- Benign filling defect of ureter and renal pelvis:
  – Air: Iatrogenic, infectious or due to fistula
  – Blood clot
  – Fibroepithelial polyp
  – Fungus ball
  – Hemangioma
  – Inflammatory lesions: Granuloma, malakoplakia, TB
  – Inverted papilloma
  – Radiolucent calculus
  – Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  – Renal papilla:
    Ectopic or end on renal papilla can be misidentified as a filling defect.
  – Sloughed papilla:

May be iatrogenic during retrograde pyelography, or due to ureteroenteric fistula, or emphysematous pyelonephritis

- Extrinsic compression on the ureter
- Mucus: Urinary diversion patients
- Protein matrix
- Ureteritis or pyelitis cystica
- Vascular impression

TREATMENT

- If positive cytology is the only sign of upper tract TCC, close follow-up is required (IVP; CT urogram; retrograde, flexible ureteroscopy where indicated, FISH urine test).
- Standard treatment is surgical for most benign and malignant lesions.

MEDICATION

- Instillation therapy with BCG or mitomycin not proven to increase survival advantage:
  - Appears to be safe, but indications and outcome are not clearly defined.
  - May be useful in multiple superficial tumors or bilateral disease
- Chemotherapy: Comparable to TCC of the bladder; useful adjuvantly in high-risk patients and may be of benefit for palliation with metastatic disease

SURGERY/OTHER PROCEDURES

- Standard treatment for urothelial carcinoma is nephroureterectomy.
- Indications for conservative, renal-sparing surgery include a single kidney, bilateral disease, reduced or nonfunction of the contralateral kidney, or tumor of low grade and stage.
- Survival more closely related to stage and grade of tumor than to treatment modality.
- Radical laparoscopic nephroureterectomy and excision of cuff of bladder:
  - 80–90% 5-yr survival (low grade and stage)
- 30–75% recurrence rate in ureteral stump
- Radical lymphadenectomy not shown to improve survival
- Endoscopic treatment (ureteroscopy):
  - Indications include solitary kidney, bilateral disease, poor renal function, moderate tumor burden, low-grade disease, high-risk surgical candidates
- Segmental ureteral resection: Option for solitary low-grade upper and mid-ureteral lesions:
  - Recurrence rate of 6%; higher if multifocal
- Distal ureterectomy and ureteroneocystostomy: Distal, solitary ureteral lesions
- Benign tumors, such as fibroepithelial polyp or inverted papilloma: Endoscopic excision and/or ablation

ADDITIONAL TREATMENT

- Radiation therapy:
  - Can be used for advanced tumors not amenable to surgery, with decreased efficacy
- Endoscopic resections: For low-grade, superficial, or solitary kidney:
  - Risk of perforation is higher than that in bladder (overall complication rate: 7%).
  - Requires close follow-up due to high recurrence rate
- Laser ablation with low-grade or multiple tumors

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Angioinfarction: For incurable disease in those deemed unfit for surgery

ONGOING CARE

PROGNOSIS

Recurrence rate reduced with more aggressive resection of tumor:

- 48% recurrence with nephrectomy
- 32% with nephrectomy plus partial ureterectomy
- 24% with nephrectomy plus subtotal ureterectomy
- 12% with nephroureterectomy.

COMPLICATIONS

- Obstruction of urinary tract
- Development of locally advanced or metastatic disease

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Cystoscopy with cytology every 3–6 mo for 2–3 yr, then yearly
- 6-mo CT urogram + chest x-ray, then annually
- Ureteroscopy is more sensitive than radiologic techniques for follow-up of upper tract TCC.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)

- Ureter and Renal Pelvis, Transitional Cell Carcinoma
- Ureter and Renal Pelvis, Squamous Cell Carcinoma

CODES

ICD9

- 223.1 Benign neoplasm of renal pelvis
- 223.2 Benign neoplasm of ureter
- 223.3 Benign neoplasm of bladder

ABBREVIATIONS

- BCG: Bacillus Calmette-Guérin
- CT: Computed tomography
- FISH: Fluorescence in situ hybridization
- IVP: Intravenous pyelogram
- MRI: Magnetic resonance imaging
- RCC: Renal cell carcinoma
- SCC: Squamous cell carcinoma
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- US: Ultrasound

URETER AND RENAL PELVIS, SQUAMOUS CELL CARCINOMA

Ahmad Shabsigh, MD
Robert R. Bahnson, MD

BASICS

DESCRIPTION

SCC arising in the collecting system (calyces, infundibuli, renal pelvis, ureters) or the ureter

EPIDEMIOLOGY

- The small number of cases in any 1 institution makes it difficult to characterize this disease.
- <1% of all GU malignancies
- 4–15% of all primary neoplasms of the upper urinary tract
- Affects older population; most often occurs in the 5th decade of life
- Male = Female

RISK FACTORS

- Strong association with renal calculi (40–80%)
- Chronic infections:
  - Recurrent pyelonephritis
  - Struvite stones
  - Renal TB
  - Parasitic infections (eg, schistosomiasis)
- Carcinogens may be risk factors, although never definitely demonstrated:
  - Cigarette smoking, benzenes, petroleum products

GENERAL PREVENTION

- Treat urologic infections and renal nephrolithiasis in timely fashion.
- Limit exposure to carcinogens.

PATHOPHYSIOLOGY

- SCC of the urinary tract is commonly associated with chronically infected states:
  - Renal calculi, staghorn calculi, TB, schistosomiasis
- Chronic infections cause irritation of the normal transitional urothelium.
- This irritation causes de-differentiation of these cells and then malignant transformation.

COMMONLY ASSOCIATED CONDITIONS

- Renal calculi
- Chronic infections:
  - Recurrent pyelonephritis
  - Struvite stones
  - Renal TB
  - Parasitic infections

DIAGNOSIS

HISTORY

- Age of patient
- Hematuria, secondary to bleeding tumor or irritation (eg, stones), may be microscopic.
- History of recurrent infections
- Flank or abdominal pain, secondary to ureteral obstruction, may be typical renal colic or dull, nonspecific pain.
- Systemic or renal TB or recent exposure
- Constitutional symptoms may prevail in more advanced disease.

PHYSICAL EXAM

- Usually a completely normal exam
- Abdominal or CVA tenderness related to renal obstruction, or active infection
- Flank mass secondary to hydronephrosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Abnormal urine analysis:
  - Hematuria in 80–90%
  - Pyuria in 83%
- Serum chemistries are usually within normal limits:
  - Serum creatinine may be elevated due to renal damage from obstruction or infection and scarring.
  - Tumor-related hypercalcemia, which resolves after tumor excision

Imaging

- Cannot make diagnosis from radiologic studies
- IVP, angiography, and US are not diagnostic; may find hydroneprhosis, nonexcretion of contrast due to obstruction or dysfunctional kidney, renal stones, filling defects.
- MRI/MRA or CT scan, should be performed if surgery is planned. These provide size and the extent of the tumor, vascular pattern of the tumor and the vascular supply to the kidney, presence of metastases

- State of native renal unit

Diagnostic Procedures/Surgery

- Cystoscopy to role out bladder urothelial cancer, selective cytology, retrograde ureteropyelogram, and ureteroscopy with biopsy are essential for appropriate diagnosis.
- Diagnosis is commonly made following definitive surgery (eg, nephroureterectomy).
- An experienced cytologist usually is needed for accurate evaluation of the urine sample.

Pathological Findings

- SCC is characterized by sheets of cells with well-defined cell borders, deeply eosinophilic cytoplasm, and focal keratin pearl formation.
- Large nuclei with prominent nucleoli usually occupy >30% of the tumor.
- Most will show areas of transition with urothelial carcinoma.
- The lesions tend to have infiltrating borders with wide invasion of the renal parenchyma.

DIFFERENTIAL DIAGNOSIS

- Malignant filling defect of ureter and renal pelvis:
  - TCC:

    The most common malignant cause of upper urinary tract filling defects
  - SCC:

    Rare malignant tumors: Adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  - RCC:

    Usually found in conjunction with a renal mass on US or CT; has been reported without associated renal mass as a filing defect in the collecting system
- Benign filling defect of ureter and renal pelvis:
  - Air: Iatrogenic, infectious, or due to fistula
  - Blood clot
  - Fibroepithelial polyp
  - Fungus ball
  - Hemangioma
  - Inflammatory lesions: Granuloma, malakoplakia, TB
  - Inverted papilloma
  - Radiolucent calculus
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Renal papilla:

Ectopic or end on renal papilla can be misidentified as a filling defect.

– Sloughed papilla:

May be iatrogenic during retrograde pyelography, or due to ureteroenteric fistula, or emphysematous pyelonephritis

– Extrinsic compression on the ureter
– Mucus: Urinary diversion patients
– Protein matrix
– Ureteritis or pyelitis cystica
– Vascular impression

TREATMENT

- Treatment of choice is surgical excision (nephroureterectomy).
- Infected patients require pre- and postoperative broad-spectrum antibiotics.

MEDICATION

Adjuvant chemo- and radiotherapy has been used with marginal results; still controversial.

SURGERY/OTHER PROCEDURES

- Surgical resection is the standard of care.
- Similar to TCC for same location and stage
- Endoscopic treatment (resection or laser ablation) may be considered for low-stage and low-grade disease especially in severely morbid patients or the rare patients with bilateral disease.
- Nephroureterectomy is the treatment of choice, including a bladder cuff resection.
- The role of retroperitoneal lymph node dissection is controversial.
- Surgery is often required for palliation in advanced disease for patients with severe gross hematuria or sepsis.

ONGOING CARE

PROGNOSIS

- Local recurrence is high.
- Survival depends on stage at the time of diagnosis.
- Average survival is short with high-grade and high-stage disease.
- Distant metastasis are commonly noted at the time of diagnosis.
- Clinical trials are needed to define the role of adjuvant chemotherapy and radiotherapy.

COMPLICATIONS

- Renal insufficiency
- Metastatic disease

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Similar to TCC of the upper tract
- Limited data for standard of care
- Cystoscopy and urine cytology every 3–4 mo for the 1st 2 yr
- Metastatic workup every 6–12 mo, depending on the stage of the disease

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See Also (Topic, Algorithm, Electronic Media Element)

- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Ureter and Renal Pelvic Tumors, General
- Ureter and Renal Pelvis, Urothelial Carcinoma
- TNM Classification

CODES

ICD9

- 189.1 Malignant neoplasm of renal pelvis
- 189.2 Malignant neoplasm of ureter

ABBREVIATIONS

- CT: Computed tomography
- CVA: Costovertebral angle
- GU: Genitourinary
- IVP: Intravenous pyelogram
- MRA: Magnetic resonance angiography
- MRI: Magnetic resonance imaging
- RCC: Renal cell carcinoma
- SCC: Squamous cell carcinoma
- TB: Tuberculosis

- TCC: Transitional cell carcinoma
- US: Ultrasound

URETER AND RENAL PELVIS, UROTHELIAL CARCINOMA (TRANSITIONAL CELL CARCINOMA AND CIS)

Nicholas T. Leone, MD

Demetrius H. Bagley, MD

BASICS

DESCRIPTION

Urothelial carcinoma (TCC) is an epithelial neoplasm of the ureter and intrarenal collecting system accounting for >90% of upper-tract urothelial tumors.

EPIDEMIOLOGY

- 5–10% of renal tumors are renal pelvis TCC.
- 2–5% of urothelial tumors occur in the UUT
- Peak incidence of 10 per 100,000/yr in 75–79 age group
- Mean age at presentation is 65.
- Incidence is increasing.

RISK FACTORS

- Bladder TCC (2–4% lifetime risk of UUT TCC):
  - Stage, grade, multiplicity, ureteral reflux, recurrent CIS after BCG, and TCC close to ureteral orifice all increase likelihood of UUT TCC in patient with bladder TCC
- Contralateral UUT TCC (1.6–6% risk):
  - Risk factors shared with bladder TCC
  - Cigarette smoking (3 times risk; only partly declines with smoking cessation)
  - Occupational exposure (4 times risk):
    Aniline dyes, -naphthylamine, benzidine, coal, coke, asphalt, or tar exposure; chemical, petroleum, or plastics industries
  - Cyclophosphamide:
    Mesna (uroprotectant) can be co-administered to neutralize acrolein (urotoxic metabolite)
- Risk factors specific to UUT TCC:
  - Balkan nephropathy (100–200 times risk):
    Typically bilateral, multifocal, low-grade
  - Analgesic abuse (3.6 times risk):
    Phenacetin, aspirin, acetaminophen, codeine
  - Papillary necrosis (6.9 times risk):

Synergistic with analgesic abuse (20 times risk)
  - Chinese weight-loss herb Aristolochia fangchi

Genetics

- Male > Female (3:1)
- White > Black (2:1)
- Lynch II syndrome (HNPCC): Familial syndrome predisposing to GI, endometrial, and UUT neoplasms

PATHOPHYSIOLOGY

- Growth patterns include papillary and nodular
- Depth of invasion can be invasive or noninvasive
- TNM staging system for UUT TCC:
  - Stage Ta: Papillary, noninvasive
  - Stage Tis: CIS
  - Stage T1: Involvement of subepithelial connective tissue
  - Stage T2: Invasion of muscularis propria
  - Stage T3: Extension into periureteral fat, perinephric fat or renal parenchyma
  - Stage T4: Adjacent organ involvement

COMMONLY ASSOCIATED CONDITIONS

- Bladder TCC: 30–50% risk of developing bladder TCC after UUT TCC
- Balkan nephropathy
- Lynch II syndrome

DIAGNOSIS

HISTORY

- Tobacco use, coffee intake
- Occupational exposures
- Medications: Analgesics (ie, phenacetin, aspirin), cyclophosphamide, exotic herbs
- Family history: Balkan family, colonic malignancy
- Gross hematuria, dull flank pain, acute renal colic

PHYSICAL EXAM

- Often asymptomatic
- Weight loss, anorexia
- CVA tenderness
- Flank or abdominal mass
- Bone pain

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis: Gross or microscopic hematuria:
  - 60–90% present with hematuria
- Voided urine cytology: Low sensitivity for low-grade TCC; better for high-grade, CIS:
  - Uroplakin staining may improve sensitivity.
- Catheterized ureteral or RP washing: 65–73% sensitive
- Brush biopsy: 91% sensitive, 88% specific:
  - Performed during retrograde pyeloureterography
- Ureteroscopic cup/basket biopsy: Most sensitive
- Electrolytes, LFTs normal in absence of urinary obstruction or metastatic disease

Imaging

- Contrast-enhanced imaging is used to detect radiolucent filling defects, obstruction, or incomplete filling of UUT.
- Differential diagnosis of UUT filling defect includes TCC, stones, blood clot, air bubble, sloughed papilla, fungus ball, ureteritis cystica, extrinsic compression.
- Study contralateral side to rule out bilateral disease and assess functionality.
- IVU:
  - Traditional study for UUT TCC
  - Combined with tomograms or renal US to better detect renal parenchymal mass
- Retrograde pyeloureterography:
  - Indications: Inadequate visualization on IVU or CTU, contrast allergy, renal insufficiency
  - More sensitive than IVU or CTU
  - Use dilute contrast (1/2–1/3).
  - Inject through cone-tip or open-ended catheter to fill entire collecting system (10–15 cc).
  - Avoid contrast extravasation due to overfilling.
- CTU:
  - 3D reconstruction image quality is equivalent to IVU for UUT TCC.
  - Can differentiate renal parenchymal mass from RP mass, or TCC from calculus
  - Can evaluate for locoregional or distant metastatic disease
- US:
  - Can help distinguish stone from tumor
  - Endoluminal US: May be used as an adjunct to ureteroscopy to define tumor size and invasion at time of ureteroscopy

Diagnostic Procedures/Surgery

- Cystoscopy: Evaluates lower urinary tract for concomitant TCC
- Ureteroscopy: Provides direct visualization of UUT TCC, aspiration for cytology, cup/basket biopsy, and treatment simultaneously

Pathological Findings

- Pathologic staging 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 (cell block).

DIFFERENTIAL DIAGNOSIS

- Malignant filling defect of ureter and renal pelvis:
  - TCC:
    The most common malignant cause of UUT filling defects
  - SCC:
    Rare malignant tumors: Adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  - RCC:
    Usually found in conjunction with renal mass on US or CT scan; has been reported without associated renal mass as a filing defect in the collecting system
- Benign filling defect of ureter and renal pelvis:
  - Air: Iatrogenic, infectious or due to fistula
  - Blood clot
  - Fibroepithelial polyp
  - Fungus ball
  - Hemangioma
  - Inflammatory lesions: Granuloma, malakoplakia, TB
  - Inverted papilloma
  - Radiolucent calculus
  - Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
  - Renal papilla:
    Ectopic or end on renal papilla can be misidentified as a filling defect.
  - Sloughed papilla:
    May be iatrogenic during retrograde pyelography, or due to ureteroenteric fistula, or emphysematous pyelonephritis

- Extrinsic compression on the ureter
- Mucus: Urinary diversion patients
- Protein matrix
- Ureteritis or pyelitis cystica
- Vascular impression

TREATMENT

- Nephroureterectomy with bladder cuff is gold standard
- Endoscopic treatment in selected cases

MEDICATION

Topical therapy: BCG, MMC, thiotepa:

- Instilled via percutaneous nephrostomy, external ureteral catheter, or into bladder with indwelling ureteral stent
- Typically given for large, multifocal, or residual tumor burden
- Role not clearly defined, as benefit has not been consistently demonstrated

SURGERY/OTHER PROCEDURES

- Open RNU with en bloc excision of peri-ureteric bladder cuff:
  - Gold standard and traditional treatment
  - Provides adequate surgical margins, control of local recurrence; obviates need for ipsilateral ureteroscopic surveillance; and provides most accurate staging information
  - Role of lymphadenectomy is unclear
- Laparoscopic RNU:
  - Skin incision positioned to allow for distal ureteral dissection and en bloc specimen removal
  - Equivalent disease-specific and overall survival rates compared with open RNU
- Nephron-sparing surgery:
  - Segmental ureterectomy:

    Used for noninvasive low-grade TCC of proximal or mid-ureter that are too large for endoscopic ablation, high-grade TCC or invasive tumors when nephron-sparing is necessary
  - Distal ureterectomy with ureteroneocystostomy:

    Used for distal ureteral TCC too large for endoscopic ablation

    Most long-term success with low-grade, low-stage 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
- No-touch technique allows for maximal preservation of ureteroscopic findings.
- Tumor biopsy with cold-cup or basket
- Treatment techniques include electrosurgical resection, fulguration, laser ablation with Nd:YAG and/or Ho:YAG
- Recurrence rates: 33% for ureteral TCC, 31% for RP TCC

ONGOING CARE

PROGNOSIS

- 5-yr survival based on grade:
  - Grade 1–2: 40–87%
  - Grade 3–4: 0–33%
- 5-yr survival based on stage:
  - Stage Ta, T1, Tis: 60–90%
  - Stage T2: 43–75%
  - Stage T3: 16–33%
  - Stage T4: 0–5%

COMPLICATIONS

Ureteral obstruction, metastatic dissemination

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- If radical RNU is performed: Cystoscopic surveillance and cytology every 3 mo for 2 yr, then every 6 mo for 2 yr, then yearly thereafter; IVP or CTU yearly
- If nephron-sparing surgery is performed: Ureteroscopic surveillance and cytology every 3 mo until tumor-free, then every 6 mo thereafter; IVP or CTU yearly

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See Also (Topic, Algorithm, Electronic Media Element)

- Filling Defect, Upper Urinary Tract (Renal Pelvis and Ureter)
- Lynch Syndrome
- TNM Staging
- Ureter and Renal Pelvic Tumors, General
- Ureter and Renal Pelvis, Squamous Cell Carcinoma

CODES

ICD9

- 189.1 Malignant neoplasm of renal pelvis
- 189.2 Malignant neoplasm of ureter

ABBREVIATIONS

- BCG: Bacilli Calmette-Guérin
- CIS: Carcinoma in situ
- CT: Computed tomography
- CTU: Computed tomography urogram
- CVA: Costovertebral angle
- GI: Gastrointestinal
- HNPCC: Hereditary nonpolyposis colorectal carcinoma
- Ho:YAG laser: Holmium YAG laser
- IVU: Intravenous urography
- LFT: Liver function test
- MMC: Mitomycin C
- Nd:YAG laser: Neodymium-doped YAG laser
- RCC: Renal cell carcinoma
- RNU: Radical nephroureterectomy
- RP: Renal pelvis
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- US: Ultrasound
- UUT: Upper urinary tract

URETER, INTRAOPERATIVE INJURY

Ivan Colon, MD

BASICS

DESCRIPTION

- Ureteral trauma is relatively rare and can be cause by penetration, blunt, or iatrogenic injury. Iatrogenic injuries can be caused by any procedure (open, laparoscopic, or endoscopic) in which the ureter is the surgical target or is in otherwise close proximity.
- Most common causes of intraoperative iatrogenic ureter injury:
  - Most common: Endourologic procedures such as ureteroscopy
  - 2nd: Hysterectomy
  - 3rd: Colorectal surgery
  - 4th: Pelvic surgery
  - Others: Abdominal vascular surgery, vertebral disk surgery, appendectomy

EPIDEMIOLOGY

- The incidence of iatrogenic ureter injuries has changed over the last decade with the advent of laparoscopy and more advanced endourologic procedures.
- Currently, endourologic procedures are the most common cause of iatrogenic ureteral injuries.
- The majority of the time (70–77%), they are identified at the time of injury and treated properly without renal damage.
- The total incidence of ureteral injury after gynecologic surgery is reported at 0.5–1.5%, and after abdominoperineal colon resection it ranges from 0.3–5.7%.
- The reported rate of ureteral injury during laparoscopic surgery varies between 0.5% (experienced surgeons) and 14% (inexperienced surgeons) after laparoscopic hysterectomy.
- In urologic laparoscopy, the initial reports were higher; today the incidence of ureteral injury with laparoscopy is about the same at 1%.

RISK FACTORS

- Bulky tumors
- Previous C-sections
- Previous abdominal, pelvic, or retroperitoneal surgery
- Radiation
- Retroperitoneal fibrosis
- Duplicated ureters
- Renal ectopia
- Ureteral injury is more likely in cases of uncontrolled bleeding.

Pregnancy Considerations

Repeat C-sections can result in an increased risk for ureteral injuries.

GENERAL PREVENTION

- Knowledge and understanding of anatomy is needed to avoid injury.
- Immediate recognition is paramount.
- Preoperative ureteral stenting may be helpful in identification of the ureters, but has not shown to prevent ureteral injuries.
- For ureteroscopic injury:
  - Abandon stone basket if an injury is noted.
  - Always perform ureteroscopy alongside a guidewire.
  - Limit ureteroscopy in the setting of a radiated field.
  - Use flexible instruments whenever possible.

PATHOPHYSIOLOGY

- Intraoperative ureter trauma is rare because of its unique location in the retroperitoneum.
- The pelvic portion of the ureter is the most common site of iatrogenic injury.
- The location of the ureter adjacent to the pelvic vessels, uterine vessels, and ligaments make it an easy target during pelvic surgery.
- Mechanisms of injuries:
  - Avulsion
  - Transection: Partial and complete
  - Ligation by suture or mechanical device such as clip or stapler
  - Devascularization
  - Crushing
  - Thermal injury: Electrocautery, cryotherapy, laser
  - Angulation with resultant obstruction
- Delayed presentation of an intraoperative ureteral injury can be highly variable:
  - Obstruction
  - Infection
  - Fistula
- Surgical procedures often associated with ureteral injury:
  - Ureteroscopy:

    Most in distal ureter

    Injury types include perforation, avulsion, intussusception, false passage, structure, prolapse

Use of thermo-ablative therapies such as cryotherapy has increased the likelihood of injury to the proximal ureter.

– Retroperitoneal lymphadenectomy for testis cancer
– Hysterectomy (open, vaginal, or laparoscopic):

Common sites: Distal ureter near where ureter passes behind uterine artery, near infundibulopelvic ligament, next to bladder

– Colorectal surgery:

Abdominal perineal resection, anterior resection

– Vascular procedures:

Repeat aortic procedures at greatest risk

Transient hydronephrosis is fairly common and often resolves spontaneously.

Stricture, fistula, or obstruction with hydronephrosis

DIAGNOSIS

HISTORY

- Immediate recognition is important. History in the setting of intraoperative injury may not be useful.
- Prior history of radiation therapy to the abdomen or pelvis can cause ureteral injury and will affect healing of any repair.
- When the diagnosis is delayed, symptoms can include abdominal bloating, nausea, vomiting, abdominal girth distention, vaginal fluid leak (urine), ileus, and renal azotemia.
- Patients can present with silent obstruction.

PHYSICAL EXAM

- If immediate recognition, either methylene blue or indigo carmine may be seen.
- If delayed, patient may present with vaginal incontinence, ascites, ileus, sepsis.
- CVA tenderness with obstruction

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- If immediate recognition: No laboratory tests needed.
- For delayed recognition, increased BUN and creatinine and other metabolic abnormalities may be seen, due to reabsorption of urine.
- Methylene blue or indigo carmine may be useful for locating site of injury.

Imaging

- In the setting of intraoperative injury, intraoperative imaging studies are seldom useful. 1-shot IVP may be used, but is seldom useful.
- US is generally not useful, except in demonstrating a urinoma or hydronephrosis.

- IVP/CT urogram
- Retrograde pyelogram
- CT with delayed images
- Sonogram may not be useful in the acute setting

Diagnostic Procedures/Surgery

- Methylene blue or indigo carmine may help identify intraoperative injuries. Too much methylene blue may stain tissues blue, making it difficult to identify the injury.
- Percutaneous nephrostomy tube placement may be necessary.
- Imaging studies are necessary for accurate diagnosis of the location, usually in the postoperative setting.

DIFFERENTIAL DIAGNOSIS

- Intraoperative ureteral injury may be classified as immediate or delayed.
- Although immediate recognition is the most important, a high degree of suspicion must be suspected when the patient

ALERT

- Although nephrectomy is an option, it is not usually advocated for any type of ureteral injury, since preservation of the kidney should be the main goal of any surgeon.
- Ligation with nephrostomy drainage and delayed repair remains an option, especially in the case of an unstable patient.

TREATMENT

- The majority of ureteral injuries are identified postoperatively.
- Intimate knowledge of the ureteral anatomy is important and predicated to avoid intraoperative ureter injury.
- Hemodynamic stability will dictate the best approach. If patient is unstable, a delayed repair may be necessary
- Intraoperative hydration or diuretic administration may enhance ureteral peristalsis and visualization.
- Methylene blue or indigo carmine may be of benefit in trying to identify location of injury.
- Stenting to reduce injury:
  - Preoperative stents may help identify the ureters, but are not definitively proven to prevent intraoperative injury.
  - Fiberoptic-lighted stents have also been advocated.
  - Ureteral stent or catheter placement has a 1% complication rate. 1–5% may experience anuria after stent removal.

MEDICATION

- Methylene blue:
  - Administered IV, colors urine green/blue to help identify urinary leak.
  - High doses (>7 mg/kg) should not be given and use is contraindicated in renal insufficiency.
  - Risk of methemoglobinemia in susceptible individuals
  - Can stain tissues, making subsequent observations difficult
- Indigo carmine (indigotindisulfonate sodium)
  - Administered IV, colors urine blue to help identify urinary leak.
  - Typical dose is 5 mL (1 ampule) IV with hydration
  - Appears in urine usually within 10 minutes

SURGERY/OTHER PROCEDURES

- Depends on the location of the injury, type of injury, and time to diagnosis (immediate vs. delayed).
- Ligated ureters: If recognized immediately, the suture should be removed and the ureter examined for viability:
  - If the ureter is viable either do nothing or place a ureteral stent endoscopically.
  - If viability is in question or ureter looks nonviable, it is preferred to do either a ureter–ureter anastomosis or reimplant (depending on the location).
- Aortic or aortofemoral bypass procedures may pose a dilemma; there has been a controversy to perform a nephrectomy vs. repair.
- Immediate repair options:
  - Upper ureter: Consider uretero–ureterostomy. Renal mobilization if necessary.
  - Mid ureter: Consider uretero–ureterostomy
  - Lower ureter: May require ureter reimplant, with or without psoas hitch.
  - Transureteroureterostomy (less desirable)
  - Nephrectomy (for severe, long ureter strictures, and in presence of normal contralateral kidney)
  - Endoscopic/ureteroscopy injury is usually best managed by immediate stenting if ureteral integrity maintained:

    Avulsion, intussusception of ureter into bladder may require open repair and ureteral reimplantation
  - Laparoscopic injury:

    Laparoscopic repair can be accomplished based on the skill of the surgeon.
- Principles of ureteral repair:

  - Debridement of devitalized tissue
  - Water-tight, tension-free anastomosis
  - Isolation of anastomosis from concomitant injuries (omental flap)
  - Drainage of repair (ureteral stent, PCN)
- Delayed repair options include ileal ureter, ureterocalicostomy, autotransplantation.

ONGOING CARE

- Ureteral stents are generally left in place for 2–3 wk after repair.
- IVP or US several weeks after stent removal will document successful repair.

PROGNOSIS

Usually good, except for complicated cases and long strictures.

COMPLICATIONS

- Ureteral stricture
- Hydronephrosis
- Loss of renal function

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Interval US monitoring of the upper tracts post repair.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Injury, Intraoperative
- Bladder Trauma
- Ureter, Obstruction
- Ureter, Stricture
- Ureter, Trauma

CODES

ICD9

- 867.3 Injury to ureter with open wound into cavity
- 997.5 Urinary complications, not elsewhere classified

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CT: Computed tomography
- CVA: Costovertebral angle
- IV: Intravenous
- IVP: Intravenous pyelogram
- PCN: Percutaneous nephrostomy
- US: Ultrasound

URETER, OBSTRUCTION

Benjamin R. Lee, MD
Mathew C. Raynor, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- Intrinsic and extrinsic processes can cause obstruction of the ureter.
- Definitions:
  - Hydronephrosis: The presence of dilatation of the renal pelvis and calyces. The term does not refer to the etiology of the dilatation as hydronephrosis can occur without obstruction
  - Hydroureteronephrosis: Dilation of the renal pelvis, calyces, and ureter
  - Obstructive uropathy: Functional or anatomic impedance to the flow of urine anywhere along the urinary tract
  - Obstructive nephropathy: Damage to the renal parenchyma from obstruction anywhere along the urinary tract
- Hydronephrosis can be caused by any obstruction from the kidney to the urethral meatus. This section refers to the specific causes of urethral obstruction that may result in hydronephrosis.
- Progressive renal damage may occur.
- Urinary infection and sepsis may be superimposed.

EPIDEMIOLOGY

- Almost any type of obstructive uropathy can result in hydronephrosis.
- Obstructive uropathy associated with congenital anomalies of the urinary tract accounts for 30–50% of all ESRD cases in children.
- More common unilateral hydronephrosis, depending on etiology

RISK FACTORS

- Blood clots
- BPH/bladder outlet obstruction
- Neurogenic bladder
- Renal nephrolithiasis
- Malignancy
- Urethral strictures

PATHOPHYSIOLOGY

- Flow of urine blocked at anatomic point and accumulates proximal to obstruction.

- With chronic obstruction, the ureter may become not only dilated but tortuous as well.
- Increased pressure
- Decreased renal blood flow
- Decreased GFR
- 3 major points of narrowing of the ureter:
  - UPJ
  - Where the ureter crosses over the pelvic brim (iliac vessels)
  - UVJ
- Women may also experience obstruction as the distal ureter crosses posterior to the pelvic blood vessels and the broad ligament.

COMMONLY ASSOCIATED CONDITIONS

- Bladder cancer
- Ureteral stricture
- Ureteropelvic junction obstruction
- Urolithiasis
- Retroperitoneal fibrosis

ALERT

A unilaterally obstructed, infected kidney in a septic patient requires immediate drainage.

DIAGNOSIS

HISTORY

- Acute obstruction can cause intense pain.
- Signs and symptoms of hydronephrosis depend upon whether obstruction is acute or chronic, partial or complete, unilateral or bilateral.
- Assess history of renal failure
- History of stone disease
- History of malignancy or radiation therapy

PHYSICAL EXAM

- CVA tenderness
- Pain radiating to scrotum
- Palpable mass (mainly in infants)

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum electrolytes: Elevated creatinine
- Urine analysis:
  - Hematuria, pyuria, crystals

– Chronic bilateral obstruction may demonstrate decreased urine to plasma creatine and increased urine sodium due to impaired concentrating ability.

– Elevated pH due to secondary destruction of nephrons within affected kidney

ALERT

A pregnancy test should be performed in any women who might be pregnant before imaging studies are performed using radiation (ie, KUB, CT).

Imaging

- Renal US: Primary screening test of choice
- CT urogram/IVP: Assess location of obstruction, determine stone size and location
- Retrograde pyelogram: Delineate anatomy
- Renal scan with Lasix washout: Assess renal function and degree of obstruction, t½ >20 min consistent with obstruction

Diagnostic Procedures/Surgery

Whitaker test can be performed in equivocal cases of obstruction

Pathological Findings

Total obstruction of urine flow with dilation of the collecting system ultimately causes complete cortical atrophy and cessation of glomerular filtration.

DIFFERENTIAL DIAGNOSIS

- Intrinsic obstruction:
  - Blood clots
  - Stones
  - Sloughed papilla
  - Ureteral or bladder cancer:
    TCC
    SCC
    Adenocarcinoma
    Others, such as sarcoma
- Extrinsic obstruction:
  - Pelvic or abdominal tumors (pregnancy, gynecologic malignancy)
  - Retroperitoneal fibrosis
  - Circumcaval/retrocaval ureter
  - Vascular lesions (abdominal aortic or iliac aneurysm, aberrant arterial anomalies), obstruction of the ureter after arterial repair or replacement, venous obstruction (ovarian vein syndrome, postpartum ovarian vein thrombophlebitis)
- Stricture disease: Congenital or acquired

- Neuromuscular dysfunction
- Bilateral ureteral hydronephrosis
- Bladder outlet obstruction
- In children:
  - Posterior urethral valves in male infants
  - UVJ obstruction
  - Ectopic ureter
  - Ureterocele
  - Megaureter

TREATMENT

- Initial management depends on clinical circumstances and determined etiology for the hydronephrosis.
- Placement of retrograde ureteral stent or percutaneous nephrostomy are the most common methods for immediate drainage.
- Hemodialysis is required in the acutely ill patient.
- After initial drainage and stabilization, the location and cause of obstruction should be determined.
- Nature of surgical intervention that may be required depends largely on the etiology of the hydronephrosis. A permanent form ofurinary drainage may be necessary in some patients.

MEDICATION

Supportive care (eg, pain medications, correction of electrolyte abnormalities)

SURGERY/OTHER PROCEDURES

- Treatment of hydronephrosis focuses upon the removal of obstruction and drainage of the urine.
- Specific treatment depends upon where obstruction lies, and whether acute or chronic.
- Acute obstruction of the upper urinary tract is usually treated by the insertion of a nephrostomy tube vs. ureteral stent.
- Chronic upper urinary tract obstruction is treated by the insertion of a ureteric stent or a laparoscopic pyeloplasty.
- Lower urinary tract obstruction (such as that caused by bladder outflow obstruction secondary to prostatic hypertrophy) is usually treated by insertion of a urinary catheter, suprapubic catheter, or transurethral resection of prostate.
- Calculi in a noninfected patient may be initially managed therapeutically with ESWL or ureteroscopy with lithotripsy, depending on location.

- Vascular lesions (aortic aneurysm) may require urgent management.
- Renal failure and electrolyte abnormalities should be corrected in conjunction with drainage.

ADDITIONAL TREATMENT

Treatment may be limited (an obstructed kidney in a terminally ill patient with a normal opposite kidney and satisfactory serum creatinine and electrolytes may require no intervention).

ONGOING CARE

PROGNOSIS

Left untreated, bilateral obstruction has a poor prognosis.

COMPLICATIONS

- Acute renal failure
- Chronic renal failure

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Renal US
- Renal scan with Lasix washout
- Serum creatinine
- Serum electrolytes:
  - Mainly for bilateral obstruction
  - Monitor for postobstructive diuresis

ADDITIONAL READING

Kumar V, Fausto N, Fausto N. Robbins and Cotran Pathologic Basis of Disease, 7th ed. Philadelphia: Elsevier Saunders, 2005:1012–1014.

See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult
- Hydronephrosis/Hydroureteronephrosis, (Dilated Ureter/Renal Pelvis), Pediatric
- Megaureter
- Postobstructive Diuresis
- Pregnancy, Urinary Tract Obstruction
- Ureteropelvic Junction Obstruction
- Ureter, Retrocaval (Circumcaval, Post Caval)
- Whitaker Test

CODES

ICD9

- 591 Hydronephrosis

- 593.4 Other ureteric obstruction
- 753.20 Unspecified obstructive defect of renal pelvis and ureter

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- CT: Computed tomography
- CVA: Costovertebral angle
- ESRD: End-stage renal disease
- ESWL: Extracorporeal shockwave lithotripsy
- GFR: Glomerular filtration rate
- IVP: Intravenous pyelogram
- SCC: Squamous cell carcinoma
- TCC: Transitional cell carcinoma
- UPJ: Ureteropelvic junction
- US: Ultrasound
- UVJ: Ureterovesical junction

URETER, TRAUMA

Benjamin R. Lee, MD
Mathew C. Raynor, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- Ureteral trauma is relatively rare and can be caused by penetrating, blunt, or iatrogenic injury. Disruption of the flow of urine by stricture, fistula, and/or leakage may result.
- Iatrogenic injury is discussed in detail elsewhere (see Section I: “Ureter, Intraoperative Injury”)

EPIDEMIOLOGY

- Ureter is involved <1% of all GU injuries caused by external trauma
- Focusing on external traumatic injury to the ureter:
  - Gunshot wounds: 91%
  - Stab wounds: 5%
  - Blunt trauma: 4%

RISK FACTORS

- Flexion/extension injuries in children
- General surgery: Colorectal surgery
- Gynecologic surgery (ie, hysterectomy, tubal ligation, laparoscopy)
- Pelvic radiation treatment
- Urologic surgery
- Penetrating injury to abdomen, lower chest or back:
  - Ureterolithotomy, ureteral reimplantation, cystectomy
  - Ureteroscopy (0.5% risk of ureteral stricture in modern series)
- Vascular surgery: Aortoiliac bypass

PATHOPHYSIOLOGY

- Ureteral injury is very rare and if encountered is almost always associated with collateral injury to other organs or structures:
  - The ureters are well protected in the retroperitoneum by dorsal muscle groups, abdominal muscles and vertebral bodies.
  - The ureters are also flexible, providing additional protection.
- Penetrating injury location:
  - Proximal ureter: 26%
  - Mid ureter: 37%

    - Distal ureter: 37%
- Most ureteral injuries are associate with injury to other organs:
    - Small bowel and colon most common
    - Other organs include liver, spleen, kidney, bladder, iliac vessels
- AAST Injury Scaling and Scoring System for Ureteral Injury:

Ureter Injury Scale
Type of injury
Description of Injury
I
Hematoma
Contusion or hematoma, no devascularization
II
Laceration
<50% transection
II
Laceration
50% transection
IV
Laceration
Complete transection with <2 cm devascularization
V
Laceration
Avulsion with >2 cm of devascularization

*Advance 1 grade for bilateral up to Grade III after Moore et al.

COMMONLY ASSOCIATED CONDITIONS

- Gunshot wounds
- Ureteroscopy
- Gynecologic surgery

DIAGNOSIS

HISTORY

- History will usually reveal cause and location of any iatrogenic injury.
- In blunt and penetrating trauma patients, a detailed history of mechanism of injury will help identify patients at risk for ureteral trauma:
  - Penetrating trauma to the lower chest, back, abdomen
  - Blunt trauma causing significant flexion and/or extension in children
- Prior history of radiation therapy to the abdomen or pelvis can cause ureteral injury and will affect healing of any repair.
- Symptoms can include pain, fever, hematuria, or urinoma causing abdominal distention, inflammation, and possible ileus.
- Urinary fistula may be present.
- Patients can present with silent obstruction.

PHYSICAL EXAM

- Penetrating trauma patients should be examined for proximity of injury to ureter.
- Associated injuries to periureteral organs can be useful in determining probability of ureteral injury.
- Physical exam may reveal abdominal distention (due to urinoma), or presence of fistula.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Creatinine may be elevated due to extravasation and reabsorption of urine or obstruction.
- Hematuria is not a reliable finding in ureteral injuries:
  - Only 74% of cases involve gross or microscopic hematuria

Imaging

- Retrograde ureteropyelography is the most useful study in detecting and evaluating ureteral injuries.

• Most trauma patients will have early CT, and ureteral trauma can be demonstrated by extravasation of contrast.

• US is generally not useful, except in demonstrating a urinoma or hydronephrosis.

• Trauma patients should have the presence of a contralateral kidney established prior to repair:

– Either by CT scan, or if the patient is being explored emergently, by a 1-shot IVP:

1-shot IVP involves the administration of high-dose (2 mL/kg) IV contrast material

Diagnostic Procedures/Surgery

• Retrograde pyelogram: Usually not practical in the acute trauma setting

• Whether a fistula originates from the bladder or ureter can be determined by instilling methylene blue or indigo carmine saline through a bladder catheter. If the fistula returns colored fluid, it originates from the bladder.

DIFFERENTIAL DIAGNOSIS

• Ureteral avulsion

• Partial disruption

ALERT

Delay in diagnosis of ureteral injury is a major contributing factor to morbidity in a trauma patient.

TREATMENT

• The initial management is often dictated by the severity of the associated injuries.

• Intraoperative recognition of ureteral injury from penetrating trauma reported in the literature: 39–92%.

MEDICATION

Methylene blue and indigo carmine may help identify the site of a ureteral perforation or transection (see Section II: “Ureter, Intraoperative Injury”)

SURGERY/OTHER PROCEDURES

• Initial management: Wide variety of both open and minimally invasive treatment options are available.

• Choice of most appropriate treatment depends on extent and location of injury and immediate vs delayed repair:

– Proximal ureter:

Ureteroureterostomy

Transureteroureterostomy

Ureterocalicostomy

Pyeloplasty with ureteral anastomosis

Ileal interposition or autotransplantation (not in acute setting)

– Mid ureter:

Ureteroureterostomy

Transureteroureterostomy

Boari flap

– Distal ureter:

Direct bladder reimplantation

Psoas hitch with reimplantation

- Open surgical management:

– Trauma patients who are being explored for other reasons, long (>2 cm) ureteral strictures, and significant iatrogenic injuries identified intraoperatively are best managed with open surgical repair.

- Principles of open surgical repair of ureteral injuries:

– Debridement of devitalized tissue to fresh edge (note: Blast effect of gun shot wound may require more extensive debridement than a laceration)

– Water-tight, tension-free anastomosis

– Spatulate edges and repair with 5–0 absorbable suture (eg, Monocryl)

– Drainage of repair; ureteral stenting

– Isolation of anastomosis from concomitant injuries (omental flap)

- Open repair options:

– Ureteroureterostomy (with renal mobilization to gain length as needed)

– Ureteroneocystostomy (with psoas hitch and/or Boari bladder flap as needed)

– Ileal ureter (less desirable in acute trauma setting)

– Transureteroureterostomy (less desirable in acute trauma setting)

– Autotransplant (useful for severe, long ureteral strictures)

– Nephrectomy (for severe damage and presence of normal contralateral kidney)

- Conservative management:

– Minor iatrogenic injuries (ie, clamping, minor suture injury) and minor trauma (minimal extravasation) may be managed with temporary stenting vs. nephrostomy tube

– Ureteral strictures <2 cm are best initially managed with balloon dilation and stenting.

– Endoluminal US can identify periureteral blood vessels to avoid during endoscopic incision.

ONGOING CARE

PROGNOSIS

- Procedures used to repair traumatically injured ureters carry a complication rate of 25%.
- Most common acute complication is prolonged urinary leakage from the anastomosis.

COMPLICATIONS

Tissue hypoxia and gross contamination play an important role in the pathogenesis of strictures, urinomas, and fistulas.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up of urinoma, abscess, or peritonitis can be treated by intraoperative placement of a drain in the retroperitoneum, thereby allowing drainage of urine and early recognition of urinary leakage from the anastomosis.
- If drains have persistently high output, check fluid for creatinine. Delayed recognition of undrained urinary leakage has been associated with sepsis, a more complicated reconstruction, and increased hospital stay.
- Ureteral stents are generally left in place for 2–3 wk after open repair, and 6–8 wk after endoureterotomy.
- IVP several weeks after stent removal will document successful repair.

ADDITIONAL READING

- Elliott SP, McAninch JW. Ureteral injuries from external violence: The 25-year experience at San Francisco General Hospital. J Urol 2003;170(4 Pt 1):1213–1216.
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- Moore EE, Cogbill TH, Jurkovich GJ, et al. Organ injury scaling. III: Chest wall, abdominal vascular, ureter, bladder, and urethra. J Trauma 1992;33(3):337–339.
- Pfitzenmaier J, et al. Trauma of the ureter. In: Hohenfellener M, Santucci RA, eds. Emergencies in Urology, 1st ed. Berlin: Springer, 2007.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Injury, Intraoperative
- Bladder Trauma
- Renal Trauma, Adult
- Ureter, Intraoperative Injury
- Ureter, Obstruction
- Ureter, Stricture

CODES

ICD9

- 867.2 Injury to ureter without mention of open wound into cavity
- 867.3 Injury to ureter with open wound into cavity

ABBREVIATIONS

- AAST: American Association for the Surgery of Trauma
- CT: Computed tomography
- GU: Genitourinary
- IVP: Intravenous pyelogram
- US: Ultrasound

URETEROCELE

Monica M. Metzdorf, MD
Julia S. Barthold, MD

BASICS

DESCRIPTION

- A cystic dilation of distal ureter
- Further classified based on the anatomic location:
  - Intravesical: Contained within bladder, may be nonobstructive
  - Extravesical: Extends into urethra, usually obstructing
  - Cecoureterocele: Intravesical orifice but submucosal extension into urethra
  - Sphincteric: Orifice of ureterocele distal to bladder neck
- Most ureteroceles are associated with the upper pole of a duplex collecting system and are often ectopic.

EPIDEMIOLOGY

1 in 500–1 in 4,000

RISK FACTORS

- More common in girls (5–7:1)
- More common in whites
- Occurs bilaterally in 10% of cases
- Extravesical ureteroceles associated with upper pole of duplex system often diagnosed in infancy or childhood

Genetics

Likely multifactorial inheritance

PATHOPHYSIOLOGY

Several hypotheses:

- Incomplete breakdown of Chwalla membrane
- Delay in canalization of lumen of ureteral bud

COMMONLY ASSOCIATED CONDITIONS

- Duplicated collecting system: 80%
- Single system: 20%
- VUR:
  - Ipsilateral lower pole in duplex system: 50–70%
  - Contralateral kidney: 10–30%
  - Into ureterocele: Uncommon; likely ectopic with orifice in urethra

DIAGNOSIS

HISTORY

- Prenatal diagnosis of hydronephrosis
- Incontinence
- UTI/sepsis
- Abdominal mass
- Abdominal pain
- Intralabial mass
- Urinary retention
- Voiding dysfunction

PHYSICAL EXAM

GU and abdominal exam:

- Abdominal mass
- Prolapsing urethral mass

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum creatinine
- Urine analysis
- Urine culture

Imaging

- Prenatal US:
  - Hydronephrosis
  - Intravesical cystic dilatation or septations in bladder
- Renal US:
  - Thin-walled cystic mass at bladder base
  - Hydroureteronephrosis, especially in ipsilateral upper pole
  - Duplex kidney/collecting system in 80%
  - May not be visualized if bladder too full or completely empty

- May be misidentified as ectopic/dilated ureter

- VCUG:
  - Smooth, broad-based filling defect near trigone
  - Visualized best in early filling phase
  - May see reflux into ipsilateral lower pole or contralateral kidney
- IVP:
  - Cobra-head sign in bladder when contrast fills the ureterocele (not usually performed)
- DMSA renal scan:
  - Evaluate renal parenchyma for scarring, differential function
- MAG-3 renal scan:
  - Evaluate drainage to determine extent of obstruction
  - May see little or no function in the upper pole moiety.

Diagnostic Procedures/Surgery

Cystoscopy:

- Findings vary, but best seen with partially empty bladder
- Assess for extension into urethra.

Pathological Findings

- Ureterocele histology; abnormal musculature
- Renal dysplasia in ~40% of upper-pole moieties associated with ureterocele; more common in association with extravesical ureteroceles

DIFFERENTIAL DIAGNOSIS

- Bladder polyps
- Ectopic ureter
- Edema
- Mesonephric duct cyst
- Tumor
- Urethral prolapse

TREATMENT

Surgical treatment is needed in most cases.

MEDICATION

- Antibiotic treatment for UTI/sepsis
- Antimicrobial prophylaxis until reflux or obstruction repaired:
  - Ampicillin 25 mg/kg/d as neonates then when older use:
  - Trimethoprim-sulfamethoxazole 2 mg/kg/d OR nitrofurantoin 1–2 mg/kg/d beyond 2 mo of age

SURGERY/OTHER PROCEDURES

- Endoscopic transurethral incision of ureterocele:
  - Usually effective in relieving obstruction
  - Risk of developing reflux in that system
  - Outpatient procedure
  - Effective for intravesical ureteroceles, less so for extravesical ureteroceles
  - Endoscopic management as definitive treatment is controversial.
  - Should be considered in patients presenting with urosepsis
- Formal surgical repair:
  - Definitive treatment but higher morbidity
  - Heminephrectomy and upper pole ureterectomy (laparoscopic or open) with or without excision of ureterocele.
  - Heminephroureterectomy alone may be treatment of choice if no VUR is present.
  - Uretero-ureterostomy if upper pole function is present
  - Excision of ureterocele with ureteral reimplantation

ADDITIONAL TREATMENT

Additional Therapies

Observation if asymptomatic; no or mild reflux or obstruction

ONGOING CARE

PROGNOSIS

Depends on extent of obstruction, infections

COMPLICATIONS

- Sepsis, loss of renal function
- Incontinence (primary or secondary)
- Persistent dilation of ureteral stump
- Ureteral obstruction
- Persistent VUR

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Renal and bladder US
- VCUG to diagnose/follow-up persistent VUR
- Monitor renal function if bilateral
- Treat UTI

ADDITIONAL READING

- Beganovi A, Klijn AJ, Dik P, et al. Ectopic ureterocele: Long-term results of open surgical therapy in 54 patients. J Urol 2007;178:251–254.

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Mass
- Collecting System, Complete Duplication
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

- 593.89 Other specified disorders of kidney and ureter
- 753.23 Congenital ureterocele

ABBREVIATIONS

- DMSA: Dimercaptosuccinic acid
- GU: Genitourinary
- IVP: Intravenous pyelogram
- MAG-3: Mercaptoacetyltriglycine
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

URETEROPELVIC JUNCTION OBSTRUCTION

Nicholas T. Leone, MD

BASICS

DESCRIPTION

- Restriction of urine flow from renal pelvis to ureter
- Most common cause of significant dilation of collecting system in fetal kidney

EPIDEMIOLOGY

1:500–1,000 newborns

- 25% diagnosed by 1 yr, 50% by 5 yr
- Adult presentation usually in 3rd–4th decade

RISK FACTORS

- Familial disposition
- Male > Female (2:1)
- Congenital renal anomalies:
  - Contralateral UPJO: 10–40% risk
  - VUR: 0.5–5% risk
  - Renal duplication: 6% risk
  - Horseshoe kidney: 15% risk
  - Ectopic kidney: 35% risk

PATHOPHYSIOLOGY

- Congenital (most common etiology):
  - Intrinsic etiologies:

    Adynamic ureteral segment due to ureteral smooth muscle maldevelopment; most common cause of pediatric UPJO

    Intrinsic stenosis due to inadequate ureteral recanalization during fetal development

    Persistent valvular mucosal folds
  - Extrinsic etiologies:

    Crossing accessory lower-pole vessel; most common cause of adult UPJO

    High ureteral insertion into renal pelvis

    Horseshoe, ectopic, or malrotated kidney causing kinking at UPJ
- Acquired:
  - Severe VUR can cause ureteral tortuosity and kinking at UPJ
  - Inflammation and scarring from trauma, urolithiasis, instrumentation, infected urinoma, retroperitoneal fibrosis

COMMONLY ASSOCIATED CONDITIONS

50% associated with another congenital anomaly:

- Contralateral renal dysplasia or MCDK
- Contralateral UPJO: Most common
- Horseshoe or ectopic kidney
- Incomplete renal duplication
- Unilateral renal agenesis
- VACTERL syndrome
- Vesicoureteral reflux

DIAGNOSIS

HISTORY

- Prenatal/neonatal presentation:
  - Hydronephrosis seen on antenatal US
  - Typically asymptomatic; but occasionally see feeding difficulties, failure to thrive, sepsis
- Childhood presentation:
  - Episodic ipsilateral colicky flank pain
  - Cyclic nausea and vomiting
  - Gross hematuria, classically after minor abdominal or flank trauma
  - UTI
- Adult presentation:
  - Episodic ipsilateral colicky flank pain, classically after diuretic or alcohol intake (aka Dietl crisis)
  - Cyclic nausea and vomiting
  - UTI or pyelonephritis

PHYSICAL EXAM

- Prenatal/neonatal or childhood presentation:
  - Palpable abdominal mass
  - Fever, failure to thrive
- Childhood presentation:
  - CVA tenderness
  - Palpable abdominal mass in small children
- Adult presentation:
  - CVA tenderness
  - 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 ureterovesical junction obstruction from UPJO
  - Defer until 2nd or 3rd day of life to avoid false-negative secondary to physiologic oliguria
- IVP:
  - Most commonly employed diagnostic study after neonatal period
  - Findings include delayed opacification of collecting system, pyelocaliectasis, non-visualization of ureter, cortical thinning
- Diuretic renal scintigraphy (Tc-99mm MAG3):
  - Provides differential renal function
  - T1/2 assesses for presence of obstruction:
    Normal T1/2 <10 min
    Indeterminate T1/2: 10–20 min
    Obstruction T1/2 >20 min

Diagnostic Procedures/Surgery

- Cystoscopy with retrograde pyelography:
  - Defines extent of ureteral involvement
  - Allows for placement of temporary ureteral stent to relieve urinary obstruction
- Whitaker test:
  - Reserved for equivocal IVP or MAG3
  - Percutaneous catheter with pressure transducer placed in renal pelvis, another placed in bladder via urethra; fluid infused into renal pelvis at 10 cc/min; measure pressure differential:
    Normal <15 cm H_2O

Equivocal: 15–22 cm H2O

Obstructed >22 cm H2O

- Helical CT scan with 3D reconstruction:
  - Allows visualization of collecting system and renal vasculature (crossing vessels)

Pathological Findings

- Hydronephrosis without hydroureter
- Elevated T1/2 >20 min on diuretic renal scintigraphy
- Elevated pressure differential >22 cm H2O on Whitaker test
- Crossing vessel on helical CT scan

DIFFERENTIAL DIAGNOSIS

- Obstructive dilation:
  - Fungal balls
  - Impacted urinary calculus
  - Intraluminal benign or malignant neoplasm
  - Sloughed papilla
- Nonobstructive dilation:
  - Prune belly syndrome
  - Renal or peripelvic cysts
  - VUR

TREATMENT

MEDICATION

- Neonatal presentation:
  - Prophylactic antibiotics to maintain sterile urine:

    UTI prophylaxis: Ampicillin 25 mg/kg/d as neonates THEN

    Trimethoprim-sulfamethoxazole 2 mg/kg/d OR nitrofurantoin 1–2 mg/kg/d beyond 2 mo of age
- Childhood and adult presentation:
  - No medical therapy appropriate except to treat active infection

SURGERY/OTHER PROCEDURES

- Restore renal function: Especially in patients with bilateral obstruction, solitary kidney, or poorly functioning contralateral kidney:
  - Percutaneous nephrostomy or ureteral stent
- Relieve severe symptoms:
  - Percutaneous nephrostomy or ureteral stent
- Treat pyonephrosis if present:

– Culture-specific antibiotics

– Percutaneous nephrostomy or ureteral stent may be necessary to ensure adequate drainage of infected urine.

- Expectant treatment:

– Neonatal hydronephrosis: Obstruction associated with unilateral neonatal hydronephrosis is 15%; a majority of neonates with hydronephrosis can be initially managed nonoperatively.

– Asymptomatic adults with normal contralateral kidney and significant comorbidities

- Definitive operative treatment:

– Open procedures: Procedures of choice in pediatric patients:

Dismembered (Anderson-Hynes) pyeloplasty: Most common open technique; success rate >90%; appropriate for high insertion, accessory vessels, massive dilation, long ureteral involvement; excise anatomic and functionally abnormal segment

Foley Y-plasty: Appropriate for high ureteral insertion

Spiral or vertical flap: Appropriate for large extrarenal pelvis and long segment of narrowed ureter

Ureterocalicostomy: 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 ipsilateral poor renal function and normal contralateral renal function, especially if differential renal function <10–15%, extensive stone disease, chronic infection, multiple failed repairs

– Laparoscopic pyeloplasty: Success rate >90%; transabdominal or retroperitoneal approach; employs dismembered or Y-V plasty technique; advantages include decreased postoperative pain, shorter convalescence, improved cosmetic result compared to open procedures.

– Endoscopic procedures: Minimally invasive alternative to open procedures in adults:

Antegrade cold-knife incision endopyelotomy: Success rate 80%; requires percutaneous access; nephrostomy tube left indwelling 24–48 hr, ureteral stent left indwelling 6 wk; appropriate for adult patients with stricture <2 cm, UPJO associated with renal calculi, children with secondary UPJO

Retrograde balloon cautery incision endopyelotomy (Acucise): Success rate 80%; performed under fluoroscopic guidance after cystoscopic placement of cutting balloon catheter; ureteral stent left indwelling 6 wk; appropriate for adult patients with stricture <2 cm; used sparingly in pediatric population with reasonable results; presence of crossing vessels may increase complication rate; incision is traditionally performed at posterolateral aspect of ureteral

wall to avoid injury to crossing vessel.

Retrograde ureteroscopic laser incision: Success rate in small series 85–90%; allows direct visualization of incision; requires specialized ureteroscopic equipment and endourologic expertise; ureteral stent left indwelling 6 wk

Balloon rupture of UPJO: Balloon is placed over guidewire across UPJ from antegrade or retrograde approach; success rate 70–80%; inflation of high-pressure balloon to 24–30 Fr under fluoroscopic guidance; appropriate for secondary UPJO with stricture <2 cm; ureteral stent left indwelling 6 wk

Chronic percutaneous nephrostomy or ureteral stent: Reserved for patients who are not candidates for definitive operative treatment

ONGOING CARE

PROGNOSIS

- Prenatal/neonatal presentation:
  - Often does not require definitive operative treatment, due to propensity to remain stable or improve spontaneously
  - Intervention in severe cases can result in greatly improved renal function.
- Childhood and adult presentation:
  - Recent investigations demonstrate lower long-term success following endopyelotomy techniques compared with pyeloplasty (75% vs. 41% 10-yr success rates, respectively).

COMPLICATIONS

Failure to treat can result in continuing symptoms, worsening renal function, urinary infection or sepsis, rarely HTN

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Expectant management in neonate:
  - Renal US or MAG3 at 1 mo, followed at 3–6 mo
  - Operative intervention is recommended if symptomatic, differential renal function >10%, worsening hydronephrosis.
- Following operative treatment:
  - IVP or MAG3 6–12 wk postop
  - 91% children will have improved MAG3 at 6–12 mo, whereas improvement in adults >30 yr is rare; IVP usually shows decreased hydronephrosis and prompt excretion.
  - Annual IVP or MAG3 s/p endopyelotomy to monitor for late failures

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Pediatric
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Prenatal

CODES

ICD9

- 593.4 Other ureteric obstruction
- 753.21 Congenital obstruction of ureteropelvic junction
- 753.3 Other specified anomalies of kidney

ABBREVIATIONS

- BUN: Blood urea nitrogen
- CT: Computed tomography
- CVA: Costovertebral angle
- HTN: Hypertension
- IVP: Intravenous pyelogram
- MAG3: Mercaptoacetyl triglycine
- MCDK: Multicystic dysplastic kidney
- UPJ: Ureteropelvic junction
- UPJO: Ureteropelvic junction obstruction
- US: Ultrasound
- UTI: Urinary tract infection
- VACTERL: Vertebral defects, imperforate anus, tracheoesophageal fistula, renal dysplasia and limb anomalies;

- VUR: Vesicoureteral reflux

URETHRA, ABSCESS (PERIURETHRAL ABSCESS)

Joseph C. Klink, MD

Judd W. Moul, MD

BASICS

DESCRIPTION

- A PUA is a potentially life-threatening infection of the male urethra and periurethral tissues associated with urinary infection and urethral stricture disease.
- In females, a urethral abscess is usually a result of a chronically infected urethral diverticulum. Management of urethral abscess in females is discussed in the Section I topic "Urethral Diverticulum."

EPIDEMIOLOGY

- Men of all ages
- More likely in diabetics or in groups at high risk for STD
- Recurrent PUAs occur in as many as 19% of patients.

RISK FACTORS

- Diabetes mellitus
- Frequent urethral instrumentation
- Gonorrhea
- HIV
- Previous PUA
- Urethral dilation
- Urethral stricture disease

GENERAL PREVENTION

- Eradicate STD such as gonorrhea.
- Sterilize the urine.
- Adequate urinary diversion away from the healing urethra
- Rehabilitation of urethral stricture:
  - Dilation
  - Internal urethrotomy
  - Staged urethral repair
  - Perineal urethrostomy

PATHOPHYSIOLOGY

- Periurethral extravasation of infected urine
- High-pressure voiding behind a stricture leads to extravasation of urine.
- Difficult dilation of urethral stricture causes urethral disruption, which leads to extravasation of infected urine.

- Bladder instability is associated with recurrent PUA.
- Often localized to bulbar urethra or spongiosum
- Once eroded through Buck fascia, PUA causes extensive necrosis of fascia and subcutaneous tissues.
- Can progress to Fournier disease, especially if immunocompromised.
- Gram-negative rods, enterococci, and anaerobes most frequent

COMMONLY ASSOCIATED CONDITIONS

- Diabetes mellitus
- Fournier gangrene
- Immunosuppression (eg, HIV)
- Urethral stricture
- Urinary infection
- Watering-pot perineum

DIAGNOSIS

HISTORY

- Urethral discharge
- Symptoms of UTI:
  - Irritative voiding symptoms, hematuria, foul-smelling urine, fever, and chills
  - Gonococcal or nongonococcal urethritis, other STDs
- Symptoms of urethral stricture, weak stream
- Neurogenic bladder:
  - Symptoms of urgency or urge incontinence
  - Catheter placement or use of intermittent catheterization
  - Use of anticholinergic medications to relieve bladder urgency
- History of any type of surgery (especially GU):
  - Previous surgery may be associated with urethral instrumentation, urethral dilation, or catheterization, all potential sources of urethral stricture or disruption.
- Pelvic radiation, cause of urethral stricture
- Diabetes

PHYSICAL EXAM

- Evaluate for sepsis: Fever, hypotension, tachycardia
- Palpate the penile shaft and perineum for masses and tenderness
- Scrotal/penile swelling: Urinary extravasation confined to Buck fascia presents with localized penile swelling.
- Scrotal edema, foul-smelling phlegmon, or fluctuance indicates urinary extravasation into the periurethral tissues.

- Necrotic tissue associated with gangrene or fasciitis (frank necrosis or discoloration) can extend around the rectum or up the abdominal wall.
- Crepitation suggests gas gangrene.
- Palpable suprapubic mass with urinary retention
- Rectal exam, primarily to exclude perirectal abscess, evaluate for perianal carcinoma
- Thorough exam of perineum, buttocks, inner thighs, and lower abdomen looking for signs of the necrosis spreading

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis of beginning of stream: Evaluate for WBCs or frank pus.
- Urine culture and sensitivity for primary or secondary UTI due to PUA
- Wound culture
- Blood culture as part of sepsis workup
- Coagulation profile/bleeding studies: Sepsis-related coagulopathy
- BUN, creatinine to assess:
  - Dehydration, renal failure
  - Aminoglycoside dose adjustment

Imaging

- CT to evaluate for subcutaneous air
- RUG: Not recommended during active infection phase:
  - Urethral stricture and fistulas; urinary extravasation is diagnostic
  - Bladder stones

Diagnostic Procedures/Surgery

Aspiration of pus if diagnosis is in doubt

Pathological Findings

Necrosis

DIFFERENTIAL DIAGNOSIS

- Fournier gangrene
- Perirectal abscess
- Follicular abscess
- Urethral carcinoma
- Carcinoma of perianal glands
- Pneumoscrotum
- Anasarca from congestive heart failure

TREATMENT

Supportive measures, as needed, for diabetes, hypotension, renal failure, or septic shock

ALERT

Failure to recognize and treat a localized urethral abscess in a male can result in life-threatening necrotizing fascitis (Fournier gangrene).

MEDICATION

- Broad-spectrum antibiotic coverage:
  - Cephalosporin and aminoglycoside
  - Consider vancomycin
  - Patient sent home on PO cephalosporin until wound clean and healing
- Antibiotic therapy tailored to culture results

SURGERY/OTHER PROCEDURES

- Incision and drainage of abscess with radical debridement of necrotic tissue
- May need repeated debridements as margin between necrotic and viable tissue becomes apparent.
- Wound vac placement after debridement if location of wound permits
- If no wound vac, pack the wound open with wet-to-dry dressings and change twice daily
- Testicles may be completely exposed and require delayed placement in the scrotum or thigh pouches.
- May need skin graft to cover skin loss or secondary closure of scrotal defect
- Biopsy to exclude urethral or perianal cancer
- Urinary diversion:
  - Suprapubic tube initially
  - Perineal urethrostomy as a secondary option in patients with an unstable bladder or where adequate urinary diversion has not occurred
- Cystoscopy for evaluation of urethral stricture disease after complete resolution of infection
- At least 6 mo after the infection has resolved, begin long-term management of urethral stricture disease:
  - Conservative (intermittent catheterization)
  - Surgical excision of diseased segment
  - Grafting procedures
  - Permanent diversion or perineal urethrostomy

ADDITIONAL TREATMENT

Wound vac and local wound care following wide tissue debridement

ONGOING CARE

PROGNOSIS

- Variable, depending on severity of presentation
- Can be life-threatening

COMPLICATIONS

- Sepsis, acute renal failure, death (1.6%)
- Progression to necrotizing fasciitis
- Extensive skin loss
- Recurrent periurethral abscess
- Necrosis of corpora spongiosa
- Urethrocutaneous fistula (watering-pot perineum)
- GI bleeding

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Frequent wound checks until healed
- Stricture disease: RUG to evaluate stricture disease after infection resolved
- Uroflowmetry
- UTI: Evaluate urine periodically to minimize the chance of recurrent PUA.
- Gonorrhea and Chlamydia testing

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Fournier Gangrene
- Urethra, Mass
- Urethra, Stricture

CODES

ICD9

597.0 Urethral abscess

ABBREVIATIONS

- BUN: Blood urea nitrogen

- CT: Computed tomography
- GI: Gastrointestinal
- HIV: Human immunodeficiency virus
- PUA: Periurethral abscess
- RUG: Retrograde urethrogram
- STD: Sexually transmitted disease
- UTI: Urinary tract infection
- WBC: White blood cell

URETHRA, CARCINOMA, GENERAL

Raymond M. Bernal, MD
Jack H. Mydlo, MD

BASICS

DESCRIPTION

- Urethral carcinoma is a rare malignancy that can arise from the various cell types of the urethra.
- Adenocarcinoma, TCC, and SCC are the most common subtypes of primary urethral carcinoma.

EPIDEMIOLOGY

- Men: 4.3 per million
- Women: 1.5 per million
- African American: 5 per million
- White: 2.5 per million

RISK FACTORS

The etiology is obscure. The following are proposed risk factors:

- Age
- Caruncles
- Chronic STDs
- HPV-16 infection has been associated with some cases of urethral carcinoma, both squamous and urothelial cell
- Leucoplakia
- Parturition
- Polyps
- Smoking
- Urethral diverticulum
- Urethral stricture disease
- Urethritis

GENERAL PREVENTION

Management of stricture disease and treatment of chronic infection may limit development of urethral carcinoma

PATHOPHYSIOLOGY

- Location of urethral carcinoma:
  - Men:

    Bulbomembranous (60%)

Penile (30%)
Prostatic (10%)
– Women:
Anterior urethra (distal 1/3), 20–40%
Posterior urethra (proximal 2/3), 60–80%

- Histology:
  - TCC (55%)
  - SCC (21.5%)
  - Adenocarcinoma (16.4%)
  - Others, including melanoma (5.3%), unclassified (1.7%)
- Spread:
  - Direct extension to adjacent structures
  - Lymphatic:
    Anterior urethra to superficial/deep inguinal/external iliac nodes
    Posterior urethra to pelvic nodes
    Palpable inguinal nodes in 20–30%; almost always represent metastatic disease

COMMONLY ASSOCIATED CONDITIONS

- Chronic urethral stricture disease: >50%
- STD: 25%
- Bladder cancer: 10%

DIAGNOSIS

HISTORY

- Age, sex, and race:
  - Incidence increases with age, most commonly >50.
  - All subtypes more common in men, except for adenocarcinoma, which is more common in black women.
  - African Americans with increased incidence.
- History of venereal disease or urethritis:
  - Possible predisposing factors
- History of bladder cancer:
  - Urethral cancer found in 10% with cystectomy
- History of exposure to carcinogens:
  - Chronic arsenic exposure has been associated with adenocarcinoma
  - Smoking has been associated with TCC
- Irritation or obstructive voiding symptoms:

  - Most common symptoms; many have a history of urethral stricture
- Gross hematuria, priapism, penile gangrene, urinary fistula, incontinence:
  - Occasionally described
- Palpable penile or perineal masses:
  - Tumors may be felt on self-exam

PHYSICAL EXAM

- Visualization:
  - May have mass protruding from urethra
- Palpation:
  - Urethra, perineum, inguinal nodes
  - Palpable inguinal nodes in 20–30%

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine cytology:
  - May return malignant cells
- Urine analysis:
  - May reveal microscopic hematuria

Imaging

- Urethrography:
  - VCUG to visualize entire urethra in women, posterior urethra in men
  - Retrograde urethrogram to visualize the anterior urethra in men
- Staging: Abdominal CT or MRI, chest x-ray
- Other considerations for surgical planning:
  - If suspected rectal involvement, barium enema
  - If suspected invasion of corporal structures or local extension, MRI

Diagnostic Procedures/Surgery

- Cystourethroscopy and biopsy
- Flexible sigmoidoscopy

Pathological Findings

- Normal female urethra proximal 1/3 transitional cells, distal 2/3 stratified
- Normal male urethra:
  - Prostatic and bulbomembranous urethra lined by transitional epithelium
  - Penile urethra is lined with pseudostratified columnar epithelium
  - Meatus is lined by stratified squamous epithelium.
- Gross:

– Irregular masses that project into the urethra and may be ulcerated.
– Melanoma may be flat or nodular, and pigmented or nonpigmented.

- Histologic:

– Nondistinctive and similar to those at other sites (urothelial and squamous carcinoma), except for melanoma, which may have absent pigment or appear papillary or spindle-shaped.

- Carcinoid, lymphoma, and small-cell carcinomas have been described.

DIFFERENTIAL DIAGNOSIS

- Caruncle
- Erosion
- Fistula
- Inflammatory phlegmon
- Leukoplakia
- Melanoma
- Nephrogenic adenoma
- Periurethral abscess
- Stricture
- Urethral diverticulum
- Urethral prolapse

TREATMENT

- The relative rarity of urethral carcinoma has made it difficult to standardize a treatment modality.
- Treatment decisions are based on histology and location of tumor.

MEDICATION

- Multimodality therapy combining chemotherapy, radiation, and surgery has shown some effectiveness in advanced urethral carcinoma.
- Neoadjuvant/adjuvant chemotherapy:
  – Men:
    MVAC for TCC
    Cisplatin, bleomycin, methotrexate for SCC
  – Women:
    5-FU + mitomycin C for SCC
    MVAC or gemcitabine for TCC
- Chemoradiation as primary treatment:
  – Mitomycin + 5-FU + 45–55 Gy radiation to pelvis (perineum to upper sacrum + 12–15 Gy to primary cancer site)

SURGERY/OTHER PROCEDURES

- Male urethral carcinoma by location:
  - Penile urethra:

    TUR, local excision, or distal urethrectomy if superficial, papillary, low grade

    Partial penectomy with 2-cm negative margin if distal and invades corpus spongiosum

    Ilioinguinal lymphadenectomy if palpable inguinal nodes and no metastatic disease

    Radical penectomy for stage Ta–T2 urethral tumors with inadequate margins for partial penectomy. May also be indicated for some distal urethral cancers that invade the corporal bodies
  - Bulbomembranous urethra:

    TUR or excision and primary anastomosis if low grade

    Cystoprostatectomy, pelvic lymphadenectomy, total penectomy for proximal T3–T4 tumors; resection of the urogenital diaphragm and pubic rami if high grade and invasion of pubis likely
- Female urethral carcinoma by location:
  - Anterior urethra (distal 1/3):

    Circumferential excision including some anterior vaginal wall
  - Posterior urethra (proximal 2/3):

    Anterior exenteration, pelvic lymphadenectomy
- Often multimodal in high-stage disease

ADDITIONAL TREATMENT

- Intravesical instillation:
  - BCG for TCC of prostate
- Radiation therapy:
  - The rarity of urethral carcinoma has made it difficult to standardize a treatment modality.
  - Men:

    Option for low-stage anterior cancers including external beam
  - Women:

    Option for low-stage anterior cancer including external beam, brachytherapy, or combined
  - Often multimodal in high-stage disease

ONGOING CARE

PROGNOSIS

- Depends ultimately on anatomic location, primary stage, and nodal status
- 5-yr overall:
  - Women:
    71% distal lesions, 48% proximal lesions, 24% involving majority of urethra
  - Men:
    69% anterior lesions, 26% posterior lesions, 83% low stage, 36% high stage

COMPLICATIONS

- Abscess
- Urethral fistula
- Urethral stricture
- Urinary incontinence

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Most local recurrences occur within the 1st 1–2 yr after treatment
- Cystourethroscopy and urine cytology every 3 months; additional biopsies as necessary, based on these results

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Incontinence (Urinary Incontinence), Adult Female (Chief Complaint)
- Periurethral Abscess
- Skene (Paraurethral) Gland Adenocarcinoma
- Skene (Paraurethral) Gland, Inflammation/Adenitis
- Urethra, Abscess (Periurethral Abscess)
- Urethra, Carcinoma, General
- Urethra, Caruncle
- Urethra, Discharge and Spotting
- Urethra, Diverticular Carcinoma
- Urethra, Leiomyoma
- Urethra, Mass (Chief Complaint)
- Urethra, Prolapse (Female)

CODES

ICD9

189.3 Malignant neoplasm of urethra

ABBREVIATIONS

- 5-FU: 5-fluorouracil
- BCG: Bacille Calmette-Guérin
- CT: Computed tomography
- MRI: Magnetic resonance imaging
- MVAC: Methotrexate, vinblastine, doxorubicin, cisplatin
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted disease
- TCC: Transitional cell carcinoma
- TUR: Transurethral resection
- VCUG: Voiding cystourethrogram

URETHRA, CARUNCLE

Deborah T. Glassman, MD

BASICS

DESCRIPTION

- A benign tumor of friable mucosa at the posterior edge of the urethral meatus in females.
- Most are asymptomatic.

EPIDEMIOLOGY

- Most commonly found in postmenopausal women
- Uncommon in childbearing years
- Extremely rare in children

RISK FACTORS

- Postmenopausal vaginal atrophy
- Chronic irritation to the urethral meatus

GENERAL PREVENTION

Prevention of vaginal atrophy

PATHOPHYSIOLOGY

Mucosal ectropion of posterior urethral wall secondary to retraction of an atrophic vagina

COMMONLY ASSOCIATED CONDITIONS

Vaginal atrophy

DIAGNOSIS

HISTORY

- Determine menopausal status, as more common in postmenopausal females
- Vaginal irritation
- Occasional dyspareunia
- Spotting on underwear
- Incidentally noted on pelvic exam
- Voiding symptoms infrequent
- Tenderness is infrequent.

PHYSICAL EXAM

- Erythematous, friable mass seen and palpated on vaginal inspection
- Usually reddish, occasionally may appear blue or black
- Usually located at the posterior urethral meatus
- May be tender to palpation

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - Examine for RBCs or epithelial cells
- Urine cytology may identify malignancy

Diagnostic Procedures/Surgery

- Urethroscopy: May help delineate extent of lesion
- Biopsy: Excisional or incisional

Pathological Findings

- Papillomatous, granulomatous, and angiomatous varieties
- Histologic:
  - Connective tissue containing many inflammatory cells and blood vessels and covered by an epithelial layer
  - Evidence of necrosis, inflammation, and hemorrhage may be present.
- Transitional or stratified squamous epithelium
- 2% of caruncles have associated malignancy

)[C]

DIFFERENTIAL DIAGNOSIS

- Urethral prolapse:
  - Evagination of urethral mucosa
  - Typically circumferential
- Malignancy:
  - Urethral carcinoma:

    Uncommon

    Peak incidence 5th–7th decade

    Usually a firm, nontender, indurated mass

    Irritative voiding symptoms associated

    Bleeding from urethra or on toilet tissue is more typical.

)[B]

  - Lymphoma
- Intestinal metaplasia
- TB
- Urethral syndrome
- Vaginal mass
- Condylomata
- Thrombosis of urethral vein:

- Bluish, swollen, very tender lesion in similar location to caruncle

TREATMENT

- Most urethral caruncles are asymptomatic and do not require definitive treatment.
- If there is any doubt concerning the diagnosis, biopsy should be performed.
- Sitz baths may alleviate discomfort.

MEDICATION

- Estrogen replacement therapy:
  - Local or systemic
- Anti-inflammatory medications for mild discomfort, PO or topical

SURGERY/OTHER PROCEDURES

- Excision:
  - Outpatient procedure performed under local

)[C]:

  - Outpatient procedure performed under local
- Cryoablation
- Laser fulguration

ADDITIONAL TREATMENT

Radiation therapy: Applicable only for certain distal urethral malignancies and not for urethral caruncle

ONGOING CARE

PROGNOSIS

Good

COMPLICATIONS

Meatal stenosis with surgical excision

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- None specific
- Routine gynecologic follow-up as this is a benign lesion

REFERENCES

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ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Urethra, Bleeding (Blood at Meatus)
- Urethra, Discharge and Spotting
- Urethra, Mass
- Urethra Carcinoma, General
- Urethra, Prolapse (Female)

CODES

ICD9

599.3 Urethral caruncle

ABBREVIATIONS

- PO: Orally
- RBC: Red blood cell
- TB: Tuberculosis

URETHRA, DIVERTICULA, FEMALE

Deborah R. Erickson, MD

BASICS

DESCRIPTION

- A protrusion or herniation of the urethra into the potential space between the periurethral fascia and anterior vaginal wall.
- It often contains a collection of urine and/or pus; usually connects to the urethra.
- Classic symptoms are dysuria, dyspareunia, and post-void dribbling.

EPIDEMIOLOGY

- Depends on avidity with which it is sought

)

)

)

RISK FACTORS

)

PATHOPHYSIOLOGY

- Congenital (uncommon)

):

  - Infection of periurethral glands
  - Glands obstruct and form abscess.
  - Abscess ruptures into urethra.
  - Diverticulum is contained within periurethral fascia.

DIAGNOSIS

HISTORY

- Classic 3 Ds (rare for all 3 to be present):
  - Dysuria: Pain during voiding
  - Dribbling (incontinence) typically due to urine leaking from the diverticulum, but patient may also have concomitant stress and/or urge incontinence
  - Dyspareunia
- Nonspecific presentations are common:
  - Frequency/urgency
  - Hematuria
  - Palpable or visible lump/bulge
  - Persistent localized pain
  - Recurrent UTIs

- Voiding symptoms or retention
- May be an incidental finding

PHYSICAL EXAM

- Inspect the anterior vaginal wall:
  - Some (but not all) diverticula are visible as a suburethral midline mass.
  - Assess bladder neck mobility.
  - Observe for stress incontinence.
- Palpate the anterior vaginal wall and test for point tenderness, which may be the only sign of a urethral diverticulum.
- A mass may be palpable:
  - Classic sign: Compressing the mass expresses urine or pus from urethral meatus.
  - If the mass does not compress, consider:
    Vaginal wall cyst
    Obstructed (noncommunicating) diverticulum
  - Most diverticula are tender (if not, consider a vaginal wall cyst).
  - 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

):

- Diverticulum has high signal intensity on T2-weighted image
- Most accurate diagnostic test
- Does not require the patient to void
- Shows noncommunicating diverticula
- Helps surgical planning: Shows size, extent, location, and presence of filling defects
- Not painful if no endoluminal coil used

):

- Advantage: Shows functional causes for symptoms, such as bladder neck or external sphincter obstruction
- Disadvantages compared to MRI:
  More invasive

Patient must be able to void
Less sensitive for diagnosis
Less anatomic detail

):

- Less sensitive than MRI
- More sensitive than VCUG
- More painful than VCUG
- Requires special radiology expertise

• US: Highly operator-dependent

Diagnostic Procedures/Surgery

):

- Much less sensitive than VCUG or MRI
- To see the entire urethra, use a scope with a short beak.
- Ostium usually in mid-urethra at 5–7 o'clock
- Main value: Rule out other pathology

):

- Not mandatory in straightforward cases
- Useful if the patient has incontinence or voiding difficulty
- Videourodynamics: Combines VCUG (may show diverticulum anatomy) with lower-tract functional evaluation in 1 procedure

Pathological Findings

):

- Transitional
- Stratified squamous
- Columnar
- Cuboidal
- Absent (wall of fibrous tissue only)

):

- Adenocarcinoma is most common
- Also: Transitional or squamous cell

• May contain stones

• May have chronic inflammation and related changes (eg, squamous or glandular metaplasia)

DIFFERENTIAL DIAGNOSIS

• Benign neoplasms:

- Hemangioma
- Adenomatous polyps
- Squamous papilloma
- Transitional cell papilloma
- Leiomyomas:
  Increased prevalence in females 30–50
- Polypoid urethritis
- Nephrogenic adenoma
- Amyloidosis
- Skene (paraurethral) gland, inflammation/adenitis

- Ectopic ureterocele
- Skene gland cyst or abscess
- Urethral prolapse or caruncle
- Urethral vein thrombosis
- Malignant neoplasms:
  - Primary urethral carcinoma; more common in females:
    Squamous cell (80%)
    Transitional cell (15%)
    Adenocarcinoma (4%)
    Melanoma (1%)
    Clear-cell adenocarcinoma has been associated with urethral diverticulum.
    Skene (paraurethral) gland adenocarcinoma
    Metastases
- Vaginal wall mass:
  - Leiomyoma
  - Vaginal wall cyst (eg, Gartner duct)

TREATMENT

- If asymptomatic, no treatment is necessary.
- Antibiotics, analgesics, and antispasmodics may control symptoms.
- With significant symptomatology, surgical excision is best.

MEDICATION

Antibiotics, analgesics, and antispasmodics may control mild symptoms.

SURGERY/OTHER PROCEDURES

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):

- Well-vascularized anterior vaginal wall flap
- Preserve periurethral fascia.
- Excise diverticulum completely.
- Watertight, tension-free urethral closure
- Cover with multiple layers (consider Martius flap).
- Avoid overlapping suture lines.
- Close dead space.
- Small urethral catheter, also suprapubic tube
- Aggressive anticholinergics to prevent bladder spasms

- Do surgery for stress incontinence (such as a fascial sling) at the same setting if:
  - Stress incontinence is present before surgery.
  - Postop stress incontinence is expected after extensive diverticular dissection.

Pregnancy Considerations

):

- Conservative treatment (antibiotics, aspiration, incision, and drainage) 1st
- Definitive surgery after delivery

- If conservative treatment fails:

)

- If so, elective cesarean section is prudent.

ONGOING CARE

PROGNOSIS

- If untreated, natural history is not well known.

)

COMPLICATIONS

- Of the diverticulum:
  - Stones
  - Carcinoma: Typically clear-cell carcinoma, but squamous cell and urothelial cell carcinoma also reported
  - Recurrent UTIs
  - Symptoms as noted above
- Of the surgery:
  - Infection
  - Bleeding
  - Incontinence:

    Stress or urge incontinence

Persistent or de novo

Pre-op SUI should be repaired at same time as diverticulum repair

- Diverticulum may return.
- Urethrovaginal fistula
- Urethral stricture or necrosis
- Bladder or ureteral injury
- Vaginal scarring or narrowing

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- VCUG after surgery
- History and exam on follow-up visits
- Additional studies if indicated based on history and exam findings

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See Also (Topic, Algorithm, Electronic Media Element)

- Dribbling, Post-Void
- Dyspareunia
- Gartner Duct Cyst
- Incontinence (Urinary Incontinence), Adult Female
- Martius Flap
- Müllerian Duct Remnants and Syndrome
- Periurethral Abscess
- Skene (Paraurethral) Gland Adenocarcinoma
- Skene (Paraurethral) Gland, Inflammation/Adenitis
- Urethra, Abscess (Periurethral Abscess)
- Urethra, Carcinoma, General
- Urethra, Caruncle
- Urethra, Discharge and Spotting
- Urethra, Diverticular Carcinoma
- Urethra, Leiomyoma
- Urethra, Mass
- Urethra, Nephrogenic Metaplasia (Adenoma)
- Urethra, Prolapse (Female)
- Urinary Tract Infection (UTI), Adult Female
- Vaginal Discharge, Urologic Considerations

CODES

ICD9

599.2 Urethral diverticulum

ABBREVIATIONS

- LUTS: Lower urinary tract symptoms
- MRI: Magnetic resonance imaging
- SUI: Stress urinary incontinence
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram

URETHRA, MASS

Kelly E. Shaffer, MD
Matthew G. McIntyre, MD

BASICS

DESCRIPTION

Urethral masses may be palpable. They are often visualized on cystoscopy or other imaging modalities.

PATHOPHYSIOLOGY

- Male urethral anatomy:
  - Male urethra is 21 cm long.
  - It is divided into the prostatic, membranous, bulbar, and penile urethra.
  - Lymphatic drainage of the distal urethra is to the superficial and deep inguinal lymph nodes. The proximal urethra drains into the external iliac, obturator, and internal iliac lymph nodes in the pelvis.
- Female urethral anatomy:
  - Female urethra is 3–5 cm long.
  - Distal 1/3 of the female urethra drains into superficial or deep inguinal lymph nodes; proximal 2/3 drains into the deep pelvic lymph nodes (external iliac and internal iliac, obturator nodes).

DIAGNOSIS

HISTORY

- Age and sex of patient:
  - Malignancy more common >50.
- Prior history of bladder cancer to suggest urethral recurrence, particularly in men
- Sexual history:
  - Genital warts, gonorrhea may predispose to malignancy
- Lower urinary tract symptoms:
  - Frequency/urgency/hematuria/dysuria may be associated with stricture or malignancy
- History of UTIs:
  - May be associated with urethral diverticulum

PHYSICAL EXAM

- General exam: Assess for lower extremity edema.
- Lymph node assessment:
  - Metastatic disease from the distal urethral can involve the superficial inguinal nodes.

- External genitalia: Examine for lesions of condyloma acuminatum.
- Urethral exam:
  - Carefully palpate the length of lesion.
  - Note location, number, consistency, degree of fixation.
  - Inspect meatus for discharge, mass, or stricture.
  - Compression or stripping of a diverticulum in females may express purulent discharge.
- Inspect the perineum for fistulous tracts.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis
- Urine culture
- Urine cytology
- Urethral swab: Culture for gonorrhea, chlamydia, and TB

Imaging

- Retrograde urethrogram to assess for location and length of urethral stricture.
- Pelvic MRI or CT to assess for urethral diverticulum, metastases to the pelvic and inguinal nodes, evidence of corporal invasion by carcinoma.

Diagnostic Procedures/Surgery

Cystoscopy allows direct visualization of the mass and allows for biopsy.

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 STDs, whereas in the older adult population it may represent primary or metastatic cancer disease.
- Congenital:
  - Benign fibroepithelial polyp
  - Retention cysts of Cowper gland ducts
- Inflammatory:
  - Stricture disease secondary to gonococcal urethritis
  - Periurethral abscess
  - Condyloma acuminata
  - TB
- Traumatic:
  - Stricture disease secondary to injury; hematoma; foreign body

- Benign neoplasms:
  - Hemangioma
  - Adenomatous polyps
  - Squamous papilloma
  - Transitional cell papilloma
  - Leiomyomas:
    Increased prevalence in females 30s–50s
  - Polypoid urethritis
  - Nephrogenic adenoma
  - Amyloidosis
  - Skene (paraurethral) gland, inflammation/adenitis
  - Urethral caruncle:
    More common in postmenopausal women
- Malignant neoplasms:
  - Primary urethral carcinoma, more common in females:
    Squamous cell (80%)
    Transitional cell (15%)
    Adenocarcinoma (4%)
    Melanoma (1%)
    Clear cell adenocarcinoma has been associated with urethral diverticulum.
    Skene (paraurethral) gland adenocarcinoma
    Metastases
- Miscellaneous:
  - Urethral prolapse:
    Interlabial, well-circumscribed mass most common in African American females age 5–7
    Stone impacted in urethra or diverticulum
    Foreign body
- Mass in corporal body in male:
  - Metastatic deposit
  - Fibrosis of corporal body from priapism or trauma
  - Peyronie disease plaque
  - Penile prosthesis
- Vaginal wall mass:
  - Leiomyoma

– Vaginal wall cyst (eg, Gartner duct)

TREATMENT

- Management is directed by the pathologic findings.
  – Cystoscopic exam with biopsy will provide the diagnosis.
  – Imaging and bimanual exam will provide staging information in the case of malignancy.
- In cases with locally advanced disease, multimodality therapy using chemotherapy with radiation is sometimes used.

MEDICATION

Condyloma of the urethra: Intraurethral 5-FU cream, biopsy with fulguration/laser ablation.

SURGERY/OTHER PROCEDURES

- Urethral stricture: Dilation, internal urethrotomy, urethroplasty.
- Urethral prolapse: Excision
- Urethral diverticulum: Excision:
  – Benign neoplasms: Biopsy for diagnosis. Excision, fulguration, laser ablation.
- Malignant neoplasms:
  – Male urethra: Partial or total urethrectomy, possible penectomy with perineal urethrostomy.
  – Female urethra: Total urethrectomy.
  – Cystectomy necessary for high-grade lesions near bladder neck for both male and female.
  – In females, this includes an anterior exenteration (urethrectomy, cystectomy with pelvic lymphadenectomy, hysterectomy with salpingectomy, and anterior vaginal wall)
  – Inguinal and pelvic node dissections are based on location of lesions.

ADDITIONAL TREATMENT

Radiation therapy:

- May be indicated in some cases of urethral cancer to decrease local recurrence
- In women, radiation therapy using brachytherapy, external beam radiation combination is a suitable alternative.

ONGOING CARE

PROGNOSIS

Depends on etiology of mass

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Cystourethroscopy and urine cytology every 6 mo for urethral carcinoma.

- Urethral condyloma require urethroscopy and retreatment for disease eradication.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Urethritis, Gonococcal and Non-Gonococcal
- Caruncle, Urethral, Urethra, Caruncle
- Fossa Navicularis, Diverticulum
- Skene (Paraurethral) Gland, Inflammation/Adenitis
- Urethra, Condyloma
- Urethra, Polyps (Fibroepithelial, Adenomatous, Inflammatory)
- Urethra, Diverticula

CODES

ICD9

- 189.3 Malignant neoplasm of urethra
- 598.9 Urethral stricture, unspecified
- 599.84 Other specified disorders of urethra

ABBREVIATIONS

- 5-FU: 5-fluorouracil
- CT: Computed tomography
- MRI: Magnetic resonance imaging
- STD: Sexually transmitted disease
- TB: Tuberculosis
- UTI: Urinary tract infection

URETHRA, SQUAMOUS CELL CARCINOMA

Matthew J. Resnick, MD

S. Bruce Malkowicz, MD

BASICS

DESCRIPTION

Tumor arising from the native squamous lining of the male and female urethra

EPIDEMIOLOGY

- Incidence (white male): 0.58 per 1,000,000
- Incidence (African American male): 2.3 per 1,000,000
- Incidence (white female): 0.43 per 1,000,000
- Incidence (African American female): 0.69 per 1,000,000
- Incidence is higher in African American patients as compared to their white counterparts.

)

RISK FACTORS

- Male SCC:
  - Chronic inflammation
  - History of frequent STDs: Nearly 25% of patients with urethral carcinoma will give history of STDs.
  - Urethritis
  - Urethral stricture disease 50% of patients with urethral carcinoma will have stricture disease.
  - HPV
- Female SCC:
  - Leukoplakia
  - Chronic irritation
  - Parturition
  - Human papilloma virus
  - Viral infections
  - Possibly urethral diverticula: 4% of female urethral carcinoma is found within diverticulum.

Genetics

)

- Notably, there have been no abnormalities described in chromosomes 9 and 17, those largely responsible for the development of TCC.

GENERAL PREVENTION

Prevention of STDs with the use of barrier protection such as condoms

PATHOPHYSIOLOGY

- Male SCC:
  - Occurs in the male membranous urethra (80% SCC), bulbar urethra (80% SCC), and penile urethra (90% SCC)
- Female 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.

COMMONLY ASSOCIATED CONDITIONS

- Condyloma acuminatum
- History of STDs
- Presence of indwelling catheter
- Urethral diverticula
- Urethral stricture disease

DIAGNOSIS

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.

HISTORY

- Particular attention must be made to risk factors and associated GU conditions.
- Male urethral SCC:
  - Urethral bleeding
  - Perineal discomfort
  - Decreased force of stream
  - Urinary frequency
  - Urinary urgency
  - Dysuria
  - Urinary fistulae
- Female urethral SCC:
  - Urethral bleeding
  - Palpable urethral mass

- Urinary frequency
- Urinary urgency
- Induration of urethra or anterior vaginal wall

PHYSICAL EXAM

- Particular attention in both men and women to potential mass arising from urethra, necessitating formal pelvic exam for female patients
- Perineal exam to evaluate male proximal urethra
- Particular attention must be made to the inguinal exam, as 20–30% of patients will present initially with metastases to the inguinal chain.
- Exam under anesthesia at time of cystoscopy including bimanual palpation of genitalia, urethra, rectum, and perineum helpful to determine extent of disease

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis
- Urine culture
- Urine PCR for gonorrhea, Chlamydia
- Cytology of 1st voided urine

Imaging

- VCUG:
  - Evaluates posterior urethra in males
  - Evaluates entire female urethra
  - Aids in assessment for stricture disease, urinary fistulae, or urethral diverticula
  - Retrograde urethrogram
  - Evaluates anterior urethra in males
- 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 TCC

Diagnostic Procedures/Surgery

Cystoscopy with biopsy/transurethral resection:

- Gold standard in histologic diagnosis of urethral carcinoma
- Cystoscopic appearance of fungating growth extending into urethral lumen
- Sigmoidoscopy/colonoscopy if concern for involvement of GI tract based upon physical exam or imaging

Pathological Findings

Fungating tumor with varied cytologic differentiation ranging from well-differentiated lesions producing keratohyaline pearls to anaplastic giant-cell tumors

DIFFERENTIAL DIAGNOSIS

- Condyloma acuminatum
- Benign neoplasms:
  - Hemangioma
  - Adenomatous polyps
  - Squamous papilloma
  - Transitional cell papilloma
  - Leiomyomas: Increased prevalence in females aged 30–50
  - Polypoid urethritis
  - Nephrogenic adenoma
  - Amyloidosis
  - Urethral caruncle: More common in postmenopausal women
- Leukoplakia
- Periurethral abscess
- Skene (paraurethral) gland, inflammation/adenitis
- Urethral diverticulum
- Urethral fistula
- Urethral stricture
- Malignant neoplasms:
  - Primary urethral carcinoma:

    Squamous cell

    Transitional cell

    Adenocarcinoma

    Melanoma

    Clear-cell adenocarcinoma has been associated with urethral diverticulum.

    Skene (paraurethral) gland adenocarcinoma

    Metastases

TREATMENT

Treatment decisions based on sex, stage, and location of tumor

MEDICATION

- The precise role for chemotherapy in the treatment of urethral SCC is poorly defined; however, chemotherapy not considered 1st-line treatment.

• In patients with advanced disease, investigators have recommended regimens of systemic cisplatin, bleomycin, and methotrexate or 5-FU and methotrexate in addition to surgical resection in the treatment of metastatic urethral SCC.

SURGERY/OTHER PROCEDURES

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– 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.

):

– Transurethral resection, fulguration, or local excision may be employed for superficial low-grade tumors.

– For tumors invading the corpus spongiosum, partial penectomy with a 2-cm margin is treatment of choice 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.

– Ilioinguinal lymphadenectomy is indicated only in presence of palpable disease, as there has been no documented benefit of prophylactic lymphadenectomy.

):

– Tumors of the distal urethra tend to be low-stage with cure rates of 70–90% with local excision alone.

– External beam radiation therapy is also therapeutic option for distal female urethral carcinoma.

):

– Far 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

• Male urethral SCC:

– Few series of radiation therapy for patients with early-stage lesions of the anterior urethra who refuse surgery

– Possible role in palliation, with occasional adjuvant use with extensive resection

• Female urethral SCC:

– Low-stage distal lesions can be treated with external beam radiation, brachytherapy, or combined therapy 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 carcinoma, the precise role of radiation therapy remains unclear.

ONGOING CARE

PROGNOSIS

):

– Overall 5-yr survival: 42.3%
– Overall 5-yr survival (superficial disease): 83.3%
– Overall 5-yr survival (invasive disease): 35.7%
– Overall 5-yr survival (anterior urethra): 69.1%
– Overall 5-yr survival (bulbar urethra): 44.7%

):

– Overall 5-yr survival: 32%
– Overall 5-yr survival (low-stage): 78%
– Overall 5-yr survival (high-stage): 33%
– Overall 5-yr survival (anterior urethra): 54%
– Overall 5-yr survival (posterior urethra): 25%

COMPLICATIONS

All typical complications associated with radical surgical intervention:

- Abscess
- Cystitis
- Incontinence
- Urethral stricture
- Urinary fistula

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Vast majority of recurrences occur within 1–2 yr following definitive therapy.
- Surveillance requires q3–6 mo cystoscopy and urinary cytology for 1–2 yr, with increasing interval between surveillance cystoscopy in the absence of recurrence.

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See Also (Topic, Algorithm, Electronic Media Element)

- Urethra, Carcinoma, General
- Urethra, Mass

CODES

ICD9

- 188.5 Malignant neoplasm of bladder neck
- 189.3 Malignant neoplasm of urethra

ABBREVIATIONS

- 5-FU: 5-fluorouracil
- CT: Computed tomography
- GI: Gastrointestinal
- GU: Genitourinary
- HPV: Human papilloma virus
- MRI: Magnetic resonance imaging
- PCR: Polymerase chain reaction
- SCC: Squamous cell carcinoma
- STD: Sexually transmitted diesease
- TCC: Transitional cell carcinoma
- VCUG: Voiding cystourethrogram

URETHRA, STRICTURE

Goutham Vemana, MD

James F. Donovan, Jr., MD

BASICS

DESCRIPTION

- In the male, a disease of the anterior urethra involving spongy erectile tissue of the corpus spongiosum.
- True stricture of the female urethra is very rare and is discussed in Section II.

EPIDEMIOLOGY

- Incidence of male urethral stricture disease is unknown.
- Can occur as high as 0.6% in susceptible populations (based on data from a population of older veterans)

RISK FACTORS

- STDs:
  - Increased among men with history of STD, particularly gonorrhea
- Recurrent infections:
  - Increased with repeated episodes of urethritis, although association is unclear
- BPH; often following resection of prostate
- Race:
  - Some data from Medicare analysis suggests that black Americans may have higher stricture rates
- Age:
  - Rates of strictures increase with age
- Frequent instrumentation of the urethra
- Trauma

GENERAL PREVENTION

- Reduce frequency of instrumentation of the urethra unless essential.
- Appropriate sized instrumentation for transurethral procedures.
- Safe sexual practices
- Antibiotic treatment for STDs
- Early treatment of urethral strictures

PATHOPHYSIOLOGY

- Anterior urethra consists of the pendulous and bulbar portions of the urethra:
  - Generally as a result of tissue injury from trauma, inflammation, or ischemia
  - Up to 10% of pelvic trauma will have an associated urethral injury.

- As defined by the WHO, a posterior urethral stricture is not included in the classic definition of urethral stricture; it is instead considered a distraction injury:
  - Posterior urethra is the membranous and prostatic urethral segments.
  - Generally secondary to trauma (pelvic fracture) or surgery such as a radical prostatectomy
- Scar forms circumferentially in response to injury of the epithelial lining of the urethra.
- Involves progressive fibrosis of the epithelium with subsequent involvement of the underlying spongiosum
- Contracting leads to smaller circumference, thus stricture

COMMONLY ASSOCIATED CONDITIONS

- LS-BXO
- STD (eg, gonorrhea)

DIAGNOSIS

HISTORY

- History of STD, transurethral surgery, or manipulation
- Obstructive voiding symptoms
- Prostatitis
- Recurrent UTIs
- Spraying or split stream
- Urinary retention

PHYSICAL EXAM

- Usually no specific findings, except with trauma
- Examine for evidence of hypospadias or penile plaque
- Discharge with abscess, urethritis, or STD

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and urine culture:
  - May demonstrate signs of a UTI
- Urinary flow rates:
  - Significant strictures will have flow rates <10 mL/s (normal, 20 mL/s)
- PVR
- Gonorrhea culture

Imaging

- Retrograde urethrogram
- Voiding cystourethrogram

- Sonography (may have limited use)

Diagnostic Procedures/Surgery

- Cystoscopy:
  - Allows for direct visualization of the stricture
- Flexible endoscopy through suprapubic access, if present
- Cystourethrography

Pathological Findings

Strictures are fibrotic narrowing composed of dense collagen and fibroblasts.

DIFFERENTIAL DIAGNOSIS

- Benign or malignant prostatic obstruction
- Urethral carcinoma
- Bladder infection
- Functional bladder disorder

TREATMENT

- It is important to determine location, length, depth, and density of the stricture.
- The depth and density of the fibrosis can be determined by physical exam; location and length is best determined by imaging and diagnostic procedures.
- Indwelling Foley catheter after dilation or urethrotomy only seems to delay reoccurrence of stricture.
- Intermittent catheterization after dilation or urethrotomy also does not prevent reoccurrence, as stricture returns after catheterization is ceased.

MEDICATION

- No primary role in management.
- Treat infections and STD with appropriate antibiotics.

SURGERY/OTHER PROCEDURES

- Dilation:
  - Goal is to stretch scar without producing additional scarring
  - Can use:
    Urethral balloon dilating catheters
    Filiform and followers
  - Reoccurrences can be redilated repeatedly
- Internal urethrotomy:

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  - Use cold knife or vaporizing laser

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- Lasers:
  - Results of laser urethrotomy are mixed
- Open reconstruction:
  - Requires vigorous mobilization of the corpus spongiosum
  - Best results are achieved when:
    Area of fibrosis is totally excised
    Urethral anastomosis is widely spatulated
    Anastomosis is tension free
  - Primary reanastomosis:

)[A]

  - Grafts used for successful reconstruction of long strictures (generally >2 cm):
    Full-thickness skin graft
    Bladder epithelial graft
    Buccal mucosal graft
    Rectal mucosal graft

ADDITIONAL TREATMENT

Urethral stents:

- Must be placed in the bulbar urethra only
- Best employed for short strictures with minimal spongiofibrosis

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- However, strictures amenable to stenting are generally candidate for definitive repair with open reconstruction.

ONGOING CARE

PROGNOSIS

Prognosis of reoccurrence of stricture depends on numerous factors such as the characteristics of the stricture as well as the intervention chosen for the stricture.

COMPLICATIONS

- Related to stricture:
  - ED
  - Periurethral abscess
  - Urethral diverticulum
  - Urethral fistula
  - Urinary infections
  - Urinary retention
- Related to surgical repair:

- ED (usually transient)
- Fistula
- Flap necrosis
- Foreign bodies (eg, hair, calcifications with use of dermal or inlay graft)
- Hematoma
- Penile curvature
- Recurrence of stricture
- Wound infection

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Can be based on patient’s symptomatic relief of the intervention
- High reoccurrence rate:

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See Also (Topic, Algorithm, Electronic Media Element)

- Sexually Transmitted Diseases (STD), General
- Urethra, Mass
- Urethra, Stricture, Female
- Urethra, Stenosis, Female
- Urethra, Trauma (Anterior and Posterior)

CODES

ICD9

- 598.00 Urethral structure due to unspecified infection
- 598.01 Urethral structure due to infective diseases classified elsewhere
- 598.1 Traumatic urethral stricture

ABBREVIATIONS

- AUA: American Urological Association
- BPH: Benign prostatic hypertrophy
- ED: Erectile dysfunction
- LS-BXO: Lichen sclerosus-balanitis xerotica obliterans
- PVR: Post-void residual
- STD: Sexually transmitted disease
- WHO: World Health Organization

URETHRA, TRAUMA (ANTERIOR AND POSTERIOR)

Audrey C. Rhee, MD

James A. Brown, MD

BASICS

DESCRIPTION

Generally described as any process that disrupts the watertight continuity of the urethra. Traumatic injury is mostly seen in male patients.

EPIDEMIOLOGY

- Uncommon in females (<2%); more common in males
- 90% of posterior urethral injuries associated with pelvic fracture

RISK FACTORS

- External genital trauma
- Pelvic fracture
- Penile fracture
- Perineal laceration
- Perineal straddle injury
- Urethral catheterization or instrumentation

GENERAL PREVENTION

Iatrogenic injury can be minimized by careful instrumentation of the urethra.

PATHOPHYSIOLOGY

- Location of injury:
  - Anterior urethra (bulbous and penile urethra)
  - Posterior urethra (membranous and prostatic)
- Anterior injuries are less common due to the mobility of the anterior urethral compared to the fixed nature of the posterior urethra.
- Mechanism of injury:
  - Blunt trauma:

    With pelvic fracture, the membranous urethra is distracted, usually at the departure of the urethra from the bulbospongiosus.

    Penile fracture can cause secondary injury to the urethra.

    Straddle injuries can be caused by falling on a fixed structure such as a bicycle crossbar.
  - Penetrating trauma:

    Gunshot wound, knife
  - Iatrogenic

- Colopinto Classification used by some authors:
  - Type I: Stretching and distortion of urethra, usually due to hematoma
  - Type II: Partial or complete urethral disruption, usually at the prostatic apex
  - Type III: Partial or complete rupture of the prostato-membranous urethra with additional damage to the bulbomembranous urethra and urogenital diaphragm (disruption both proximal and distal to the genitourinary diaphragm)

COMMONLY ASSOCIATED CONDITIONS

- Pubic rami fracture
- Pelvic hematoma

Pediatric Considerations

Associated bladder neck injuries more common

DIAGNOSIS

HISTORY

- Description of trauma
- Voiding history subsequent to trauma:
  - Document if patient has urinated
  - Urinary retention
  - Hematuria or blood per urethra

PHYSICAL EXAM

- Clinical triad:
  - Bloody urethral discharge (does not correlate with severity of injury)
  - Inability to urinate
  - Palpable, full bladder
- DRE: If pelvic fracture and associated pelvic hematoma, can expect high-riding prostate
- Anterior urethral injury:
  - If confined by Buck fascia, classic finding of ecchymosis and swelling limited to penile shaft
  - If Buck fascia is violated, the hematoma is then confined by Colles fascia and will appear as butterfly ecchymosis of the perineum

ALERT

Findings in the evaluation of children with straddle injuries to the external genitalia that should raise concern for sexual abuse:

- Presence of other nonurogenital trauma
- Patient <9 mo

- Perianal, rectal injury without history of penetrating trauma
- Findings of more extensive or severe trauma
- Lack of correlation between reported history and physical findings

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- None specific, but otherwise related to the overall trauma evaluation:
  - CBC, type and cross, electrolytes, BUN, creatinine,
- Urine analysis; urine for culture and sensitivities

Imaging

- RUG: Small volume of contrast, ideally under fluoroscopy:
  - Obtain plain pelvic film to evaluate for pelvic fracture.
  - Place patient in 30-degree oblique position to aid visualization of urethra.
  - Pass a 14 F Foley 2–3 cm into the urethra (just into the fossa navicularis).
  - Gently inflate balloon with 2–3 mL of water to seal the urethra.
  - Under fluoroscopy, with penis on traction, gently inject ~25 mL of diluted contrast into catheter.
  - A Brodney penile clamp can also be used instead of a catheter.
- With a partial urethral tear, contrast can often be seen in the bladder. With complete transection, contrast extravasates and usually does not reach the bladder.
- If multiple injuries sustained during trauma, abdominal and pelvic CT (or single-shot excretory urography, as appropriate)
- Note that CT is inadequate to diagnose and evaluate urethral trauma.
- Once RUG demonstrates urethra intact and Foley catheter is placed, CT trauma cystogram or true trauma cystogram can be obtained.

Diagnostic Procedures/Surgery

Flexible cystoscopy in certain cases (often with placement of a stenting or an aligning Foley catheter)

DIFFERENTIAL DIAGNOSIS

- Urethral transection: Complete or partial
- Urethral contusion
- Injury to other urologic organs, ie bladder, kidney, ureter, bladder neck
- Penile corporal injury, labial/vaginal injury

ALERT

With blood at meatus or high-riding prostate in a trauma, perform RUG if patient is clinically stable before placing urethral stent. This may prevent converting a partial urethral disruption to a complete disruption.

TREATMENT

- If suspicion of urethral injury, perform RUG 1st. If RUG is negative, can safely place Foley catheter.
- If catheter has already been placed, do not remove it. Perform pericatheter RUG with either a pediatric feeding tube or a small angiocatheter.
- Urethral injury is usually confirmed by:
  - Evidence of urinary extravasation on RUG or VCUG
  - Visual confirmation on cystoscopy of urethral disruption or injury

MEDICATION

- Analgesics
- Broad-spectrum antibiotics in all cases:
  - Ancef 1 gm IV q8h
  - Gentamicin 80 mg IV q8h or 24-hr dosing protocol with kinetic monitoring with piperacillin 3 mg IV q6h
  - Ciprofloxacin 400 mg IV q12h or 500 mg PO q12h

SURGERY/OTHER PROCEDURES

- If patient has sustained multiple injuries, stabilize the patient:
  - Unstable with pelvic fracture: Consider external fixation; if continues unstable, then angiography with embolization of arterial extravasation or emergent exploratory laparotomy with packing of pelvis.
  - Place suprapubic catheter
  - If stable patient, can place an aligning urethral catheter (may be performed up to 1 wk after trauma).
- Posterior urethral injury (see above)
- Anterior urethral injury: Usually urethral catheter will suffice:
  - When in doubt, place suprapubic catheter
  - Penetrating trauma: If low-velocity projectiles, immediate reconstruction is highly successful; if high-velocity projectile, immediate reconstruction less reliable because extent of blast effect unknown.
- Iatrogenic urethral injury: Place indwelling Foley for 7–10 days and then give trial of voiding.

ONGOING CARE

PROGNOSIS

- Posterior urethral injury: Prognosis varies, depending on extent of injury and any associated trauma

- Anterior urethral injury: Good prognosis after primary repair
- Iatrogenic urethral injury: Good prognosis if appropriately managed

COMPLICATIONS

- Urethral strictures
- Fistulas
- Incontinence
- ED

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Anterior urethral injury: Catheter is typically kept in place for 2–3 wk with follow-up RUG or VCUG.
- Posterior urethral injury:
  - After immediate urethral reconstruction, realignment or suprapubic tube placement is accomplished, urine should be diverted for 3–4 mo
  - At 3–4 mo, perform RUG or VCUG
  - If concerning, cystourethroscopy
  - If necessary, reconstructive or endoscopic procedures at 4–6 mo

ADDITIONAL READING

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- Koraitim MM. Pelvic fracture urethral injuries: The unresolved controversy. J Urol 1999;161(5):1433–1441.

See Also (Topic, Algorithm, Electronic Media Element)

- Penis, Trauma
- Urethra, Strictures, Male

CODES

ICD9

- 867.0 Injury to bladder and urethra without mention of open wound into cavity
- 867.1 Injury to bladder and urethra with open wound into cavity

ABBREVIATIONS

- BUN: Blood urea nitrogen

- CBC: Complete blood count
- CT: Computed tomography
- DRE: Digital rectal exam
- ED: Erectile dysfunction
- IV: Intravenous
- RUG: Retrograde urethrogram
- VCUG: Voiding cystourethrogram

URETHRITIS, GONOCOCCAL AND NONGONOCOCCAL

Costas D. Lallas, MD

BASICS

DESCRIPTION

- GU and NGU urethritis in men are STDs usually characterized by dysuria and associated with urethral discharge.
- Neisseria gonorrhoeae (gram-negative diplococci) on Gram stain or cultured differentiates GU from NGU.

EPIDEMIOLOGY

- Gonorrhea is the most common reportable disease in the US.
- Gonorrhea is most common in teenagers and in racial and ethnic minorities.
- Young men are prime candidates for contracting NGU.
- NGU more often affects men of higher economic status than does GU.

RISK FACTORS

- GU:
  - The risk of infection following a single episode of intercourse with an infected partner is ~17%.
  - Risk increases as the number of sexual contacts increases.
  - May also be transmitted through oral/anal sex with infected partner
- NGU:
  - Urethritis in homosexual males is more likely to be gonococcal than nongonococcal.

GENERAL PREVENTION

GU and NGU: Proper use of condoms, if multiple sexual partners

PATHOPHYSIOLOGY

- GU caused by N. gonorrhoeae
- NGU caused by several bacteria; most common:
  - Chlamydia trachomatis, recovered in 25–60% of heterosexual men with NGU
  - Mollicutes: Ureaplasma urealyticum, Mycoplasma hominis, and M. genitalium have been implicated in up to 40% of NGU cases.
  - Trichomonas vaginalis, HPV, and CMV have also been isolated in NGU.
- Both GU and NGU are STDs acquired during intercourse.
- The usual incubation period is 3–10 days for GU and 7–21 days for NGU.
- The urethra is the most common site of infection in all men.
- NGU occurs >50% of the time.

- C. trachomatis is cultured from the urethra in 4–35% of men with gonorrhea.

COMMONLY ASSOCIATED CONDITIONS

- Other STDs
- Urethral stricture

DIAGNOSIS

HISTORY

- GU:
  - Urethral discharge: Usually purulent, copious, and green, yellow, or white. Infrequently may be scant, watery, or absent.
  - Dysuria usually as mild to severe burning. May present as urethral itching and occasionally no symptoms other than urethral staining on underwear
  - Rarely presents with systemic symptoms
- NGU:
  - Urethral discharge: Usually mild to moderate, clear or whitish. On rare occasion may be thick and purulent. May be absent or only noted as stain on underwear
  - Dysuria: May present as mild burning or not present at all
  - Urethral itching may be the only complaint.
  - Rarely presents with systemic symptoms
- GU and NGU:
  - Relationship to sexual activity: When, type (vaginal, anal, oral)
  - 1st episode or recurrent
  - Number of sexual partners
  - Severity of symptoms (ie, burning, itching, frequency and urgency of urination)
  - Description of discharge: Scant or copious, purulent or clear; when noted (morning, constant, any time)
  - Symptoms relating to other body systems: GI, bronchopulmonary, musculoskeletal, cutaneous, neurologic
  - GU symptoms are usually more severe; urethral discharge is purulent and more copious than with NGU, which is often more scant and watery.

PHYSICAL EXAM

GU and NGU:

- Pendulous urethra may be tender to palpation
- Abdomen and flanks palpated for masses, tenderness, and bladder distention
- Scrotal contents examined for testicular and epididymal size, consistency, and tenderness

- DRE for prostatic size, consistency, and tenderness; a prostatic smear should be obtained.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - 15 polymorphonuclear leukocytes in HPF of spun sediment in the 1st-void urine specimen correlate with urethritis.
  - A positive leukocyte esterase dipstick test in the absence of urinary tract infection suggests urethritis.
  - NAAT: Can be performed on an intraurethral swab or urine specimen (less sensitive)
- GU:
  - Gram-stained urethral smear and plated culture (Thayer-Martin) obtained 1–4 hr after voiding
  - Calcium alginate swab inserted 2–4 cm into urethra used to obtain specimen
  - Leukocyte esterase urine dipstick test
  - Midstream urine analysis to rule out urinary tract infection
  - NAAT (swab or urine)
- NGU:
  - Same as above to rule out GU
  - Endourethral swab for C. trachomatis culture
  - NAAT (swab or urine)
  - Mollicutes will not grow in routine culture media and require specialized agar.

DIFFERENTIAL DIAGNOSIS

Reiter syndrome: Reactive urethritis associated with conjunctivitis, arthritis, and reactive tenosynovitis: No growth on culture, minimal number of leukocytes in urethral smear or urinalysis

TREATMENT

- GU:
  - Sexual intercourse should be avoided until cure.
  - Sexual partners should be evaluated and treated.
  - In GC, assume treatment for concomitant Chlamydia
- NGU:
  - Determine if syndrome is caused by different organisms that respond differently to treatment, and if results are inconsistent.

– Current recommendations from the CDC are based on chlamydial infection.

– Sexual intercourse should be avoided or condoms used until cure: Sexual partners should be evaluated and treated.

ALERT

Gram stain of urethral discharge is no longer considered essential for diagnosis since it rarely changes plan for antibiotic therapy.

MEDICATION

First Line

- GU:
  - Ceftriaxone 125 mg IM once; efficacious in 99% of uncomplicated cases
- NGU:
  - Azithromycin 1 gm PO once, or doxycycline 100 mg PO b.i.d. for 10–14 days

Second Line

- GU:
  - Ciprofloxacin 500 mg once
  - Ofloxacin 400 mg once
  - Cefixime 400 mg oral once
  - Spectinomycin 2 g IM once; can be used in pregnancy
- NGU:
  - Erythromycin 500 mg q.i.d. for 7 days
  - Ofloxacin 300 mg PO b.i.d. for 10–14 days

ADDITIONAL TREATMENT

- Patient education
- Patients should be instructed regarding the proper use of condoms.
- Having multiple sexual partners increases the risk: Patients should be instructed to inform sexual partners regarding evaluation and treatment.

ONGOING CARE

PROGNOSIS

- Generally good with treatment for both GU and NGU.
- Systemic manifestations of gonococcal dissemination are rare today and include arthritis, dermatitis, meningitis, and endocarditis.

COMPLICATIONS

- GU:
  - Periurethritis, which may lead to abscess
  - Urethral fibrosis, leading to stricture

- Epididymitis, which may lead to infertility or testicular atrophy
- Prostatitis, which may lead to abscess if untreated
- Systemic manifestations of gonococcal dissemination are rare.

• NGU:

- Emotional problems are common. Fear of loss of sexual function or guilt may produce depression.
- May result in epididymitis and/or nonbacterial prostatitis
- Usually does not cause severe physical complications in men

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- GU: Negative urethral smear and culture post-therapy
- NGU: Negative urethral smear and culture post-therapy

ADDITIONAL READING

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- Frenkel T, Potts J. Sexually transmitted diseases. In: Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007.
- www.cdc.gov/std/Gonorrhea/STDFact-gonorrea.htm

See Also (Topic, Algorithm, Electronic Media Element)

- Gonorrhea
- Sexually Transmitted Diseases (STD), General
- Urethra, Stricture, Male
- Urethra, Discharge
- Urethra Discharge Algorithm

CODES

ICD9

- 098.0 Gonococcal infection (acute) of lower genitourinary tract
- 099.40 Other nongonococcal urethritis, unspecified
- 099.41 Other nongonococcal urethritis, chlamydia trachomatis

ABBREVIATIONS

- CMV: Cytomegalovirus
- DRE: Digital rectal exam
- GC: Gonococcal chlamydia

- GU: Gonococcal urethritis
- HPF: High-power field
- HPV: Human papilloma virus
- NAAT: Nucleic acid amplification test
- NGU: Nongonococcal urethritis
- STD: Sexually transmitted disease

URGENCY, URINARY (FREQUENCY & URGENCY)

Timothy R. Yoost, MD

Gary W. Bong, MD

BASICS

DESCRIPTION

- Frequency is the complaint by the patient that he or she voids too often:
  - Typically, the patient will complain of voiding 5–6 times per day or >2 times per night.
- Urgency is the sudden impulse to void, which is difficult to defer.
- Uncontrolled voiding after this impulse is termed urge incontinence.

EPIDEMIOLOGY

- Not well known
- Female > Men (2:1) in US
- Estimated at >1 in 20 or 4.78% or 13 million people in US

RISK FACTORS

Depends on etiology (see Differential Diagnosis)

PATHOPHYSIOLOGY

- Frequency:
  - Increased urine output (polyuria)
  - Inflammation/irritation: Infection, malignancy, calculus, fistula, etc.
  - Bladder abnormalities: Nerve-mediated excitation of the detrusor muscle:
    Damage to the brain
    Damage to the spinal cord
    Damage to the sacral synapse
    Damage to peripheral nerves to the bladder
  - Muscle-mediated spontaneous contractions of the detrusor
  - Autonomous upregulation of localized modular contraction of the detrusor
- Adjacent pathology:
  - Pelvic masses, vaginitis, neurologic disease, etc.
- Urgency is usually a severe form of frequency.

COMMONLY ASSOCIATED CONDITIONS

- Interstitial cystitis
- UTI
- Frequency-urgency syndrome

DIAGNOSIS

HISTORY

- Irritative voiding symptoms:
  - Urgency, frequency, urge incontinence, nocturia
- Obstructive voiding symptoms
  - Hesitancy, slow stream, post-void dribbling, straining to void, retention
  - Consider causes of bladder outlet obstruction (eg, BPH, strictures, cancer)
- Incontinence (stress, urge, mixed, etc.):
  - Female stress incontinence may be related to pelvic prolapse.
- Symptoms of UTI or prostatitis
- Hematuria
- History of stone disease
- Fluid intake
- Change in bowel habits or sexual function:
  - May imply neurologic etiology
- History of gynecologic or GI problems
- Current medications
- History of tobacco use
- History of caffeine use
- Family history, particularly for bladder, prostate, or upper tract urothelial cancers

PHYSICAL EXAM

- Genital exam in men should include an evaluation for phimosis, meatal stenosis, or urethral scarring.
- DRE:
  - Prostate size, nodules, and estimation of PVR
  - Rectal masses, fecal impaction
  - Perineal sensation, anal sphincter tone, and bulbocavernosus reflex
- Pelvic exam for masses; pelvic floor support in females:
  - Fibroids, gynecologic cancers, pelvic floor relaxation, urethral lesions, urethral diverticula
  - Valsalva maneuver should be employed to detect stress urinary incontinence or pelvic floor prolapse.
- General exam for edema may explain nocturia
- Palpable abdominal masses:
  - Retention, fibroids, or uterine masses
- Neurologic:

- Mental status, cognitive defects
- Motor deficits
- Sensory deficits
- Reflexes, particularly bulbocavernosus, cremasteric, anal

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - Specific gravity: Poorly concentrated urine suggests polydipsia
  - Leukocyte esterase, nitrate, pyuria: Suggests UTI
  - RBCs: Suggests the need for a hematuria workup to rule out stone, tumor, etc.
  - Glucosuria: Rule out diabetes mellitus
  - Proteinuria: Suggests nephritis or nephrotic syndrome
- Urine culture should be obtained if a urinalysis suggests UTI.
- BUN and creatinine:
  - If neurogenic bladder, severe bladder obstruction, or retention is suspected

Imaging

- Renal US:
  - If neurogenic bladder is suspected, severe bladder outlet obstruction or retention
  - If renal insufficiency is found
- Pelvic US:
  - If adnexal mass or uterine enlargement is noted on pelvic exam
  - Estimate of PVR
- CT:
  - A triphasic CT urogram should be employed to rule out upper-tract TCC in the setting of hematuria
- Noncontrasted CT should be obtained to rule out stones when stones are suspected.

Diagnostic Procedures/Surgery

- Voiding diary:
  - Documents voiding pattern and incontinence
- Cystoscopy:
  - If hematuria, pyuria, or persistent/worsening symptoms
  - May detect bladder stones, bladder tumors, bladder outlet obstruction
- Urodynamics (CMG, EMG, uroflow, PVR, video urodynamics with fluoroscopy):
  - PVR is very important to rule out retention
  - Evaluates for neurogenic causes

- Evaluates for incontinence, bladder outlet obstruction
- Defines treatment options.

Pathological Findings

Based on specific etiology

ALERT

Careful evaluation is needed for UTI, cancer, stones with upper tract study and cystoscopy.

DIFFERENTIAL DIAGNOSIS

- Congenital/inherited:
  - Spina bifida and other neurologic malformations:
    Posterior urethral valves and other urologic malformations
- Traumatic:
  - Pelvic trauma: Bladder or urethral injury
  - Neurologic trauma: Bladder or spinal cord
  - Iatrogenic trauma: Surgical injury to the brain, spinal cord, pelvic nerves, bladder or urethra
  - Foreign body: Foley catheter, ureteral stents, etc.
- Inflammatory:
  - UTI: Most common cause of frequency/urgency. Also causes dysuria, fever, bacteriuria, and pyuria.
  - Specific infections: TB, schistosomiasis
  - Radiation cystitis: Pelvic irradiation for malignancy (cervical, prostate, etc.)
  - Urethritis: STD, usually from Chlamydia, gonorrhea, etc.; also causes dysuria and urethral discharge
  - Interstitial cystitis
- Metabolic
- Polyuria:
  - Excessive fluid intake
  - Diabetes mellitus, usually with glucosuria; poorly controlled or undiagnosed
  - Diabetes insipidus
- Urinary calculi: Bladder or intramural ureter
- Neoplastic:
  - BPH: Bladder outlet obstruction can induce urgency, frequency, nocturia, and obstructive symptoms
  - Prostate cancer: Also the mechanism is bladder outlet obstruction

  - Bladder cancer and CIS
  - Urethral cancer
  - Nonurologic cancers by local extension
  - Metastatic cancer, rare
- Miscellaneous
- Drugs:
  - Diuretics
  - Caffeine
  - Alcohol
- Neurologic:
  - Cerebral or brainstem
  - Spinal cord
  - Peripheral neuropathies
- GI
- Gynecologic

TREATMENT

Treatment is based on underlying disorder.

MEDICATION

ALERT

Anticholinergics are contraindicated in people with narrow-angle glaucoma.

First Line

- Anticholinergics are used to inhibit detrusor overactivity:
  - Oxybutynin 5 mg b.i.d.–t.i.d.
  - Oxybutynin XL 10–15 mg/d
  - Tolterodine 2–4 mg/d
  - Trospium XR 60 mg/d
  - Solifenacin 5–10 mg/d
  - Hyoscyamine XR 0.375 mg b.i.d.
  - Transdermal oxybutynin patch 3.9 mg/d
  - Fesoterodine 4–8 mg/d
- -Blockers decrease outflow obstruction due to BPH:
  - Terazosin (start 1 mg/d to max 20 mg)
  - Doxazosin (start 1 mg/d to max 8 mg)
  - Tamsulosin (start 0.4 mg/d to max 0.8 mg)
  - Alfuzosin (10 mg/d)

  - Silodosin (8 mg/d)

- 5-Reductase inhibitors block intracellular DHT conversion; generally best for larger glands, may take 6–12 mo for improvement:
  - Finasteride (5 mg/d)
  - Dutasteride (0.5 mg/d)

Second Line

Other agents are occasionally used: Imipramine, topical estrogens (in postmenopausal women)

SURGERY/OTHER PROCEDURES

- Correction of pelvic floor prolapse
- Correction of bladder outlet obstruction due to BPH
- If disabling and associated with incontinence: Bladder augmentation or urinary diversion
- Implantable neurostimulator device (InterStim®):
  - Mechanism not well understood
- Botox injection of the bladder submucosa:
  - Decreases frequency of bladder contractions
  - Not FDA approved

ADDITIONAL TREATMENT

- Behavioral treatment:
  - Bladder training involves suppressing urges to void and delaying voiding.
  - Timed voiding or prompted voiding involves scheduled voiding to preempt urgency.
- Kegel exercises to strengthen the pelvic floor musculature may improve stress urinary incontinence and inhibit urgency.
- Biofeedback involves using electronic measurements to assist patients in changing or inhibiting bladder behavior.

ONGOING CARE

PROGNOSIS

- 30% improvement in symptoms is generally seen with pharmacotherapy.
- Improvement of symptoms with surgery is excellent in properly selected patients.

COMPLICATIONS

Common side effects of pharmacotherapy include dry mouth and constipation.

Geriatric Considerations

Anticholinergics may cause decreased mentation in the elderly population.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Periodic follow-up depends on etiology, treatment, and response: Often consists of a voiding diary, uroflow, and PVR check.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Dysuria
- Incontinence, Urinary, Adult Male
- Interstitial Cystitis (IC)
- Incontinence, Urinary, Adult Female
- Neurogenic Bladder, General
- Overactive Bladder (OAB)
- Prostate, Benign Hyperplasia/Hypertrophy (BPH)

CODES

ICD9

- 788.31 Urge incontinence
- 788.41 Urinary frequency
- 788.63 Urgency of urination

ABBREVIATIONS

- BPH: Benign prostatic hyperplasia
- BUN: Blood urea nitrogen
- CIS: Carcinoma in situ
- CT: Computed tomography
- DHT: Dihydrotestosterone
- DRE: Digital rectal exam
- GI: Gastrointestinal
- IC: Interstitial cystitis
- OAB: Overactive bladder

- PVR: Post-void residual
- RBC: Red blood cell
- TCC: Transitional cell carcinoma
- US: Ultrasound
- UTI: Urinary tract infection

URINARY RETENTION, GENERAL

J. Nathaniel Hamilton, MD
Avi C. Weiss, MD

BASICS

DESCRIPTION

Inability to properly empty the urinary bladder. It can be further classified as acute or chronic.

- Acute: Sudden onset of the inability to void more than small volumes of urine; associated with an uncomfortable sensation and a distended bladder
- Chronic: Longstanding inability to completely void, with occasionally large PVRs, but not usually associated with discomfort:
  - Common symptoms include frequency, urgency, incontinence (overflow) and weak urinary stream

EPIDEMIOLOGY

- Incidence increases with age in males (~10% in men age 70).
- The incidence in females is less well recorded.
- Exact prevalence is difficult to estimate.

RISK FACTORS

- General: Diabetes, herpes zoster, drugs, psychogenic, neurologic disease, bladder stone, recent surgery (especially with epidural or spinal anesthesia), groin surgery such as hernia repair, prostate brachytherapy, trauma to pelvis, stroke
- Elderly men: BPH; prostate cancer; history of retention, urologic procedures, or instrumentation; medications, cysto-prostatitis; bladder cancer (rare cause)
- Women: Pelvic organ prolapse, urethral diverticulum, vulvovaginitis
- Medications:
  - Antihistamines
  - Anticholinergics: Atropine, belladonna, benztropine mesylate, cyclic antidepressants, phenothiazines, ipratropium bromide
  - Antispasmodics
  - Tricyclic antidepressants
  - -Agonists (induce bladder neck hypertonicity): Cold preparations, ephedrine derivatives, amphetamines
  - Narcotics
  - Detrusor muscle relaxants: Tolterodine, trospium, darifenacin, oxybutynin, solifenacin, hyoscyamine

- NSAIDs

Genetics

- BPH thought to be heritable in pattern consistent with AD pattern
- Increased risk of moderate to severe symptoms in men with + family history

GENERAL PREVENTION

- Treatment of bladder outlet obstruction in men with BPH:
  - Medications: -Blockers, 5-reductase inhibitors
  - Definitive therapy such as TURP, microwave hyperthermia, etc.
- Increased length of postoperative catheterization in patients at risk

PATHOPHYSIOLOGY

- Most commonly occurs in patients with pre-existing bladder outlet obstruction or with a known history of neurologic voiding dysfunction.
- Infection, bleeding, or overdistension is the usual precipitating event.
- Drainage of bladder results in prompt symptomatic relief.

COMMONLY ASSOCIATED CONDITIONS

- Diabetes
- Disease of prostate: BPH, prostate cancer, prostatitis
- Neurologic conditions: Neurogenic bladder, spinal cord damage/defect, demyelinating disorders
- UTI

DIAGNOSIS

HISTORY

- May suggest infection or BPH:
  - Symptoms of bladder outlet obstruction: Weak stream, hesitancy, incomplete voiding, dribbling
  - Symptoms of irritative voiding: Frequency, urgency, dysuria, nocturia
- Previous urinary retention
- Any urologic procedures or instrumentation suggests scarring, stricture, clot retention
- STD or strictures
- Medication use: See “Risk Factors”
- Pain: Bone pain and weight loss suggest prostate cancer.
- Recent gross hematuria suggests clot retention.
- Spinal cord injury or pelvic trauma
- Recent surgery, especially in those with spinal or epidural anesthesia
- Diabetes mellitus can cause bladder dysfunction in up to 50%.

PHYSICAL EXAM

- Palpable abdominal mass (bladder with >150 mL of urine should be palpable or percussible, depending on the size of the patient):
  - Assess for severe urgency and/or pain on suprapubic palpation.
- DRE:
  - Symmetrically enlarged prostate with BPH; nodularity suggests cancer; boggy, tender, warm prostate suggests prostatitis.
- Complete neurologic exam if suspicion for a neurologic etiology exists:
  - Anal tone (S2) and levator muscle tone (S3–S4) should be assessed.
  - Check sensation over the penis (S2), perianal area (S2–S3), outside of the foot (S2), sole of the foot (S2–S3), and large toe (S3).
  - When extremity findings do not parallel perineum findings (ie, absent sensation and tone in the feet but partial tone or sensation in the perineum), suspect spina bifida or meningomyelocele.
- Examine genitalia for rashes or lesions (herpes zoster flare).
- Female pelvic exam for prolapse

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Chemistry: BUN and creatinine may be elevated in retention if hydronephrosis is present:
  - With postrenal obstructive renal failure, increased postobstructive diuresis risk.
- Urine analysis and culture:
  - Leukocyte esterase or nitrite positivity with pyuria suggests infection.
  - Hematuria is suggestive of infection, tumor, or calculi.
- PSA is not usually checked acutely due to false positive with prostatitis, recent prostate surgery, etc.

Imaging

- Bedside bladder scan accurately shows PVR and is useful for diagnosis of acute and chronic urinary retention
- Formal renal and bladder US can be obtained if diagnosis is uncertain and can also show hydronephrosis and/or bladder wall thickening.
- Abdominal and pelvic CT: Can show bladder stones, prostate size, hydronephrosis, bladder thickening, obstructing masses, and foreign objects; frequently, findings of urinary retention are incidental on CT.
- Any history of pelvic trauma with new urinary retention should be evaluated with a retrograde urethrogram to rule out urethral injury.

Diagnostic Procedures/Surgery

- Placement of catheter for bladder drainage is diagnostic of retention and curative. Normal PVR is <30 mL but can vary.
- Cystoscopy for definitive diagnosis or acutely to place catheter
- Urodynamic studies (uroflowmetry, cystometrogram, electromyography, urethral pressure profile, pressure flow studies) usually not performed in the acute setting

DIFFERENTIAL DIAGNOSIS

Generally either bladder outlet obstruction or bladder dysfunction:

- Anatomic:
  - Penis: Phimosis, paraphimosis, meatal stenosis, foreign-body constriction
  - Urethra: Tumor, foreign body, calculus, urethritis, stricture, clot retention, meatal stenosis (female), diverticulum (female), hematoma
  - Prostate: BPH, prostate cancer, bladder neck contracture, prostatitis, prostatic infarction
  - Pelvic organ prolapse (cystocele, rectocele)
- Trauma: Urethral disruption
- Neurologic:
  - Motor paralytic: Spinal shock, spinal cord syndromes (eg, spina bifida, meningomyelocele)
  - Sensory paralytic: Tabes dorsalis, diabetes, multiple sclerosis, pernicious anemia
  - Syringomyelia, myasthenia gravis
  - Herpes zoster, poliovirus
  - Herniated disks
- Drugs (see “Risk Factors”)
- Miscellaneous: Vulvovaginitis

TREATMENT

- Acute retention: Catheterization for decompression.
  - In men with BPH, consider immediate -blocker therapy to improve likelihood of successful catheter removal.
  - Some consider SPT superior in the management of short term retention
- Chronic retention: Clean intermittent catheterization preferred over long-term indwelling catheter
- If standard Foley catheter placement is difficult (ie, 16F Foley), attempts can be made with different size/types of catheters. In older males, coudé catheters can help in large prostate.

• Workup for precipitating factors for urinary retention should be undertaken. Definitive management may involve medications, surgical intervention, or chronic catheterization strategies.

• Patient may require urodynamic study after acute events are resolved to establish diagnosis.

• Treatment should be directed toward cause, with goal of preventing future episodes.

• IVF as needed to correct dehydration or for postobstructive diuresis.

• Antibiotics as indicated for infection

• Decrease or stop medications that can contribute to voiding dysfunction if possible.

• Silver alloy–impregnated Foley catheters lower the rate of UTI.

MEDICATION

First Line

• Most medications are used for BPH

• -Blockers: Work to relax smooth muscle of bladder neck and prostate to improve urine flow

– Side effects include hypotension, syncope, floppy iris syndrome, retrograde ejaculation

– 1-Specific: Tamsulosin (0.4 mg PO q.h.s.) or alfuzosin (10 mg PO q.h.s.)

– 1-Nonspecific: Doxazosin (start 1 mg PO q.h.s. and increase to 8 mg PO q.h.s. max); terazosin (start 1 mg PO q.h.s. and increase to 20 mg PO q.h.s. max)

• 5-reductase inhibitors: Work by blocking conversion of testosterone to 5-dihydrotestosterone, which shrinks prostate over time and improves urine flow:

– Reduces long-term risk of retention, especially when combined with -blockers.

– Dutasteride (0.5 mg/d PO); finasteride (5 mg/d PO)

– Side effects: Decreased libido, decreased ejaculate volume, impotence, gynecomastia

Second Line

Bethanechol (10–50 mg PO t.i.d.–q.i.d.):

• Direct cholinergic stimulant; increases detrusor tone (infrequently used)

• Many side effects: Diarrhea, nausea, bronchospasm, hypotension, tachycardia, seizure

SURGERY/OTHER PROCEDURES

• If catheter placement fails, bedside or intraoperative cystoscopy can be performed:

– Cystoscopy is usually diagnostic and can show urethral stricture, false passages, bladder neck contractures and obstructing prostate tissue.

– Once bladder is entered under direct vision, a wire can be placed and dilations, if necessary, can be carried out. The wire can then be used to allow passage of Council tip

catheter.

- If cystoscopy is unsuccessful, consider SPT placement
  - Open SPT preferable in patients with history of multiple surgeries
  - If no prior surgery, place SPT via various percutaneous approaches (requires 200–300 mL of urine in bladder or bladder US guidance):

    Rousch or Stamey kit
- For definitive surgery specific to outlet obstruction urinary retention due to BPH see Section I: “Bladder Outlet Obstruction (BOO).”

ADDITIONAL TREATMENT

- Chronic retention can be managed with clean intermittent catheterization.
- Surgery for BPH, if a factor, can often be beneficial.

ONGOING CARE

PROGNOSIS

- >30% 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 major hemorrhage secondary to bladder mucosal disruption and tearing of bladder vessels or postobstructive diuresis.
- Significant hypotension may occur secondary to a vaso-vagal response.
- Longstanding uncorrected urinary retention can lead to reflux nephropathy and permanent bladder dysfunction.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Monitoring and fluid replacement for postobstructive diuresis (>200 mL/h), especially after chronic or prolonged retention and when BUN and creatinine are significantly elevated
- Patients with signs of infection or decreased renal function should be admitted and observed.

ADDITIONAL READING

- Curtis LA, Dolan TS, Cespedes RD. Acute urinary retention and urinary incontinence. Emerg Med Clin N Am 2001;19(3):591–620.
- Edwards JL. Diagnosis and management of benign prostatic hyperplasia. Am Fam Physician 2008;77(10):1403–1410.
- Kaplan SA, Wein AJ, Staskin DR, et al. Urinary retention and post-void residual urine in men: Separating truth from tradition. J Urol 2008;180(1):47–54.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Neck Contracture
- Bladder Outlet Obstruction
- Foley Catheter Problems
- Lower Urinary Tract Symptoms (LUTS)
- Prostate Cancer
- Prostatitis
- Suprapubic Pain
- Urethra Trauma
- Urethra, Stricture
- Urinary Retention Following Brachytherapy
- Urinary Retention, Male Algorithm
- Urinary Retention, Postoperative

CODES

ICD9

- 788.20 Retention of urine, unspecified
- 788.21 Incomplete bladder emptying
- 788.29 Other specified retention of urine

ABBREVIATIONS

- AD: Autosomal dominant
- BOO: Bladder outlet obstruction
- BPH: Benign prostate hypertrophy
- BUN: Blood urea nitrogen
- CT: Computed tomography
- DRE: Digital rectal exam
- NSAID: Nonsteroidal anti-inflammatory drug
- PSA: Prostate-specific antigen
- PVR: Postvoid residual
- SPT: Suprapubic tube
- STD: Sexually transmitted disease
- TURP: Transurethral resection of the prostate
- UTI: Urinary tract infection

URINARY TRACT INFECTION (UTI), ADULT FEMALE

Arun K. Srinivasan, MD

Robert M. Moldwin, MD

BASICS

DESCRIPTION

- Symptomatic urothelial inflammation due to microbial invasion; characterized by bacteriuria and pyuria
- Bacteriuria: The presence of bacteria in the urine, which is normally free of bacteria. In the absence of pyuria, bacteriuria indicates colonization or contamination.
- Most UTIs in adult females are uncomplicated.
- Complicated UTI: UTI in women with anatomical urinary tract abnormalities, immunocompromised, elderly, indwelling catheter, diabetes, recurrent UTI or resistant organism, recent instrumentation, hospital-acquired infection, and symptoms >7 days at presentation

EPIDEMIOLOGY

- Considered the most common bacterial infection, it accounts for nearly 7 million office visits, 1 million ER visits, and 100,000 hospital admissions annually
- Bacteriuria is 3.5%; increases from 1% in school-aged girls to 4% in young adulthood and then by an additional 2% for every decade of life
- Increased prevalence in hospitalized and institutionalized women

RISK FACTORS

- Age, postmenopausal, instrumentation, immunocompromised states, indwelling catheter, fecal soiling of perineum
- In young, sexually active women, associated with recent sexual intercourse, delayed postcoital voiding, recurrent UTI, and use of diaphragm with spermicide as method of contraception
- Anatomic urinary tract anomalies: Urinary obstruction, presence of calculi, vesicoureteral reflux, cystocele, bladder diverticula

Genetics

Increased bacterial adherence resulting in increased susceptibility to UTI in women with HLA-A3 and non-secretor Lewis antigen

GENERAL PREVENTION

- Hygiene, postcoital voiding, hydration, good glycemic control; treat underlying immunocompromised state when possible
- Antibiotic prophylaxis in patients with structural urinary tract anomalies, pregnancy (history of recurrent UTI)

PATHOPHYSIOLOGY

- Patterns of UTI:
  - Isolated infection: 1st UTI or UTI occurring at least 6 mo after a previous infection
  - Unresolved UTI: Failure of the initial treatment course to eradicate bacteria from the urine, usually due to preexisting or acquired antimicrobial resistance, noncompliance, or insufficient antibiotic dosing, or from disorders that decrease drug bioavailability (ie, azotemia, urinary calculus)
  - Reinfection: Most common cause of recurrent UTIs. Following resolution of a UTI, a new infection with a different organism ascending from rectum to vagina
  - Bacterial persistence: Recurrent UTI following sterilization of the urine and resolution of a prior UTI, caused by the same bacteria as the preceding infection, usually arising from an underlying abnormality (ie, renal stone). Relapse is often used interchangeably.
- Urinary pathogens:
  - Community-acquired UTI: Escherichia coli most common (85%); also Proteus, Klebsiella, Enterococcus faecalis, and Staphylococcus saprophyticus (young females)
  - Nosocomial UTI: E. coli most common (50%), also Enterococcus, Klebsiella, Citrobacter, Serratia, Pseudomonas, and Providencia.
- Routes of infection:
  - Ascending route: Most common in normal females; fecal flora from perianal area into bladder
  - Hematogenous route: Uncommon, occurs in Staphylococcus bacteremia or candidal fungemia
- Bacterial virulence vs. host resistance:
  - Increased bacterial virulence in E. coli strains with hemolysin to serologic 0 groups (01, 04, 06, 018, and 075), K antigens, and certain types of surface adhesin molecules
  - >90% of E. coli responsible for pyelonephritis express P fimbriae:

    Type 1 (mannose-sensitive) fimbriated E. coli cause most cases of bacterial cystitis.

    Increased epithelial cell receptivity for E. coli in patients with HLA-A3 antigen expressions, Lewis blood group Le (a+b) (nonsecretor) phenotypes

    Increased binding of E. coli to vaginal fluid at alkaline pH (postmenopausal conditions)
  - In premenopausal woman, estrogen promotes vaginal Lactobacillus colonization that lowers vaginal pH and inhibits adherence of bacteria by competing for receptor sites.
  - In postmenopausal women, loss of estrogen is associated with increased bacterial adherence.

Pregnancy Considerations

UTI/Pyelonephritis in pregnancy might be complicated by premature delivery and pregnancy loss and hence is always a complicated UTI. It should be managed aggressively with antibiotics and hydration.

COMMONLY ASSOCIATED CONDITIONS

- Postmenopausal
- Diabetes
- Nephrolithiasis
- Structural urinary tract anomalies

DIAGNOSIS

HISTORY

- Typical symptoms of bacterial cystitis: Urinary frequency, urgency, dysuria, small-volume voiding, nocturia, or suprapubic pain or pressure
- Atypical symptoms (fever, flank pain, and chills) may indicate acute pyelonephritis.
- Vaginal discharge, foul vaginal odor, and pruritus suggest vaginitis or urethritis.
- Gross or microhematuria that does not resolve may be due to tumor or stones.
- Assess risk factors for UTI:
  - Correctable factors that facilitate bacterial ascent into the bladder
  - Anatomic or functional urinary tract abnormalities that may be complicating factors
- Community-dwelling or institutionalized:
  - Different pathogens involved in nosocomial than in community-acquired UTI
- Frequency of UTIs:
  - >2 UTIs in a 12-mo period should raise suspicion of structural or functional urinary tract abnormality, relapsing infection, or reinfection.
  - Treatment and treatment results:

    Determine if the infection was treated appropriately, if the infection responded appropriately, if the infection is likely to respond to or be resistant to a particular empiric antibiotic.
  - Determine if the patient was therapy compliant.
- Previous urine culture results:
  - Establish infection pattern; patient may have a relapse with the same organism (bacterial persistence) or reinfection with different organism.
- Medical/surgical history, including childhood UTIs and current medications:
  - Identify any complicating structural or functional urinary tract abnormalities or immuno-compromising factors.

– Determine if the patient has had a recent hospitalization that might have led to infection with nosocomial rather than community organisms.

– The patient may have had recent urinary tract catheterization or instrumentation, which may have led to a UTI.

- Gynecologic history, including STDs:

– Loss of estrogen in postmenopausal associated with increased bacterial adherence in the vagina.

– A history of STDs: Rule out urethritis or vaginitis in patients with appropriate symptoms.

PHYSICAL EXAM

- Bladder distention/suprapubic tenderness indicates urinary retention, which may promote UTIs due to urinary stasis.
- Urosepsis with profound hemodynamic instability must be looked for and appropriately treated in a monitored setting.
- Flank tenderness suggests pyelonephritis or possible upper tract obstruction.
- Abdominal tenderness and peritoneal signs may indicate other intraabdominal pathology.
- Pelvic exam:

– Vaginal/urethral discharge may be present in patients with vaginitis or urethritis.

– Vaginal mucosal atrophy may reflect estrogen status in perimenopausal women.

– An anterior vaginal wall mass with purulent urethral discharge expressed during palpation can be seen with urethral diverticulum.

– A large cystocele should raise a suspicion of incomplete voiding and urinary stasis.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:

– Dipstick: Leukocyte esterase (50% positive predictive value, 92% negative predictive value), nitrate (sensitivity 35%–85%), false-negatives common in setting of low dietary nitrate, diuretics, and infections with Staphylococcus, Enterococcus, Pseudomonas

– Microscopy (if positive dipstick): Pyuria 10 WBCs/L urine, bacteriuria 1 organism per oil immersion field of uncentrifuged urine correlates with 105 CFU/mL (90% sensitivity/specificity). Bacterial counts >30,000/mL for detection.

- Urine culture:

– Gold standard: 105 CFU/mL urine; however, this limit excludes 30–50% of women with classic symptoms of acute bacterial cystitis. Treatment indicated if 102 CFU/mL in a symptomatic patient, particularly if with pyuria

– Obtain prior to treatment if atypical symptoms (suspected pyelonephritis), negative pyuria/hematuria/bacteriuria on urinalysis, recent antibiotic use, symptom duration >7 days, age >65, diabetes, pregnant, immunosuppressed, recent urinary tract instrumentation, indwelling catheter

Imaging

- Only for cases of suspected complicated UTI
- Indications: Persistent fever after 72 hr of treatment, Proteus in culture with urine pH 8.0 (struvite calculi), bacterial persistence, unexplained hematuria, suspected upper tract obstruction, history of calculi, neurogenic bladder dysfunction, analgesic abuse, diabetes
- Renal US: Most appropriate initial study to rule out suspected hydronephrosis, abscess, bladder or renal stones
- Noncontrast spiral CT: Alternative screening study when IV contrast contraindicated (best for stones)
- CT ± IV contrast: Further evaluation of suspected acute focal bacterial nephritis or renal abscess, renal mass, or radiolucent renal calculus
- VCUG: Used to detect vesicoureteral reflux in patients with a history of reflux or neurogenic bladder, or to evaluate the uncommon patient with a urethral diverticulum

Diagnostic Procedures/Surgery

- Cystoscopy: If urine cultures grow unusual organisms, persistent bacteriuria, or hematuria in the absence of infection
- Urodynamic testing: Indicated for urinary retention, voiding difficulty with history of diabetes, or neurologic disease

Pathological Findings

Generalized nonspecific inflammation of the urinary bladder; may reveal bacteria in the submucosal layer of the bladder wall

DIFFERENTIAL DIAGNOSIS

- Bladder tumor: Older patients with hematuria, urgency/frequency; standard evaluation includes urine cytology, cystoscopy, upper tract imaging
- Bladder calculus: Usually associated with urinary stasis
- Vaginitis: Characterized by pruritus, vaginal discharge/odor, dyspareunia
- Urethritis: Urethral discharge, dysuria, pruritus, initial hematuria, history of STD risk factors or urethral instrumentation:
  – Culture of initial 10 mL of voided urine and urethral swab may show pyuria and causative organism.
- Interstitial cystitis: Chronic urgency, frequency, and pain with bladder filling, which decreased in severity after voiding:

– Diagnosis of exclusion

– Have decreased bladder capacity, glomerulations, or Hunner ulcer on cystoscopy.

TREATMENT

Pregnancy Considerations

- UTI during pregnancy poses significant risk to fetus and mother (prematurity, premature labor, others)
- Ampicillin, amoxicillin, and oral cephalosporins safe
- Amoxicillin/clavulanic acid (Augmentin) for resistant organisms
- Nitrofurantoin is safe for the fetus but potentially toxic to the mother
- Fluoroquinolones should be avoided in pregnancy.
- Hydration
- Treat obstructive or functional pathology
- Counsel patient regarding prevention strategies

MEDICATION

First Line

- Outpatient oral antibiotic treatment with nitrofurantoin, trimethoprim-sulfamethoxazole, fluoroquinolones, as appropriate (see “Section I: Cystitis, General”)
- In recurrent UTI, it may be appropriate to have patients start the 1st dose of antibiotics at home.

Second Line

- If unresponsive or if patient is systemically unwell with signs of sepsis, use IV antibiotics:
  – Broad-spectrum antibiotics like 3rd-generation cephalosporins or extended spectrum penicillins (see “Section I: Pyelonephritis, Acute”)
- Urinary tract imaging
- In postmenopausal women, estrogen replacement—local or systemic—has been shown to decrease the rate of recurrent UTI.

SURGERY/OTHER PROCEDURES

- Rarely indicated acutely:
  – Urinary tract obstruction with urosepsis is a surgical emergency and requires drainage of the obstructed system
- If patient has emphysematous pyelonephritis or pyonephrosis, may need nephrectomy to prevent worsening sepsis

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Cranberry juice: Meta-analysis of randomized trials shows decrease incidence of UTI particularly in women with recurrent UTI. Optimal dose guidelines still not available

ONGOING CARE

PROGNOSIS

Usually good but might have recurrent problems

COMPLICATIONS

Urosepsis, pyonephrosis, emphysematous cystitis, emphysematous pyelonephritis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

Routine urine cultures not recommended

ADDITIONAL READING

- Foxman B, et al. Urinary tract infection: Self-reported incidence and associated costs. Ann Epidemiol 2000;10:509–515.
- Hooton TM. Current management strategies for community acquired urinary tract infection. Infect Dis Clin N Am 2004;17(2):303–332.
- Hooton TM, Scholes D, Hughes JP. A prospective study of risk factors for symptomatic urinary tract infection in women. N Engl J Med 1996;335:468–474.
- Infectious Diseases Society of America guidelines on management of UTI 2007. Available at www.idsociety.org/Content.aspx?id=9088.

See Also (Topic, Algorithm, Electronic Media Element)

- Cystitis, General
- Pregnancy, Bacteruria, Pyuria, and UTI
- Pyelonephritis

CODES

ICD9

- 041.3 Friedlander’s bacillus infection in conditions classified elsewhere and of unspecified site
- 041.4 Escherichia coli (E. coli) infection in conditions classified elsewhere and of unspecified site
- 599.0 Urinary tract infection, site not specified

ABBREVIATIONS

- CFU: Colony forming units
- CT: Computed tomography
- IV: Intravenous
- STD: Sexually transmitted disease
- US: Ultrasound
- UTI: Urinary tract infection

- VCUG: Voiding cystourethrogram
- WBC: White blood cell

URINARY TRACT INFECTION (UTI), ADULT MALE

Anthony John Schaeffer, MD
Trinity J. Bivalacqua, MD

BASICS

DESCRIPTION

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- Defined by source of infection:
  - Cystitis: Infection of bladder; dysuria, frequency, urgency, suprapubic pain, hematuria.

    Isolated cystitis in men rare, usually associated with prostatitis or pyelonephritis
  - Pyelonephritis: Infection of kidney; chills, fever, flank pain ± 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 reinfection in a healthy young male with normal urinary tract; urethritis or prostatitis
  - Complicated: Infection associated with:

    Structurally abnormal urinary tract (eg, bladder outlet obstruction/BPH), or

    Functionally abnormal urinary tract (eg, neurogenic bladder)

    Impaired host defense (eg, immunosuppression/diabetes)

    Increased bacterial virulence

    Most UTIs in men are complicated.
- Defined based on chronicity:
  - Unresolved: 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

    Reinfection: A recurrent UTI from reintroduction of bacteria into previously sterilized urine

    Bacterial persistence: A recurrent UTI due to a source of bacterial colonization (eg, infected stone, prostate, or foreign body)
- Other definitions (and suggested therapies):
  - Emphysematous cystitis/emphysematous pyelonephritis: Complicated UTIs associated with gas in bladder wall or renal parenchyma; typically found in diabetic population; associated with gas-forming organisms and obstruction (in pyelonephritis); treated with parenteral antimicrobials; pyelonephritis may require nephrectomy

– Xanthogranulomatous pyelonephritis:

Chronic renal infection associated with obstruction, nephrolithiasis; massively enlarged, nonfunctioning kidney; presenting signs of flank pain, fever, and persistent bacteriuria

– Asymptomatic bacteriuria in men:

102 CFU/mL of single organism from catheterized specimen or 105 CFU/mL from single clean catch in men without symptoms of UTI

)[C]

Prophylaxis in those at risk (ie, spinal cord injury or other cause for indwelling catheter) is not recommended; treat only when symptomatic.

EPIDEMIOLOGY

- Increases with age

)[C]

- The prevalence of symptomatic UTI in men increases with age to >10% in men >65
- Asymptomatic bacteriuria in elderly men approaches 60–80%

RISK FACTORS

Risk factors for complicated UTI:

- Male gender
- Elderly
- Diseases: Diabetes mellitus; recent UTI immunosuppression; chronic steroids
- Recent antimicrobial use
- Indwelling urinary catheter
- Recent urologic intervention or hospital infection
- Urinary tract obstruction (eg, BPH, urethral stricture disease); urinary stasis
- Urinary calculi
- Uncircumcised
- Spinal cord injury
- Unprotected anal intercourse
- History of childhood UTI

Genetics

Certain individuals (including those with HLA-A3) prone to recurrent UTIs have increased epithelial cell receptivity for uropathogenic Escherichia coli.

GENERAL PREVENTION

- Safe sex practices; avoidance of unprotected anal insertive intercourse
- See “Complimentary & Alternative Medicine.”

PATHOPHYSIOLOGY

):

– Ascending: Via inoculation of urethra/urethral catheter with bowel flora: Most common

– Hematogenous seeding of kidney

– Lymphatic spread

• Males are more resistant to UTI than females due to longer urethra, antibacterial nature of prostatic fluid, drier periurethral environment.

• UTIs occur as a result of interaction between host defense mechanisms and bacterial virulence:

– Inherent host defense mechanisms:

Urinary flow helps to decrease retrograde infection; conversely, residual urine/obstruction increases risk of infection

Urine: Urea, pH, organic acids help prevent growth; glucose provides environment conducive for bacterial growth and increases risk of infection

Bladder: 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 (mediate attachment to cells); pyelonephritis bacteria contain P pili

• Common community-acquired uropathogens: E. coli (most common), Proteus, Klebsiella pneumonia, Enterococcus faecalis, Staphylococcus saprophyticus

• Common nosocomial uropathogens include: E. coli, Klebsiella, Enterobacter, Citrobacter, Serratia, Pseudomonas, Enterococcus faecalis, Providencia, S. epidermidis

COMMONLY ASSOCIATED CONDITIONS

See "Risk Factors."

DIAGNOSIS

HISTORY

• Assess for any of risk factors listed above.

• For 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.

PHYSICAL EXAM

• Obtain vital signs to assess severity of infection, presence of systemic disease.

• Assess for suprapubic pain, flank pain, urethral discharge rectal exam for tenderness

• Uncircumcised: May increase risk of infection

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis: Quality of specimen grossly assessed by presence (poor) or absence (good) of squamous cells
- Microscopic analysis for bacteria: False-positive from foreskin contamination if poor-quality specimen; false-negative if 102–104 bacteria/mL (too few to be seen under slide)
- Dipstick:
  - WBC must be present for infection but WBC without bacteriuria may be present with renal stones, indwelling stent, tuberculous infection
  - Nitrite: Bacterial reduction of nitrate in urine
  - Leukocyte esterase: Presence of WBC
  - Sensitivity of nitrite and leukocyte esterase positivity varies greatly; does not replace microscopic analysis for bacteria
- Culture:
  - Midstream clean catch: Reduce bacterial contamination of culture in uncircumcised men by retracting foreskin and cleansing
  - 102–103 CFU/mL in dysuric male with pyuria is indicative of infection (clean catch).
- For lower UTI, consider localization studies (see Section I: “Prostatitis, General”).

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 (ie, persistence), when obstruction suspected
- CT urogram or MRI: Provide excellent detail, evidence of urinary tract abnormalities, stones, or foreign bodies, among others

Diagnostic Procedures/Surgery

- Cystoscopy: Same indications as listed under “Imaging”; allows direct visualization of bladder to assess for foreign body, ectopic ureters, diverticula, stones, or other abnormalities
- PVR: Should be considered in men with BPH, voiding dysfunction; high residual with stasis increases risk of infection
- Localization studies: Selective cultures from each kidney via ureteral catheterization and prostatic cultures are helpful in identifying source of bacterial persistence.

DIFFERENTIAL DIAGNOSIS

- Prostatitis:
  - NIH Class I: Acute bacterial prostatitis, sudden onset

– NIH Class II: Chronic bacterial prostatitis; insidious onset, relapsing, recurrent UTI

– NIH Class III: CP/CPPS

IIIA: Inflammatory: Inflammatory cells in prostatic secretion, seminal fluid, post-prostatic massage urine

IIIB: Noninflammatory: Insignificant inflammatory cells

• For cystitis: Interstitial cystitis vs. urethritis

• For pyelonephritis: Pancreatitis vs. appendicitis vs. diverticulitis vs. acute focal/multifocal nephritis

TREATMENT

• See Section I: “Prostatitis, General”

• If severe infection or toxicity is present, CT should be obtained to rule out obstructive pyelonephritis; if found, decompression is critical.

MEDICATION

):

– Trimethoprim-sulfamethoxazole: Inexpensive, covers staphylococci, streptococci, and most gram-negatives except

Pseudomonas

– Fluoroquinolones: More expensive (levofloxacin > ciprofloxacin), cover staphylococci and most gram-negatives including Pseudomonas

• Commonly parenteral antimicrobials:

– Ampicillin: Covers streptococci, enterococci, E. coli, Proteus; addition of -lactamase inhibitor covers Klebsiella and Haemophilus; no pseudomonal coverage; good 1st-line IV drug

– Gentamicin: Staphylococci, most gram-negatives including Pseudomonas; augments ampicillin for coverage in pyelonephritis

)[C]:

– Take into account local resistance profiles

– No controlled trials, recommendations are limited; oral antimicrobials are based on local resistance patterns, previous culture sensitivity (if possible)

– 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.

)[C]:

– For men, pyelonephritis is a complicated UTI and outpatient therapy is initiated only after treatment of complicating factors is initiated.

– Renal/perirenal abscess is suspected if indolent/recurrent fever >72 hr 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

– Outpatient therapy:

Fluoroquinolone (7 days) is more effective than trimethoprim-sulfamethoxazole (14 days)

Tailor antimicrobial to culture sensitivities.

If no improvement, use IV therapy

– Inpatient therapy:

)[C]

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

SURGERY/OTHER PROCEDURES

As needed for cause of recurrent UTI, such as stone, foreign body, or enlarged prostate

COMPLEMENTARY AND ALTERNATIVE MEDICINE

)[B]

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.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

See recommended repeat culture time points listed above

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See Also (Topic, Algorithm, Electronic Media Element)

- Prostatitis, Acute, Bacterial (NIH 1)
- Prostatitis, Chronic, Nonbacterial, Noninflammatory (NIH CP/CPPS III B)
- Prostatitis, Chronic, Bacterial, (NIH II)
- Prostatitis, Chronic, Nonbacterial, Inflammatory (NIH CP/CPPS III A)
- Prostatitis, General
- Pyelonephritis
- Urethritis, Acute Male
- Urinary Tract Infection (UTI), Pediatric

CODES

ICD9

- 041.4 Escherichia coli (E. coli) infection in conditions classified elsewhere and of unspecified site
- 595.9 Cystitis, unspecified
- 599.0 Urinary tract infection, site not specified

ABBREVIATIONS

- BPH: Benign prostatic hyperplasia
- CFU: Colony-forming units
- CP/CPPS: Chronic prostatitis/chronic pelvic pain syndrome
- CT: Computed tomography
- IV: Intravenous
- MRI: Magnetic resonance imaging
- PO: By mouth
- PVR: Post-void residual
- UTI: Urinary tract infection
- WBC: White blood cell

URINARY TRACT INFECTION (UTI), PEDIATRIC

Timothy J. LeRoy, MD

Michael J. Erhard, MD

BASICS

DESCRIPTION

- Inflammatory changes in the urinary tract caused by the presence of an invasive infections agent
- Spectrum of severity, from local infection to urosepsis

EPIDEMIOLOGY

- Males <1 yr are 2.5–4 times more likely to have a UTI
- After 6 mo of age, females are up to 20 times more likely to have a UTI
- 0.7% of all pediatric office visits each year
- Overall 5–9% of febrile infants:
  - Comparing infants
  - Uncircumcised males (21.3%)
  - Females (5.0%)
  - Circumcised males (2.3%)
  - White children have a 2–4 times higher risk than black children.
- Prevalence is more variable and closer to an adult level as age groups increase.

RISK FACTORS

- Previous UTI:
  - ~25% 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 and steroid use
- Anatomic abnormalities of the urinary tract:
  - Vesicoureteral reflux, ureterocele, ureteropelvic junction obstruction, bladder diverticula, posterior urethral valves, etc.
- Functional abnormalities of the urinary tract:
  - Neurogenic bladder, dysfunctional voiding/elimination behaviors, etc.
- Urologic instrumentation (catheters)
- Older children: Sexual activity
- Circumcision:
  - Uncircumcised males <1 yr of age have the highest rate of UTI of all gender and age groups.
  - This is also a 10-fold greater risk than those males who are circumcised.

– The protective benefit of circumcision is thought to decrease after 1 yr.

Genetics

- Incompletely understood
- Multifactorial including expression of uropathogen receptors to P fimbriae

GENERAL PREVENTION

- Good voiding/eliminating habits
- Treatment of constipation
- Treatment of underlying urologic conditions

PATHOPHYSIOLOGY

- The most common pathogen is Escherichia coli (~85%).
- Other uropathogens include Klebsiella, Proteus, Enterobacter, Citrobacter, Staphylococcus saprophyticus, and Enterococcus.
- Intestinal flora colonization of the female introitus and male preputial epithelium often serve as a nidus for infection.
- Both humoral and cellular responses result in inflammation of the urinary tract, peaking 2–5 days from initiation of infection.
- Terminal fimbria (bacterial surface adhesion molecules) adheres to uroepithelial cell surfaces and interstitium to promote bacterial colonization.
- P-fimbria on E. coli contributes to bacterial ascent to the upper tracts even in the absence of reflux.
- 40% of children with 1st febrile UTI will have VUR on VCUG.

DIAGNOSIS

HISTORY

- Vague in infants and nonverbal children:
  – Symptoms: Fever, irritability, poor feeding, vomiting, diarrhea, abdominal distention, new onset incontinence, jaundice.
- Older children may complain of dysuria, incontinence, voiding dysfunction, lower abdominal pain, enuresis, etc.
- Presence and severity of fever
- Previous UTIs and how documented (urine analysis, culture, etc).
- Prenatal history including ultrasounds
- Previous GU/GI surgery
- Family history of infections and/or GU anomalies

PHYSICAL EXAM

- Infrequently, any specific findings in infants

• Older children may have suprapubic, flank, abdominal and/or upper quadrant tenderness.

• CVA tenderness points to pyelonephritis.

• A scrotal exam will help rule out epididymitis.

• Careful external genital exam to rule out trauma, local irritation, discharge, foreign body, and anatomic abnormalities

• Circumcised patient

• Palpable renal mass (can manifest severe hydronephrosis) and/or a palpable bladder

DIAGNOSTIC TESTS & INTERPRETATION

Lab

)[A]:

– Microscopic exam after dipstick urine analysis increases the test's sensitivity and specificity. It can also yield clues to contamination (epithelial cells), or WBC/RBC casts (indicative of renal involvement).

– Positive leukocyte esterase (manifests WBCs in the urine) is about 75% sensitive and specific.

– Positive nitrite (many gram-negative bacteria produce this substance) has a sensitivity of 30–45%, but a specificity that nears 100%.

– Combined positive nitrite-leukocyte esterase 80–90% sensitive and 60–98% specific

– >10 WBCs per HPF on an unspun specimen or >5 WBCs on a spun sediment is usually indicative of infection.

– Bacteria seen on Gram stain has a sensitivity and specificity better than that of a dipstick evaluation for nitrite and leukocyte esterase.

)[A]:

– >100,000 CFU/mL for a voided specimen, and >10,000 CFU/mL for a suprapubic aspirate cath specimens defines a clinical infection.

– In febrile children <2 yr, >50,000 CFU/mL is also consistent with a clinical UTI.

– Depending on the patient's presentation, lower numbers may also be significant.

– The method of collection is vital for accuracy:

From most to least accurate: Suprapubic aspirate (rarely performed), catheterized urine, midstream voiding samples from older females and circumcised males, and bag collection specimens in infants (multiple organisms suspicious for contamination and should be confirmed with a catheterized specimen)

• Blood tests are unreliable to delineate clinical urinary infection.

Imaging

)[B]; however, it may be indicated at follow-up or for a febrile UTI:

– 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.

– Abdominal US and VCUG at a convenient time.

)[A]

)[B]

)[C]

Diagnostic Procedures/Surgery

None specific, although cystoscopy may be performed for associated conditions or chronic infections as indicated

DIFFERENTIAL DIAGNOSIS

- UTIs present similarly to other infections:
  - Bacteremia and sepsis
  - Epididymitis
  - Gastroenteritis
  - Pinworms
  - Sexual abuse
  - STD in a sexually active child
  - Vaginitis
- Also consider:
  - Appendicitis
  - Diabetes
  - Dysfunctional voiding/elimination behaviors
  - Pregnancy in postpubertal females
  - Urolithiasis
  - Urinary obstruction

ALERT

Findings suggestive of an STD infection in a child should raise concern for sexual abuse.

TREATMENT

- 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 mo and nontoxic children with suspected pyelonephritis can be treated as outpatients as long as compliance is not an issue.

• There is much debate to the role of antibiotic prophylaxis in promoting resistant bacteria that must be weighed in this clinical decision.

• Children with asymptomatic bacteriuria may not require treatment with antibiotics if their urinary system is otherwise normal.

MEDICATION

ALERT

Fluoroquinolones should not be a 1st-line choice and are limited to resistant organisms.

First Line

• Infants <2 mos (IV therapy):

– Ampicillin 50–100 mg/kg/d divided dose q6h; maximum PO dose: 2–3 g/d

)[A]

)[A]

• Children >2 mo:

)[A]:

Cefixime 8–16 mg/kg/d PO divided q12–24h; 400 mg/d maximum

Cefdinir 14 mg/kg/d PO divided in 2 doses; 600 mg/d maximum

Ceftibuten 9 mg/kg/d PO in single dose; 400 mg/d maximum

• Children <2 yr of age should be treated with therapeutic doses (IM, IV, PO, or combination) for 10 days.

• School-aged children without systemic signs may be treated with 3–5 days of an oral broad-spectrum antibiotic such as SMZ-TMP, nitrofurantoin, amoxicillin/clavulanate, cephalexin, and cefixime

)[A]

)[B]:

– Antibiotic prophylaxis should be continued until the radiographic imaging is complete

– Appropriate for children with frequent symptomatic UTIs (even in the absence of VUR):

3 in 6 mo or >4 in 1 yr

Recommended in children with VUR with history of UTI

– Antibiotics are typically given in 1/4–1/2 of the typical therapeutic dose:

Nitrofurantoin (in children without G6PD) 1–2 mg/kg PO once or twice daily

SMZ-TMP (except children <3 mo) 1–2 mg/kg TMP, 5–10 mg/kg SMZ

Cephalexin (in infants <3 mo)

Ampicillin should not be used due to high incidence of resistant E. coli

Second Line

Other antibiotics appropriate for pediatric use, age, and local bacterial resistance patterns

SURGERY/OTHER PROCEDURES

May be indicated following resolution of infection if child has specific urinary abnormalities causing obstruction, reflux, etc.

ADDITIONAL TREATMENT

Treatment of dysfunctional voiding/elimination behaviors is paramount to these patients' long-term management.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Cranberries may be effective in decreasing bacterial adherence, but there are no specific recommendations for children at present.

ONGOING CARE

PROGNOSIS

- Most children do not have any long-term sequelae from a UTI.
- Prompt, efficacious treatment can prevent systemic sequelae.
- Recurrence is common, especially in those with anatomic/functional abnormalities.

COMPLICATIONS

- Renal insufficiency/failure: Renal scarring in ~8% of children overall
- HTN
- Urosepsis

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

If scarring is present, consider a nephrology consult to monitor for evaluation of HTN, proteinuria, and renal insufficiency.

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See Also (Topic, Algorithm, Electronic Media Element)

- Urinary Tract Infection, Pediatric Algorithm
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

- 041.4 Escherichia coli (E. coli) infection in conditions classified elsewhere and of unspecified site
- 599.0 Urinary tract infection, site not specified
- 771.82 Urinary tract infection of newborn

ABBREVIATIONS

- CVA: Costovertebral angle
- DMSA: Technetium99m dimercaptosuccinic acid
- GI: Gastrointestinal
- GU: Genitourinary
- HPF: High-power field
- HTN: Hypertension
- IM: Intramuscular
- IV: Intravenous
- PO: By mouth
- RBC: Red blood cell
- SMZ/TMP: Sulfamethoxazole/trimethoprim
- STD: Sexually transmitted disease
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

- WBC: White blood cell

UROLITHIASIS, ADULT, GENERAL

Benjamin R. Lee, MD
Gordon L. Fifer, MD
Raju Thomas, MD

BASICS

DESCRIPTION

Urolithiasis may occur in any portion of the urinary tract and may be associated with mild to severe symptoms.

EPIDEMIOLOGY

- More common in Caucasians than African Americans
- Peak incidence: 4th–6th decades
- Within the US, more common in the Northwest, Southeast, and Southwest
- ~1:272 or 0.37% or 1 million people
- Accounts for 7–10 of every 1,000 hospital visits.
- Increasing incidence with increased obesity
- Estimated 10% of people in US will have a kidney stone at some point in their lives.

RISK FACTORS

- Upper urinary tract calculi:
  – Calcium oxalate stones most common; also uric acid, cystine, struvite (magnesium ammonium phosphate), calcium phosphate
  – Calcium stone formation may be due to dietary excess, hyperparathyroidism, sarcoidosis, multiple myeloma, leukemia, inappropriate loss of calcium in urine through renal tubules (renal leak), excessive intestinal absorption, inadequate levels of stone inhibitors in urine, or idiopathic.
  – Uric acid stone formation may be due to dietary excess, gout, myeloproliferative disorders, chronic dehydration, Lesch-Nyhan syndrome, ingestion of uricosuric drugs (salicylates, thiazides), or idiopathic.
  – Struvite stones are associated with UTI with urease-splitting organisms (Proteus, Klebsiella, and others), leading to alkaline urine and magnesium ammonium phosphate crystallization.
  – Cystine stones are rare and associated with inherited disorder of renal tubular reabsorption of cystine.
- Lower urinary tract calculi
- Bladder stones are seen in patients with foreign material in bladder; inadequate bladder emptying as in neurogenic bladder or chronic bladder outlet obstruction (most often due to benign prostatic hyperplasia).

Genetics

- In general, urolithiasis is associated with a polygenic defect and partial penetrance.
- Cystinuria, an unusual cause of urolithiasis, is a homozygous recessive disorder.
- RTA is inherited and is associated with urolithiasis.

GENERAL PREVENTION

- Adequate hydration
- Allopurinol for uric acid stones
- Decreased protein diet
- Decreased sodium intake
- Diuretics
- Increase urinary citrate
- Limit grapefruit juice consumption:
  - 1 study showed a 44% increase in calcium oxylate stones.
- Restrict oxalate consumption

PATHOPHYSIOLOGY

- Supersaturation: Urine becomes oversaturated with certain types of crystal (ie, uric acid, cystine), which then come out of solution; the saturation level is variably pH-dependent, based on type of crystal.
- Inhibitor deficiency: Inhibitors may limit crystal growth and aggregation (citrate and magnesium important inhibitors of urolithiasis).

COMMONLY ASSOCIATED CONDITIONS

- Crohn disease
- Dehydration
- Intestinal bypass
- Medullary sponge kidney
- Renal tubular acidosis

DIAGNOSIS

HISTORY

- Acute onset of severe pain; if stone partially obstructive, may have more chronic, mild to moderate pain:
  - Pain radiates to groin or lower abdomen
- Gross hematuria may be present.
- Previous history of kidney stones or UTIs
- Family history of urolithiasis
- Change in urination patterns:

– Frequency and urgency suggests stone in distal ureter or bladder calculi.

- History of neurogenic voiding dysfunction or obstructive urinary symptoms

PHYSICAL EXAM

- Fever present if associated infection:

– Moderate, deep tenderness in flank common; greater tenderness suggests possible pyelonephritis.

- An abdominal mass suggests another cause for pain besides urolithiasis:

– Elevated heart rate and BP secondary to pain

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:

– Microscopic hematuria unless stone has caused complete obstruction and no urine from affected side; pyuria may be present to mild degree, if significant, pyuria suggests concomitant UTI

– Crystalluria may provide important information regarding the type of calculus present.

- Leukocytosis may be present if secondary infection:

– Elevated creatinine may be present if bilateral obstruction or stone in solitary kidney

Imaging

- Assessment of acute renal colic may be carried out using several different techniques:

– CT: Noninfused helical CT scanning: Rapid study, no need for contrast

– 1st-line test of choice for most patients with acute renal colic; all stones readily visible

– Pathology in other abdominal organs can also be assessed; the degree of hydronephrosis and size and location of stones can be reliably determined.

– No information regarding renal function

– Hydronephrosis does not define obstruction.

- IVP:

– Requires IV contrast; delayed x-rays needed if high-grade obstruction present and contrast not immediately excreted; some stones radiolucent; can assess renal function

- US:

– Noninvasive; operator-dependent; generally cannot visualize ureter in adult; its use in this setting is largely superseded by availability and greater information provided by CT:

Pregnancy

- Retrograde pyelography:
  - Invasive; allows for simultaneous removal of stone and/or placement of ureteral stent to relieve obstruction

Pathological Findings

Stone analysis useful:

- 80% calcium stones:
  - Most calcium oxalate
  - Less often, calcium phosphate
- Uric acid
- Struvite (magnesium ammonium phosphate)
- Mixed stones, such as calcium oxalate and uric acid often seen
- Indinavir rarely in HIV infected patient on therapy
- Other rare types include matrix, melamine, triamterene, and xanthine

DIFFERENTIAL DIAGNOSIS

- Abdominal aortic aneurysm
- Appendicitis
- Bowel obstruction
- Cholecystitis or biliary colic
- Gastritis, pancreatitis, peptic ulcer
- Mesenteric ischemia
- Musculoskeletal back pain
- Pyelonephritis, urinary tract infection
- Sloughed renal papilla
- UPJ obstruction
- Urolithiasis: Calcium oxylate, calcium phosphate, uric acid, struvite, indinavir, matrix, triamterene, xanthine, mixed

ALERT

The presence of pyuria, fever, leukocytosis, or bacteriuria suggests the possibility of a urinary infection and the potential for an infected obstructed renal unit or pyonephrosis. Such a condition is potentially life-threatening and should be treated as a surgical emergency.

TREATMENT

- Stones 2–3 mm have 80% probability of passing with conservative measures (hydration, analgesia, symptomatic relief)
- Stones 4–5 mm have 50% probability of passing with conservative measures
- Stones 7–8 mm have 20% probability

- Stones >1 cm are unlikely to pass spontaneously.
- Hydration and adequate pain control
- Increase hydration
- Patients with likelihood of spontaneously passing a stone (<4–5 mm in size) may be sent home with analgesics; should be instructed to return if pain worsens, or severe vomiting or fever
- Controversy exists regarding maximum period of observation for partially obstructing stone without development of significant irreversible renal dysfunction; generally, should intervene if stone has not passed within 4–6 wk.
- Indications for intervention:
  - Fever and/or infection
  - Intractable pain
  - Unable to tolerate oral fluid and at risk for dehydration
  - Progressive renal deterioration; obstruction of solitary functioning kidney

MEDICATION

- Patients with evidence of active UTI should be treated with broad-spectrum antibiotics (eg, ampicillin and gentamicin, 3rd-generation cephalosporin).
- Antiemetics if acute colic is associated with nausea and vomiting.
- Medical expulsive therapy:
  - -Blockers (ie, terazosin, tamsulosin) or calcium-channel blockers (eg, nifedipine) can relax musculature of the ureter and lower urinary tract. Recent studies support their benefit in reducing pain associated with stone passage, increasing frequency of stone passage, and reducing need for surgical intervention.
- Uric acid stones and cystine stones can be dissolved with medical therapy; calcium stones and struvite stones cannot be dissolved:
  - Uric acid stones: Alkalinize urine with potassium citrate or bicarbonate, to maintain urinary pH between 6.5 and 7.0:

    Urinary pH >7.5 can precipitate calcium phosphate with resulting stone formation.

    May dissolve up to 1 cm per month
  - Cystine stones: Alkalinize urine with potassium citrate or bicarbonate, to maintain urinary pH >7.5. Difficult to dissolve.

SURGERY/OTHER PROCEDURES

- Patients with active UTI/sepsis: 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)

– Ureteral calculi: ESWL or ureteroscopic stone removal; the approach depends on size and location of stone and patient and physician preference.

– Stent placement in anticipation of ureteral dilation and subsequent spontaneous stone passage is an option for patients with smaller ureteral calculi.

– >2 cm: Percutaneous nephrolithotomy or if >1.5 cm in lower pole.

ADDITIONAL TREATMENT

- 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.
- Drink 2 L/d

Pregnancy Considerations

- Urolithiasis during pregnancy increases risk of preterm delivery.
- If standard US not helpful, and stone disease suspected, consider transvaginal US in the pregnant female.
- 75–80% will pass spontaneously due to physiologic dilation of ureters (see Section I: “Pregnancy, Urolithiasis”)

ONGOING CARE

PROGNOSIS

- 24-hr urine collection for metabolic analysis should be performed 1 mo after patient is stone-free.
- Metabolic workup after 2nd episode

COMPLICATIONS

- Surgery carries standard risks of bleeding, infection, ureteral stricture.
- Pneumothorax with nephrostomy access

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Drink enough water to make 2–2.5 L of urine per 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

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Calculi
- Pregnancy, Urolithiasis
- Urolithiasis, Indinavir
- Urolithiasis, Pediatric, General
- Urolithiasis, Calcium Oxylate/Phosphate
- Urolithiasis, Staghorn
- Urolithiasis, Ureteral Calculi Algorithm
- Urolithiasis, Uric Acid

CODES

ICD9

- 592.0 Calculus of kidney
- 592.1 Calculus of ureter
- 592.9 Urinary calculus, unspecified

ABBREVIATIONS

- BP: Blood pressure
- CT: Computed tomography
- ESWL: Extracorporeal shockwave lithotripsy
- IV: Intravenous
- IVP: Intravenous pyelogram
- RTA: Renal tubular acidosis
- US: Ultrasound

UROLITHIASIS, CALCIUM OXALATE/PHOSPHATE

Grant I.S. Disick, MD

Ravi Munver, MD

BASICS

DESCRIPTION

- Formation of calcium salts in the urinary tract may result in a urinary calculus.
- Calcium oxalate in its pure form or mixed with calcium phosphate (hydroxyapatite) is the most common type of calculus in industrialized countries

EPIDEMIOLOGY

- US annual stone incidence: 16.4 in 10,000
- Male > Female (3:1–2.0)
- Age of peak incidence: 20–40 yr
- 1 in 8 men, 1 in 20 women lifetime risk
- Stone incidence by composition: calcium oxalate 30–56%; mixed calcium oxalate and calcium phosphate: 11–31%
- 10–15% US prevalence of stone disease
- 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; white males; other illnesses: (IBD, etc.), elevated PTH, medullary sponge kidney, recurrent UTI
- Anatomic: UPJ obstruction, horseshoe kidneys
- Extrinsic risk factors: Geography/climate
- Diet: Elevated dietary protein, oxalates, refined sugars, and calcium, and low fiber intake; high salt intake increases UCa
- Water intake: Low consumption increases risk
- Occupation: Sedentary occupations

Genetics

- Calcium oxalate: Multifactorial; hypercalciuria an autosomal dominant trait
- Idiopathic hypercalciuria: 5–10% of normals and 30–60% with calcium nephrolithiasis
- Familial tendency to form stones

PATHOPHYSIOLOGY

- Hypercalciuria may be heterogeneous.
- Normocalcemic hypercalciuria (idiopathic hypercalciuria): 30–60% of calcium oxalate stones

- AH: Intestinal hyperabsorption of calcium:
  - Hypercalciuria due to increased filtered load and decreased renal tubular reabsorption due to decreased PTH
  - Renal loss of calcium compensates for absorption, maintains normal SCa
  - Hypercalciuria: >4 mg/kg weight/24 hr on random diet (>250 mg/24 hr), OR >200 mg/24 hr after 1 wk diet to 400 mg calcium and 100 mEq sodium/d (1)
  - AH type I: Uncommon, most severe form; persistent hypercalciuria >250 mg/24 hr on random diet or restricted diet with normal SCa and normal or slightly decreased PTH level; 2-hr fasting UCa normal.
  - AH type II: Most common, mild form; hypercalciuria >250 mg/24 hr on random diet but normocalciuria on calcium/sodium-restricted diet, normal SCa and PTH
- Renal hypercalciuria (renal leak):
  - Impaired renal tubular reabsorption of calcium; decreased in SCa; elevated PTH; elevated vitamin D3, and increased intestinal hyperabsorption
  - SCa normal, mild secondary elevated PTH
  - UCa elevated on both random and restricted diets; 2-hr fasting UCa elevated
- Resorptive hypercalciuria:
  - Primary elevated PTH; elevated SCa and UCa secondary to increased PTH secretion, causing excessive resorption of bone and an increased intestinal absorption of calcium due to increased PTH and increased renal synthesis of vitamin D3
  - 2-hr fasting UCa is elevated
- Unclassified hypercalciuria:
  - Hypercalciuria with normal SCa, normal PTH, and elevated 2-hr fasting UCa
  - Sodium cellulose phosphate may help to distinguish AH by eliminating problem of inadequate dietary preparation prior to fast and load calcium studies; renal hypercalciuria by reducing the suppressive effect of absorbed calcium on parathyroid stimulation
- Other causes calcium oxalate stones:
  - Hyperuricosuria (urinary uric acid >600 mg/24 hr); only abnormality in 10% of calcium stones; up to 40% of calcium stone-formers with other physiochemical abnormalities
  - May initiate calcium oxalate stones by direct induction of heterogeneous nucleation of calcium oxalate crystals, or by absorption of certain macromolecular inhibitors
- Hyperoxaluria:
  - Urinary oxalate >45 mg/24 hr
  - Mild hyperoxaluria (45–80 mg/24 hr) is as important a risk factor for idiopathic calcium oxalate stones as hypercalciuria and is found in 37% of patients with calcium oxalate stones

– Activity of stone disease correlates better with level of urinary oxalate than calcium.

– Most common: Intestinal hyperabsorption of oxalate: Intestinal resection (enteric hyperoxaluria), IBD, celiac, gastric/small bowel resection; jejunoileal bypass

– Bile salts and fatty acids increases large-bowel oxalate absorption.

– Fat malabsorption causes calcium to complex with bile acids and form calcium soap, which decreases free calcium in the intestinal lumen, which can complex with oxalate, and decrease oxalate for absorption.

– Stone formation due to hyperoxaluria but also contributed to by low-volume urinary output, low citrate secondary to hypokalemia, chronic metabolic acidosis

– Low magnesium levels may also be secondary to intestinal malabsorption.

– Primary hyperoxaluria type I:

Autosomal recessive, defect of AGT

Elevated urinary oxalic, glycolic, glyoxylic acids

Clinically, nephrocalcinosis, tissue deposition of oxalate, and renal failure, with death by age 20 if untreated

2/3 have undetectable AGT on liver biopsy; glyoxylate oxidized to oxalate

– Primary hyperoxaluria type II:

Rare (21 cases) deficiency of D-glycerate dehydrogenase and glyoxylate reductase

Elevated urinary oxalate and glycerate; nephrocalcinosis and renal failure

– Dietary hyperoxaluria:

Excess oxalate-rich foods (dark green vegetables, tea, cola, concentrated fruit juices, chocolate); vitamin C >1000 mg/d

Pyridoxine (vitamin B6) deficiency, ethylene glycol toxicity, hepatic conversion to glycoaldehyde and glycolic acid, methoxyflurane anesthesia, converted in liver to oxalate

• Hypocitraturia:

– Citrate <220 mg/24 hr; sole abnormality in 10%; 15–60% with other calcium stones causes

– Acidosis most important factor in hypocitraturia; decreases urinary citrate secondary to increased renal tubular reabsorption and decreased synthesis

– Causes of metabolic acidosis: IBD, chronic diarrhea; thiazide-induced hypokalemia, and intracellular acidosis; purine-rich diet (high acid-ash); strenuous exercise (lactic acid); RTA (type I, distal); increased sodium intake. UTI with bacteria-degrading citrate decreases urinary calcium salts by forming soluble complexes with calcium.

- Hypomagnesuria:
  - Urinary Mg <50 mg/24 hr; coexists with hypocitraturia in 2/3 and with low urine volume (<1 L/24 hr) in 40%
  - Pathogenesis is not known; may be dietary (IBD and malabsorption)

COMMONLY ASSOCIATED CONDITIONS

IBD, chronic pancreatitis, chronic diarrhea states, elevated PTH, medullary sponge kidney, UTIs

DIAGNOSIS

HISTORY

- See “Flank Pain” and “Urolithiasis, General.”
- Review stone history, family history, and the intrinsic and extrinsic risk factors noted earlier

PHYSICAL EXAM

See “Flank Pain” and “Urolithiasis, General.”

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Abbreviated protocol for low-risk single-stone formers (history, dietary habits, basic metabolic panel including calcium, PTH, and uric acid, urinalysis/pH, radiologic imaging, stone analysis)
- Most physicians do not perform a comprehensive metabolic evaluation (with calcium fast and load test) in recurrent stones and those with an increased risk for stone formation. Rather, a simple metabolic evaluation (metabolic panel and 1–2 24-hr urines):
  - 24-hr urine (volume, calcium, creatinine, oxalate, citrate, sodium, phosphate, magnesium, pH, uric acid, sulfate)
  - Data best on a diet at least 1 month after stone passage or 1 wk after IVP studies
  - Discontinue drugs that may affect the tests (vitamins, antacids, diuretics, acetazolamide, allopurinol, or other stone medications)

Imaging

- CT: Most sensitive
- US
- KUB
- IVP
- MRI not useful for calcifications/urinary calculi

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 program is 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 gout or major stone complications; history of metabolic stone (uric acid or cystine), infection stone (struvite), or pure calcium 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
– Solitary kidney; age at onset <20

Pathological Findings

• Stone analysis: Varying percent composition from calcium oxalate and/or calcium phosphate

• Crystals: Calcium oxalate monohydrate (dumbbell/hourglass), calcium oxalate dehydrate (envelope/bipyramidal), calcium phosphate-apatite (amorphous)

DIFFERENTIAL DIAGNOSIS

• Hypercalcemia: Primary elevated PTH, RTA, vitamin D excess, immobilization, sarcoidosis, metastatic malignancies, milk-alkali syndrome, hyperthyroidism, myxedema, adrenal insufficiency, furosemide administration

• See Section I: “Filling Defect-Upper Urinary Tract.”

• Flank pain: See Section I: “Flank Pain.”

TREATMENT

MEDICATION

• Absorptive hypercalciuria type I:

– Thiazide (not a selective therapy for AH as does not decrease intestinal calcium; limited long-term effect):
– Hydrochlorothiazide 25 mg b.i.d.
– Consider potassium citrate (20 mEq b.i.d.)
– Alternates: Trichlormethiazide 2.5 mg/d or chlorthalidone (25–50 mg/d):

Restrict dietary oxalate

Magnesium supplementation

Sodium cellulose phosphate out of favor (GI effects); use if UCa >500 mg/d; after all other treatment options tried

• Absorptive hypercalciuria type II: Moderate calcium restriction (600 mg/d or 1–2 servings dairy/d); sodium restriction; thiazide if conservative approach is not effective; potassium citrate supplementation

• Renal hypercalciuria: Thiazide to increase tubular calcium reabsorption; hydrochlorothiazide 25 mg b.i.d.; potassium citrate supplementation (Polycitra K syrup 15–30 mL b.i.d.; Polycitra K crystals 1 packet b.i.d.; Urocit K 10–20 mEq b.i.d.); sodium restriction (2 g sodium diet; keep urinary sodium <100 mg/d)

• Hyperuricosuric calcium nephrolithiasis: Increase fluid intake; reduce dietary purine (eg, red meat); urinary alkalization (pH 6.5–7.0), potassium citrate; reduce endogenous uric acid production (allopurinol 300 mg/d); if serum uric acid >8 mg/dL, or if urinary uric acid >800 mg/24 hr

• Hypocitraturic calcium nephrolithiasis: Potassium citrate, increases intracellular pH, which increases citrate production

• Hyperoxaluria: High fluid intake; low-oxalate diet; potassium citrate (60–120 mEq/d), calcium supplementation (calcium citrate, TUMS); therapy to control diarrhea

• Type I RTA: Potassium citrate

SURGERY/OTHER PROCEDURES

See “Urolithiasis, Adult, General.”

ADDITIONAL TREATMENT

General Measures

• Patients with evidence of an active UTI should be treated with broad-spectrum antibiotics.

• Medical expulsion therapy for a symptomatic ureteral stone (1)[C] (See “Urolithiasis, General”)

• Prevention should be tailored to patient need.

• 1st-time stone-formers at low risk for recurrence should follow a conservative approach.

• Conservative treatment is appropriate for all stone-forming patients, regardless of cause.

– High fluid intake, daily urine output of 2 L; sodium and oxylate restriction

– Restrict protein (8 oz of meat, chicken, or fish/d); vitamin C <2 g/d

– Avoid excess calcium intake. 1 serving with each meal acceptable; avoid late at night

– Calcium citrate: Stone-friendly calcium supplement

– Avoid stone-provoking drugs: Vitamin D, antacids, furosemide, uricosurics, triamterene

ONGOING CARE

PROGNOSIS

- Untreated recurrence rate for calcium oxalate stones: 10% at 1 yr, 35% at 5 yr, 50% at 10 yr
- Medical therapy effective in decreasing new stone formation; remission >80%, and >90% recurrence reduction

COMPLICATIONS

- An obstructing calculus can lead to sepsis and/or progressive renal damage.
- An unobstructing renal calculus may (but not always) grow and cause eventual chronic obstruction and deterioration of renal function.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

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

ADDITIONAL READING

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- Preminger GM, et al. 2007 AUA Guidelines for the Management of Ureteral Calculi.

See Also (Topic, Algorithm, Electronic Media Element)

- Urolithiasis, Adult, General
- Hypercalcuria

CODES

ICD9

- 592.0 Calculus of kidney
- 592.1 Calculus of ureter
- 592.9 Urinary calculus, unspecified

ABBREVIATIONS

- AGT: Alanine-glyoxylate aminotransferase
- AH: Absorptive hypercalciuria
- Ca: Calcium
- CT: Computed tomography
- ESWL: Extracorporeal shock-wave lithotripsy
- IBD: Inflammatory bowel disease
- IVP: Intravenous pyelogram
- KUB: Kidneys, ureters, bladder
- PTH: Parathyroid hormone
- RTA: Renal tubular acidosis
- SCa: Serum calcium
- UCa: Urinary calcium
- UPJ: Uteropelvic junction
- URS: Ureteroscopy
- US: Ultrasound
- UTI: Urinary tract infection

UROLITHIASIS, PEDIATRIC, GENERAL

Michael J. Erhard, MD

BASICS

DESCRIPTION

- When crystals precipitate in the urine because of an imbalance between stone promoters and inhibitors, they can coalesce to form distinct stones.
- Many stones will pass unnoticed, but some cause significant symptoms, and possibly renal damage.

EPIDEMIOLOGY

- Male = Female pediatric patients
- White > African American
- 75% of stones contain mostly calcium: Calcium oxalate 60% all stones
- 1/50th of adults (US)
- Southeastern US most common

RISK FACTORS

Genetics

- Cystinuria: Autosomal recessive
- Primary hyperoxaluria: Autosomal recessive
- RTA: Autosomal dominant (small subset)
- Xanthinuria: Autosomal recessive

GENERAL PREVENTION

Maintain adequate hydration and fluid volume

PATHOPHYSIOLOGY

- Stone formation:
  - Crystals precipitate when the equilibrium between stone-promoting and stone-inhibiting factors becomes unbalanced.
- Infection:
  - Urea-splitting organisms produce urease, which catalyzes the hydrolysis of urea.
  - Magnesium ammonium phosphate (struvite) and calcium phosphate stones
  - Urine is alkaline due to urease.
  - Most often present in patients with an anatomic abnormality that leads to chronic infection (neurogenic bladder, reflux, obstruction, etc.)
- Anatomic:
  - Ureteropelvic/vesical obstruction
  - Neurogenic bladder

– Previous bladder neck surgery

- Hypercalciuria:

– Renal: Impaired tubular reabsorption of calcium causes increased parathyroid hormone release, which normalizes serum calcium.

– Absorptive: Increased absorption from intestines causes decreased parathyroid hormone and therefore decreased calcium tubular reabsorption:

Type 1: Severe

Type 2: Mild

– Resorptive (exceedingly rare):

Results from primary hyperparathyroidism

Elevated PTH and serum calcium, low serum phosphorous, high urine calcium

– Iatrogenic (medications): Loop diuretics (furosemide), corticosteroids, methylxanthines (theophylline, aminophylline)

– Infant nephrocalcinosis: Most common in preterm infants treated with loop diuretics, excess calcium intake, excess vitamin D intake, metabolic acidosis and immobility:

>60% resolve spontaneously and <10% develop significant stone disease

- RTA: Inability to acidify urine in response to an acid load:

– Metabolic acidosis; high urine pH

– Type I (distal) most common: Disorder of hydrogen ion excretion that leads to bone demineralization and thus hypercalciuria

– Most common stone is calcium phosphate, which results from hypercalciuria, hypocitraturia, and elevated urine pH

- Uric acid stones/hyperuricosuria:

– Rare in children; high purine intake, uricosuric drugs (probenecid, sulfinpyrazone, allopurinol), renal tubular disorders, cyanotic congenital heart disease, hemolysis, and myeloproliferative disorders

– Lesch-Nyhan syndrome and type I glycogen storage disease: Increased uric acid

– Acute diarrheal states and inflammatory bowel disease: Fluid and bicarbonate losses

- Cystinuria: Autosomal recessive disorder of amino acid transport; excessive excretion of COLA

- Hyperoxaluria:

– Primary type I and II are rare autosomal recessive disorders with hepatic enzyme defects

– Type I: More severe; organ failure

– Secondary: Excessive intake of ethylene glycol, ascorbic acid, methoxyflurane, or increased intestinal absorption due to bowel disease/resection, gastric bypass

COMMONLY ASSOCIATED CONDITIONS

- Cystic fibrosis
- Indinavir therapy
- Ketogenic diet
- Lowes syndrome

DIAGNOSIS

HISTORY

- Patient: Prematurity, medications, dietary habits, fluid consumption, malignancies, previous intestinal disorder/surgery, hematuria
- Family: Cystinuria, primary hyperoxaluria, RTA, uric acid lithiasis
- Abdominal/flank pain ± nausea/vomiting

PHYSICAL EXAM

Nonspecific; occasional flank tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis:
  - Crystals (hexagonal = cystine)
  - pH (RTA, 2nd morning void >5.5)
  - Look for infection
- Serum electrolytes and creatinine
- Urine spot calcium to creatinine ratio
- Serum calcium, uric acid, phosphorous, parathyroid hormone (if appropriate)

Imaging

- Abdominal plain film has low yield (may be helpful in follow-up)
- Renal US:
  - Hydronephrosis; Not sensitive for detecting small stones; useful as follow-up test
- Noncontrast spiral CT:
  - 96% sensitive and specific
  - Downside: Radiation exposure; tailor usage

Diagnostic Procedures/Surgery

- Metabolic evaluation: 24-hr urine collection:
  - Appropriate for all pediatric stone formers
  - >50% will have an identifiable abnormality

– Parameters: Volume, pH, calcium, citrate, creatinine, cystine, magnesium, oxalate, phosphate, potassium, sodium, uric acid
  – Pre–toilet-trained children will require a catheter to ensure adequate collection.
  – Delay collection until at least 1 mo after acute episode.
  – If any abnormalities, repeat collection after treatment modifications.
- Stone analysis to determine composition
- Fasting calcium load test:
  – Sodium and calcium restriction
  – Check urine prior to calcium load.
  – Give hydration and calcium load and check urine sodium and calcium 4 hr after:
    Absorptive hypercalciuria: Normal fasting, elevated after load
    Renal hypercalciuria: Elevated fasting

DIFFERENTIAL DIAGNOSIS

See Section I: “Urolithiasis, Adult, General.”

TREATMENT

- The acute management of kidney stones is similar for adults and is discussed in Section I: “Urolithiasis, Adult, General.”
- Evaluate all children for underlying metabolic disorder.
- Prevent additional stones.
- Hydration:
  – Water preferred; avoid caffeine, sodium (sports drinks), calories
  – 50 mL/kg/d input
  – 35 mL/kg/d urine output
- Dietary restrictions when applicable
- 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)

MEDICATION

- Medical expulsive therapy:
  – 1-Receptor antagonists, corticosteroids, calcium channel blockers
  – Efficacy in pediatric population to be defined
- Infectious stones:
  – Proper bladder irrigation to avoid mucus
  – Long-term antibiotics with specificity to urea-splitting bacteria
  – Urease inhibitor acetohydroxamic acid (Lithostat)
- Renal leak hypercalciuria:

- Hydrochlorothiazide:
  <6 mo: Up to 3.3 mg/kg/d 2 divided doses
  6 mo–12 yr: 2–2.2 mg/kg/d 2 divided doses
  >12 yr: 25–100 mg/d or divided b.i.d.
- Potassium citrate: 1 mEq/kg/d

- Absorptive hypercalciuria:
  - Low calcium diet: 400–600 mg/d
  - Hydrochlorothiazide
  - Sodium cellulose phosphate:
    25–35 mg/kg/d in 4 divided doses
    May cause magnesium depletion or secondary hyperoxaluria
- RTA:
  - Correct systemic acidosis
  - Potassium citrate (2 mEq HCO3/mL), or sodium citrate (1 mEq HCO3/mL), or baking soda (1 tsp = 42 mEq HCO3)
    Children: 0.5–3 mEq/kg/d in 4 divided doses
    Adolescents: 30–60 mEq HCO3 t.i.d.–q.i.d.
- Uric acid stones:
  - Limit dietary sodium
  - Alkalinization of urine to pH >6.5:
    Oral medications (see RTA)
    IV: 1/6 molar lactate at 0.5–1 mL/kg/hr
    Avoid pH >8.5 (calcium phosphate)
    Test urine with Nitrazine paper
  - Allopurinol (decrease uric acid production) 200 mg/d
  - Limit purine intake if necessary
- Cystinuria:
  - Create high urine volume (>1.5 L/m2/d)
  - Urine alkalinization (see RTA) pH >7.5
  - Chelating agents (bind cystine): Use cautiously:
    Thiola
    D-penicillamine
    Tiopronin
- Hyperoxaluria:
  - Limit sodium and oxalate-rich foods (eg, spinach, rhubarb, nuts, tea, wheat bran, strawberries)

- Supplemental citrate, magnesium, phosphorous (stone inhibitors)
- Pyridoxine 1.5–3 mg/kg/d
- Avoid excess of vitamin C and D

- Hypocitraturia: Potassium citrate supplementation (see RTA)
- Hypomagnesuria (uncommon):
  - Can be associated with inflammatory bowel disease
  - Magnesium oxide 6.5 mg/kg/d

SURGERY/OTHER PROCEDURES

- SWL:
  - Renal and proximal ureteral stones, <1 cm
    All ages, including low-birth-weight infants
    Use for distal stones not well defined
  - Success rate depends upon many variables:
    Stone size and location, energy utilized, density of stone, anatomic abnormalities
  - Complications (renal):
    Subcapsular hematoma: Self-limiting
    Interstitial fibrosis: Insignificant unless multiple procedures
  - Complications (surrounding organs):
    Shield lung fields in small children
- Ureteropyeloscopy:
  - Rigid and flexible endoscopes permit access to almost all areas of the collecting system in nearly all children:
    Distal stones more successful than mid/proximal ureteral and intrarenal stones
    Pre-placement of stent is sometimes necessary to passively dilate the ureter.
    Active dilation (balloon, graduated dilator)
    Access sheaths (with/without pre-stenting) facilitate procedures requiring multiple endoscope passes.
  - All forms of lithotripsy are safe; holmium laser most effective
  - Postoperative stent not always needed; use after complicated procedures; dangler string facilitates removal without anesthesia
  - Complications: Significant ureteral reflux is theoretical; ureteral injury is managed initially with stent; further procedures are based on severity.
- Percutaneous:
  - Appropriate for large intrarenal/proximal ureteral stones:
    Also failed primary procedures (SWL, ureteroscopy), and with associated anatomic abnormalities (congenital, acquired, postsurgical)

– Access at same time as or prior to surgery:

Sheath size as small as possible to allow for success of procedure and to accommodate flow of irrigant around scope

Place site in position to allow best access to stone burden.

Multiple tracts are safe.

– Irrigation (saline): Warmed for young children

– Lithotripsy: All forms safe; vacuum devices require larger scopes with a straight channel.

– Postoperative management: Appropriate drainage:

Confirm stone-free status/antegrade urine flow prior to removal of percutaneous tube drains; 2nd-look procedure if necessary

Chest x-ray in recovery room (high access)

– Complications:

Bleeding: Place tube (traction if necessary); embolize if significant

Perforation/extravasation: If significant, stop procedure and place drain

Infection: Appropriate antibiotics; confirm patency of tube/stent

Pleural effusion/pneumothorax: Chest tube, needle drainage

Intestinal injury: Expectant management; colostomy tube

• Open/laparoscopic pyelolithotomy (rare): Large pelvic/staghorn stones

ONGOING CARE

COMPLICATIONS

See above.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Repeat 24-hr urine 3–4 mo after instituting therapy and if stone recurs after initial stabilization.

• Assess periodically for stone growth or new stone disease with US/abdominal plain film.

ADDITIONAL READING

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• Milliner DS. Urolithiasis. In: Avner ED, et al., eds. Pediatric Nephrology, 5th ed. Philadelphia: Lippincott, 2003.

• Minevich E, Defoor W, Reddy P, et al. Ureteroscopy is safe and effective in prepubertal children. J Urol 2005;174:276–279.

See Also (Topic, Algorithm, Electronic Media Element)

- Cystinuria
- Hypercalcuria (Absorptive, Renal, and Resorptive)
- Renal Tubular Acidosis
- Renal and Ureteral Calculi (Nephrolithiasis)
- Urolithiasis, Adult, General
- Urolithiasis, Cysteine and Cystinuria

CODES

ICD9

- 592.0 Calculus of kidney
- 592.1 Calculus of ureter
- 592.9 Urinary calculus, unspecified

ABBREVIATIONS

- COLA: Cystine, ornithine, lysine and arginine
- CT: Computed tomography
- PTH: Parathyroid hormone
- RTA: Renal tubular acidosis
- SWL: Shockwave lithotripsy
- US: Ultrasound

UROLITHIASIS, STAGHORN

Benjamin R. Lee, MD
Mathew C. Raynor, MD
Raju Thomas, MD

BASICS

DESCRIPTION

- A staghorn calculus is a branching calculi that fills the majority of the intrarenal collecting system.
- Complete staghorns involve the renal pelvis and branch into minor/major infundibulum and calyces.
- Partial staghorn: Incomplete filling of the intrarenal collecting system
- Typically consist of pure forms or combinations of:
  - Struvite (magnesium ammonium phosphate or triple phosphate), usually due to infection
  - Calcium carbonate apatite
  - Cystine stones: Calcium oxylate and calcium phosphate (very uncommon)

EPIDEMIOLOGY

More common in women

RISK FACTORS

- Chronic indwelling catheters
- Metabolic disorders such as hyperoxaluria, cystinuria, or hypercalciuria
- Propagated by states of stasis and/or obstruction
- Recurrent UTIs
- Reflux of urine, neurogenic bladder, preexisting stone disease, stricture disease
- Urinary diversions

PATHOPHYSIOLOGY

- Any type of calculus can form a staghorn
- ~75% of staghorn calculi are composed of struvite-infected material:
  - Magnesium-ammonium-phosphate (also called urease stones)
  - Can often grow in size rapidly
- UTI important in pathogenesis of struvite stones:
  - Bacteria reside inside of the stones.
  - Bacteria produce urease.
  - Proteolytic enzyme: Hydrolyzes urea into ammonia, bicarbonate, and carbonate
  - Urease production: Mostly Proteus sp. and Ureaplasma urealyticum; some Pseudomonas, Klebsiella, Staphylococci, Escherichia coli, etc.

- Bicarbonate causes alkaline urine, and this induces supersaturation of the urine.

- Many other organisms, including yeast species, have been implicated.
- Crystallization is enhanced by stasis caused by obstruction or pyelocalyceal paralysis (from bacterial endotoxins).
- Chronic infections lead to stone formation:
  - This cycle involves infundibular obstruction with or without stricture, possibly hydronephrosis, further stone formation and obstruction, and loss of renal parenchyma.
- Metabolic calculi (calcium) can also form a staghorn.
- Staghorn stones may sometimes be mixed (eg, struvite and calcium oxalate or calcium phosphate)
- Can progress to more severe XGP and abscess

COMMONLY ASSOCIATED CONDITIONS

Proteus bacterial in UTI

DIAGNOSIS

HISTORY

- Usually discovered during a diagnostic workup for recurrent UTIs, as symptoms are often vague
- History of prior calculi
- Constitutional signs, including fever, malaise, weight loss
- Hematuria
- Flank pain or abdominal mass
- Neurogenic bladder
- Undiagnosed severe metabolic disorders:
  - Cystinuria
  - Primary hyperoxalosis
  - Primary hyperparathyroidism

PHYSICAL EXAM

- May have CVA tenderness
- Palpable mass: High-grade hydronephrosis

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Assess existing renal function:
  - BUN and creatinine
- CBC may demonstrate chronic anemia
- Urine analysis:

- pH of >7.0 is suggestive of a urea-splitting UTI and possible struvite stone.

• Urine culture may identify typical organism (ie, Proteus sp.) associated with struvite stone and staghorn calculus.

• PT/PTT for preoperative workup

Imaging

• Must have functional renal study; nonfunction with XGP:
  - Excretory urogram
  - Nuclear medicine scan
  - CT with and without IV contrast
• Plain films of the abdomen may demonstrate the presence of a large calculus:
  - Stones in the presence of Proteus or Klebsiella UTIs are likely struvite stones:
    Lightly calcified and relatively less dense on plain film
  - Stones in the presence of Pseudomonas, some Streptococcus and Staphylococcus:
  - Relatively dense: Increased calcium content
• If surgical intervention is planned, additional imaging is helpful:
  - CT/spiral CT:
    Provides 3-dimensional location of the stone
    Evaluates cortical thickness
    Measured most commonly by their longest diameter
    Computer-assisted volumes have also been used to better estimate stone burden.
• Broad branches vs. tight narrow branches:
  - Tight branches and associated infundibular stenosis: More difficult to treat
• MRI has limited or no utility in urolithiasis

Pathological Findings

• Microscopically, magnesium ammonium phosphate crystals resemble coffin lids.
• Chronic infection can cause parenchymal scarring and thinning.

DIFFERENTIAL DIAGNOSIS

• Malignant filling defect of ureter and renal pelvis:
  - TCC
  - SCC
  - Rare malignant tumors: Adenocarcinoma, sarcoma, angiosarcoma, and carcinosarcoma
  - Renal cell carcinoma
• Benign filling defect of ureter and renal pelvis:

- Air: Iatrogenic, infectious or due to fistula
- Blood clot
- Fibroepithelial polyp
- Fungus ball
- Hemangioma
- Inflammatory lesions: Granuloma, malakoplakia, TB
- Inverted papilloma
- Radiolucent calculus
- Rare benign tumors: Leiomyoma, neurofibroma, cholesteatoma
- Renal papilla
- Ectopic or end on renal papilla can be misidentified as a filling defect.
- Sloughed papilla
- Mucus: Urinary diversion patients
- Protein matrix
- Pyelitis glandularis
- Pyelitis cystica

TREATMENT

- Due to the infectious nature of the struvite material, all portions must be removed to maximize therapeutic response.
- Medical therapy alone is not commonly used, unless the patient is too ill to tolerate a surgical procedure.
- In 2005, the AUA published guidelines on the management of the staghorn calculus.
- Observation with supportive care (eg, hydration and antibiotics):
  - Reserved for those patients who would not tolerate surgical therapies
  - 28% of patients with staghorn calculi had significant morbidity while on long-term watchful waiting.
- Dietary phosphorus restriction to slow stone growth is not practical for most patients

MEDICATION

- Control any active UTI with antibiotics based on culture and sensitivity.
- Acetohydroxamic acid (AHA, Lithostat):
  - May reduce recurrence of struvite stones
  - Inhibits bacterial urease enzymes, thereby decreasing urinary ammonia production by urea-splitting organisms.
  - Adult dose: 12 mg/kg/d PO t.i.d.–q.i.d. on empty stomach; 1.5 g/d maximum
  - Pediatric dose: 10 mg/kg/d PO; titrate

– Associated with many significant side effects:

Anemia, bone marrow suppression, hepatotoxicity DVT, palpations, edema, nausea, vomiting, diarrhea, headache, loss of taste, hallucinations, rash, abdominal discomfort, others

– Follow CBC and liver function tests with chronic use.

– Cannot be used in cases of severe renal insufficiency; contraindicated with Cr of >2.5 mg/dL.

SURGERY/OTHER PROCEDURES

- Removal of all stone and infectious material is required:
  - The stone may regrow over weeks if not completely cleared.
  - Infection will persist because the stone itself is infected.
- Broad-spectrum antibiotics are needed prior to stone manipulation and treatment.
- General surgical approaches include:
  - Open surgery
  - PCNL
  - ESWL
  - Combination of PCNL and ESWL
- Often multiple procedures are needed to produce a stone-free state.
- 1st-line therapy:

– Endoscopic clearance via percutaneous nephrostolithotomy is generally considered primary approach, as the need for subsequent procedures is reduced.

– Complementary endoscopes and lithotripsy are applied.

– Ureteroscopy: Helpful in complex cases (eg, bleeding diathesis, comorbid conditions, obesity)

- ESWL as monotherapy is not the usual treatment of choice for a staghorn. Must have wide infundibulum to allow fragment passage.
- Open surgery: Rarely done today with improvements in minimally invasive techniques:
  - Pyelolithotomy
  - Nephrolithotomy
  - Anatrophic nephrolithotomy: Once the most widely performed procedures for staghorn calculi; very useful for stenotic infundibuli
  - Incision along a posterior lateral avascular plane (Brodel white line), between the areas supplied by the anterior and posterior branches of the renal artery
- Nephrectomy: Option for kidney with very poor function, if contralateral kidney is normal:

    - Open or laparoscopic techniques
- Tight infundibular stenosis: Severe stenosis requiring infundibuloplasty

ADDITIONAL TREATMENT

Prophylactic antibiotics in chronic infection

ONGOING CARE

PROGNOSIS

- Excellent once stone-free
- Once the stone burden is cleared, prevent further infections.

COMPLICATIONS

- Of the struvite staghorn calculus:
    - Death
    - Pyelonephritis
    - Renal failure
    - Sepsis
- Of treatment:
    - Blood loss with transfusion
    - Colon injury
    - Death
    - Fistula
    - Hydrothorax/pneumothorax
    - Nephrectomy
    - Perforation of the renal pelvis or ureter
    - Perirenal hematoma
    - Prolonged urine leak
    - Renal impairment
    - Repeat intervention
    - Residual fragments
    - Sepsis
    - Stent migration
    - Urinoma
    - Vascular injury (arterial or venous)
    - Wound infection

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patients are monitored postoperatively with routine renal US and plain films (imaging).

- Serial urine cultures are obtained to ensure a noninfected state.
- Metabolic analysis with 24-hr urine collection

ADDITIONAL READING

- Healy KA, Ogan K. Pathophysiology and management of infectious staghorn calculi. Urol Clin N Amer 2007;34(3):363–374.
- Preminger GM, Assimos DG, Lingeman JE. AUA guideline on management of staghorn calculi: Diagnosis and treatment recommendations. J Urol 2005;173(6):1991–2000.
- Segura JW. Staghorn calculi. Urol Clin N Amer 1997;24(1):71–80.

See Also (Topic, Algorithm, Electronic Media Element)

- Urinary Tract Infection (UTI), Adult
- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General
- Xanthogranulomatous Pyelonephritis

CODES

ICD9

592.0 Calculus of kidney

ABBREVIATIONS

- AUA: American Urological Association
- BUN: Blood urea nitrogen
- CBC: Complete blood count
- Cr: Creatinine
- CT: Computed tomography
- CVA: Costovertebral angle
- DVT: Deep vein thrombosis
- ESWL: Extracorporal Shock wave lithotripsy
- PCNL: Percutaneous nephrolithotomy
- PT/PTT: Prothrombin time/partial thrombin time
- SCC: Squamous cell carcinoma
- TB: Tuberculosis
- TCC: Transitional cell carcinoma
- US: Ultrasound
- UTI: Urinary tract infection
- XGP: Xanthogranulomatous pyelonephritis

UROLITHIASIS, URIC ACID

Paul Crow, MD

Francis X. Keeley, MD

BASICS

DESCRIPTION

- Urinary stones composed primarily of uric acid
- Uric acid is more likely to precipitate in acidic urine.

EPIDEMIOLOGY

- Account for 5–10% of all urinary tract stones
- 1/1,000 adults

RISK FACTORS

- Excretion of excessively acidic urine
- Strenuous exercise, dehydration
- Crohn disease, regional ileitis
- Ulcerative colitis, ileostomy, short-bowel syndrome
- Hyperuricosuria, gout:
  - Uric acid nephrolithiasis occurs in 10–25% of patients with gout
- Purine gluttony
- Inborn errors of metabolism:
  - Lesch-Nyhan syndrome: HGPRT
  - Phosphoribosylpyrophosphate synthetase overactivity
  - Glucose-6-phosphate deficiency
- Myeloproliferative states: Neoplasia, leukemia, hemolytic anemia, chemotherapy
- Decreased urinary volume
- Diabetes associated with metabolic syndrome (hyperglycemia, hyperinsulinemia, obesity, dyslipidemia, and HTN)
- Persistent acid urine pH

Genetics

The familial variety is autosomal dominant.

GENERAL PREVENTION

- Dietary considerations: Reduction of dietary protein (purine) in at-risk population.
- Encourage fluid intake.

PATHOPHYSIOLOGY

- Uric acid crystallization caused by the supersaturation of urine with respect to undissociated uric acid

- Uric acid is a weak acid with limited solubility and 2 dissociable protons:
  - pKa 1 is 5.5; pKa 2 is 10.3 (nonphysiologic).
- At a pH of 5.35, 1/2 of the uric acid is urate salt and 1/2 is free uric acid.
- At a pH of 6.5, 90% of the uric acid is soluble.
- Uric acid may serve as a nidus for calcium oxalate stone formation.
- Other renal conditions that may be related to hyperuricemia or gout are acute and chronic nephropathy.
- Uric acid nephropathy, acute (acute gouty nephropathy): Acute renal failure due to deposition of uric acid crystals in the renal tubules:
  - Often due to tumor lysis syndrome associated with the treatment of myelogenous malignancies such as leukemia and lymphoma
- Uric acid nephropathy, chronic: Chronic renal insufficiency due to sodium urate crystal deposition in the renal tubules:
  - Uncommon today; previously associated with tophaceous gout (tophi are monosodium urate crystals deposited in the soft tissues of the body)

COMMONLY ASSOCIATED CONDITIONS

- Diabetes and metabolic syndrome
- Gout
- Inflammatory bowel disease
- Lesch-Nyhan syndrome
- Myeloproliferative disease

DIAGNOSIS

HISTORY

- Acute presentation of urolithiasis:
  - Pain, fever, chills, nausea, vomiting secondary to renal colic.
- Purine gluttony:
  - Diet high in red meats, fish, and poultry
- Increased physical activity with dehydration; poor urine output; poor urine volume
- Gout, family history of uric acid stones
- Short-bowel syndrome, inflammatory bowel disease, ileostomy
- Myeloproliferative disorders

PHYSICAL EXAM

CVA tenderness

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Serum uric acid level may be normal or elevated >380 mol/L or 6.4 mg/100 mL
  - Latent hyperuricemia (borderline uric acid elevation) may require a purine loading test.
- Urine analysis:
  - pH: Generally <5.8
  - Presence of WBCs, RBCs
  - Crystals: Uric acid appearance of coffin-lid crystals
- 24-hr urine collection for uric acid; volume suggestive of uric acid:
  - Volume <2 L/d
  - pH <6.0
  - Uric acid >4.0 mmol/d

Imaging

- Plain KUB x-ray:
  - Uric acid stones are often radiolucent (noncalcified), therefore the plain film is often not useful.
- Renal US
- IV urogram
- Noncontrast abdominal spiral CT: Gold standard imaging modality

Diagnostic Procedures/Surgery

- Stone analysis
- 24-hr urine collection for uric acid

Pathological Findings

- Long-term deposition of crystals in the renal parenchyma can cause chronic urate nephropathy.
- Microtophi cause a giant-cell inflammatory reaction, causing proteinuria and inability of the kidney to concentrate urine.

DIFFERENTIAL DIAGNOSIS

- Renal stones:
  - Uric acid
  - Calcium oxalate monohydrate
  - Calcium oxalate dihydrate
  - Cysteine
  - Struvite (magnesium ammonium phosphate)
- Filling defect on IV urogram (see also Section I: “Filling Defect, Upper Urinary Tract”):
  - Can be differentiated on noncontrast CT

- Uric acid stone; urothelial neoplasm (eg, TCC)
- Blood clot, fungus ball, sloughed renal papilla, crossing renal vessel

- Bladder calculi: 50% consist of uric acid

TREATMENT

ALERT

Do not allow urinary pH to chronically rise above 7.0. This may cause the precipitation of other urinary calcium salts such as calcium phosphate.

- Acute renal colic and emergency management of urolithiasis is discussed in Section I: "Urolithiasis, Adult, General"
- Uric acid stones are often amenable to medical therapy.
- General approach:
  - Low-protein/low-purine diet (decrease red and organ meats)
  - >2 L fluid intake/d
  - Alkalinize urine

MEDICATION

First Line

- Oral alkalinization therapy to maintain a urine pH of 6.5 to 7.0:
  - May require 3–4 mo to dissolve stone
  - Do not exceed pH 7, as stones of other composition can precipitate, such as calcium phosphate.
  - Requires patient to self-monitor urine pH daily, with pH paper or Nitrazine paper
  - Use potassium citrate 30–60 mEq/d (Polycitra-K or Urocit-K).
  - Alternative: Sodium bicarbonate 650 mg q6–8h:

    Note that potassium citrate is preferred to sodium bicarbonate due to the high sodium load.

Second Line

Allopurinol:

- For hyperuricemia or urinary uric acid secretion >1,000 mg/d
- If no response to standard alkalinization
- Dose 100–600 mg/d in additional to PO alkalinization
- Allopurinol inhibits conversion of hypoxanthine and xanthine to uric acid.
- Side effects: Skin rash, fever, or acute attack of gout.

SURGERY/OTHER PROCEDURES

- Depends on size and position of stone together with patient factors and preference
- ESWL

- Ureteroscopic lithotripsy
- Percutaneous nephrolithotomy
- Open/laparoscopic nephrolithotomy
- Alkaline irrigation via nephrostomy tube

ONGOING CARE

PROGNOSIS

Depends on etiology and stone characteristics.

COMPLICATIONS

- Sepsis
- Obstructive renal failure

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up includes urinalysis for pH, crystals, RBCs/WBCs.
- Follow stone size with US or CT every 2–3 mo on therapy.

ADDITIONAL READING

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- Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: Urolithiasis. J Urol 2005;173:848–857.
- Shekarriz B, Stoller ML. Uric acid nephrolithiasis: Current concepts and controversies. J Urol 2002;168(4 Pt 1):1307–1314.

See Also (Topic, Algorithm, Electronic Media Element)

- Bladder Calculi
- Pregnancy, Urolithiasis
- Urolithiasis, Adult, General
- Urolithiasis, Pediatric, General
- Urolithiasis, Calcium Oxylate/Phosphate
- Urolithiasis, Staghorn

CODES

ICD9

- 274.10 Gouty nephropathy, unspecified
- 274.11 Uric acid nephrolithiasis
- 592.9 Urinary calculus, unspecified

ABBREVIATIONS

- CT: computed tomography
- CVA: Costovertebral angle

- ESWL: Extracorporeal shock wave lithotripsy
- HGPRT: Hypoxanthine guanine phosphoribosyl transferase deficiency
- HTN: Hypertension
- IV: Intravenous
- KUB: Kidneys, ureters, bladder
- RBC: Red blood cell
- TCC: Transitional cell carcinoma
- WBC: White blood cell

UROSEPSIS (SEPTIC SHOCK)

Brett S. Carver, MD
Joel Sheinfeld, MD

BASICS

DESCRIPTION

- Sepsis is the systemic inflammatory response to infection, with urosepsis identifying the source of the infection as originating somewhere in the urinary tract.
- It is estimated that in 50% of sepsis cases the urinary tract is the source.

EPIDEMIOLOGY

- Estimated that sepsis occurs in >750,000 patients in the US annually
- The mortality rates associated with sepsis syndrome and septic shock are 13% and 28%, respectively.

RISK FACTORS

- Elderly
- Diseases such as diabetes mellitus, malignancy, immunosuppression, cachexia, immunodeficiency, alcoholism
- Obstructive uropathy: BPH, prostate cancer, stricture, urolithiasis, neurologic voiding dysfunction, retroperitoneal masses, and fibrosis, sloughed papilla, endometriosis
- Abnormal/congenital anatomy: UPJ obstruction, polycystic kidneys, ureterocele, vesicoureteral reflux, phimosis
- Inflammatory/infectious diseases:
  - Pyelonephritis, acute bacterial prostatitis [NIH category I], renal abscess, paranephric abscess, epididymoorchitis, Fournier gangrene
- Precipitating interventional/nosocomial events resulting in bacteremia and subsequent urosepsis:
  - Indwelling catheters, urologic instrumentation/surgery such as prostate biopsy, transurethral surgery

GENERAL PREVENTION

- Urine culture and appropriate antibiotic coverage prior to a urologic procedure
- Silver-impregnated urethral catheters and closed urinary drainage systems further reduce incidence of nosocomial UTI.

PATHOPHYSIOLOGY

- The most common etiology of urosepsis is secondary to a bacterial infection with Escherichia coli, Klebsiella, Pseudomonas aeruginosa, Proteus sp., or Enterococcus (E. faecalis).

- P. aeruginosa, Enterobacter sp., and Serratia sp. are rare and associated with urologic instrumentation.
- Obstruction in an infected urinary tract further contributes to the development of sepsis.
- 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.
  - These components activate numerous humoral pathways and cells involved in the inflammatory process.
- The primary initiator of gram-negative bacteria septic shock is endotoxin, a lipopolysaccharide component of the bacterial cell membrane.
- The intravascular activation of inflammatory systems results in the overproduction of cytokines such as TNF tumor necrosis factor and IL-1.
- 1 of the earliest signs of sepsis is increased respiratory rate with respiratory alkalosis.
- Sepsis is a clinical syndrome that is a complication of severe infection that results in systemic inflammation and extensive tissue injury. This is often manifested as MODS, and is usually the cause of death in severe sepsis.
- SIRS and sepsis:
  - Noninfectious processes, such as acute pancreatitis, may also be complicated by tissue injury secondary to the inflammatory system. SIRS refers to the dysregulated host inflammatory response in the absence of infection.
  - It is essential to distinguish an underlying disease (infection or noninfection) and the host response (sepsis or SIRS).
- International Sepsis Definitions Conference Definitions:
  - SIRS: 2 of:

    Temperature >38.5°C or <35.0°C

    Heart rate >90 beats/min

    Respiratory rate of >20 breaths/min or $PaCO_2$ of <32 mm Hg

    WBC count of >12,000 cells/mL, <4,000 cells/mL, or >10% bands
  - Sepsis SIRS in response to documented infection (culture or Gram stain of blood, urine, etc., positive for pathogenic microorganism; or focus of infection identified by visual inspection, eg, wound with purulent discharge)
  - Severe sepsis: Sepsis with at least 1 of the following signs of organ hypoperfusion/dysfunction:

    Mottled skin

    Capillary refilling of 3 sec

Urine output of <0.5 mL/kg for at least 1 hr, or renal replacement therapy (eg, hemodialysis)

Lactate >2 mmol/L

Abrupt change in mental status or abnormal EEG

Platelets <100,000 cells/mL or DIC

Acute lung injury/ARDS

Cardiac dysfunction on EKG

– Septic shock: Severe sepsis and 1 of the following:

Systemic mean BP of <60 mm Hg after 20–30 mL/kg hetastarch or 40–60 mL/kg saline bolus, or PCWP 12–20 mm Hg

Need for dopamine >5 g/kg/min, or norepinephrine or epinephrine of <0.25 g/kg/min to maintain mean BP at >60 mm Hg

– Refractory septic shock: Need for dopamine at >15 g/kg/min, or norepinephrine or epinephrine at >0.25 g/kg/min to maintain mean BP at >60 mm Hg (80 mm Hg if previously hypertensive)

COMMONLY ASSOCIATED CONDITIONS

- Acute pyelonephritis
- Lower UTI
- Urolithiasis
- Urologic procedure/instrumentation

DIAGNOSIS

HISTORY

- A thorough history should be obtained, with emphasis on identifying the primary etiology:

– The classical presentation of fever and chills followed by hypotension is manifested in only ~30% of patients.

- A history of hydronephrosis, urolithiasis, flank pain, UTIs, 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: Hyperthermia, hypothermia, tachycardia, tachypnea, and hypotension.
- Examine for all urologic and nonurologic sources of bacteremia:

– Purulent subcutaneous fluid collections; chest exam; costovertebral tenderness; abdominal or suprapubic tenderness; exam of the scrotum, testis, perineum; prostatic fluctu-

ance; extremities for tenderness or swelling.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC with differential: Usually shows elevated WBC count with elevated neutrophil count. However, patients may also have neutropenia.
- Comprehensive metabolic and liver profile: May show evidence of end-organ dysfunction
- Blood, urine, and wound culture and Gram stain for preliminary identification and to document etiology and sensitivity to antibiotics:
  - Obtain before starting empiric antibiotics

Imaging

Obtained based on presumptive initiating event and clinical symptoms

Diagnostic Procedures/Surgery

Diagnostic procedures should be tailored to identifying the initiating event.

DIFFERENTIAL DIAGNOSIS

- Upper urinary tract source:
  - Emphysematous pyelonephritis
  - Pyelonephritis
  - Pyonephrosis
  - Renal and perirenal abscess
  - Renal TB
  - Xanthogranulomatous pyelonephritis
- Lower urinary tract source:
  - Acute bacterial prostatitis
- External genitalia:
  - Cellulitis
  - Epididymitis/orchitis
  - Fournier gangrene
  - Pyoderma gangrenosum
  - Testicular abscess
- Common nonurologic causes of sepsis:
  - Catheter-related bacteremia (usual central line in place for prolonged period)
  - Empyema
  - Endocarditis
  - Mediastinitis

– Intra-abdominal processes: Pancreatic infection, cholecystitis, cholangitis, peritonitis, diverticular abscess, appendical abscess, tubo-ovarian abscess, etc.)
  – Pneumonia
  – Prosthetic device infection
  – Septic arthritis
  – Sinusitis
  – Soft tissue infection
- Noninfectious conditions that mimic sepsis:
  – Acute adrenal insufficiency
  – Acute GI bleed
  – Acute myocardial infarction
  – Acute pancreatitis
  – Acute pulmonary embolus
  – Adverse drug reactions
  – Emboli: Amniotic fluid, fat, pulmonary
  – Procedure-related transient bacteremia
  – Transfusion reactions

TREATMENT

- Early supportive care:
  – Volume expansion with isotonic fluids
  – Supplemental oxygen with or without intubation and assisted ventilation if indicated
  – Monitor for cardiac decompensation; vasoactive agents (dopamine, etc.) may be utilized to maintain adequate BP and perfusion.
  – Maintain glycemic control.
- Distinguish true sepsis from SIRS:
  – With an infection, treat as soon as possible.
  – Administer empiric antibiotics
  – Surgical drainage or decompression as indicated (catheter, stent, nephrostomy, percutaneous drainage)

MEDICATION

First Line

- Broad-spectrum antibiotic coverage (against both gram-positive and gram-negative bacteria) should be instituted immediately.
- Ampicillin (vancomycin if penicillin allergic) and gentamicin are usually sufficient.
- Monotherapy for urosepsis due to aerobic gram-negative bacilli:

– Aztreonam: 2 g IV q6–8h; max 8 g/d
– Levofloxacin: 500 mg IV q24h
– 3rd-generation cephalosporins:
Ceftriaxone: 1–2 g IV q12–24h
Cefotaxime: 2 g IV q6–8h
Ceftazidime: 500 mg IV q8–12h
– 4th-generation cephalosporin:
Cefepime: 2 g IV q12h

Preferred monotherapy for urosepsis due to enterococci (E. faecalis) is with ampicillin (or vancomycin if penicillin-allergic).

• Monotherapy for suspected enterococci (E. faecalis) urosepsis: Ampicillin or vancomycin (penicillin-allergic).
• Nosocomial urosepsis monotherapy:
– Piperacillin, imipenem, or meropenem
– Community-acquired urosepsis infection:
Levofloxacin, aztreonam, or an aminoglycoside plus ampicillin.
• Fournier gangrene:
– Penicillin G: 3–5 million IU IV q6h for gram-positive coverage.
– Imipenem: 500–1,000 mg IV q6h for polymicrobial coverage.
– Clindamycin: 600–1,200 mg/d (divided dose) for anaerobic coverage if Clostridia are suspected.
– Add vancomycin 1 g IV b.i.d. if MRSA suspected.

Second Line

• Culture-specific antibiotic coverage should be instituted when sensitivity results are available.
• Switch to PO antibiotics when clinically stable for at least 48 hr and usually complete a 14-day course based on the cause of the infection.

SURGERY/OTHER PROCEDURES

Patients should undergo surgical drainage of purulent collections, removal of foreign bodies, and relief of urinary tract obstruction.

ADDITIONAL TREATMENT

Definitive correction of any correctible factors when patient stabilized

ONGOING CARE

PROGNOSIS

• Mortality associated with sepsis syndrome and septic shock are 13% and 28%, respectively.

- 5 factors have been associated with a higher risk of mortality from sepsis: Fever, WBC count, creatinine level, diabetes mellitus, and serum albumin levels.

COMPLICATIONS

Renal insufficiency, hepatic dysfunction, end organ failure, cardiac events, death

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Patient should be continued on appropriate antibiotic coverage for 2–3 wk.
- Repeat cultures should be obtained to ensure that treatment is adequate.

ADDITIONAL READING

- Annane D, Bellissant E, Cavaillon JM. Septic shock. Lancet 2005;365:63.
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- Mackenzie I, Lever A. Management of sepsis. BMJ 2007;335(7626):929–932.
- Wagenlehner FM, Weidner W, Naber KG. Optimal management of urosepsis from the urological perspective. Int J Antimicrob Agents 2007;30(5):390–397.

See Also (Topic, Algorithm, Electronic Media Element)

- Epididymitis
- Fournier Gangrene
- Prostatitis, Acute, Bacterial (NIH I)
- Pyelonephritis, Acute
- Pyelonephritis, Emphysematous
- Pyelonephritis, Xanthogranulomatous
- Pyonephrosis
- Renal and Perirenal Abscess
- Retroperitoneal Abscess

CODES

ICD9

- 038.9 Unspecified septicemia
- 785.52 Septic shock
- 995.92 Severe sepsis

ABBREVIATIONS

- ARDS: Acute respiratory distress syndrome
- BP: Blood pressure
- BPH: Benign prostatic hyperplasia
- CBC: Complete blood count
- DIC: Disseminated intravascular coagulation
- EEG: Electroencephalogram
- EKG: Electrocardiogram
- IV: Intravenous
- MODS: Multiple organ dysfunction syndrome
- MRSA: Methicillin-resistant Staphylococcus aureus
- PCWP: Pulmonary capillary wedge pressure
- SIRS: Systemic inflammatory response syndrome
- TB: Tuberculosis
- TNF: Tumor necrosis factor
- UPJ: Ureteropelvic junction
- UTI: Urinary tract infection
- WBC: White blood cell

UROSTOMY PROBLEMS

Nicholas T. Karanikolas, MD
Leonard G. Gomella, MD

BASICS

DESCRIPTION

- Complications of the abdominal urinary stoma (urostomy) is the most common problem encountered in the postoperative period in patients undergoing urinary diversion.
- Urostomy is an incontinent 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 distal ileum being the most common bowel segment used:
  - Also called ileal conduit, cutaneous uretero-ileostomy if made up of ileum
  - Colon conduit, if made up of segment of large bowel.
  - Very rarely, a urostomy can consist of the ureters being directly anastomosed to the skin (cutaneous ureterostomies). These are uncommon in adults but are sometimes performed in children.
- This section focuses on the chronic issues that often involve a urostomy.

EPIDEMIOLOGY

- 2.8–19% of patients develop stomal stenosis with ileal conduits.
- 10–20% of patients with colon conduits develop stenosis.
- Parastomal hernia:
  - Occurs in 2–6.6% of patients with loop ileostomies
  - Rare with end stomas (1–4%)
  - More commonly occur with loop stomas (4–20%)
- Nearly all patients will have a stomal-related complication at some point.

RISK FACTORS

- Obesity
- Chronic cough
- Wound infection
- Abdominal distension
- Malnutrition
- Immunosuppression/steroid use
- Poor surgical technique
- Lack of proper stomal 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 to the skin.

GENERAL PREVENTION

• Parastomal skin care can reduce bleeding, stomal stenosis, and dermatitis.

• Surgical technique ensuring a properly formed stoma in an appropriate location based on the abdominal wall contours

• Proper site location by an experienced stoma nurse preoperatively takes into account many variables, including the contour of the abdomen in the sitting and standing positions and the type of belts and garments worn by the patient.

• Proper selection of pouching system:

– Compatibility with abdominal contours

– Proper sizing of the pouch opening to minimize urine exposure on the skin

– The opening on the adhesive skin barrier should be no more than 1/8-inch larger than the stoma to help keep urine off the skin.

• Emptying pouch appropriately such that excessive weight of the pouch will not disrupt the skin adhesion (usually when about 1/3 full)

• 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.

PATHOPHYSIOLOGY

• A pouching system (also called an appliance) is used to collect the urine that exits from the stoma:

– 2 styles of pouching systems are available:

Both include an adhesive faceplate, flange, skin barrier, or wafer (the part that sticks to the skin), and a urine collection pouch.

1-piece pouches are fused to the skin barrier.

2-piece systems have a face plate and a pouch that can be removed from the barrier.

• Patients should be encouraged to empty the pouch as needed but at least every 2–4 hr.

• 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 ~1.5 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 initially 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:
  – Stomal necrosis can result in retraction and a flush ostomy that is difficult to apply an appliance to.
- Early stomal retraction can be caused by an insufficient length of bowel segment or improper technique in securing and eversion of the stoma.
- Stomas stenosis can develop with or without obstruction:
  – Reported in 2.8–19%
  – May be asymptomatic, painful, or cause appliance fit problems
  – Stomal stenosis is less for loop stoma than end stomas.
  – Multifactorial causes: Fascial or muscular constriction, ischemia, and retraction allowing skin edges to overgrow opening (hyperkeratosis)
- Parastomal hernia:
  – Gap between the intestinal segment forming the stoma and the surrounding fascia
  – Factors include obesity, malnutrition, chronic cough, wound infection.
  – Placement of the intestinal segment through the rectus fascia minimizes the risk of herniation.
  – Stomas placed lateral to the rectus fascia are more likely to develop a parastomal hernia (2.8% in rectus fascia vs. 21% lateral to rectus fascia).
  – Most parastomal hernias tend to worsen with time.
- Poorly fitting appliances can cause social embarrassment and skin irritation and breakdown:
  – Urine contact (alkaline) with the skin can cause stomal encrustation, stomal epithelization, and eventual stenosis due to hyperkeratosis.
  – Unless contraindicated, maintaining the urine in an acid state is more protective of the skin (see below).
- Irritative adhesives
- Fungal infections cause severe redness and pruritus.
- Bleeding from varices associated with portal HTN.
- Urine pH:
  – Most fruits and vegetables give an alkalinized urine. Meats and cereals will usually lead to an acidic urine.
  – Unless contraindicated, urine should be kept in an acidic pH range.
  – This protects the skin and limits the deposition of urine crystals in and around the stoma.

- Calcifications and small stones due to exposed staples usually pass spontaneously

COMMONLY ASSOCIATED CONDITIONS

- Congenital anomalies such as exstrophy or myelodysplasia
- Urothelial carcinoma
- Urethral carcinoma

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 parastomal skin lesions, bleeding, or dermatitis
- Problems with the adhesives, paste, tape, or pouch material

PHYSICAL EXAM

- Peristomal skin lesions:
  - Irritative parastomal lesions that are manifested by hypopigmentation, hyperpigmentation, and skin atrophy
  - Erythematous erosive lesions that are macular, scaling with loss of epidermis
  - Pseudo-verrucous appear wartlike
- Minor bleeding from the exposed mucosa is common. Significant bleeding can be seen in cases of ileal conduit varices.
- Examine for evidence of parastomal herniation:
  - Defect along fascial region of urostomy
  - Reducible
- Evidence of stomal stenosis or hyperkeratosis:
  - Calibrate ostomy with a sterile catheter if stomal stenosis present.
- Note if any urinary crystals are present on the skin edge.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

Usually not necessary

Imaging

- Not usually necessary. However, in the setting of severe stomal stenosis or prolapse, CT or US may identify dilation of the intestinal segment or evidence of hydronephrosis.
- Loopogram to identify if there is reflux or obstruction of the ureters with prolapse or parastomal herniation.

Diagnostic Procedures/Surgery

Calibration of the stoma with a red rubber catheter and determination if there is retained urine may be useful.

DIFFERENTIAL DIAGNOSIS

- Cutaneous allergic reaction or fungal infection
- Parastomal hernia
- Peristomal skin breakdown
- Stomal bleeding
- Stomal prolapse
- Stomal retraction
- Stomal stenosis

TREATMENT

- Proper initial surgical technique will minimize short- and long-term stomal problems.
- Proper stomal care and problem-solving is often accomplished by consultation with a certified ostomy care health provider:
  - WOCNCB provides certification in ostomy nursing
- A proper pouching system should have the following characteristics:
  - Secure, with a good 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 urostomy system tends to be more flexible that a 2-piece unit and 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.
- Allergic reaction to adhesive or other components can be addressed by switching to another product.
- Urine crystals on the skin or stoma (whitish gritty particles) are caused by alkaline urine:
  - Cranberry juice in place of citrus juices (citrus juices makes the urine more alkaline)
  - Consider vitamin C daily

– Some acid ash foods (make urine acidic) include: Most meats, breads and cereals, cheese, corn, cranberries, eggs, macaroni, 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 skin barrier dry and reduce the incidence of superficial fungal infections where the pouch hangs down and contacts the skin.

MEDICATION

- 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.

SURGERY/OTHER PROCEDURES

- Surgical repair for parastomal hernias:
  - High likelihood of recurrence with or without relocation of the fascial opening
  - Suprafascial synthetic mesh wrap may decrease recurrence rates.
  - Period of conservative management appropriate
  - Laparoscopic repair reported
- Surgical revision for stomal stenosis
- Surgical revision of retracted stoma
- Liposuction has been used to correct inverted stoma in obese patients
- Looposcopy to remove calculi

ADDITIONAL TREATMENT

Radiation therapy: Some limited reports of radiation to treat stomal stenosis–related hyperkeratosis

ONGOING CARE

PROGNOSIS

Very good when intervention is applied in a timely fashion to prevent irreversible upper tract deterioration from stomal stenosis.

COMPLICATIONS

- Recurrent stomal stenosis
- Recurrent parastomal hernia
- Recurrent skin irritation from poor ostomy care
- Appliance leakage

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Stomal wound care
- Cancer surveillance as per protocol

ADDITIONAL READING

- American Cancer Society Urostomy Guide:http://www.cancer.org/docroot/CRI/content/CRI_2_6x_Urostomy.asp (Accessed April 2009)
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See Also (Topic, Algorithm, Electronic Media Element)

Catheterizable Stoma Problems

CODES

ICD9

- 996.39 Other mechanical complication of genitourinary device, implant, and graft
- 997.5 Urinary complications, not elsewhere classified
- V55.6 Attention to other artificial opening of urinary tract

ABBREVIATIONS

- CT: Computed tomography
- HTN: Hypertension
- US: Ultrasound
- WOCNCB: Wound Ostomy Continence Nursing Certification Board

VAGINITIS/VULVOVAGINITIS

Deborah R. Erickson, MD

BASICS

DESCRIPTION

- Vaginitis is infection or inflammation of just the vagina. Vulvovaginitis involves both the vagina and vulvar areas.

)

- Can be infectious, noninfectious (chemical or irritants), or hormonal
- Bacterial vaginitis (BV) is the most common cause of vaginal discharge in women of childbearing age.

EPIDEMIOLOGY

):

- BV: 22–50%
- Candidiasis: 17–39%
- Trichomoniasis: 4–35%

RISK FACTORS

- Depends on etiology

)

):

  - Broad-spectrum antibiotics
  - Corticosteroids
  - Diabetes mellitus
  - Immunosuppression
  - Pregnancy

- Risk for any STD is increased with:
  - Number of partners
  - Number of partners' partners
  - Unprotected sexual contact

GENERAL PREVENTION

)

- Wash external skin with water alone or mild soap.
- Avoid tight clothing.
- For STDs, treat partners as applicable.
- Avoid douching, a risk factor for BV.
- For trichomoniasis and other STDs:

– Abstain from sexual contact, or be in a long-term mutually monogamous relationship with an uninfected partner.
– Latex male condoms

PATHOPHYSIOLOGY

- Depends on etiology
- BV: Normal vaginal Lactobacillus are replaced with anaerobic bacteria, Gardnerella vaginalis and Mycoplasma hominis (some of these are normal vaginal flora; their overgrowth leads to clinical BV)
- VVC: Overgrowth of Candida
- Trich and other STDs: Infection with organism
- Atrophic vaginitis: Lack of estrogen

COMMONLY ASSOCIATED CONDITIONS

STDs are associated with other STDs.

DIAGNOSIS

HISTORY

- Potential predisposing factors:
  - Prior vaginitis
  - Antibiotic use
  - Pregnancy
  - Diabetes
  - Sexual intercourse
  - Method of contraception
  - STD history
- Symptoms of current condition:
  - Duration
  - Response to prior treatment
  - Any current treatments that have been self-administered (OTC products)
  - Itching, burning
  - Color, consistency, and odor of discharge

ALERT

)

PHYSICAL EXAM

- Inspect the vulva, vagina, and cervix for:
  - Erythema or skin lesions
  - Degree of estrogenization

- Discharge
- Foreign body (eg, forgotten tampon)
- Friable cervix: Consider Chlamydia or gonorrhea

- Characterize discharge if present:
  - BV: White or gray, homogeneous, thin, coats the vaginal walls, can have fishy odor
  - Candida: White, thick, curdy, not malodorous
  - Trich: Yellow or yellow-green, malodorous, can be profuse and frothy
  - Cervicitis: Purulent, comes from cervix
- Palpate for tenderness:
  - Vulvar tenderness without discharge suggests atrophic vaginitis, vulvodynia, or dermatologic condition

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and culture if dysuria is present
- Evaluate discharge by wet mount and KOH:
  - Put a drop of discharge on a glass slide
  - Add a drop of saline to the discharge, add cover slip, and look under microscope for Trichomonas and clue cells
  - Repeat with another slide, using a drop of 10% KOH instead of saline. Wait 2 minutes for KOH to dissolve most of the cells. Yeast cells or hyphae remain undissolved.
- Diagnosis of BV is controversial. Generally need 3 (ref 2) or 2 (ref 1) of Amsel's criteria:
  - Abnormal gray discharge
  - Vaginal pH >4.5 (sample from mid-vagina)
  - Positive amine test (fishy odor before or after addition of 10% KOH)
  - >20% of epithelial cells on wet mount are clue cells:

    Vaginal epithelial cells studded with adherent coccobacilli that are best appreciated at the edge of the cell
- Diagnosis of candidiasis:
  - Hyphae or yeast cells on KOH or wet mount
  - If Candida suspected but not seen on KOH or wet mount, send discharge for yeast culture
- Diagnosis of trichomoniasis:

)

)
  - OSOM Trichomonas Rapid Test
  - Affirm™ VP III
- Culture is the most accurate test for trich

):
  - Purulent discharge
  - Discharge has leukocytes on microscopy
  - Friable cervix
  - Symptoms of PID (pelvic pain, fever)
  - Patient in high-risk group for STDs

Diagnostic Procedures/Surgery

- Not needed in most cases
- Biopsy may be indicated for vulvar dermatologic disorders or to rule out cancer.

Pathological Findings

Vulvar dermatologic disorders and cancer have characteristic histology.

DIFFERENTIAL DIAGNOSIS

- The most common vaginal infections that cause discharge are:
  - BV
  - VVC
  - Trichomoniasis, an STD
- Cervicitis due to Chlamydia or gonorrhea can present with discharge.
- Noninfectious etiologies:
  - Atrophic vaginitis
  - Foreign body
  - Vulvar dermatologic conditions
  - Vulvodynia

TREATMENT

- See “General Prevention.”
- Attempt to identify specific cause based on history, lab testing to avoid shotgun management.

MEDICATION

First Line

):
  - Metronidazole 500 mg PO b.i.d. for 7 days
  - Single dose 2 g not recommended currently

– Metronidazole gel 0.75% 1 applicator (5 g) per vagina every day for 5 days
– Clindamycin cream 2% 1 applicator (5 g) per vagina at bedtime for 7 days
):
– Multiple topical azole regimens, or single PO dose 150 mg fluconazole:
)
Fluconazole has many drug interactions.
):
– Defined as severe disease (extensive erythema, edema, excoriation, fissures), recurrent disease, not Candida albicans, uncontrolled diabetes, debilitation, immunosuppression, or pregnancy
– Start with same drugs but give longer courses.
– Correct underlying conditions if possible.
– If azoles fail, use 600 mg of boric acid in a gelatin capsule, per vagina daily for 2 wk
):
)
– Gel is much less effective than PO dose.
)
Second Line
):
– Clindamycin 300 mg PO b.i.d. for 7 days
– Clindamycin ovules 100 mg per vagina at bedtime for 3 days
)
)
ALERT
)
)
Pregnancy Considerations
):
– BV in pregnancy is associated with preterm birth.
– Definitely treat in pregnancy if symptoms are present.
– Screen pregnant women who are at high risk for preterm birth; treat if positive.
– If low or average risk for preterm birth, no benefit to screening
):
Metronidazole 500 mg PO b.i.d. for 7 days

Metronidazole 250 mg PO t.i.d. for 7 days

Clindamycin 300 mg b.i.d. for 7 days

Topical clindamycin should not be used in the 2nd half of pregnancy.

)

):

– Trich in pregnancy is associated with adverse outcomes, but no strong evidence that treatment improves outcomes, therefore:

No need to screen

Do treat 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.

ADDITIONAL TREATMENT

For atrophic vaginitis, if estrogen cannot be used, moisturizers and lubricants may help symptoms.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

)

ONGOING CARE

PROGNOSIS

Depends on etiology

COMPLICATIONS

)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

):

)

)

)

):

– No follow-up needed unless symptoms persist or recur within 2 mo.

– No partner treatment, unless he has balanitis or if she has frequent recurrences.

):

– Treat partners and avoid sexual contact until both partners have completed treatment and are asymptomatic.

– No follow-up needed if symptoms resolve in both

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ADDITIONAL READING

See Also (Topic, Algorithm, Electronic Media Element)

- Candidiasis, Cutaneous, External Genitalia
- Chlamydia Sexually Transmitted Disease
- Gonorrhea
- Lichen Sclerosis et Atrophicus
- Menopause, Urologic Considerations
- Pregnancy, Urologic Medications Use With
- Sexually Transmitted Diseases, General
- Vaginal Atrophy, Urologic Considerations
- Vaginal Discharge Algorithm
- Vaginal Discharge, Urologic Considerations
- Vulvar Malignancy, Urologic Considerations
- Vulvodynia

CODES

ICD9

- 112.1 Candidiasis of vulva and vagina
- 131.01 Trichomonal vulvovaginitis
- 616.10 Vaginitis and vulvovaginitis, unspecified

ABBREVIATIONS

- BV: Bacterial vaginosis
- HIV: Human immunodeficiency virus
- KOH: Potassium hydroxide
- PID: Pelvic inflammatory disease
- OTC: Over the counter
- STD: Sexually transmitted disease
- VVC: Vulvovaginal candidiasis

VARICOCELE, ADULT

Ashley E. Ross, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- A dilation of the pampiniform plexus of veins situated within the spermatic cord)[C]
- Can be symptomatic, asymptomatic, or alter spermatogenesis

EPIDEMIOLOGY

- 15–20% of postpubertal males:
  - Left hemi-scrotum in majority of cases
  - Bilateral in 33%
  - If prior to puberty or unilateral right varicocele (rare), suggests underlying pathology (See “Varicocele, Pediatric”)
- 40% of men with primary infertility
- 80% of men with secondary infertility
- Decreases with increasing BMI
- Increases with age
- Increased among 1st-degree relatives with varicocele

RISK FACTORS

- Congenital absence of valves in spermatic vein
- Acquired incompetence of valves, extrinsic compression increasing intravascular pressure (eg, inguinal hernia repair, retroperitoneal pathologic process)

Genetics

- Contribution ill defined
- Possible hereditary behavior

PATHOPHYSIOLOGY

- Varices:
  - Dilation of pampiniform plexus of veins in scrotum due to absent competent venous valves in spermatic vein
  - Lack/incompetence of valves may be congenital or acquired
  - Higher intravascular pressure in left renal and therefore left spermatic vein (nutcracker effect on left renal vein may contribute)
  - Gradual dilation of spermatic vein, separation of valves, retrograde flow of blood
  - Rarely, tumor or renal vein thrombus from renal tumor can occlude renal vein and lead to varix.

- Infertility due to varicoceles:
  - Poorly defined, many theories
  - Increased testicular temperature:
    Varix increases intratesticular temperature compared to controls (0.6–0.8°C)
    Loss of countercurrent testicular cooling mechanism
  - Increased testicular hypoxia and oxidative stress (possibly affecting Leydig cells)
  - Altered adrenal hormone metabolism from retrograde flow

COMMONLY ASSOCIATED CONDITIONS

- Infertility
- Testicular atrophy
- Rarely, tumor, renal vein thrombus

ALERT

- The development of an acute varicocele on either side suggests the possibility of a tumor compressing or causing thrombosis of the internal spermatic vein.
- This should be suspected when the varicocele is exclusively right-sided or if the varix remains engorged when the patient is placed in the supine position.

DIAGNOSIS

HISTORY

- Infertility:
  - Primary: Failure to conceive despite >12 mo of unprotected intercourse
  - Secondary: Those who have previously conceived
- Pain:
  - Most are asymptomatic
  - Dull ache, heavy sensation, sensation of increased heat
  - Increases with activity or standing and with Valsalva or strenuous activity (including intercourse)
  - Relieved by recumbency
- Acute onset suggests obstruction of renal or spermatic vein.

PHYSICAL EXAM

)[C]:

  - Examine in warm room after patient has been standing for 10 min.
  - Examine with patient supine and upright and while performing Valsalva in upright position.
- Varicocele feels like a bag of worms:
  - More prominent when patient upright or during Valsalva

- Grading:
  - Grade I: Small, not grossly visible, palpated only during Valsalva
  - Grade II: Moderate size, not grossly visible, easily palpable in standing position
  - Grade III: Large and grossly visible

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Seminal fluid analysis:
  - Needed prior to ligation to confirm male-factor subfertility
  - Typical findings for male-factor infertility due to varicocele
  - Sperm density <20 million/mL; motility <60%; motile sperm/ejaculate <40 million
  - Young men with varicocele and normal semen analysis should be followed every 1–2 yr for progression
- Endocrine screen, as needed, to evaluate for infertility

Imaging

)[B]

- Radiographic testing should therefore only be used when presence is uncertain on physical exam, recurrence is suspected, or varicocele is persistent after treatment.
- US:
  - Helps exclude other intrascrotal pathology
  - A normal spermatic vein at the inguinal canal is typically 2.2 mm, with an allowable increase to 2.7 mm with Valsalva.

)[C]

- Internal spermatic venography:
  - Potentially diagnostic and therapeutic
  - Invasive
- Abdominal imaging if renal or other retroperitoneal mass suspected of causing varicocele

Diagnostic Procedures/Surgery

Venography, as described above

Pathological Findings

- Histologic changes on testicular biopsy:
  - Tubular thickening
  - Interstitial fibrosis
- Decreased spermatogenesis
- Maturation arrest

DIFFERENTIAL DIAGNOSIS

- Infertility: See Section I: “Infertility, Urologic Considerations.”
- Spermatic cord mass:
  - Adenomatoid tumor of the cord
  - Epidermoid cyst
  - Epididymitis/epididymoorchitis
  - Fibrous pseudotumor
  - Filarial hydroceles
  - Funiculitis
  - Hernia
  - Hemangioma
  - Hydrocele/hydrocele of the cord
  - Inguinal lymphadenopathy
  - Leiomyoma
  - Malignant tumor: Liposarcoma, rhabdomyosarcoma, leiomyosarcoma, malignant fibrous histiocytoma
  - Mesothelioma
  - Metastatic: Melanoma and others
  - Polyorchidism
  - Sarcoid
  - Sperm granuloma
  - Spermatocele
  - Testis tumor
  - TB of the cord (tuberculoma)
  - Undescended/retractile testicle
  - Vasitis and vasitis nodosa (usually associated with epididymitis)

TREATMENT

)[A]

- Pain from symptomatic varicocele or testicular atrophy are also indications for repair.

MEDICATION

- Infertility: No medical therapy unless associated with hypogonadism
- Pain: Analgesics (eg, NSAIDs) usually are not durable therapy.

SURGERY/OTHER PROCEDURES

)[B]:

  - Couple with known infertility

– Female has normal fertility or potentially treatable cause of infertility:

Varicocele is palpable on physical exam or if suspected, presence is corroborated by US.

Male partner has abnormal semen analysis

- Operative therapy can be classified by anatomic site of varix ligation or surgical technique used:
  - Anatomic site of ligation

Scrotal approach now obsolete

Inguinal (Ivanissevitch): Inguinal incision, ligation of spermatic veins within inguinal canal; allows for coincident hernia repair (recurrence rates up to 16% and hydrocele rate up to 30% if non-microsurgical)

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 (vasal, cremasteric artery); recurrence is common (11–15%), hydrocele rate ~7%

Subinguinal: The standard in recent years; incision over the cord below external ring; number of veins requiring ligation is greater and magnification is recommended to salvage spermatic artery and lymphatics.

  - Surgical techniques:

Open with or without magnification (magnification preferred to spare arteries and lymphatics and allow for ligation of small venous tributaries)

Laparoscopic: High ligation; should only be performed by experts, recurrence rate <2%, hydrocele rate 5–8%, 5% patients experience transient anterior thigh numbness

)[A]

ADDITIONAL TREATMENT

- Scrotal support may help with mild symptoms
- Scrotal hypothermia device (Zorgniotti):
  - Equivocal fertility success at best
- Interventional radiology:
  - Venography with access through femoral or internal jugular (internal jugular access offers advantage for right sided varicocele)
  - Quicker recovery (3–4 days) but high recurrence rate (up to 25%)

COMPLEMENTARY AND ALTERNATIVE MEDICINE

- Assisted reproduction for varicocele-associated infertility
- IVF-ICSI:

- Less cost effective

ONGOING CARE

PROGNOSIS

- See “Surgery” for recurrence rates of individual techniques
- Semen quality improved in 70% men
- Spontaneous post-repair pregnancy rate up to 61%:
  - Result depends on sperm count
  - Men with <5 million sperm/mL only had 8% spontaneous pregnancy rate after repair
- Pain or relief of pain typically immediate after recovery from surgery

COMPLICATIONS

- Hydrocele
- Testicular artery injury
- Nerve injury (see subheading under “Surgery” for complication rates of individual techniques)

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Varicocele recurrence:
  - Monitor at 3-mo intervals
  - Recurrence usually evident within 6–13 mo
- Infertility:
  - Semen analysis at 3-mo intervals; semen should be monitored regularly for at least 1 yr or until pregnancy has been achieved

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See Also (Topic, Algorithm, Electronic Media Element)

- Infertility, Urologic Considerations
- Spermatic Cord Mass and Tumors
- Varicocele, Pediatric

CODES

ICD9

456.4 Scrotal varices

ABBREVIATIONS

- BMI: Body mass index
- IVF-ICSI: In vitro fertilization with intracytoplasmic sperm injection
- NSAID: Nonsteroidal anti-inflammatory drug
- US: Ultrasound

VARICOCELE, PEDIATRIC

Job K. Chacko, MD

T. Ernesto Figueroa, MD

BASICS

DESCRIPTION

A pediatric varicocele is defined as an abnormal dilatation of the pampiniform plexus of the spermatic cord in a male generally <18 yr of age.

EPIDEMIOLOGY

- ~15% of adolescent males but unusual pre-puberty
- 90% left sided
- 1–7% right sided
- 2% bilateral
- No racial, cultural or geographic predilection
- More common in tall, thin males

RISK FACTORS

- Congenital absence of valves in spermatic vein
- Acquired incompetence of valves, extrinsic compression increasing intravascular pressure (eg, inguinal hernia repair, retroperitoneal pathologic process)

PATHOPHYSIOLOGY

- Insertion of spermatic vein into left renal vein compared to IVC; left vein is 8–10 cm longer than the right vein
- “Nutcracker” phenomenon of left renal vein passing between aorta and SMA
- Incompetence or absence of valves of internal spermatic vein
- Erect posture (no varicoceles 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
  - Decreased proliferation and increased apoptosis of germ cells
  - Heat shock protein A2, oxidative stress patterns, calcium channels and DNA fragmentation affected
- Testicular hypotrophy: Significant testicular volume loss in 30–70% of adolescents with a varicocele:
  - Most rapid growth of testis between ages 11 and 16 yr

- Testicular hypotrophy reversible in 90% of patients after varicocelectomy

- Venous stasis:
  - Possible oxygen depletion in testis
  - Human studies do not support theory.
- Adrenal/renal reflux:
  - Theory of toxic exposure to testis from reflux of adrenal and renal metabolites
  - Data inconclusive
- Endocrine imbalance:
  - Abnormal response in patients with varicocele to GnRH stimulation
  - Unclear how affects future fertility or hypotrophy

COMMONLY ASSOCIATED CONDITIONS

Secondary causes can include retroperitoneal tumor, renal mass with renal vein extension, renal vein thrombosis, retroperitoneal fibrosis

DIAGNOSIS

HISTORY

- Usually asymptomatic
- Symptomatic-dull ache or fullness in scrotum, worsened with activity
- Occasional testicular pain due to venous congestion
- Change in size with position or Valsalva
- Found after routine pediatric physical

PHYSICAL EXAM

- Examine patient upright and supine, with and without Valsalva
- Grading criteria:
  - Grade I: Palpable only with Valsalva
  - Grade II: Palpable without Valsalva
  - Grade III: Visible through scrotal skin
- Check patient in supine position—Idiopathic varicoceles may disappear, while secondary varicoceles persist if caused by tumor, especially on right side
- “Bag of worms” superior to testicle
- Negative transillumination
- Examine for bilateral varicocele and lymphedema
  - If present, rule out secondary varicocele
- Testicular exam:
  - Visual inspection
  - Orchidometer-Prader vs. disk to determine testicular volume of each testicle and the comparison between the two testes

Prader orchidometer: Consists of 12 solid ellipsoid testis shaped models ranging in volume from 1 to 25 mL (1–6, 8, 10, 12, 15, 20, and 25 mL), against which the testis is compared

Disk or Rochester orchidometer: Series of 15 punched-out elliptical rings; volumes ranging from 1 to 30 mL (1–6, 8, 10, 12, 14, 16, 19, 22, 26, and 30 mL).

- 2 cc or 20% size discrepancy suggests testicular hypotrophy

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Semen analysis: Rarely performed in adolescents
- Response to GnRH stimulation: Not useful for surgical decision making.

Imaging

- Scrotal US
- Gold standard to measure testicular volume
- Decrease in volume of 2 cc or 20% size warrants intervention

Diagnostic Procedures/Surgery

Diagnosis confirmed by physical exam ± ultrasound

DIFFERENTIAL DIAGNOSIS

- Epididymal cyst (spermatocele)
- Hydrocele:
  - Communicating
  - Scrotal
  - Spermatic cord
- Inguinal hernia
- Lipoma of cord
- Paratesticular rhabdomyosarcoma

TREATMENT

- Management is either observation or surgical intervention
- Surgical indications in the pediatric population:
  - 2 cc or 20% size discrepancy between testicles based on ultrasound or orchidometer measurements
  - Bilateral varicoceles
  - Solitary testis with varicocele
  - Symptomatic

SURGERY/OTHER PROCEDURES

- Surgical technique based on comfort and experience of surgeon

- Techniques described in more detail in Section I: “Varicocele, Adult”
- Testicular artery sparing
  - Doppler can help identify
  - Preferred in adults because of concerns with infertility
  - Should be considered in adolescents
- Techniques:
  - Retroperitoneal
  - High ligation of vessels (Palomo)
  - Closer to left renal vein; usually fewer veins to ligate
- Inguinal:
  - External inguinal ring opened to isolate spermatic cord
- Subinguinal:
  - Spermatic cord isolated below inguinal ring at the level of the pubic tubercle
- Microsurgical dissection:
  - Adjunct often used with inguinal and subinguinal approaches that helps with artery and lymphatic sparing
- Laparoscopic:
  - Magnification helps with artery/lymphatic sparing
  - Results approaching open techniques
- Radiographic embolization:
  - Generally reserved for recurrent/persistent varicocele
- 90% of patients demonstrate catch-up growth

ONGOING CARE

PROGNOSIS

No definitive evidence that adolescents with varicocele will have impaired fertility in future or that surgical correction will improve/prevent infertility

COMPLICATIONS

- Recurrence or persistence of varicocele:
  - 1–15% depending on technique
- Postoperative hydrocele (1–9%)
- Testicular atrophy
- Failure of catch-up growth
- Possible decreased fertility

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- If asymptomatic and no testicular size discrepancies, observe with bi-annual or annual exams
- If postsurgical, assess for testicular catch-up growth and hydrocele formation after 3 mo with ultrasound. Then monitor biannually or annually.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Infertility, Urologic Considerations
- Spermatic Cord Mass and Tumors
- Varicocele, Adult

CODES

ICD9

456.4 Scrotal varices

ABBREVIATIONS

- GnRH: Gonadotropin-releasing hormone
- IVC: Inferior vena cava
- SMA: Superior mesenteric artery
- US: Ultrasound

VAS DEFERENS, CONGENITAL ABSENCE

Wilmer B. Roberts, MD, PhD
Arthur L. Burnett, MD

BASICS

DESCRIPTION

- Congenital bilateral absence of the vas deferens (CBAVD, agenesis of the vas deferens) may occur unilaterally or bilaterally.
- CBAVD blocks the transport of spermatozoa from testicular or epididymal structures to the outer genital tract.
- This results in azoospermia, or absence of sperm in the ejaculate.
- Often related to CF, CBAVD is 1 of the most consistent features of the disease, afflicting over 98% of CF patients, compared to the more commonly thought of respiratory symptoms that are present in only about 50% of patients.

EPIDEMIOLOGY

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- 1.3% of all infertile men
- Ipsilateral renal anomalies present in 91% of men with unilateral absence of the vas
- The most common CFTR mutation, F508del, ~70% in Northern European populations

RISK FACTORS

CF

Genetics

Mutations of the CFTR; multiple mutations often identified

PATHOPHYSIOLOGY

- CF, general:
  - Altered chloride transport leads to thick, viscous secretions in multiple organ systems (lungs, pancreas, liver, intestine, reproductive tract).
  - Typical CF presentation: Multisystem disease involving several organs
- Genetics of CF as it relates to CBAVD:
  - CF results mostly secondary to point mutations in CFTR
  - CFTR gene encodes a glycosylated transmembrane protein, which functions as a chloride channel.
  - CFTR is expressed in epithelial cells of exocrine tissues, such as the lungs, pancreas, sweat glands, and vas deferens

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- CBAVD patients have mutations on both CFTR genes:

– ~88% carry 1 severe mutation and 1 mild mutation.

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• CF patients: ~88% of the CF patients carry severe mutations on both CFTR genes:

)

• Absence of the vas deferens is a Wolffian (mesonephric) duct anomaly.

• Originally thought to exist apart from CFTR mutations, recent data have challenged this concept:

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• Agenesis of the vas deferens may be associated with unilateral or bilateral hypoplasia or absence of other portions of the Wolffian duct derivatives.

COMMONLY ASSOCIATED CONDITIONS

• With unilateral agenesis of the vas:
  – 75% of patients have only the caput of the epididymis present.
  – 20% have no ipsilateral epididymis.
  – 86% have ipsilateral agenesis of the seminal vesicle.
  – 20% have bilateral seminal vesicle agenesis.
  – Incidence of renal anomalies (usually agenesis) is 26–79%
• With bilateral vas agenesis:
  – 68% have absence of a portion of the epididymis bilaterally.

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  – Incidence of renal anomalies is 14–21%
• Unilateral or bilateral absence of the ejaculatory duct
• Unilateral or bilateral epididymal obstruction
• Obstructive azoospermia
• CAUV

DIAGNOSIS

HISTORY

• Developmental history:
  – Testicular descent, pubertal development
• Sexual function and libido: Prior fertility assessments
• Chronic medical illnesses: Sinopulmonary symptoms

PHYSICAL EXAM

• Performed to evaluate for the presence of the vasa as well as any areas of atrophy or agenesis

- Measure testicular size and examine consistency:
  - Normal adult male testis size: 3.5 cm in length and 2–3 cm in diameter
- Evaluate spermatic cords:
  - Presence of vasa and epididymides bilaterally
  - Evaluate for skip lesions
  - Assess for varicocele and hernia

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Semen analysis:
  - Presence of sperm rules out bilateral absence/obstruction of the vasa.
- Post-ejaculatory urine analysis:
  - To assess for sperm deposited in the bladder due to retrograde ejaculation
- If vasa not palpable on exam: Perform CFTR testing

Imaging

- TRUS: To evaluate presence of seminal vesicles, vasa, and for ejaculatory duct obstruction:
  - If abnormally large seminal vesicles with presence of vasa, aspirate seminal vesicles to assess for sperm
  - Normal TRUS values in men without obstruction of the ductal structures:
    Diameter of the vas: 0.3–0.5 cm
    Diameter of the ampulla of vas: 0.2–0.6 cm
    Seminal vesicle width: 0.3–1.5 cm
    Seminal vesicle length: 1.4–4.6 cm
    Diameter of the ejaculatory duct: 0.0–0.1 cm
- Renal US:
  - To screen all men with vasal agenesis to evaluate for renal anomalies/agenesis
- Vasography (see below)

Diagnostic Procedures/Surgery

Vasography:

- Assess patency of the vasa by fluoroscopic injection of contrast material
- Only perform at time of planned microsurgical reconstruction of the vasa
- See Section II: “Vasography, Technique and Indications.”

DIFFERENTIAL DIAGNOSIS

- Decreased spermatogenesis vs. obstruction/absence of vas
- Failure of hypothalamic-pituitary function:

  - Hypogonadotropic hypogonadism
  - Pituitary tumor
- Primary failure of spermatogenesis:
  - Congenital chromosomal abnormalities (Y-chromosome micro deletions)
  - Gonadotoxin exposure
  - Spermatogenic abnormalities
  - Varicocele
- Ductal obstruction:
  - Obstruction of the ejaculatory ducts
  - Unilateral or bilateral epididymal obstruction
  - Vasal obstruction

TREATMENT

Assisted reproductive techniques, including sperm retrieval with IVF, are the primary techniques used to achieve pregnancy.

MEDICATION

Specific endocrine therapy is only for men whose infertility results from hypogonadotropic hypogonadism.

SURGERY/OTHER PROCEDURES

- MESA using a glass micropipet technique followed by ICSI.
- IVF-ICSI
- May perform with autologous vs. donor semen
- If autologous semen is used, see “Patient Monitoring” below.

ADDITIONAL TREATMENT

Adoption reduces the risks of CF and CBAVD to that seen in the general population.

ONGOING CARE

PROGNOSIS

- Fertilization rate with IVF-ICSI is ~60%.
- Pregnancy rate ~20% (largely facility dependent).

COMPLICATIONS

For a couple with CBAVD associated with CFTR defects, planning to have their own genetic children, the risk for both male and female offspring of having CF or related diseases, and for male offspring to have CBAVD, depends on whether or not the female partner is a carrier.

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Genetic testing for CFTR mutations should be offered to the couple prior to ICSI.
- Genetic analysis is able to prove but not to exclude the diagnosis of a genital form of CF.
- The risk of CF or CBAVD in the offspring is unpredictable when rare mutations are identified in the male or the female.
- A negative mutation screen reduces, but does not eliminate, the risk of being a carrier.

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5. Schlegel PN, Shin D, Goldstein M. Urogenital anomalies in men with congenital absence of the vas deferens. J Urol 1996;155(5):1644–1648.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Assisted Reproductive Technologies (ART)
- Cystic Fibrosis, Urologic Considerations
- Infertility, Urologic Considerations

CODES

ICD9

752.89 Other specified anomalies of genital organs

ABBREVIATIONS

- CAUV: Congenital absence of the uterus and vagina
- CBAVD: Congenital bilateral absence of the vas deferens
- CF: Cystic fibrosis
- CFTR: Cystic fibrosis transmembrane regulator
- ICSI: Intracytoplasmic sperm injection
- IVF: In vitro fertilization
- MESA: Microsurgical epididymal sperm aspiration
- TRUS: Transrectal ultrasound
- US: Ultrasound

VESICOURETERAL REFLUX, ADULT

Paul Crow, MD

Francis X. Keeley, MD

BASICS

DESCRIPTION

- 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 pathology. It 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 HTN in this population.

EPIDEMIOLOGY

- 5% of adults have VUR.
- Female > Male

RISK FACTORS

- 85% of childhood reflux occurs in girls; likely to be similar in adults.
- Family history of VUR
- Conditions that predispose to secondary VUR (eg, neuropathic bladder)

Genetics

Having a parent or sibling with VUR increases the risk of childhood VUR.

GENERAL PREVENTION

None. Long-term renal damage can be limited by appropriate prevention of infection and management of secondary cause of VUR.

PATHOPHYSIOLOGY

- Primary VUR:
  - 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 (ileal conduit) or bladder replacement (orthotopic neobladder, catheterizable diversions) commonly have VUR.

– Bacterial cystitis can cause often transient ureteral reflux due to inflammation.

– Genitourinary TB can cause the ureteral orifices to become fixed and relatively patulous.

- International Reflux Study Committee classifies VUR into 5 grades:
  - Grade I: Reflux partly up to the ureter
  - Grade II: Reflux up to the pelvis and calyces without dilatation; normal calyceal fornices
  - Grade III: Same as grade II, but with mild dilatation and tortuosity of the ureter and minimal blunting of the fornices
  - Grade IV: Moderate dilatation and tortuosity of the ureter, pelvis, and calyces; complete blunting of fornices
  - Grade V: Gross dilatation and tortuosity of the ureter, pelvis, and calyces; absent papillary impressions in the calyces
- Mild reflux: Grades I and II
- Moderate reflux: Grade III
- Severe reflux: Grades IV and V
- Reflux associated with diversions such as ileal conduit is considered to be low-pressure with minimal long-term damage to upper tracts.

COMMONLY ASSOCIATED CONDITIONS

- See causes of high bladder storage pressure mentioned above.
- Renal transplantation: Extravesical refluxing anastomosis typical

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

- CVA tenderness with pyelonephritis
- Digital rectal exam for BPH
- Palpable bladder
- Neurologic impairment

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Blood testing is not necessary, except for severe cases in which renal function should be evaluated.
- Urine analysis and culture should demonstrate the presence of infection if the patient is symptomatic:
  - Between infections, the urine will often be normal.

Imaging

- US can show hydroureteronephrosis 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.

Diagnostic Procedures/Surgery

Video urodynamic studies combine the information provided by the VCUG with physiologic information on bladder filling and voiding.

Pathological 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 (loin) pain and infection (eg, renal colic, ureteropelvic junction obstruction) (see Section I: “Flank Pain”)
- Other causes of hydroureteronephrosis or ureteral obstruction (See Section I: “Hydronephrosis/Hydroureteronephrosis [Dilated Ureter/Renal Pelvis], Adult”)

TREATMENT

- Treatment of secondary VUR is directed at the primary cause (ie, management of BPH, treatment of UTI, etc.).
- Early treatment of cystitis can prevent progression to pyelonephritis.

MEDICATION

First Line

- Patients with recurrent UTI may benefit from prophylactic antibiotics.
- Primary asymptomatic adult VUR does not otherwise require ongoing medical therapy as risk of progressive renal impairment is low.

Pregnancy Considerations

Pregnant women with known VUR should be given antibiotic prophylaxis until delivery (eg, amoxicillin 250 mg/d PO).

Second Line

Secondary VUR may benefit from medical treatment of underlying cause:

- Anticholinergic preparations in detrusor overactivity
- -Blockade or 5-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, extravisually, or by a combination of both:

  Some common techniques include: Cohen cross-trigonal, Politano-Leadbetter, Lich-Gregoir (extravesical) reimplantations.

ADDITIONAL TREATMENT

Additional therapeutic options in the treatment of the underlying condition for secondary VUR include intra-detrusor botulinum toxin and sacral neuromodulation.

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Some data suggest cranberry juice and live-culture yogurt can be effective in preventing UTI.

ONGOING CARE

PROGNOSIS

Depends on underlying etiology and severity of VUR

COMPLICATIONS

- Chronic pyelonephritis
- HTN
- Reflux nephropathy
- Renal impairment rare in primary VUR unless pre-existing from childhood, but can be encountered in secondary VUR

- UTI
- Urolithiasis

FOLLOW-UP RECOMMENDATIONS

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.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Heikel-Parkkulainen Reflux Classification System
- Hydronephrosis/Hydroureteronephrosis (Dilated Ureter/Renal Pelvis), Adult
- Reflux Nephropathy
- Pyelonephritis, Chronic
- Vesicoureteral Reflux, Pediatric

CODES

ICD9

- 593.70 Vesicoureteral reflux unspecified or without reflux nephropathy
- 593.71 Vesicoureteral reflux with reflux nephropathy, unilateral
- 593.72 Vesicoureteral reflux with reflux nephropathy, bilateral

ABBREVIATIONS

- BPH: Benign prostatic hypertrophy
- CVA: Costovertebral angle
- HTN: Hypertension
- MAG3: Mercapto Acetyl Tri Glycine
- MRI: Magnetic resonance imaging

- MS: Multiple sclerosis
- TB: Tuberculosis
- US: Ultrasound
- UTI: Urinary tract infection
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

VESICOURETERAL REFLUX, PEDIATRIC

Ashley B. King, MD

Harry P. Koo, MD

BASICS

DESCRIPTION

- Abnormal condition due to incompetence of the UVJ, resulting in retrograde flow of urine
- VUR in the presence of bacteria is a risk factor for pyelonephritis and may lead to upper-tract pathology. It may be unilateral or bilateral, primary or secondary.

EPIDEMIOLOGY

- 1–2% of healthy infants; although true incidence is difficult to determine due to the invasive diagnostics required. In children with a history of symptomatic UTI, the incidence of VUR has been estimated at 20–50%.
- Up to 9% of newborns with hydronephrosis discovered on antenatal US
- 25–32% of the siblings of patients with VUR

RISK FACTORS

- Congenital deficiency in the functional integrity of the ureter or a defect in the anatomic composition of the UVJ; examples include laterally ectopic ureter associated with duplication, prune belly syndrome, bladder exstrophy
- Decreased bladder compliance due to neurogenic bladder or bladder outlet obstruction; causes include myelodysplasia, posterior urethral valves, and severe voiding dysfunction
- Infection and inflammation may predispose marginally competent UVJ to demonstrate reflux.
- Iatrogenic: Prior ureteral surgery, ureterocele incision or resection

Genetics

- Primary VUR tends to be familial.
- Prevalence in siblings is 25–32%; up to 100% in identical twins
- 2/3 of children with parents with known VUR have evidence of reflux.
- Autosomal dominant inheritance with a complicated multigene mechanism that has yet to be elucidated.

GENERAL PREVENTION

Maintenance of sterile urine may help reduce risks of reflux and renal damage.

PATHOPHYSIOLOGY

- Reflux in the presence of bacteruria is a risk factor for upper UTI. Reflux allows bacteria to reach the kidney and prevents proper emptying of the urinary tract, thus perpetuating infection.

- Factors including age, renal papillary anatomy, host susceptibility and response, and bacterial virulence, which determine the degree of local tissue damage and scarring.
- The risk of renal scarring after pyelonephritis is inversely related to age. Children <5 are at greatest risk.

COMMONLY ASSOCIATED CONDITIONS

- Bladder diverticula
- Bladder exstrophy
- Megaureter
- Multicystic dysplastic kidney disease
- Neurogenic bladder
- Posterior urethral valves
- Prune belly syndrome
- Severe voiding dysfunction
- Ureteral duplication
- Ureterocele
- Ureteropelvic junction obstruction

DIAGNOSIS

HISTORY

- In children, pyelonephritis can present with fever alone or occasionally abdominal pain and diarrhea.
- Some may present with asymptomatic pyelonephritis, in which the incidental findings of pyuria and bacteriuria are the only clues.
- With the common use of prenatal US, a large proportion of children with significant VUR are diagnosed in the perinatal period, prior to presenting with UTI.
- Family history of VUR
- Review of systems:
  - Symptoms of neurogenic bladder may prevail: Incontinence, retention or large postvoid residual volume
  - Voiding dysfunction/urinary tract obstruction: Girls may present with symptoms of hesitancy and intermittency secondary to spasm of periurethral striated muscle. In males, a slow stream may be due to posterior urethral valves (infants).

PHYSICAL EXAM

- General exam: Neurogenic deficit looking for spina bifida occulta
- Abdominal and pelvic exam:
  - Inspection: A mass visible in the upper abdominal area may indicate hydronephrosis.

– Palpation: During an episode of acute pyelonephritis, renal tenderness may be elicited; however, chronic renal infection is usually painless.

– Palpation of the suprapubic area may reveal a distended bladder secondary to obstruction or neurogenic disease.

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Urine analysis and culture:

– Bacteruria and/or pyuria; the method of collection is very important to reduce false positives.

– Clean-catch specimen is the best option in patients who can comply.

– In infants, with clinical suspicion for UTI, catheterized specimen is preferable; suprapubic needle aspiration most accurate, but invasive.

- Creatinine may be elevated in the advanced stage of renal damage.

Imaging

- Plain pelvic x-ray: In case of a neurologic deficit, a plain film may reveal absence of the sacrum or other forms of spina bifida.
- Assessment of the lower tract:

– US: May show high PVR bladder volume in cases of obstruction distal to bladder neck

– VCUG or RNC are the gold standards to diagnosis reflux. The VCUG may also reveal changes compatible with dysfunctional voiding in girls or findings diagnostic of posterior urethral valves in young boys.

– Cystoscopy with PIC cystogram is performed by some investigators to investigate each ureter under cystoscopy and fluoroscopy for presence of reflux.

- Assessment of the upper tract:

– Renal US: May show hydronephrotic changes of the kidney, and has replaced the use of excretory urograms to monitor renal changes over time. A normal US study cannot rule out the presence of VUR.

– Renal scintigraphy with DMSA is useful for detection of renal scarring. DMSA scanning has been employed to detect acute pyelonephritis.

– Excretory urogram (IVU) and MRU are helpful in evaluation of ureteral duplication and ureteral ectopia that may be associated with reflux.

Diagnostic Procedures/Surgery

- Uroflowmetry to assess any degree of bladder outlet obstruction or hypocontractility
- Cystoscopy: Routine use should be avoided. However, it may be helpful preoperatively to assess position of the ureteral orifices, presence of duplication, or diverticula.

• Urodynamics: Especially helpful in evaluating bladder compliance and function in children with secondary reflux due to neurogenic bladder or posterior urethral valves

Pathological Findings

• Graded according to International Reflux Study Committee system:

– Grade I: Reflux partly up to the ureter

– Grade II: Reflux up to the pelvis and calyces without dilatation; normal calyceal fornices

– Grade III: Same as grade II, but with mild dilatation and tortuosity of the ureter and minimal blunting of the fornices

– Grade IV: Moderate dilatation and tortuosity of the ureter, pelvis, and calyces; complete blunting of fornices

– Grade V: Gross dilatation and tortuosity of the ureter, pelvis, and calyces; absent papillary impressions in the calyces

• Mild reflux: Grades I and II

• Moderate reflux: Grade III

• Severe reflux: Grades IV and V

DIFFERENTIAL DIAGNOSIS

• VUR should be differentiated from other causes of hydroureter or hydronephrosis, in the absence of reflux.

• Occlusive: UPJ obstruction, obstructed megaureter, ureteral occlusion (tumor, stone, foreign body)

• Nonocclusive: Nonobstructed and nonrefluxing megaureter

TREATMENT

• Goal of intervention is to prevent renal damage, allow normal renal growth, and prevent long-term complications such as HTN and renal insufficiency.

• Grades I–III: Likelihood that reflux will disappear as the bladder matures; antibiotic suppression is currently the most common form of therapy in the pediatric population.

• Surgical treatment is warranted if medical treatment is unsuccessful or if there is evidence of progressive renal damage.

MEDICATION

Antimicrobial for UTI, followed by chronic suppressive therapy allowing for the possibility of spontaneous resolution while protecting the upper tract from infection

• Children 2 mo: Trimethoprim, amoxicillin, or cephalexin

• Children >2 mo: Trimethoprim-sulfamethoxazole, nitrofurantoin

ALERT

• Children 2 mo are unable to clear sulfamethoxazole; use of trimethoprim-sulfamethoxazole will result in jaundice.

SURGERY/OTHER PROCEDURES

• With the availability of minimally invasive procedures, some families are choosing endoscopic treatment over long-term prophylactic antibiotics.

• Ureteral reimplantation surgery:

– Creates a passive flap valve; allows the ureter to occlude temporarily while the intravesical pressure rises within the bladder, therefore preventing VUR from occurring.

– A mucosal tunnel with a length-to-ureteral diameter ratio of 5:1 should correct the reflux.

– Ureteral reimplantation successfully corrected reflux in 98% of cases with complication rates of <2%.

– Some common techniques include Cohen cross-trigonal, Politano-Leadbetter, Lich-Gregoir (extravesical) reimplantations.

– Complications: Persistent reflux, contralateral reflux, obstruction

• Endoscopic treatment: Injection of bulking agents below the ureteral orifice:

– 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.

Autologous chondrocytes

• Laparoscopic/robotic ureteral reimplantation is also being performed at select centers. Technical challenges remain in performing the procedures in pediatric patients.

ADDITIONAL TREATMENT

• Children with dysfunctional voiding may benefit from elimination retraining program and selective use of anticholinergic medications (eg, oxybutynin).

• Consider screening siblings (controversial).

ONGOING CARE

PROGNOSIS

• The natural history of reflux is often spontaneous resolution. This is more likely with low-grade reflux than high-grade reflux; the earlier the age of diagnosis, the more likely that spontaneous resolution will occur.

– Grades I and II: 80% at 5 yr

– Grade III: In older children (up to 10 yr old) and bilateral reflux: <20% resolve over a 5-yr period; 70% resolution in younger children (up to 2 yr) if unilateral VUR.

– Grade IV: 60% resolution in unilateral VUR and <10% in bilateral VUR over a 5-yr period

– Grade V: Spontaneous resolution rare

- Surgical repair: >98% success
- Endoscopic treatment: >90% success

COMPLICATIONS

- Hydroureteronephrosis
- HTN: In the later stages of atrophic pyelonephritis
- Impaired somatic growth
- Pyelonephritis, acute and chronic
- Renal failure
- Renal growth retardation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Follow-up during medical treatment should include annual renal US (growth/scarring).
- Periodic urine monitoring for protein is recommended. Urine cultures should be performed if a child presents with signs and symptoms of UTI. RNC can be performed every 1.5 yr until VUR resolves.
- After open surgical correction of VUR, evaluate upper tracts in 4–6 wk for signs of obstruction. Follow-up VCUG is frequently made optional for the parents.
- Following endoscopic treatment, US should be performed in 4–6 wk. VCUG is performed in 3–4 mo. If there is incomplete correction of reflux, a 2nd endoscopic treatment may be performed in about 6 mo.

ADDITIONAL READING

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See Also (Topic, Algorithm, Electronic Media Element)

- Heikel-Parkkulainen Reflux Classification
- Reflux Nephropathy
- Urinary Tract Infection (UTI), Pediatric
- Vesicoureteral Reflux, Adult

CODES

ICD9

- 593.70 Vesicoureteral reflux unspecified or without reflux nephropathy
- 593.71 Vesicoureteral reflux with reflux nephropathy, unilateral
- 593.72 Vesicoureteral reflux with reflux nephropathy, bilateral

ABBREVIATIONS

- DMSA: Dimercaptosuccinic acid
- HTN: Hypertension
- MRU: Magnetic resonance urography
- PIC: Positioning instillation of contrast at the ureteral orifice
- PVR: Post void residual
- RNC: Radionucleotide cystogram
- US: Ultrasound
- UTI: Urinary tract infection
- UVJ: Ureterovesical junction
- VCUG: Voiding cystourethrogram
- VUR: Vesicoureteral reflux

VON HIPPEL-LINDAU DISEASE/SYNDROME

Gennady Bratslavsky, MD
Inger Rosner, MD
W. Marston Linehan, MD

BASICS

DESCRIPTION

A multisystem neoplastic syndrome characterized by a predisposition to develop cystic as well as solid tumors of the kidney and pancreas, pheochromocytomas, CNS hemangioblastomas, retinal angiomas, endolymphatic sac tumors, and cystadenomas of the epididymis and broad ligament.

EPIDEMIOLOGY

- 1 in 35,000 live births
- Considered a rare disease by ORD of the NIH
- Prevalence in the US: About 7,000
- No gender or racial predilection

RISK FACTORS

Inheritance of a mutated VHL allele

Genetics

- VHL is a tumor suppression gene.
- VHL is located on chromosome 3p25–26.
- Each affected individual inherits 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).
- In autosomal dominant inheritance, the chance of inheriting the mutated gene from the affected parent is 50%.
- Present technology allows identification of the mutated gene in 100%.

GENERAL PREVENTION

The best prevention of VHL sequelae is close surveillance of affected individuals and timely intervention.

PATHOPHYSIOLOGY

- Mutated VHL leads to aberrant VHL protein (pVHL).
- Abnormal pVHL is unable to target HIF for degradation.
- Excessive accumulation of HIF protein upregulates downstream genes such as VEGF, GLUT-1, PDGF, TGF-, Epo, and many others, leading to tumor formation.

COMMONLY ASSOCIATED CONDITIONS

- Multifocal and bilateral clear RCC (seen in 50%):
  - Renal cysts seen in up to 70%
- Pheochromocytomas (seen in about 20%):
  - Extraadrenal pheochromocytomas (<5%)
- CNS hemangioblastomas (seen in 75%)
- Retinal angiomas (seen in 50–55%)
- Pancreatic neuroendocrine tumors (15–20%):
  - Pancreatic cysts are seen in up to 60%
- ELST (5–10%)
- Papillary cystadenomas of the epididymis or broad ligament (<5%)
- Rare VHL-associated lung cysts/tumors (<1%)
- Rare VHL-associated ovarian tumors (<1%)

DIAGNOSIS

HISTORY

- Family history of RCC or pheochromocytoma, CNS or pancreatic surgeries, hearing or vision problems is often elicited.
- Patients may present with 1 symptoms related to the organ involved:
  - Clear RCC:

    Most commonly detected during screening by imaging in asymptomatic VHL patients

    May present with hematuria, flank pain, abdominal fullness, weight loss, cachexia in more advanced disease
  - Pheochromocytoma:

    Headaches, palpitations, episodic sweating, anxiety attacks, personality changes

    Occasionally severe HTN leading to hemorrhagic stroke

    May be asymptomatic

    Rarely may present with weight loss, cachexia, bone pain, or cough in setting of metastatic disease.
  - CNS hemangioblastomas:

    Headaches, vertigo, ataxia, vomiting, wide-based gait, sensory loss, seizures

    Often asymptomatic

    Size and location of the lesion(s) often determine symptoms.
  - Retinal angiomas:

    Blurred or decreased vision, eye pain

    Undetected, may present with blindness

– Pancreatic neuroendocrine tumors and cysts:

Most are asymptomatic.

Diarrhea, steatorrhea and diabetes may occur if pancreas is replaced by cysts.

Early satiety if pancreatic cysts are large and compressing the stomach

Bone pain and painless jaundice in rare cases of extrinsic compression of the biliary system or metastatic disease

– ELST:

Hearing decrease or loss, tinnitus, vertigo

– Cystadenomas of epididymis:

Scrotal or testicular tenderness or mass

PHYSICAL EXAM

- Careful urologic, neurologic, and ophthalmologic exam can often help with diagnosis of VHL.
- Clear RCCs:
  - Usually undetected on exam unless large in size or cause marked varicocele
  - Occasionally, skin lesions or jaundice may be appreciated in metastatic RCC.
- Pheochromocytoma:
  - HTN, tachycardia, arrhythmias
- CNS hemangioblastomas:
  - Nystagmus, papilledema, loss of proprioception, sensory deficits
- Retinal angiomas:
  - Decreased visual acuity, characteristic retinal hemangiomas, retinal detachment
- Pancreatic neuroendocrine tumors:
  - Usually undetected on exam unless large in size, metastatic, or causing obstruction
- ELST:
  - Decrease or loss of hearing
  - Need exam and testing by otologist
- Papillary cystadenomas of the epididymis:
  - Paratesticular tenderness and palpable epididymal masses

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- Elevated erythropoietin levels or erythrocytosis may be seen in patients with CNS involvement.
- Elevated plasma and urine catecholamines are seen in patients with pheochromocytoma:

  - Norepinephrine or normetanephrine are most commonly elevated in VHL patients.
  - Other catecholamines may also be elevated.
- Similar to sporadic RCC:
  - Hypercalcemia, erythrocytosis, anemia, or elevated LFTs may be seen as paraneoplastic laboratory abnormalities.

Imaging

- Brain and spine MRI for detection of CNS hemangioblastomas and ELSTs
- Abdominal US (in children) and CT or MRI of the abdomen for detection of renal or pancreatic masses, as well as adrenal and extraadrenal pheochromocytomas
- MIBG scan is often helpful in localizing active pheochromocytoma in those with symptoms of pheochromocytoma or elevated catecholamines.
- Chest CT or MIBG may be helpful for extra-abdominal pheochromocytomas.

Diagnostic Procedures/Surgery

- None is usually required.
- Occasionally, the glucagon stimulation test or clonidine suppression test may be helpful with diagnosis of pheochromocytoma.

Pathological Findings

- Clear RCCs:
  - Usually multifocal and bilateral
  - Growth rate similar to sporadic counterpart of about 3 mm on average per year
  - May be up to several hundreds of gross and microscopic lesions in a single kidney
  - Most commonly Fuhrman nuclear grade II
  - Cysts commonly lined by clear cells
  - Metastatic potential increases with tumor size >3 cm
- Pheochromocytoma:
  - Generally encapsulated, highly vascular, frequently multifocal and bilateral
  - Microscopically seen are nests of cells in round clusters
- CNS hemangioblastomas:
  - Solitary or multiple lesions in cerebellum, spinal cord, brainstem, or cerebrum
  - Benign vascular lesions
- Pancreatic neuroendocrine tumors:
  - Usually multifocal intermixed with cysts
  - Solid lesions may metastasize to liver or bones unless resected in timely manner
  - Well demarcated, unencapsulated nodules
  - Nests of polygonal cells with vesicular nuclei

- ELST:
  - Locally aggressive; usually slow growing
  - Microscopically show low-grade papillary adenocarcinomas
- Papillary cystadenomas of the epididymis:
  - Benign lesions
  - Well circumscribed but unencapsulated
  - Histologically, papillary and tubular architecture with a fibrous stroma
  - Histologically identical to benign cystadenoma of the broad ligament

DIFFERENTIAL DIAGNOSIS

- Metastatic RCC or other primary
- MEN-2
- Non-VHL familial bilateral multifocal RCC
- Other familial types of hereditary renal carcinoma syndromes
- Polycystic kidney disease
- Sporadic form of bilateral RCC
- SDHB syndrome in the presence of pheochromocytoma and renal masses

TREATMENT

- Vigilant surveillance of kidneys, adrenals, pancreas, retina, brain, and spinal cord are the most important measures for timely intervention.
- Surgery is still the mainstay of VHL treatment.
- Nephron-sparing surgery is recommended when the largest solid tumor reaches 3 cm in the largest dimension.

MEDICATION

- Directed to address immediate presenting symptoms (commonly antihypertensives) in patients presenting with pheochromocytoma
- May be required for the management of related diseases such as RCC
- Preoperative blockade in a patient with a known pheochromocytoma:
  - NCI regimen: Phenoxybenzamine 10 mg b.i.d. and metyrosine 250 mg t.i.d. for 2 wk pre-op

SURGERY/OTHER PROCEDURES

- Dozens of tumors may be resected from the same kidney in a single setting with adequate renal preservation:
  - To minimize ischemic damage, most of the surgery is performed without hilar clamping.
  - Some surgeries may be safely performed laparoscopically or with the use of robotic assistance.

– Special technical challenges and increased morbidity are seen in patients previously operated on the same kidney or after the ablation.

– Bilateral nephrectomies and renal transplantation may be a valid option for some patients.

• Laparoscopic or open partial adrenalectomies are performed to preserve maximal adrenal function and avoid steroid dependence.

• Resection of pancreatic neuroendocrine tumors is the most definitive treatment:

– The type of surgical resection and procedure is determined by tumor size and location.

• Resection of ELSTs or hemangiomas

• Laser ablation or cryotherapy of retinal angiomas

ADDITIONAL TREATMENT

• A few clinical trials are presently in progress for treatment of VHL-associated tumors.

• Genetic counseling

• Radiation therapy: Occasional stereotactic irradiation of the metastatic disease or CNS hemangioblastomas not amendable to surgical resection

ONGOING CARE

PROGNOSIS

• Much depends on the stage of the renal lesions at presentation.

• No metastasis is seen with solid RCC lesions <3 cm

• 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 neuroendocrine tumors also increase metastatic potential with increase in size.

COMPLICATIONS

May occur from involvement of any of the systems involved. Most serious include:

• Hypertensive crisis resulting in hemorrhagic stroke

• Severe neurologic deficit or paralysis

• Blindness

• Metastatic disease from either RCC, pheochromocytoma, or pancreatic NET

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

• Radiographic surveillance is performed every 1–2 yr with CT or MRI for kidneys, adrenal, pancreas; and MRI for brain or spinal cord

• More frequent surveillance for active lesions

- Ophthalmology exams yearly
- Otology exams every 5 yr

Pediatric Considerations

- Yearly ophthalmologic exam from birth
- Yearly urinary catecholamine from age 2
- Yearly abdominal US from age 10

Pregnancy Considerations

- Higher risk of miscarriage with active pheochromocytoma
- Treatment of pheochromocytoma is preferred before pregnancy or early in the pregnancy.

ADDITIONAL READING

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- Duffey BG, Choyke PL, Glenn G, et al. The relationship between renal tumor size and metastases in patients with von Hippel-Lindau disease. J Urol 2005;72(1):63–65.
- Linehan WM, Vasselli J, Srinivasan R, et al. Genetic basis of cancer of the kidney: Disease-specific approaches to therapy. Clin Cancer Res 2004;15 (10 Pt 2):6282S–6289S.
- www.vhl.org
- Zbar B, Glenn G, Merino M, et al. Familial renal carcinoma: Clinical evaluation, clinical subtypes and risk of renal carcinoma development. J Urol 2007;177(2):461–465.

See Also (Topic, Algorithm, Electronic Media Element)

- Adrenal Mass
- Epididymis, Mass (Epididymal Tumor and Cysts)
- Pheochromocytoma
- Renal Cell Carcinoma, General
- Renal Cell Carcinoma, Localized (T1–T2)
- Renal Cysts (Intrarenal, Peripelvic, and Parapelvic)
- Renal Mass

CODES

ICD9

759.6 Other congenital hamartoses, not elsewhere classified

ABBREVIATIONS

- CNS: Central nervous system
- CT: Computed tomography
- ELST: Endolymphatic sac tumors

- HIF: Hypoxia inducible factor
- HTN: Hypertension
- LFT: Liver function test
- MEN-2: Multiple endocrine neoplasia type 2
- MIBG: Metaiodobenzylguanidine scan
- MRI: Magnetic resonance imaging
- NCI: National Cancer Institute
- NET: Neuroendocrine tumors
- NIH: National Institutes of Health
- ORD: Office of Rare Diseases
- RCC: Renal cell carcinoma
- SDHB: Succinate dehydrogenase B deficiency
- US: Ultrasound
- VHL: Von Hippel-Lindau

WILMS TUMOR (NEPHROBLASTOMA)

Job K. Chacko, MD

T. Ernesto Figueroa, MD

BASICS

DESCRIPTION

- The most common primary malignant renal tumor in childhood
- Represents 6% of all childhood cancers
- Most present in children with abdominal mass
- Symptoms may include pain, HTN, or hematuria.

Pediatric Considerations

Wilms tumor is considered a pediatric renal tumor, but does rarely occur in adults.

EPIDEMIOLOGY

- 6% of all childhood tumors
- 80% of cases occur in age <5
- 7% bilateral (present at mean age 2.5)
- 12% multifocal within a single kidney
- Rare >10 yr and <6 mo
- Median age 3.5 yr
- 8 per million children every year

RISK FACTORS

- Increased frequency in children with:
  - Beckwith-Wiedemann syndrome: 1 in 10 children develop a tumor of the liver, adrenal cortex, or kidney.
  - Hemihypertrophy (2% risk)
  - Denys-Drash syndrome
  - WAGR syndrome (30% risk)
  - Perlman syndrome
  - Sotos syndrome (2–3% risk)
- Presence of nephrogenic rests:
  - 1% of kidneys on infant postmortems
  - 35% of unilateral Wilms
  - Almost 100% of bilateral Wilms
  - Considered premalignant lesion
  - Perilobar-limited to periphery of renal cortex
  - Intralobar-occur randomly in renal lobe

- Monitor for recurrence if present on pathology

- Higher risk in African American compared to Caucasians for Wilms tumor
- Lower risk in Asians compared to Caucasians

Genetics

- WT1 (11p13): Denys-Drash and WAGR syndromes
- WT2 (11p15): Beckwith-Wiedemann syndrome
- FWT1 (17q), FWT2 (19q): Familial; 1–2% of cases
- 16q, loss of long arm in 20% of cases
- 1p. loss of short arm in 10% of cases
- p53 mutation not important in Wilms

PATHOPHYSIOLOGY

- An abnormal renal development marked by proliferation of metanephric blastema composed of 3 cell types: Blastemal, stromal, epithelial
- Histology: Favorable vs. unfavorable (ie, anaplasia in pathology)
- Anaplasia seen in 5%

COMMONLY ASSOCIATED CONDITIONS

- Congenital anomalies occur in 15% of Wilms tumors.
- GU anomalies: Renal anomalies, cryptorchidism, hypospadias, ureteral duplication, ambiguous genitalia (4%)
- Hemihypertrophy (3%)
- Aniridia (1%)
- Denys-Drash syndrome (male pseudohermaphroditism, renal mesangial sclerosis, renal failure)
- WAGR syndrome
- Beckwith-Wiedemann syndrome (macroglossia, organomegaly, hemihypertrophy)
- Perlman syndrome (autosomal recessive overgrowth: Fetal gigantism, organomegaly, renal hamartomas, and nephroblastomatosis)
- Sotos syndrome (overgrowth of face and extremities, cognitive delay)

DIAGNOSIS

HISTORY

- Abdominal mass
- Fever, anorexia, weight loss
- Hematuria

PHYSICAL EXAM

- Most common presentation is abdominal mass

- HTN: 20–25% from activation of RAAS
- Occasionally present as acute abdomen from tumor rupture

DIAGNOSTIC TESTS & INTERPRETATION

Lab

- CBC: Anemia, polycythemia
- Liver function tests
- BUN, creatinine
- Serum calcium
- Urine analysis: 25% with microhematuria

Imaging

- Abdominal US: Initial study
- CT of abdomen and chest: To detect smaller lesions in either renal unit not detected by US; chest imaging to evaluate for pulmonary metastasis
- Bone scan: If history of bone pain or elevated alkaline phosphatase or serum Ca

Diagnostic Procedures/Surgery

- NWTSG recommends surgical diagnosis, followed by adjuvant treatment.
- SIOP treatment involves preoperative chemotherapy followed by surgery. Histology and staging are potentially altered.
- Percutaneous biopsy is not recommended.

Pathological Findings

- Gross: Tan or grayish, fleshy tumor with a pseudocapsule
- Microscopic (3 features): Stromal (immature spindle cells and can have muscle cartilage or fat), epithelial (recapitulates kidney with glomeruli and tubules), 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
  - Anaplasia: Unfavorable marker of chemoresistance

DIFFERENTIAL DIAGNOSIS

- Solid renal mass in children
- Clear cell sarcoma, rhabdoid tumor, neuroblastoma, multilocular cystic nephroma, mesoblastic nephroma, multicystic dysplastic kidney, renal cell carcinoma, renal medullary carcinoma

TREATMENT

- Multimodality therapy combining surgery, radiation, and chemotherapy
- 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 NWTSG and SIOP; they are difficult to compare directly due to the fact that 1 is based on surgical staging and the other is based on surgical staging following chemotherapy (see Section VII).
  - NWTSG: Commonly used in the US and Canada; based on surgical evaluation prior to chemotherapy.
  - SIOP: Commonly used in Europe, based on surgical findings following chemotherapy.
- Treatment recommendations based on NWTSG Type evidence

MEDICATION

First Line

- Chemotherapy recommendations based on NWTSG, which is given adjuvantly postoperatively
- SIOP studies favor preoperative chemotherapy.
- Pulse-intensive dactinomycin plus vincristine (18 wk) for:
  - Stage I: Favorable histology, age >2 yr, or tumor <550 g
  - Stage I: Anaplasia
  - Stage II: Favorable histology
- Pulse-intensive dactinomycin, vincristine, and doxorubicin (24 wk) for:
  - Stages III–IV: Favorable histology
  - Stages II–IV: Focal anaplasia
  - Stage V: Doxorubicin, vincristine, cyclophosphamide, etoposide
  - Stages II–IV: Diffuse anaplasia

Second Line

The optimal salvage chemotherapy regimen is unknown. Recurrent/persistent tumors have been treated with cyclophosphamide, ifosfamide, carboplatin, etoposide, and cisplatin combinations

SURGERY/OTHER PROCEDURES

- Choose incision that provides adequate exposure:
  - Transabdominal
  - Thoracoabdominal

- Chevron
- Unilateral tumor:
  - Radical nephrectomy
  - Contralateral exploration not needed if not seen on adequate preoperative imaging
- Bilateral tumor:
  - Biopsy both sides based on preoperative imaging
  - Consider initial partial nephrectomy if peripheral, <2 cm
  - Reimage 6 wk after chemo; excise residual disease
  - Renal preservation is key to avoid renal failure; important for patient with syndromes at high risk for metachronous disease
- Lymph node: Sample perihilar, pericaval, and para-aortic nodes; excise suspicious nodes
- Tumor spillage:
  - Local: Percutaneous anterior/posterior percutaneous biopsy; open incisional biopsy (stage II)
  - Peritoneal spillage or tumor thrombus spillage is more extensive (stage III).
- Local invasion: Usually can be dissected freely; if not, biopsy and treat with chemotherapy.

ADDITIONAL TREATMENT

- Ongoing studies of NWTSG to assess modifying treatment based on risk stratification
- Radiation therapy:
- Stage III favorable histology and stages II–III focal or diffuse anaplasia:
  Abdominal/flank irradiation 10.8 Gy
- Stage IV favorable histology and stage IV focal or diffuse anaplasia:
  Abdominal/flank irradiation 10.8 Gy
  Lung radiation 12 Gy with lung metastasis

ONGOING CARE

PROGNOSIS

- 5-yr overall survival: 90%
- 4-yr post nephrectomy overall survival:
  - Favorable histology:
  - Stage I: 98%
  - Stage II: 96%
  - Stage III: 95%

- Stage IV: 90%

- Unfavorable histology:
  - Stage I: 82.6%
  - Stage II: 81.2%
  - Stage III: 72%
  - Stage IV: 37.5%
  - Stage V: 55.2%
- 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 involve biologic markers (ie, loss of heterozygosity, aneuploidy).

COMPLICATIONS

- Treatment related
- Surgical:
  - Bowel obstruction (5.1%)
  - Hemorrhage (1.9%)
  - Wound infection (1.9%)
  - Vascular injuries (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
    Unilateral disease risk in Denys-Drash
  - Cardiotoxicity:
    Congestive heart failure in patients treated with doxorubicin
    Dose dependent
  - Hepatotoxicity:
    Vincristine and dactinomycin; dose related
  - Secondary malignancies:
    Highest risk in patients treated with both doxorubicin and radiation
    Occur in radiation field; mean 16.1 yr post therapy
- Radiation:
  - Short stature, muscle atrophy, scoliosis
  - Highest risk in age <1

– Thyroid disease and mammary tissue damage in chest radiation

– Pregnancy complications increased in females receiving high-dose abdominal radiation

FOLLOW-UP RECOMMENDATIONS

Patient Monitoring

- Screen patients with aniridia, hemihypertrophy, and Beckmann-Wiedemann syndrome with abdominal US every 3–4 mo to age 7.
- 1% of children develop contralateral Wilms within 6 yr of 1st diagnosis
- Majority of Wilms tumor recurrence occurs within 2 yr of nephrectomy.
- Favorable histology, <24 mo, and tumor weight <550 g

– Chest x-ray, abdominal US every 3 mo for 1st 2 yr after diagnosis, then every 6 mo for 1 yr, then yearly for 2 yr

- All others:

– Chest x-ray 6 wk and 3 mo after surgery; then every 3 mo for 15 mo, every 6 mo for 18 mo, and yearly for 2 yr

– Abdominal US every 3 mo for 2 yr, then every 6 mo for 3 yr

ADDITIONAL READING

- Ahmed HU, Arya M, Tsiouris A, et al. An update on the management of Wilms' tumour. ESJO 2007;33:824–831.
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- Kalapurakal JA, Dome JS, Perlman EJ, et al. Management of Wilms' tumour: Current practice and future goals. Lancet Oncol 2004;5:37–46.
- Metzger ML, Dome JS. Current therapy for Wilms' tumor. Oncologist 2005;10:815–26.
- National Wilms' Tumor Study 1–5 summaries. Available at http://www.nwtsg.org/bibliography/bibliography.html.

See Also (Topic, Algorithm, Electronic Media Element)

- Abdominal Mass, Newborn/Child, Urologic Considerations
- Renal Mass
- Wilms Tumor Staging System National Wilms' Tumor Study Group (NWTSG)
- Wilms Tumor Staging System: International Society of Pediatric Oncology (SIOP)

CODES

ICD9

189.0 Malignant neoplasm of kidney, except pelvis

ABBREVIATIONS

- BMP: Basic metabolic panel
- BUN: Blood urea nitrogen
- CBC: Complete blood count
- CT: Computed tomography
- HTN: Hypertension
- NWTSG: National Wilms’ Tumor Study Group
- RAAS: Renin-angiotensin-aldosterone system
- SIOP: International Society of Pediatric Oncology
- US: Ultrasound
- WAGR: Wilms tumor, Aniridia, Genital anomalies, mental Retardation

SECTION II SHORT TOPIC SECTION A to Z

11--HYDROXYLASE (CYP11B1) DEFICIENCY

DESCRIPTION Comprises 5–8% of congenital adrenal hyperplasia (CAH) cases. Autosomal recessive disorder that manifests as childhood hypertension, hypokalemia, and muscle weakness. Low plasma renin activity is a hallmark. Caused by an enzyme deficiency, leading to low cortisol levels and high adrenocorticotropic hormone level, causing adrenal hyperplasia. Afflicted females are virilized and may have male-appearing genitalia. Males may be hyperdeveloped. Diagnosed by high levels of deoxycorticosterone and/or 11-deoxycortisol in serum or their tetrahydro-metabolites in a 24-hr urine. (See also Section I: “Disorders of Sexual Development [DSD]”; Section II: “Congenital Adrenal Hyperplasia.”)

TREATMENT

- Oral hydrocortisone (10–20 mg/m2/d)
- Refractory hypertension treated with spironolactone, amiloride, and/or calcium channel blockers
- Surgical correction of ambiguous genitalia in females
- Prenatally treated with steroid administration to mother

REFERENCE

1. Mantero F, et al. 11 beta-hydroxylase deficiency. J Endocrinol Invest 1995;18(7):545–549.

21-HYDROXYLASE (CYP21A2) DEFICIENCY

DESCRIPTION Responsible for >90% of congenital adrenal hyperplasia cases. This enzyme deficiency leads to low cortisol levels and high ACTH level, leading to adrenal hyperplasia. It is the most common cause of female pseudohermaphrodism. Most have aldosterone deficiency, which can lead to fatal salt wasting. Untreated are tall as children but short as adults. Untreated females may have secondary amenorrhea or polycystic ovarian syndrome. Males may have small testes with precocious secondary sexual characteristics. Diagnosed by elevated 17--hydroxyprogesterone levels in serum with ACTH stimulation test. (See also Section I: “Disorders of Sexual Development [DSD]”; Section II: “Congenital Adrenal Hyperplasia.”)

TREATMENT

- Oral hydrocortisone (10–20 mg/m2/d)
- 9--fluorohydrocortisone for salt wasters
- Surgical correction of ambiguous genitalia in females
- Prenatally treated with steroid administration to mother

REFERENCE

2. New MI. Steroid 21-hydroxylase deficiency (congenital adrenal hyperplasia). Am J Med 1995;98(1A):2S–8S.

5-ALPHA-REDUCTASE DEFICIENCY

DESCRIPTION An autosomal recessive disorder characterized by a 46,XY 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 dihydrotestosterone (DHT) during fetal development. Hypoplasia or absence of the prostate and a blind-ending vagina are common. Virilization occurs at puberty. Diagnosed by normal-to-high male plasma testosterone levels, abnormal ratios of serum testosterone to DHT, or abnormal ratios of urinary 5-- to 5--steroid metabolites. (See also Section I: “Disorders of Sexual Development [DSD].”)

TREATMENT

- Male gender assignment: Genital reconstruction and supplemental androgen
- Female gender assignment: Orchiectomy, estrogen/progesterone therapy, and vaginoplasty

REFERENCE

3. Imperato-McGinley J. 5 alpha-reductase-2 deficiency. Curr Ther Endocrinol Metab 1997;6:384–387.

AARSKOG SYNDROME (FACIODIGITOGENITAL SYNDROME)

DESCRIPTION A malformation syndrome carried by both an X-linked and an autosomal dominant form. Primary diagnostic criteria include short stature, hypertelorism, short nose with anteverted nares, maxillary hypoplasia, a crease below the lower lip, mild interdigital webbing, clinodactyly, and shawl scrotum. Cardiac abnormalities are also reported. There is no specific treatment.

REFERENCE

4. Teebi AS, et al. Aarskog syndrome: Report of a family with review and discussion of nosology. Am J Med Genet 1993;46(5):501–509.

ABDOMINOPERINEAL RESECTION (APR), UROLOGIC CONSIDERATIONS

DESCRIPTION Commonly performed for rectal cancers in which the rectum, anus, and a portion of the sigmoid colon are removed (also known as Miles resection or abdominal perineal proctosigmoidectomy).

The extensive pelvic dissection can lead to a number of urologic problems. Urinary retention and urinary incontinence represent 2 distinct urologic complications after abdominoperineal resection. Injury to detrusor branches of the pelvic nerve can cause detrusor denervation and urinary retention. In addition, injury to intrapelvic branches of the pelvic and pudendal nerves to the urinary sphincter can result in intrinsic sphincter deficiency and urinary incontinence. Impotence and urinary retention can occur in males; urinary incontinence and altered sexual function may occur in females, secondary to removal of the anterior vaginal wall. Damage to the ureters is not uncommon during the procedure.

TREATMENT

- Stent placement preoperatively may help in identifying the ureters.
- Intermittent catheterization for retention; TURP or other bladder outlet procedure may be considered preoperatively in men with BPH.
- A penile prosthesis is often necessary for impotence.

REFERENCE

5. Kodner IJ, et al. Colon, rectum and anus. In: Schwartz SI, et al. Principles of Surgery, 6th ed. New York: McGraw-Hill, 1994.

ABRAMS-GRIFFITHS NOMOGRAM

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, a point can be plotted on the nomogram that determines whether the bladder outlet is obstructed, unobstructed, or equivocally obstructed. For those that fall in the equivocal zone, further criteria for the mean slope of the pressure–flow plot and the minimal voiding detrusor pressure are used to determine whether obstruction is present. The nomogram has shown excellent prognostic value in multiple studies in predicting the outcome of prostatectomy. Although the Abrams-Griffiths nomogram and number are somewhat simplistic, none of the more complex methods of pressure–flow analysis has been shown to be a better predictor of treatment outcome to date. (See also Section II: “Pressure Flow Studies and Urodynamics, Indications and Normal Values.”)

REFERENCE

6. Lim CS, Abrams P. The Abrams-Griffith nomogram. World J Urol 1995;13:34.

ACQUIRED RENAL CYSTIC DISEASE

DESCRIPTION The cause of development of renal cysts in patients with long standing ESRD or severe chronic renal insufficiency 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 compared to the general population (individual risk 4–7%). Tumors tend to be very aggressive, with a high incidence of metastasis. Risk increases with increased time on dialysis. (See also Section I: “Renal Cysts.”)

TREATMENT

- Close follow-up for early detection of malignancy
- Renal transplantation can reverse growth of cysts, but malignancy can still occur.

REFERENCE

7. Farivar-Mohseni H, et al. Renal cell carcinoma and end stage renal disease. J Urol 2006;175(6):2018–2020.

ACROSOME REACTION ASSAY

DESCRIPTION The acrosome is a membrane-bound organelle covering the anterior 2/3 of the sperm head. This organelle contains numerous enzymes whose release, termed the acrosome reaction, is required for penetration of the hard zona pellucida of the ovum. It is hypothesized that human sperm bind to the ovum, after which the acrosome reaction is induced by one or more of the zona pellucida glycoproteins. Abnormalities of any aspect of this reaction may be a source 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

8. Agarwal A. Assessing sperm function. Urol Clin North Am 2008;35(2);157–171.

ACTINOMYCOSIS, RENAL

DESCRIPTION Actinomycosis is a chronic granulomatous infection caused by gram-positive anaerobic Actinomyces bacteria, usually A. israelii. No pathognomonic findings are common; it can reach the kidney by hematogenous spread or instrumentation. Fibrosis and fistulas are common. The infection can present as sepsis with negative urine culture. Imaging can reveal renal abscesses and hydronephrosis, and the condition has been typically diagnosed post-operatively due to a renal mass prompting nephrectomy; it is diagnosed by gram-positive organisms on stain and prolonged incubation of bacteria. Microscopic examination of the organism can appear as yellow bodies called sulfur granules.

TREATMENT

- Usually nephrectomy of involved renal unit is necessary.
- Aggressive antibiotic therapy with long-term penicillin followed by doxycycline and ciprofloxacin

REFERENCE

9. Dhanani NN, et al. Medical management of renal actinomycosis. J Urol 2004;171(6 Part 1): 2373–2374.

ACUTE KIDNEY INJURY (AKI)

DESCRIPTION Acute renal failure (ARF) has been defined as the abrupt loss of kidney function resulting in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes. While this loss in kidney function is detected by elevated serum creatinine, several problems are associated with the use of this measure to quantitatively define ARF, particularly the lack of consensus in the quantitative definition. The Acute Dialysis Quality Initiative (ADQI) has proposed a graded definition of ARF called the RIFLE criteria. The Acute Kidney Injury Network modified the RIFLE criteria to include less severe ARF, a time constraint of 48 hr, and to allow for correction of volume status and obstructive causes of ARF prior to classification. The Acute Kidney Injury Network uses the term acute kidney injury (AKI) to represent the spectrum of acute renal failure. The proposed diagnostic criteria for AKI are: An abrupt (<48 hr) increase in creatinine concentration of 0.3 mg/dL (26.4 mmol/L) from baseline, a percentage increase in the serum creatinine 50%, or oliguria of <0.5 mL/kg/hr for >6 hr. (See also Section I: “Renal Failure, Acute” and Section II: “Rifle Criteria for Acute Renal Injury.”)

REFERENCE

Levin A, et al. Improving outcomes from acute kidney injury: report of an initiative. Am J Kidney Dis 2007;50:1.

ADENOFIBROMA, METANEPHRIC, PEDIATRIC

DESCRIPTION Metanephric adenofibroma is a very rare benign tumor 1st described as nephrogenic adenofibroma by Hennigar and Beckwith in 1992. This tumor appears to affect predominantly young people (mean, 14 yr; range, 20 mo–35 yr). The most common symptom is hematuria, but a significant proportion of patients are asymptomatic. Polycythemia is a peculiar incidental finding that resolves after resection of the tumor. The radiologic appearances are nondiagnostic and indistinguishable 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 mesoblastic nephroma in cytologic appearance. At present, all metanephric adenofibroma lesions should be excised to establish diagnosis, but no further adjuvant therapy is required.

REFERENCE

Hennigar RA, Beckwith JB. Nephrogenic adenofibroma. A novel kidney tumor of young people. Am J Surg Pathol 1992;16:325–334.

Palese, MA. Metanephric stromal tumor: A rare benign pediatric renal mass. Urology 2001;58:462.

ADRENAL CALCIFICATIONS

DESCRIPTION Adrenal calcifications may be the result of hemorrhage (secondary to trauma, venous thrombosis, stress, or bleeding diatheses), infection (usually granulomatous diseases), or may be associated with different tumors. Necrosis and calcification are more common in association with adrenal carcinoma but are not diagnostic. Bilateral calcified adrenal glands may be seen in adrenal insufficiency or secondary Addison disease. Calcifications may be detected on MRI because of their susceptibility artifact but are much better appreciated on CT images.

REFERENCE

Kenney PJ, Stanley RJ. Calcified adrenal masses. Urol Radiol 1987;9:9–15.

ADRENAL CYSTS AND PSEUDOCYSTS

DESCRIPTION A rare (0.064–0.18% on autopsy studies) condition, more often detected on imaging. 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: Endothelial, pseudocyst, epithelial, and parasitic, in order of decreasing incidence. Parasitic cysts arise primarily from Equinococcus granulosus infection. Adrenal pseudocysts are thought to result from infarction or hemorrhage of a cyst or tumor.

TREATMENT

- >3.5 cm: Aspiration for fluid analysis and cytology to rule out malignancy
- <3.5 cm: Observe with serial US or CT scan.

REFERENCE

Ulusoy E, et al. Giant adrenal cyst: Preoperative diagnosis and management. Urol Int 1997;58(3): 186–188.

ADRENAL CYTOMEGALY

DESCRIPTION Found infrequently in children and adults and 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 that demands increased functional capacity and proliferation of adenocytes.

REFERENCE

Noguchi S, et al. Adrenal cytomegaly: Two cases detected by prenatal diagnosis. Asian J Surg 2003;26(4):234–236.

ADRENAL HEMORRHAGE

DESCRIPTION Adrenal hemorrhage (AH) is a collection of blood producing a mass effect in one or both adrenal glands, with or without adrenal necrosis and insufficiency. It occurs in up to 30% of selected neonatal intensive care patients, 14–22% of newborns at autopsy, and up to 15% at autopsy of adult patients dying in shock. Signs and symptoms include fever, flank or abdominal pain, tachycardia, nausea, vomiting, respiratory distress, and weakness. Unilateral AH may be an incidental finding during imaging. Adrenal hemorrhage may result from multiple mechanisms: Stress, sepsis (Waterhouse-Friderichsen syndrome), anticoagulation-related hypotension, vascular spasm, adrenal venous thrombosis, or heparin-associated thrombocytopenia.

Workup may show dropping hemoglobin and electrolyte abnormalities (hyponatremia, hyperkalemia in 56% of bilateral AH). Treatment includes 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 abscess formation is suspected.

REFERENCE

Simon DR, Palese MA. Clinical update on the management of adrenal hemorrhage. Curr Urol Rep 2009;10(1):78–83.

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, as in pituitary agenesis. Congenital adrenal hypoplasia (primary) is an inherited disorder, with several forms identified. The major form of adrenal hypoplasia is X-chromosome linked and traced to the DAX-1 (AHCH) gene. This gene is in close proximity to other genes encoding for glycerol kinase and Duchenne muscular dystrophy (both associated with adrenal hypoplasia). Hypogonadotrophic hypogonadism is also a common finding. It typically presents in the neonatal period or with adrenal crisis (dehydration, hyponatremia, hyperkalemia, hypotension, hypoglycemia). Disorders of the external genitalia may include micropenis, undescended testes, or hypospadias. It can be detected by biochemical testing (serum cortisol, corticotrop-in-releasing hormone (CRH) stimulation test, etc.). Antenatal maternal estriol screening can also detect adrenal hypoplasia. Treatment is replacement of adrenal hormones.

Diagnosis must be made early, or it can be fatal secondary to salt wasting.

REFERENCE

Ferraz-de-Souza B, Achermann JC. Disorders of adrenal development. Endocr Dev 2008;13:19–32.

ADRENAL INCIDENTALOMAS

DESCRIPTION Incidentally discovered adrenal lesions—adrenal incidentalomas—are by-products of increased availability and use of advanced imaging. Adrenal masses are found in ~4% of patient 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; cyst/pseudocyst; 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. Incidentaloma <4 cm are likely benign. A 1-mg dexamethasone suppression test and measurement of plasma-free metanephrines is recommended for all patients with an adrenal incidentaloma, as well as a serum potassium and plasma aldosterone concentration-plasma rennin activity ratio for patients with hypertension.

TREATMENT

- Surgical removal is indicated with hormonally active tumors, as well as any tumors >6 cm.
- Observation is warranted for any mass <4 cm and nonfunctioning. A repeat CT 6–12 mo after the initial study is reasonable for follow-up.

REFERENCE

Grumbach MM, et al. Management of the clinically inapparent adrenal mass (incidentaloma). Ann Intern Med 2003;138(5):424–429.

ADRENAL MEDULLARY NEUROBLASTOMA

DESCRIPTION Neuroblastoma specifically arising from the adrenal medulla or other paraganglionic tissues of neural crest origin. Neuroblastoma is the most common malignant tumor in infancy and most common extracranial solid tumor of childhood, with a U.S. annual incidence of 10 per 1 million live births. Lesions of adrenal origin have worse survival rates than those with nonadrenal origin. Favorable prognostic factors include young age at diagnosis (<1 yr), low stage (I or II), favorable histology (high degree of differentiation), and stage IVS (>80% survival rate); 2-yr survival without evidence of disease is usually equivalent to cure. Treatment is typically surgical if resectable or localized; locally advanced disease receives neoadjuvant chemotherapy, followed by surgical resection. (See also Section I: “Neuroblastoma.”)

REFERENCE

Park JR, et al. Neuroblastoma: Biology, prognosis, and treatment. Pediatr Clin N Am 2008;55:97–120.

ADRENAL METASTASES

DESCRIPTION The 4th most common site of metastatic tumor spread. Common metastases include lung and breast (most common), kidney, stomach, pancreas, and melanoma. (See also Section I: “Adrenal Mass.”)

REFERENCE

Gittens PR Jr, et al. Surgical management of metastatic disease to the adrenal gland. Semin Oncol 2008;35(2):172–176.

ADRENAL MYELOLIPOMA (ADRENAL MYOLIPOMA)

DESCRIPTION Referred to as myolipoma and myelolipoma in the literature, this rare, usually nonfunctioning lesions are composed of adipose and hematopoietic cells may represent extramedullary hematopoiesis. It is rarely metabolically active (Cushing or Conn syndrome) and usually asymptomatic, except when very large or if hemorrhage occurs. It can be diagnosed radiographically and is more typically incidentally discovered at 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, while T2-weighted images are moderately intense. The main diagnostic similarity is well-differentiated liposarcoma. (See also Section I: “Adrenal Mass.”)

Treatment is excision if symptomatic or if diagnosis cannot be confirmed radiographically or on needle biopsy.

REFERENCE

Lamont JP, et al. Giant adrenal myelolipoma. Am Surg 2002;68(4):392–394.

ADRENALITIS

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, hemorrhage, metastatic neoplasms, sarcoidosis, amyloidosis, and adrenal leukodystrophy. Autoimmune adrenalitis can be associated with thyroiditis, diabetes mellitus, pernicious anemia, vitiligo, hypoparathyroidism, and mucocutaneous candidiasis (autoimmune polyendocrine syndrome type 1, also known as candidiasis-hypoparathyroidism-Addison disease syndrome), or with autoimmune polyendocrine syndrome type 2 (also known as Schmidt syndrome). HIV with opportunistic CMV adrenalitis accounts for an increasing number of cases.

TREATMENT

- Replacement of adrenal and other hormones, as necessary
- Treatment of underlying cause, as indicated

REFERENCE

Perry R, et al. Primary adrenal insufficiency in children: Twenty years experience at the Sainte-Justine Hospital, Montreal. J Clin Endocrinol Metab 2005;90(6):3243.

ADRENOGENITAL SYNDROME

DESCRIPTION This is the most common cause of ambiguous genitalia, caused by an inborn error of metabolism involving cortisol synthesis. At fault is a defect in any 1 of 5 enzymes involved in the cortisol biosynthetic pathway (21-hydroxylase, 11-hydroxylase, 3-hydroxysteroid dehydrogenase, 20.22-desmolase, or 17-hydroxylase), which may result in congenital adrenal hyperplasia (CAH). Usually presents with an autosomal recessive inheritance. (See also Section I: “Disorders of Sexual Development [DSD]”; Section II: “Congenital Adrenal Hyperplasia.”)

SYNONYMS

- Congenital adrenal hyperplasia
- Female pseudohermaphrodite
- Male pseudohermaphrodite

COMPLICATIONS

- For untreated females:
  - Premature pubic and axillary hair development
  - Rapid somatic maturation, premature epiphyseal closure, short adult stature
  - No breast development or menstruation until excessive androgen production is suppressed
- For untreated males:
  - Sexual and somatic precocity within 1st 2 yr of life
  - Premature epiphyseal closure, short adult stature
- Untreated males and females with salt-losing variant:
  - 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 consequences
- Steroid replacement with cortisone, fluorohydrocortisone as needed
- Surgical genital reconstruction may be necessary early in life, based on specific findings

REFERENCE

Newman K, et al. The surgical management of infants and children with ambiguous genitalia. Lessons learned from 25 years. Ann Surg 1992;215: 644–653.

Pang S. Congenital adrenal hyperplasia. Endocrinol Metab Clin North Am 1997;26:853–891.

ADRENOLEUKODYSTROPHY

DESCRIPTION Rare, X-linked recessive metabolic disorder occurring in boys (formerly called Schilder disease), and characterized by adrenal atrophy and widespread, diffuse cerebral demyelination. It produces mental deterioration, corticospinal tract dysfunction, and cortical blindness. There is laboratory evidence of adrenal cortical dysfunction. Two 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. Lorenzo's oil (a mixture of glyceryl trioleate and glyceryl trierucate oil) has been tried in this disease, with some delay in neurologic symptoms. Bone marrow transplantation is under study.

REFERENCE

Moser HW, et al. Lorenzo's oil therapy for X-linked adrenoleukodystrophy: Rationale and current assessment of efficacy. J Mol Neurosci 2007; 33(1):105.

AGING MALE SURVEY

DESCRIPTION The Aging Male Survey (AMS) is a questionnaire developed to detect hypogonadism in adult men. It has three domains: Psychological, Somato-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 Somato-vegetative domain. The higher the score, the more severe the symptoms. The AMS has been shown to have a sensitivity (83%) and specificity (39%) similar to those of the Shorter ADAM Survey. (See also Section II: “Androgen Deficiency in the Aging Male (ADAM) and ADAM Survey.”)

REFERENCE

Moore C, et al. The Aging Males Symptom Scale (AMS) as outcome measure for treatment of androgen deficiency. Eur Urol 2004;46:80–87.

AL GHORAB CORPORAL SHUNT

DESCRIPTION To treat priapism, a small transverse incision is made on the dorsum of the glans. A section of septum between the glans spongiosa and the corpora cavernosa is removed to create a shunt. (See also Section I: “Priapism.”)

REFERENCE

Thomas AJ, Surgery for priapism. In: Novick AC, et al., eds. Stewart’s Operative Urology. Baltimore: Williams & Wilkins, 1989:826–832.

ALAGILLE SYNDROME

DESCRIPTION Also known as Alagille-Watson syndrome, 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 dysplasia and renal failure. This autosomal dominant disorder is mapped to chromosome 20; it is treated by renal replacement therapy as needed.

REFERENCE

Krantz JD, et al. Alagille syndrome. J Med Genet 1997;34(2):152–157.

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 source 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 seminoma.

REFERENCE

Koshida K, et al. Significance of placental alkaline phosphatase in the monitoring of patients with seminoma. Br J Urol 1996;77(1):138–142.

ALKAPTONURIA

DESCRIPTION An inherited inborn error 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). Alkali can accelerate this process. Ochronosis (deposition of a bluish-black pigment noted in the connective tissue) may lead to arthropathy. Of urologic interest, renal failure occurs, rarely, with longstanding disease. Even more rarely, HGA stones can occur. It is caused by a single gene defect, causing absence of HGA oxidase. It is treated by dietary restriction of phenylalanine and tyrosine and large doses of ascorbic acid; otherwise, treatment is symptomatic.

REFERENCE

Venkataseshan VS, et al. Alkaptonuria and renal failure: A case report and review of the literature. Mod Pathol 1992;5(4):464–471.

ALOPECIA GENITALIUM

DESCRIPTION A poorly understood and clinically insignificant condition marked by isolated loss of pubic hair.

REFERENCE

Pavona, NA. Alopecia genitalium: Personal observation. Tech Derm Urol 1981;10:24.

-FETOPROTEIN

DESCRIPTION A single-chain glycoprotein (MW 70,000) that aids in the management of testicular cancer. It is normally produced by the liver, yolk sac, and GI tract of the fetus; its half-life is 5 (3.5–6) days. Serum -fetoprotein (AFP) levels are normally elevated in the 1st 8 mo of life. The normal adult level is <8 ng/mL; this can be elevated in 38% of cases of embryonal cell carcinoma, 64% of teratocarcinoma, and in yolk sac tumors. Other reasons for elevation include neuroblastoma, hepatoblastoma (hepatoma), hepatocellular, neural tube defects, fetal death, ataxia-telangiectasia, and some cases of benign hepatic disease.

REFERENCE

Ritchey ML, et al. Pediatric urologic oncology. In: Gillenwater JY, et al., eds. Adult and Pediatric Urology, 3rd ed. St Louis: Mosby, 1996.

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 uremia. Family history 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

Gregory MC, et al. Alport syndrome—clinical phenotypes, incidence, and pathology. Contrib Nephrol 1996;117:1–28.

ALSTRöM-EDWARDS SYNDROME

DESCRIPTION Also called Alström syndrome, a progressive autosomal recessive genetic disorder affecting multiple organ systems. It may be detected at birth or in early childhood. Clinically, patients with Alström 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, dilated cardiomyopathy, and progressive renal and hepatic failure. Alström 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.

REFERENCE

Mendioroz J, et al. Alström syndrome: Clinical and genetic features, and a diagnostic guide to foresee complications. Med Clin (Barc) 2008;131(19): 741–746.

ALZHEIMER DISEASE, UROLOGIC CONSIDERATIONS

DESCRIPTION Alzheimer disease is the principal cause of dementia in the elderly patient population. The urologic manifestations include urinary incontinence, overactive bladder, and erectile dysfunction. Patients may be difficult to treat due to limited cooperation with the treatment plan; toileting schedules can help with early incontinence episodes. 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 correctable causes before ascribing urinary tract problems to this disease specifically. (See Section I: “Incontinence, Urinary, Adult Male”; Section I: “Incontinence, Urinary, Adult Female.”)

REFERENCE

Resnick NM, et al. The pathophysiology and clinical correlates of established urinary incontinence in frail elderly. N Engl J Med 1989;320:1–7.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA ORGAN SEVERITY SCALE: KIDNEY INJURIES

DESCRIPTION Numerous classifications of traumatic renal 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: "Renal Trauma, Adult"; Section I: "Renal Trauma, Pediatric.")

American Association for the Surgery of Trauma Organ Injury Severity Scale for the Kidney

Grade	Type	Description
I	Contusion	Microscopic or gross hematuria, urologic studies normal
	Hematoma	Subcapsular, nonexpanding without parenchymal laceration
II	Hematoma	Nonexpanding perirenal hematoma confined to renal retroperitoneum
	Laceration	<1 cm parenchymal depth of renal cortex without urinary extravasation
III	Laceration	>1 cm parenchymal depth of renal cortex without collecting system rupture or urinary extravasation
IV	Laceration	Parenchymal laceration extending through renal cortex, medulla, and collecting system
	Vascular	Main renal artery or vein injury with contained hemorrhage
V		

Laceration

Completely shattered kidney

Vascular

Avulsion of renal hilum, devascularizing the kidney

REFERENCE

Santucci RA, et al. Validation of the American Association for the Surgery of Trauma organ injury severity scale for the kidney. J Trauma 2001;50(2): 195–200.

AMINOACIDURIA

DESCRIPTION Excretion of an overabundance of amino acids in the urine, most often due to an inborn error of metabolism. Aminoaciduria 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 kidney, such as diabetes mellitus and diabetes insipidus.

REFERENCE

Neithercut WD, et al. Persistent nephrogenic diabetes insipidus, tubular proteinuria, aminoaciduria, and parathyroid hormone resistance following long term lithium administration. Postgrad Med J 1990; 66(776):479–482.

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 (<16 mmol/L). The normal result is urine pH <5.4; distal RTA exists if pH >5.4. (See also Section II: “Renal Tubular Acidosis.”)

REFERENCE

Osther PJ, et al. Screening renal stone formers for distal renal tubular acidosis. Br J Urol 1989;63(6): 581–583.

AMMONIUM URATE UROLITHIASIS

DESCRIPTION Extremely rare form of stone disease (<0.5%), endemic in countries with poor nutrition and in patients with Crohn disease. In contrast to uric acid stones, these grow only in urine with pH <6.5. Caused mostly by infection, usually mixed with struvite stones. Treatment involves clearing infection and increasing urine output to >2.5 L/d. Chemolitholysis not possible, and surgical intervention may be necessary. Encourage a balanced diet.

REFERENCE

Hossain RZ, et al. Urolithiasis in Okinawa, Japan: A relatively high prevalence of uric acid stones. Int J Urology 2003;10(8):411–415.

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–S4 in the pudendal nerve. A hypoactive sphincter suggests a lower motor neuron lesion, whereas a hyperactive 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 bulbocavernosus reflex, which is widely used in evaluating urinary incontinence and erectile dysfunction, requires anal sphincter contraction in response to squeezing the glans of penis.

REFERENCE

Magee MC. Basic Science for the Practicing Urologist. New York: Cambridge University Press, 1983.

ANDERSON-HYNES PYELOPLASTY

DESCRIPTION Used to treat ureteropelvic junction (UPJ) obstruction. The UPJ is excised, and excess renal pelvis is removed. The widely spatulated ureter is reanastomosed to the renal pelvis with interrupted chromic sutures, and the excess renal pelvis is closed with simple or running suture. After nephrostomy, a ureteral stent is placed. (See also Section I: “Ureteropelvic Junction Obstruction.”)

REFERENCE

Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, et al., eds. Stewart’s Operative Urology. Baltimore: Williams & Wilkins, 1989:220–233.

ANDROGEN/ANABOLIC STEROID ABUSE

DESCRIPTION Androgens are steroid hormones that include testosterone and its derivatives, including androstenedione, dihydrotestosterone, and dromostanolone. In the medical realm, androgens at physiologic doses treat androgen deficiency due to hypothalamus, pituitary, or testis disorder of genetic or acquired etiology. The use of androgens at supraphysiologic 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 bodies, 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 deficient spermatogenesis. Abnormalities in sperm motility and morphology are commonly seen, and usually recover spontaneously within 4 mo after cessation of abuse.

REFERENCE

Dohle GR, et al. Androgens and male fertility. World J Urol 2003;21(5):341–345.

ANDROGEN 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, melatonin, and dehydroepiandrosterone. Clinical manifestations include fatigue, depression, decreased libido, and erectile dysfunction, as well as changes in cognition and mood. The ADAM questionnaire is a screening tool to detect late-onset hypogonadism, 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 3 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?

REFERENCE

Morales A, et al. Andropause: A misnomer for a true clinical entity. J Urol 2000;163(3):705–712.

Morley JE, et al. Validation of a screening questionnaire for androgen deficiency in aging males. Metabolism 2000;49:1239–1242.

ANDROGEN DEPRIVATION SYNDROME (ADS)/METABOLIC SYNDROME

DESCRIPTION Long-term androgen deprivation therapy, 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: Hot flushes, impotence, loss of libido, emotional lability, anemia, hyperglycemia, increased triglycerides and cholesterol, muscle atrophy, decreased muscle strength, testicular atrophy, osteoporosis, depression, anxiety, malaise, fatigue, and memory difficulties. Metabolic syndrome defined by the NIH Adult Treatment Panel III criteria is also part of this spectrum and may include abdominal obesity, hyperglycemia, hypertriglyceridemia, elevated HDL cholesterol, and hypertension. Treatment of the metabolic syndrome includes:

- Management of underlying causes (overweight/obesity and physical inactivity): Weight management, increased physical activity
- Treat lipid and nonlipid risk factors if they persist despite these lifestyle therapies: Treat hypertension; use aspirin for coronary heart disease (CHD) patients to reduce prothrombotic state; treat elevated triglycerides and/or low HDL

REFERENCE

Braga-Basaria M, et al. Metabolic syndrome in men with prostate cancer undergoing long-term androgen-deprivation therapy. J Clin Oncol 2006;24(24):3979–3983.

National Cholesterol Education Program. Available at http://www.nhlbi.nih.gov/guidelines/cholesterol/atglance.htm.

ANDROGEN INSENSITIVITY SYNDROME (AIS; OR ANDROGEN RESISTANCE SYNDROME), COMPLETE AND PARTIAL

DESCRIPTION An X-linked recessive disorder with a prevalence range from 1 in 20,400 genetic males to 1 in 99,000 genetic males. The typical mode of presentation is an adolescent female who has breast development with a pubertal growth spurt but has not had her menarche. Insensitivity can be complete insensitivity or partial.

Clinical Features of Complete Androgen Insensitivity Syndrome

Karyotype

46, XY

Inheritance

X-linked recessive; mutations in AR gene

Genitalia

Female with blind vaginal pouch

Wolffian duct derivatives

Often present, depending on mutation type

Müllerian duct derivatives

Absent or vestigial

Gonads

Testes

Habitus

Scant or absent pubic and axillary hair; breast development and female habitus at puberty; primary amenorrhea

Hormone and metabolic profile

Increased LH and testosterone levels; increased estradiol (for male reference range); FSH levels often normal or slightly increased. Resistance to androgenic and metabolic effects of testosterone

Management of complete (severe) androgen insensitivity relates primarily to the optimal timing of gonadectomy. 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 puberty is complete. In partial androgen insensitivity, the external genitalia may be ambiguous at birth, but the prototypic phenotype is characterized by perineoscrotal hypospadias, micropenis, and a bifid scrotum. The testes may also be undescended.

Clinical Features of Partial Androgen Insensitivity Syndrome

Karyotype

46, XY

Inheritance

X-linked recessive; mutations in AR gene

External genitalia

Ambiguous with blind vaginal pouch, under-masculinized, isolated hypospadias, normal male with infertility (mild AIS)

Wolffian duct derivatives

Often normal

Müllerian duct derivatives

Absent

Gonads

Testes (usually undescended)

Habitus

Decreased to normal axillary and pubic hair, beard growth, and body hair; gynecomastia common at puberty

Hormone and metabolic profile

Increased LH and testosterone concentrations; increased estradiol (for men); FSH levels may be normal or slightly increased

Partial resistance to androgenic and metabolic effects of testosterone

REFERENCE

Hughes IA, Deeb A. Androgen resistance. Best Pract Res Clin Endocrinol Metab 2006;20(4):577–598.

ANGIOKERATOMA OF FORDYCE (PENILE AND SCROTAL ANGIOKERATOMAS)

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. Usually asymptomatic, but can cause annoying bleeding either spontaneously or with scratching or intercourse. Cause is not known but possibly related to increased regional venous pressure; some believe an association with varicocele exists. Typically seen in older patients; these are distinct from congenital scrotal hemangiomas (see Section II: “Scrotum, Hemangioma.”)

TREATMENT

Electrosurgery and lasers are effective, but rarely necessary.

REFERENCE

Schiller PI, Itin PH. Angiokeratomas: An update. Dermatology 1996;193(4):275–282.

ANGIOLYMPHOID HYPERPLASIA, PENILE

DESCRIPTION A subtype of a broad class of histiocytoid hemangiomas in which 4 features are found: (1) Vacuolated histiocytoid cells, (2) tumor vessels that are thick-walled or capillaries consisting only of histiocytoid endothelial cells, (3) interstitial eosinophils, and (4) lymphoid infiltrates. These are usually confined to the skin of one area of the body.

SYNONYMS

- Pseudopyogenic (or atypical pyogenic) granuloma
- Inflammatory angiomatous nodule
- Subcutaneous angioblastic hyperplasia with eosinophilia
- Epithelioid hemangioma
- Intravenous atypical vascular proliferation

TREATMENT

Local surgical excision or laser (CO_2) ablation.

REFERENCE

Allen PW, et al. The histiocytoid hemangiomas and other controversies. Pathol Ann 1992;27[Pt 2]: 51–87.

ANGIOMYXOMA, PERINEAL

DESCRIPTION Benign lesion of the pelvic soft tissue, but may very rarely metastasize. Characterized by slow, infiltrative growth. May present as mass in the pelvis. Histologically, demonstrates wavy collagen fibrils 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

Hong RD, et al. Aggressive angiomyxoma of the perineum in a man. J Urol 1997;157(3):959–960.

ANGIOSARCOMA, GENITOURINARY

DESCRIPTION A very rare malignancy that grossly 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 VIII immunohistochemically. These sarcomas can be widely metastatic and have persistent local recurrence. Bladder angiosarcoma has been reported post-radiation for treatment of other malignancies; chronic lymphedema, foreign bodies, and other toxins have been implicated.

TREATMENT

- Radical resection of affected area (penectomy, cystectomy with diversion)
- Lymph node dissection for presence of lymphadenopathy
- Adjuvant radiation may be useful; chemotherapy for adjuvant or metastatic disease is not usually effective.

REFERENCE

Webber RJS, et al. Angiosarcoma of the penis. Urology 1998;51:130–131.

ANOGENITAL INTRAEPITHELIAL NEOPLASIA

DESCRIPTION Genital warts are caused by human papilloma virus (HPV), a DNA-containing virus that is spread by direct skin-to-skin contact; 100 different types of HPV exist, and over 30 types can infect the genital area. Risk factors for acquiring HPV include multiple sexual partners, early age at onset of sexual intercourse, and having a sexual partner with HPV. Most infections are subclinical and asymptomatic.

Anogenital HPV infection is common in HIV-infected men who have sex with men. These patients have a strongly increased risk of HPV-induced anal cancer and its precursor lesion, anal intraepithelial neoplasia (AIN), and a moderately increased risk for penile cancer. Many of these men also have penile intraepithelial neoplasia, a penile cancer risk factor. Some authors recommend that all HIV positive men who have sex with men be screened for penile intraepithelial neoplasia.

REFERENCE

Kreuter A, et al. Penile intraepithelial neoplasia is frequent in HIV-positive men with anal dysplasia. J Invest Derm 2008;128, 2316–2324.

ANORGASMIA/DYSORGASMIA

DESCRIPTION Anorgasmia is the complete inability to achieve an orgasm; this condition impacts 0.14% of the general population and 0.39% of men seeking fertility treatment. The primary etiology of this dysfunction is thought to be psychological, and it is believed that such men lack sensual self-awareness. Treatment of this condition is difficult and mainly utilizes cognitive-behavioral sex therapy techniques that 1st help these men become comfortable with touch and later assists them in translating sexual pleasure into orgasm. Fertility issues associated with anorgasmia can be addressed easily with techniques for producing orgasm or collecting sperm, including prostatic massage, rectal electroejaculation, the collection of nocturnal sperm, and microsurgical sperm aspiration.

Dysorgasmia is defined as postorgasm–associated pain. Very little is known about its incidence in the general population. Although believed to be generally uncommon, evidence suggests that men who have undergone a prostatectomy or pelvic radiation and young men suffering from chronic pelvic pain disorder experience high rates of dysorgasmia. Dysorgasmia may be associated with pelvic floor muscle or bladder neck spasm. Tamsulosin, an -blocker specific to the smooth muscle tissues of the prostate and bladder, has been shown to alleviate pain associated with treatments affecting the prostate, with 77% reporting improvement and 13% indicating complete resolution of their pain. (See also Section I: “Ejaculatory Disturbances.”)

REFERENCE

Mulhall JP, Nelson CJ. Male orgasmic disorders: What do we know? Contemp Urol 2007;Feb 1.

ANTERIOR URETHRAL VALVES

DESCRIPTION Much less common than posterior urethral valves, this condition is characterized by obstruction of the anterior urethra, usually associated with a urethral diverticulum. It is caused by a diverticulum acting as valves, although cusps without diverticulum have been reported. It usually presents with voiding symptoms or bulging diverticulum on the ventral shaft with voiding. Diagnosed by VCUG and renal US. Retrograde urethrogram 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

- Foley catheter if azotemia occurs
- Endoscopic valve fulguration or single-stage urethroplasty if urethra is adequate
- Staged urethroplasty for large diverticulum
- Vesicostomy for reflux or persistent azotemia

REFERENCE

Van Savage JG, et al. An algorithm for the management of anterior urethral valves. J Urol 1997;158[3 Pt 2]:1030–1032.

ANTIANDROGEN WITHDRAWAL SYNDROME

DESCRIPTION A decrease of PSA levels occurs in 15–40% of patients upon withdrawal of nonsteroidal antiandrogen in those treated for advanced prostate cancer with total androgen blockade. This is possibly caused by a mutation in the androgen receptor, which then acts to stimulate growth of tumor when bound by the agent. Initially reported for flutamide, butbicalutamide and nilutamide have also shown this effect. This effect should be sought before adding other more cytotoxic agents to patients with hormone-refractory prostate cancer, and could partially explain the activity of some salvage therapies.

REFERENCE

Smith DC. Secondary hormonal therapy. Semin Urol Oncol 1997;15(1):3–12.

ANTISPERM ANTIBODIES

DESCRIPTION Antisperm antibodies develop when a disruption occurs in the blood–testis barrier; they may be a cause of infertility. Causes can include ductal obstruction (i.e., vasectomy), infection, cryptorchidism, and varicocele, 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. Condoms, antibiotics, steroids, and sperm washing have all been utilized, with variable results. Presently, assisted reproductive techniques such as in vitro insemination are most effective. (See also Section I: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Terminology”; “Semen Analysis, Technique and Normal Values.”)

REFERENCE

Turek P. Immunopathology and infertility. In: Lipshultz, Howards SS, eds. Infertility in the Male, 3rd ed. St. Louis: Mosby, 1997.

APHTHOUS ULCER, EXTERNAL GENITALIA

DESCRIPTION Aphthae are localized, painful, shallow, round to oval ulcers often covered by a gray fibromembranous slough and surrounded by an erythematous halo. Complex aphthosis involves almost constant, multiple, oral or oral and genital aphthae. Those involving both oral and genital aphthae are termed bipolar aphthosis (BA) of Neumann. Most specialists consider bipolar aphthosis to be a forme fruste of Behçet disease (BD). The prevalence of genital aphthae in BD varies from 60–90% in various reports. Genital aphthae are most commonly seen in male patients on the scrotum and in female patients on the vulva. In females, genital aphthae tend to be larger and deeper, sometimes even leading to perforations. Genital aphthae, especially those that are larger, may be confused with STDs; a common misdiagnosis is genital herpes or donovanosis.

REFERENCE

Somesh G, et al. Bipolar aphthosis presenting as mutilating genital ulcers in women. Indian J Dermatol Venereol Leprol 2004;70(6):357–360.

ARTERIOVENOUS FISTULA (AVF), RENAL (OR ARTERIOVENOUS MALFORMATION, AVM)

DESCRIPTION Renal AVF or AVM are uncommon lesions. They can be congenital, acquired, or idiopathic. Most (70%) are iatrogenic and occur as a result of renal biopsy, blunt or penetrating trauma, inflammation, malignancy, or renal surgery. Congenital fistulas account for ~20% and are often found under the mucosa, accounting for the bleeding presentation. The right kidney is more often involved than the left, and women twice as often as men. May rarely present as a renal mass. The peak incidence occurs in patients 30–40 yr old. Acquired or idiopathic lesions are usually aneurysmal. Congenital renal AVF frequently causes hematuria. Symptoms can include abdominal bruit, hypertension, headache, and palpitation. Indications for treatment include progressive increase in the size of the fistula, recurrent or persistent hematuria, and hemodynamic effects (cardiac decompensation, hypertension, high-output heart failure). Arteriography is the gold standard for evaluating renal AVF (demonstrating simultaneous visualization of major arteries and veins). Doppler US is a good screening tool. CT or MRI angiography can usually demonstrate the lesion adequately. Endovascular techniques are used even for giant aneurysms with AVFs. For small renal AVFs, macroparticules or methyl cyanoacrylate glue should be used. For larger fistulas, coils or detachable balloons are used. With any concerns for the possibility of systemic and pulmonary embolism, high-flow AVF should be managed by open resection or ligation.

REFERENCE

Dönmez FY, et al. Noninvasive imaging findings of idiopathic renal arteriovenous fistula. Diagn Interv Radiol 2008;14:103–105.

ARTIFICIAL INSEMINATION (AI)

DESCRIPTION The process by which semen is introduced into the female reproductive tract by artificial means, for the purpose of improving the chance for conception in fertile couples with patent tubes. Variations include controlled ovarian hyperstimulation, intrauterine insemination (IUI), direct interperitoneal insemination (DIPI), a combination of IUI and DIPI, fallopian tube sperminfusion (FSI), and peritoneal oocyte and sperm transfer. Other related means of improving fertility include in vitro fertilizations, such as zygote intrafallopian transfer (ZIFT) and tubal embryo stage transfer (TEST) techniques.

REFERENCE

Abyholm T, Tanbo T. GIFT, ZIFT, and related techniques. Curr Opin Obstet Gynecol 1993;5:615–622.

ASK-UPMARK KIDNEY

DESCRIPTION Also called segmental renal hypoplasia, these are small kidneys with areas of normal architecture separated by grooves overlying dilated calices without pyramids. The parenchyma of the grooved areas contain thyroid-like tubules and lack glomeruli. Cause is unknown, but vesicoureteral reflux and ascending infection have been implicated. They are typically unilateral and associated with vesicoureteral reflux, and commonly present as malignant hypertension, but cases of nonmalignant hypertension and recurrent UTIs occur. Nephrectomy of the affected side for refractory hypertension is the treatment.

REFERENCE

Zezulka AV, et al. The association of hypertension, the Ask-Upmark kidney and other congenital abnormalities. J Urol 1986;135(5):1000–1001.

ASOPA HYPOSPADIAS REPAIR

DESCRIPTION The dorsal preputial foreskin’s inner rectangular graft is tubularized to form the neourethra, and the outer opposing skin, which shares the same blood supply, serves as the outer penile shaft skin cover.

REFERENCE

Wacksman J. Use of the Hodgson XX (modified Asopa) procedure to correct hypospadias with chordee: Surgical technique and results. J Urol 1986;136(6): 1264–1265.

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 aspergilloma or pseudotumor has been reported in patients with AIDS. Urine cultures can be negative, but aspiration and cytology can demonstrate typical septated hyphae. Therapy is systemic amphotericin B and at least 3 mo of itraconazole. Amphotericin B irrigations into the involved renal unit have been used to supplement systemic therapy. (See also Section I: “Fungal Infections, Genitourinary.”)

REFERENCE

Wise GJ, Freyle J. Changing patterns in genitourinary fungal infections. AUA Update Series, Volume XVI, Lesson 1, 1997.

ASPERMIA

DESCRIPTION A condition of no ejaculate, which should be differentiated from azoospermia, where an ejaculate is present but the sperm are absent from the fluid. (See also Section I: “Infertility and Ejaculatory Disturbances”; Section II: “Semen Analysis, Technique and Normal Values”; Section II: “Semen Analysis, Abnormal Findings and Terminology.”)

CAUSES

- Complete bilateral obstruction of ejaculatory duct
- Congenital anorchidism, imperforate anus, and other congenital anomalies
- Medication (chlorpromazine, -blockers, methyldopa, imipramine, -blockers)
- Radical prostatectomy
- Retrograde ejaculation; failure of seminal emission
- Surgical (bladder neck dysfunction secondary to TURP, TUIP, retroperitoneal lymph node dissection)

TREATMENT

See also Section I: “Ejaculatory Disturbances.”

REFERENCE

Dunetz GN, Krane RJ. Successful treatment of aspermia secondary to obstruction of ejaculatory duct. Urology 1986;27(6):529–530.

ASSISTED REPRODUCTIVE TECHNOLOGY

DESCRIPTION Assisted reproductive technology (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: Aspiration of sperms from epididymis 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
- IUI or AI: Also not ART by strict definition; however these are methods for fertility performed during ovulation by inserting a catheter into the cervical os and injecting concentrated sperm into the uterus, thereby bypassing the cervical mucus barrier.

The following are classical methods of ARF:

- Gamete intrafallopian transfer (GIFT): Oocytes and semen are retrieved, the semen is concentrated, then both are placed into the fallopian tube by laparoscopy.
- In vitro fertilization (IVF): Fertilization by either incubating sperms with oocytes or by injecting 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.
- Zygote intrafallopian transfer (ZIFT): After in vitro fertilization of an egg, the resultant embryo is placed into the fallopian tube laparoscopically, instead of through the cervix.

REFERENCE

Carbone Jr DJ. Male reproductive physiology and assisted reproductive technology. AUA Update Series, Vol. XVIII, Lesson 21:162, 1999.

ASTHENOSPERMIA

DESCRIPTION A general term for defects in sperm movement, usually a decrease in sperm motility to <50–60% of normal. It can be detected on semen analysis and can be a cause of male factor infertility. (See also Section I: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Terminology.”)

CAUSES

- Antisperm antibodies
- Hypoandrogenic state
- Idiopathic
- Immotile cilia (Kartagener syndrome and immotile cilia syndrome)
- Infection
- Partial ejaculatory duct obstruction
- Varicocele (most common surgically correctable abnormality)

TREATMENT

- Aimed at offending agent (i.e., antibiotics for infection, sperm washing for antibodies, varicocelectomy)
- Interest has been noted in vitamins C and E and other free-radical scavengers
- Assisted reproductive techniques

REFERENCE

Meacham RB, et al. Male infertility. In: Gillenwater JY, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

ATHLETIC HEMATURIA

DESCRIPTION Also called sport-related or exercise-induced hematuria. Hematuria, 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 foot-strike hemolysis, renal ischemia, release of a hemolyzing factor, direct trauma to bladder or kidney, dehydration, myoglobinuria, increased circulation, and NSAIDs. Treatment includes adherence to sensible training guidelines and hydration.

REFERENCE

Jones GR, Newhouse I. Sport-related hematuria: A review. Clin J Sport Med 1997;7(2):119–125.

ATOPIC DERMATITIS (ECZEMA), UROLOGIC CONSIDERATIONS

DESCRIPTION Also called eczema, disseminated neurodermatitis, atopic eczema, and Besnier prurigo, this chronic pruritic eczematous condition affects characteristic sites. In adults, the genitalia is a common site. Patients present with itching, excoriation, 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 diseases (allergic rhinitis, asthma).

TREATMENT

Topical corticosteroids such as triamcinolone 0.1% b.i.d.; nighttime sedation with antihistamines or other agent. Treat stress and remove irritants (soaps, solvent, fabrics made of wool or nylon).

REFERENCE

Edwards L, Lynch PJ. In: Sams WM, et al., eds. Principles and Practice of Dermatology. New York: Elsevier, 1998:960–961.

ATYPICAL ADENOMATOUS HYPERPLASIA OF THE PROSTATE (ADENOSIS)

DESCRIPTION Also described in the literature as small gland hyperplasia, atypical adenosis, atypical small acinar hyperplasia. 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 prostatic 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 acinar adenocarcinoma. It is recommended to stain for 34E12, which detects basal cell–specific cytokeratin. If basal cell staining is present, this helps to rule out carcinoma. Although the biologic significance of AAH is uncertain, its light 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 prostate (ASAP), which appears to be more associated with prostate cancer. In AAH, rebiopsy is not usually indicated. (See also Section II: “Atypical Small Acinar Hyperplasia, Prostate (ASAP)”; Section II: “Postatrophic Hyperplasia of the Prostate Gland.”)

REFERENCE

Armah HB, Parwani AV. Atypical adenomatous hyperplasia (adenosis) of the prostate: A case report with review of the literature. Diagn Pathol 2008; 3:34.

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 concurrent or subsequent invasive prostate carcinoma. (See also Section I: “Prostatic Intraepithelial Neoplasia”; Section II: “Atypical Adenomatous Hyperplasia and Postatrophic Hyperplasia of the Prostate.”)

REFERENCE

Bostwick DG, Meiers, I. Atypical small acinar proliferation in the prostate: Clinical significance. Arch Pathol Lab Med 2006;130(7):952–957.

AUA (AMERICAN UROLOGIC ASSOCIATION) SYMPTOM INDEX FOR BPH

DESCRIPTION Also called the BPH symptom index, and the AUA symptom score or AUA-SS 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 used widely used. (See Section VII for the questionnaire.) The AUA Index consists of 7 questions that assess emptying, frequency, intermittency, urgency, weak stream, and straining, with each graded on a score of 0–5. Scores can range from 0–35. The index currently categorizes symptoms as:

- Mild (score 7)
- Moderate (score 8–19)
- Severe (score 20–35)

The International Prostate Symptom Score (I-PSS) 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 (or "delighted") to 6 (or "terrible").

It is suggested that patients with mild symptoms (AUA-SS 7) and patients with moderate or severe symptoms (AUA-SS 8) 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 (-blockers with or without 5-reductase inhibitors or 5-reductase alone prior to any surgical intervention). Surgical options includes TURP, transurethral incision of the prostate, open prostatectomy, or minimally invasive therapies (such as transurethral microwave thermotherapy, transurethral needle ablation, and water-induced thermotherapy). (See also Section II: "International Prostate Symptom Score [IPSS]"; Section VII: "AUA Symptom Index for BPH/IPSS.")

REFERENCE

AUA Guidelines on Management of Benign Prostatic Hyperplasia. Chapter 1: Diagnosis and treatment recommendations. J Urol 2003;170:530–547.

Kaplan S. AUA Guidelines and their impact on the management of BPH: An update. Rev Urol 2004;6(Suppl 9):S46–S52.

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 post-ejaculate 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 examination for the presence of vas deferens and hormone studies are indicated. Treatment is based on the underlying cause. (See also Section I: Infertility; Section II: Semen Analysis, Abnormal Findings and Terminology.)

CAUSES

- Congenital absence of vas deferens
- Ductal obstruction
- Germ cell failure
- Gonadotoxins
- Hypogonadotropic hypogonadism
- Idiopathic
- Testicular failure (Klinefelter syndrome)

REFERENCE

Practice Committee of American Society for Reproductive Medicine in collaboration with Society for Male Reproduction and Urology. Evaluation of the azoospermic male. Fertil Steril 2008;90(5 Suppl): S74–577.

SHORT TOPIC SECTION B

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 hemorrhage or infarction
- Gynecologic: Neoplasm of uterus or ovary, dysmenorrhea, salpingitis, uterine prolapse
- Infectious: Osteomyelitis, subarachnoid or spinal abscess, tuberculosis, meningitis, basilar pneumonia
- Mechanical: Pregnancy, obesity, fatigue, scoliosis
- Medication: Tadalafil-incidence of back pain and/or myalgia in 9.4% in patients receiving tadalafil 10 mg; 8.3% in patients receiving tadalafil 20 mg, and 3.7% in placebo-treated patients.
- Neoplastic: Myeloma, Hodgkin disease, carcinoma of pancreas, metastatic neoplasm from breast, prostate, lung
- Renal: Hydronephrosis, calculus, neoplasm, renal infarction, pyelonephritis
- Trauma: Injury to bone, joint, internal organs, or ligament

REFERENCE

1. Gerber GS, Brendler CB. Evaluation of the urologic patient: History, physical examination, and urinalysis. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders.

2. Seftel AD, et al. A three-part study to investigate the incidence and potential etiologies of tadalafil-associated back pain or myalgia. Int J Impot Res 2005;17(5):455–461.

BALANITIS XEROTICA OBLITERANS (BXO)

DESCRIPTION BXO is an inflammatory lesion of the glans and foreskin, now considered to be synonymous with Lichen Sclerosis et atrophicus (LSA). The term BXO is used when the skin of the genitalia is affected. BXO can cause itching and decreased sensitivity in the head of penis, but the hallmark is urethral meatal stenosis or distal urethral stricture. Differential diagnosis includes leukoplakia, Bowen disease, erythroplasia of Queyrat, or squamous cell carcinoma of the glans or preputial skin; biopsy is necessary to confirm the absence of malignancy. (See also Section I: “Penis, Lesion, General.”)

TREATMENT

- Local therapy with steroid, estrogen, or testosterone cream
- Surgical therapy with circumcision (when appropriate) and flap reconstruction of fossa navicularis for severe cases; meatal or urethral dilation rarely gives durable response.

REFERENCE

3. Akporiaye LE, et al. Balanitis xerotica obliterans (BXO). AUA Update Series, Vol. XVI, Lesson 21, 1997.

BALANITIS, ZOON

DESCRIPTION Also called balanoposthitis chronica circumscripta plasma cellularis and plasma cell balanitis. Can be confused clinically with erythroplasia of Queyrat. Grossly, it appears as a shiny, glazed-red macular erythematous lesion with multiple, pinpoint, bright red “cayenne pepper” spots. Histologically, a subepidermal inflammatory infiltrate of plasma cells and dermal red cell extravasation is present. No malignant transformation is reported. Proposed etiologies include Mycobacterium smegmatis, heat, poor hygiene, or constant friction. Treated by circumcision.

REFERENCE

4. Jolly BB, et al. Zoon’s balanitis. Urol Int 1993;50(3): 182–184.

BALKAN NEPHROPATHY

DESCRIPTION An interstitial 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 end in ESRD. Anemia, proteinuria, and hypertension can be severe. Renal biopsy has no specific markers for the disease. A strong association with increased incidence of upper tract transitional cell carcinoma (TCC) has been documented, although bladder TCC incidence is normal. No proven etiologic entity is known, but mycotoxin, long-acting virus, or hereditary causes are theorized. Treatment involves aggressive surveillance for TCC and renal replacement therapy, as necessary.

REFERENCE

5. Plestina R. Some features of Balkan endemic nephropathy. Food Chem Toxicol 1992;30(3): 189–192.

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.”)

The Banff Schema Simplified

Biopsy Findings

Banff Classification

Possible Clinical Approach

Normal, minor changes, or infiltrates without tubular invasion

Normal or “other” (non-specific changes)

No treatment, or treat other entity

Mild lymphocytic invasion of tubules (tubulitis)

Borderline changes

No treatment, or treat other entity

Widespread interstitial infiltrate with moderate invasion of tubules

Mild acute rejection (Grade I)

Treat for rejection if there are clinical signs

(A) Widespread interstitial infiltrate with severe invasion of tubules and/or (B) mild or moderate intimal arteritis

Moderate acute rejection (Grade II)

Treat for rejection, consider ALG/OKT3 if refractory to steroids

Severe intimal arteritis and/or “transmural” arteritis, fibrinoid change, and medial smooth muscle cell necrosis often with patchy infarction and interstitial hemorrhage

Severe acute rejection (Grade III)

Treat for rejection unless clinical course suggests rejection cannot be reversed in which case consider abandoning the graft

Hyaline arteriolar thickening (new onset, not present in implantation biopsy), and/or extensive isometric vacuolization of tubules, smooth muscle degeneration, thrombotic microangiopathy.

“Other,” cyclosporine toxicity

Reduce cyclosporine therapy

Tubular cell loss and necrosis, regenerative changes

“Other,” acute tubular necrosis

Await recovery

Interstitial fibrosis, tubular atrophy (new onset arterial fibrous intimal thickening suggests chronic rejection)

Chronic transplant nephropathy

Temporize

REFERENCE

6. Solez K, et al. International standardization of criteria for the histologic diagnosis of renal allograft rejection: The Banff working classification of kidney transplant pathology. Kidney Int 1993;44(2): 411–422.

BARCAT-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 parameatal flap. The full-thickness parameatal and urethral plate grafts are tubularized together and laid to rest in the new urethral groove.

REFERENCE

7. Duckett JW. Hypospadias. In: Walsh PC, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:2093–2119.

BARTTER SYNDROME

DESCRIPTION Congenital abnormality that usually presents in childhood with metabolic acidosis, hypereninemic hyperaldosteronism, and hypokalemia. Presenting symptoms are muscle weakness, polyuria, and sometimes growth retardation. Patients are normotensive. Renal biopsy reveals juxtaglomerular hyperplasia. Defective platelet aggregation and decreased vascular responsiveness to pressors are also noted. Pathophysiology includes decreased sodium transport in the thick ascending loop of Henle; decreased vascular responsiveness and increased prostaglandin secretion may also play a role.

This condition is incurable; potassium supplementation, prostaglandin synthesis inhibitors, aldosterone antagonists, and ACE inhibitors can help greatly to ameliorate symptoms.

REFERENCE

8. Clive DM. Bartter's syndrome: The unsolved puzzle. Am J Kidney Dis 1995;25(6):813–823.

BASHFUL BLADDER (PARURESIS, SHY BLADDER SYNDROME)

DESCRIPTION Also referred to as “pee-shy,” this is the inability to urinate with others present; it is a relatively common, but poorly researched and little understood phobia. According to DSM-IV TR, this disorder is classified as social phobia.

REFERENCE

9. Hammelstein P, et al. Is “shy bladder syndrome” (paruresis) correctly classified as social phobia? Anxiety Disord 2006;20(3):296–311.

BCG REFRACTORY TRANSITIONAL CELL CARCINOMA (TCC)

DESCRIPTION TCC that recurs 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. Additionally, 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.

REFERENCE

Sengupta S, Blute ML, The management of superficial transitional cell carcinoma of the bladder. Urology 2006;67(3 Suppl 1):48–54.

BCL-2, UROLOGIC CONSIDERATIONS

DESCRIPTION The protein product of the gene bcl-2 acts as an apoptosis-blocking agent. It appears to be required for normal morphogenesis of the kidney, and may be unimportant as a prognostic factor in renal cell carcinoma. It is seen in higher levels in prostatic intraepithelial hyperplasia but is variable in prostate cancer. Levels increase during XRT. Expression is increased in high-grade bladder tumors.

REFERENCE

King ED, et al. Incidence of apoptosis, cell proliferation and bcl-2 expression in transitional cell carcinoma of the bladder: Association with tumor progression. J Urol 1996;155(1):316–320.

BECKWITH-WIEDEMANN SYNDROME

DESCRIPTION Also referred to as EMG syndrome (exomphalos, macroglossia, and gigantinism), this condition is characterized by macroglossia, abdominal wall defects, adrenal cytomegaly, and neonatal hypoglycemia. Other characteristic features include gigantism, earlobe creases and pits, facial nevus flammeus, and prominent eyes with infraorbital creases. Most ominous is the increased risk of neoplasia, of which Wilms tumor, adrenal cortical carcinoma, and hepatoblastoma are most common. Mental retardation is not associated. Most cases are sporadic, but a genetic cause is widely suspected. Close follow-up early in life is recommended for tumor surveillance.

REFERENCE

Weng EY, et al. Beckwith-Wiedemann syndrome. An update and review for the primary pediatrician. Clin Pediatr 1995;34(6):317–326.

BEER NEPHROURETERECTOMY

DESCRIPTION Refers to a retroperitoneal two-incision approach to a nephroureterectomy through a flank and a separate Gibson or a midline Czerny incision.

REFERENCE

Bergman H, Lockhart J. Surgery of the ureteral stump. In: Kaufman JJ, eds. Current Urologic Therapy. Philadelphia: Saunders, 1986:212–214.

BEER POTOMANIA

DESCRIPTION A hypo-osmolality syndrome of beer drinkers, usually with hyponatremia. Patients with beer potomania have a history of significant beer drinking, often long term, 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 involves: Fluid restriction, ICU monitoring, and serial serum sodium levels, with slow correction of hyponatremia.

REFERENCE

Sanghvi SR, et al. Beer potomania: An unusual cause of hyponatremia at high risk of complications from rapid correction. Am J Kidney Dis 2007;50:673–680.

BEHçET DISEASE

DESCRIPTION A syndrome characterized by oral and genital ulcers (vulvar and penile), uveitis, vascular involvement (venous thrombosis, vasculitis), and non–mucous membrane skin lesions of unknown etiology. Lesions on the genitalia are herpetiform and can be painful. Other genital ulcers, such as syphilis, herpes, and chancroid, must be ruled out first. Genital ulcers are treated with local moisture-retaining dressings, topical anesthetics, and steroids. Occasionally, systemic immunosuppressive agents may be used.

REFERENCE

Kovacova E. Behcet’s syndrome. Bratisl Lek Listy 2005;106(12):386–389.

BELLINI DUCT CARCINOMA (COLLECTING DUCT CARCINOMA)

DESCRIPTION A variant of renal cell carcinoma 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 mucicarminophilic material, which is not seen in RCC. Radical nephrectomy for localized disease is the treatment of choice. Chemotherapy is used (interferon-–based) for metastatic disease. (See also Section I: “Renal Mass.”)

REFERENCE

Kirkali Z, et al. Bellini duct (collecting duct) carcinoma of the kidney. Urology 1996;47(6):921–923.

BELT PROCEDURE

DESCRIPTION Named for 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

Belt E, et al. A new anatomic approach in perineal prostatectomy. J Urol 1939;41:482–497.

BENCHEKROUN ILEAL VALVE

DESCRIPTION A hydraulic ileal 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 invaginating an ileal segment that then serves as the efferent continent limb.

REFERENCE

Benson MC, Olsson CA. Continent urinary diversion. In: Walsh PC, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3190–3245.

BERGER DISEASE (IGA NEPHROPATHY)

DESCRIPTION Sometimes referred to as idiopathic immunoglobulin A nephropathy, this condition was 1st described by Berger and Hinglas in 1968. 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 IgA deposits in the mesangium on immunofluorescence staining.

TREATMENT

- Recent promise seen in corticosteroids, fish oil, and ACE inhibitors
- Research in high-dose immunoglobulins
- Renal transplant for cases of renal failure

REFERENCE

Donadio JV Jr, Grande JP. Immunoglobulin A nephropathy: A clinical perspective. J Am Soc Nephrol 1997;8(8):1324–1334.

BERGMAN SIGN

DESCRIPTION In urologic radiography, the Bergman sign occurs when the ureter is dilated immediately below a neoplasm, rather than collapsed, as below an obstructing stone, thus showing a chalice shape. Retrograde pyelography demonstrates an irregular ureteral filling defect with complete obstruction and distal ureteral dilation, producing the chalice appearance; a ureteral catheter tends to curl in this segment. The Bergman sign is pathognomic for neoplasm.

REFERENCE

Bergman H (ed.). The Ureter, 2nd ed. New York: Springer-Verlag, 1981.

HCG (HUMAN CHORIONIC GONADOTROPIN)

DESCRIPTION Glycoprotein with a molecular weight of 38,000 and a half-life of 2 days. It is produced normally by the syncytiotrophoblast cells in pregnancy. hCG is composed of 2 subunits, and . The -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 urothelial tumors and secreting polyembryoma. Therapeutically can be given exogenously to stimulate Leydig 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 weeks. The hCG test is used to diagnose anorchia in underscended testicles; a failure to increase testosterone after administration suggests anorchia. (See also Section I: “Testis, Cancer, General”; Section I: “Testis, Nonseminomatous Germ Cell Tumors, General.”)

REFERENCE

Bower M, Rustin GJ. Serum tumor markers and their role in monitoring germ cell cancers of the testis. In: Comprehensive Textbook of Genitourinary Oncology, 2nd ed. Vogelzang NJ, et al., eds. Philadelphia: Lippincott Williams & Wilkins; 2000.

BETHANECHOL SUPERSENSITIVITY TEST

DESCRIPTION A variation of urodynamic testing wherein bethanechol is administered subcutaneously 20 min before testing. Usually considered when normal bladder contraction is weak or absent. If positive, a rise in filling pressure of >20 cm of water and a shift in the filling curve to the left are noted. A positive test represents bladder denervation. No change during the test represents myogenic damage.

REFERENCE

Snyder JA, Lipsitz DU. Evaluation of female urinary incontinence. Urol Clin North Am 1991;18(2): 197–209.

BEZOARS (FUNGUS BALLS)

DESCRIPTION Fungal infections of the kidney occur most commonly in the setting of diabetes, immunosuppression, urinary obstruction, or indwelling urinary catheters or stents. Most commonly Candida species such as C. albicans and tropicalis are involved. Other fungi such as Torulopsis glabrata and Aspergillus may cause renal infections, although less commonly. These infections can cause the formation of fungal balls or bezoars, which can be seen on imaging as a renal pelvic mass or filling defect and may cause obstruction; in the bladder, they may cause irritative voiding symptoms. Urinary tract imaging in the setting of candiduria (funguria) is needed in patients who have persistent candiduria and are at increased risk of bezoars (diabetics, or other urologic abnormalities). Urinary tract fungal bezoars are managed with a combination of surgical and medical therapy. (See also Section I: “Fungal Infections, Genitourinary”; Section II: “Funguria.”)

TREATMENT

- Treat medically until endoscopic procedure to remove the bezoar has been accomplished, symptoms have resolved, and cultures are negative.
- Candida bezoars: Fluconazole (200–400 mg/d [3–6 mg/kg/d] PO)
- Alternative regimen: Amphotericin B (0.5–0.7 mg/kg/d IV) with or without flucytosine (100 mg/d PO divided into 4 doses)
- Aspergillosis bezoars: Use voriconazole load: 6 mg/kg q12h for 2 doses; then maintenance of 4 mg/kg q12h
- With upper tract involvement, amphotericin B mixed 50 mg/L of sterile water by ureteral catheter, or nephrostomy can be considered.

REFERENCE

Pappas PG, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48:503.

BIFID SCROTUM

DESCRIPTION A congenital anomaly in which the scrotal folds are completely separate. This is generally seen in conjunction with other anomalies, and may be present in congenital adrenal hyperplasia and 5-reductase deficiency, almost always associated with hypospadias.

REFERENCE

Palmer JS. Genitourinary manifestations in boys and girls associated with genetic diseases. J Men’s Health Gend 2006;3(1):71–79.

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 expensive electronic systems (utilizing EMG or pressure probes). Biofeedback is applied in urology for improvement of urinary incontinence, generally by strengthening pelvic floor muscles. Biofeedback has also been used to teach patients to stop uninhibited detrusor contractions, teach relaxation of the pelvic floor and promote normal voiding in children, and control pelvic muscle spasms to alleviate pelvic pain syndromes.

REFERENCE

Bo K, et al. Lower urinary tract symptoms and pelvic floor muscle exercise adherence after 15 years. Obstet Gynecol 2005;105:999–1005.

BIOTHESIOMETRY, PENILE

DESCRIPTION A simple, inexpensive method of testing the vibratory sensitivity threshold when evaluating neurogenic causes of impotence. It is performed by measuring vibratory thresholds, usually in at least three 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 tibial evoked potentials, pudendal evoked potentials, and bulbocavernosus reflex latency. (See also Section I: “Erectile Dysfunction/Impotence, General.”)

REFERENCE

Bemelmans BL, et al. Comparison of biothesiometry and neuro-urophysiological investigations for the clinical evaluation of patients with erectile dysfunction. J Urol 1995;153(5):1483–1486.

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 (FLCN) 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 hybrids of these tumors. However, many will develop clear cell tumors as well. These tumors are more likely to be multiple and bilateral.

REFERENCE

Adley BP, et al. Birt-Hogg-Dubé syndrome: Clinicopathologic findings and genetic alterations. Arch Pathol Lab Med 2006;130(12):1865–1870.

BITES TO PENIS, ANIMAL AND HUMAN

DESCRIPTION Bites to the penis can result in significant morbidity. 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 for polymicrobial contamination and, in the case of dog bites, penicillin-VK may be given to treat Pasteurella multocida, which may be present in 20–25% of bites. Human bites tend to present later and pose a significant risk for infection. These should be copiously irrigated, broad-spectrum antibiotics should be administered, and wound closure is generally avoided. (See also Section I: “Penis, Trauma.”)

REFERENCE

Cummings JM, Boullier JA. Scrotal dog bites. J Urol 2000;164:57–58.

Wessells H. Penile and genital injuries. Urol Clin North Am 2006;33(1):117–126.

BK VIRUS, UROLOGIC CONSIDERATIONS

DESCRIPTION A common member of the human polyoma DNA virus, with a sero-positivity rate of 60–100% of the general population; it rarely presents any symptoms in immunocompetent hosts, and is not known to cause malignancy. During states of immunosuppression (eg, chemotherapy, AIDS, transplantation), this virus can reactivate and become a significant pathogen. BK virus often affects the urinary tract, with infections of the kidney and bladder being most common due to affinity to urothelial cells. In kidney transplant recipients, it can cause tubulointerstitial nephritis and ureteral stenosis. It has been shown to cause nephropathy in AIDS patients. BK virus has been found in the urine of immunosuppressed patients (viruria) having hemorrhagic cystitis (0.5–5 mo after bone marrow transplantation), causing both life-threatening hematuria and dysuria, as well as asymptomatic infections. Other causes of hemorrhagic cystitis in the differential include cyclophosphamide toxicity and adenovirus infection. The urine cytology–detectable abnormality of polyomavirus-infected cells is an enlarged nucleus with a single large basophilic intranuclear inclusion known as a “decoy cell”; this appears to be the best diagnostic test. Viral urine cultures and PCR are not useful in the diagnosis. It is named after the 1st patient (B.K.) in whom the virus was identified. (See also Section I: “Cystitis, Hemorrhagic [Infectious, Noninfectious, Radiation].”)

REFERENCE

Sukov WR, et al. BK virus-associated nephropathy in a patient with AIDS. Am J of Kidney Dis 2008; 51(4):15–18.

BLACK-WATER FEVER

DESCRIPTION Blackwater fever is a clinical entity characterized by acute intravascular hemolysis, classically occurring after the introduction of quinine for treatment of malaria. It is a rare but serious condition, in which hemolysis and anemia produce characteristically dark-colored urine. The condition has become exceptional since 1950, when quinine was replaced by chloroquine. Currently, it has reemerged from increased reutilization of quinine because of the development of resistance to chloroquine. Treatment of blackwater fever is supportive, including stopping the offending drug, blood transfusion for severe anemia, and a short course of steroids.

REFERENCE

Tombe M. Images in clinical medicine. Hemoglobinuria with malaria. N Engl J Med 2008;358(17):1837.

BLADDER AGENESIS

DESCRIPTION Rare and usually lethal congenital abnormality that has been reported in <20 living patients. Associated abnormalities include renal agenesis, retroiliac ureters, crossed fused renal ectopia, malrotation of the gut, colonic duplication, anal atresia, intraperitoneal iliac arteries, and bicornuate uterus. It is caused by a urogenital sinus abnormality during weeks 5–7 of development.

TREATMENT

- Separation of urinary and fecal stream
- Other reconstructive surgeries as appropriate

REFERENCE

Kaefer M, Adams MC. Penis and bladder agenesis in a living male neonate. J Urol 1997;157(4):1439–1440.

BLADDER CHORIOCARCINOMA

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. Metastases and -hCG elevation were seen in the majority of reported cases. A full metastatic workup including scrotal exam and ultrasound are mandatory. Three of the 7 cases were treated with resection and then chemotherapy, and all 3 showed good response (1 patient died of pulmonary embolus during therapy), the other 4 patients died of the disease. (See also Section I: “Bladder Cancer, General.”)

REFERENCE

Hanna NH, et al. Primary choriocarcinoma of the bladder with the detection of isochromosome 12p. J Urol 2002;167(4):1781.

BLADDER DIVERTICULUM

DESCRIPTION A bladder diverticulum is a herniation of the vesical mucosa through the detrusor muscle. Bladder diverticula may be congenital or acquired. Most acquired diverticula are associated with longstanding bladder outlet obstruction (high intravesical pressures) and are most commonly seen in older men with benign prostatic hypertrophy 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 rarely at the dome. Since the acquired diverticuli have no muscle wall components, they do not empty well and cause urinary stasis with increased risk of infection, stones, and urothelial carcinoma (intradiverticular tumors have a prevalence of 1–10%). The lack of a muscular wall makes urothelial carcinoma more likely to extend outside the bladder early. Congenital bladder diverticula are uncommon and occur almost exclusively in boys. When next to the ureteral orifice (Hutch 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 calculi. Treatment for cancers within diverticula may include transurethral resection (can be complicated by narrow ostia and thin diverticular wall), laser ablation, diverticulectomy, partial cystectomy, and radical cystectomy with or without intravesical therapy.

REFERENCE

Zeman PA, et al. Lower urinary tract symptoms. In: Siroksy MB, et al., eds. Handbook of Urology, 3rd ed. Philadelphia: Lippincott, 2004.

BLADDER EARS

DESCRIPTION Transient bladder outpouchings into the inguinal ring of male infants <6 mo old. This close association of the bladder with the internal ring resolves spontaneously. Inguinal herniorrhaphy 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

Redman JF, et al. Cystectomy: A catastrophic complication of herniorrhaphy. J Urol 1985; 133(1):97–98.

BLADDER FILLING DEFECTS

DESCRIPTION Filling defect on a contrast study of the urinary bladder (cystography) may be the result of:

- Air: Artifactual, post-instrumentation, vesicoenteric fistula
- Benign tumor: Prostatic enlargement, inverted papilloma, endometriosis
- Blood clot
- Calculus
- Congenital: Ureterocele
- Extrinsic compression by pelvic organ or mass, pelvic lipomatosis
- Fungus ball (bezoar)
- Infective, inflammatory: Inflammatory edema
- Instruments (catheters), foreign body
- Malignant tumor: Bladder and prostate malignancy, tumors invading urinary bladder from contiguous organs (eg, uterus, colon)
- Radiological atrifact: Fold in nondistended bladder

See also Section II: “Bladder Wall Mass.”

BLADDER HEMANGIOMA

DESCRIPTION A bladder anomaly most often associated with Klippel-Trenaunay syndrome (extensive port wine stains on extremities), bladder hemangioma is a rare, benign tumor. It presents with gross hematuria, at times severe. Bladder hemangiomas may be solitary or multiple.

TREATMENT

- Endoscopic treatment with Nd:YAG laser ablation
- Partial cystectomy can be required for large lesions or uncertainty in diagnosis.

REFERENCE

Kato M, et al. Endoscopic neodymium:yttrium aluminium garnet (Nd:YAG) laser irradiation of a bladder hemangioma associated with Klippel-Weber syndrome. Int J Urol 2000;7(4):145–148.

BLADDER HERNIA

DESCRIPTION Sometimes called a scrotal cystocele, 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 scrotum; bladder infarction and obstruction has been reported. In women, herniation of the bladder into the anterior vaginal wall is technically a cystocele. 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

Bisharat M, et al. Complications of inguinoscrotal bladder hernias: A case series. Hernia 2009; 13(1):81.

BLADDER HYPOPLASIA

DESCRIPTION Lack of urinary bladder development, leading to inadequate function and storage capacity. Hypoplasia is caused either the failure of production or storage of urine, or from complete bypass of the bladder. Causes include urogenital sinus abnormalities, severe epispadias, bilateral renal agenesis, severe renal dysplasia, and bilateral ureteral ectopia. Bladder reconstruction with bowel segments can be attempted.

REFERENCE

Canning DA, et al. Anomalies of the bladder and cloaca. In: Gillenwater JY, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

BLADDER, INFLAMMATORY PSEUDOTUMOR

DESCRIPTION A benign spindle cell lesion in patients who have not had surgery (as opposed to postoperative spindle cell nodule). Most patients are from 20–50 yr old 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 myxoid sarcomatoid carcinoma and myxoid leiomyosarcoma. Resection is the treatment.

REFERENCE

Young RH, Eble JN. Non-neoplastic disorders of the urinary bladder. In: Bostwick DG, Eble JN, eds. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

BLADDER LEIOMYOMA

DESCRIPTION The most common mesodermal tumor of the bladder, but very rare overall, with <200 cases reported. Presents as a mass or with voiding symptoms; the cause is unknown. US is reported to be useful for visualizing the lesion. It is differentiated from leiomyosarcoma on the basis of nuclear abnormalities.

TREATMENT

- Pedunculated lesions are amenable to transurethral resection.
- Sessile or large tumors may require partial cystectomy.

REFERENCE

Kabalin JN, et al. Leiomyoma of bladder. Report of two cases and demonstration of ultrasonic appearance. Urology 1990;35(3):210–212.

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 decade. 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 MALT (extranodal marginal zone B-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

Kempton CL, et al. Malignant lymphoma of the bladder: Evidence from 36 cases that low-grade lymphoma of the MALT-type is the most common primary bladder lymphoma. Am J Surg Pathol 1997;21(11):1324–1333.

BLADDER MASS, DIFFERENTIAL DIAGNOSIS

Malignant

Benign

Urothelial carcinoma (TCC)

Inverted papilloma

Squamous cell carcinoma

Nephrogenic adenoma

Adenocarcinoma

Leiomyoma

Small-cell (neuroendocrine) tumor

Hemangioma

Sarcoma

Granulomas

Sarcomatoid tumors

Abscess

Melanoma

Bladder diverticulum

Metastatic disease

Inflammatory pseudotumor

Filling defect (calculi, air, clot, foreign body, fungus ball)

(See also Section II: “Bladder Filling Defect and Bladder Wall Thickening.”)

REFERENCE

Abol-Enein H. Nonurothelial cancer of the bladder. Urology 2007;69(1 Suppl):93–104.

BLADDER, METASTASIS TO

DESCRIPTION The bladder may become involved by metastatic cancer from nearly any site. The most common are thought to be the prostate, ovary, uterus, breast, kidney, lung, and stomach. Others include melanoma, leukemia, and lymphoma.

REFERENCE

Messing EM, Catalona W. Urothelial tumors of the urinary tract. In: Walsh PC, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998.

BLADDER NECK CONTRACTURE

DESCRIPTION Scarring and stenosis of the bladder neck occurs most commonly as a postoperative complication of transurethral resection of the prostate or radical prostatectomy at the site of vesicourethral 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 site or foreign bodies such as surgical clips. Management consists of dilation, endoscopic incision (laser, cold cut, electrosurgical) or resection, and, in severe cases, open repair.

REFERENCE

Blumenthal KB, et al. Bladder neck contractures related to the use of Hem-o-lok clips in robot-assisted laparoscopic radical prostatectomy. Urology 2008;72(1):158–161.

BLADDER NECK HYPERTROPHY

DESCRIPTION Hypertrophy of the bladder neck is often seen in conjunction with BPH and may lead to obstructive symptoms and dysfunctional high-pressure voiding. Pure bladder neck hypertrophy has also been implicated in chronic pelvic pain syndrome and may respond best to -adrenergic blockade. (See also Section I: “Bladder Outlet Obstruction [BOO].”)

REFERENCE

Hruz P, et al. Non-inflammatory chronic pelvic pain syndrome can be caused by bladder neck hypertrophy. Eur Urol 2003;4:106–110.

BLADDER, NEUROFIBROMA

DESCRIPTION A benign tumor of the nerve sheath from overgrowth of Schwann cells, these lesions originate in bladder from ganglia in the wall. They can present in childhood as obstruction or voiding symptoms. Malignant degeneration is rare. The condition is sporadic or related to neurofibromatosis.

Conservative resection, as needed is the usual treatment. With severe obstruction or intolerable symptoms, cystectomy may be needed.

REFERENCE

Winfield HN, Catalona WJ. An isolated plexiform neurofibroma of the bladder. J Urol 1985;134(3): 542–543.

BLADDER, PARAGANGLIOMA

DESCRIPTION Exceedingly rare tumor, with 15% being malignant. Accounts for 10% of extra-adrenal pheochromocytomas. Catecholamine release is sometimes triggered by voiding, bladder distention, defecation, or intercourse. Typical symptoms are those of a pheochromocytoma (diaphoresis, paroxysmal hypertension, palpitations, headaches, syncope). The lesion may arise from embryonic nests of chromaffin cells in the sympathetic plexus of the detrusor muscle. Cystoscopy should be accompanied by adrenergic blockade; routine biopsy should be avoided. Transurethral resection is considered inadequate, since most lesions involve the entire thickness of the bladder wall. Treatment for smaller lesions consists of partial cystectomy with pelvic lymph node dissection. Radical cystectomy is recommended with large tumors or if lymphatic involvement is present.

REFERENCE

Dahm P, Gschwend JE. Malignant non-urothelial neoplasms of the urinary bladder: A review. Eur Urol 2003;44(6):672.

BLADDER, PHEOCHROMOCYTOMA

DESCRIPTION Similar to pheochromocytomas in other areas of body; 10% are malignant. They are thought to arise from paraganglionic cells in bladder, usually around the trigone. Most are hormonally active and can present with hypertension during bladder emptying and filling. 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

Piedrola G, et al. Malignant pheochromocytoma of the bladder: Current controversies. Eur Urol 1997; 31(10):122–125.

BLADDER SARCOMA (LEIOMYOSARCOMA/RHABDOMYOSARCOMA)

DESCRIPTION Types of sarcoma that have been described in the bladder include angiosarcoma, leiomyosarcoma, rhabdomyosarcoma, liposarcoma, chondrosarcoma, and osteosarcoma. These, combined, account for less than 1% of all malignant tumors of the bladder. They usually present with hematuria or voiding symptoms. Sarcomas of the bladder are rare aggressive malignancies. Leiomyosarcoma is the most common malignant mesenchymal tumor that arises in the bladder of adults. It occurs more frequently in men. On histology, parallel bundles of spindle cells are seen. The mainstay of treatment is aggressive excision (4–5 cm margins), but even with such treatment the 5-yr disease-specific survival is 62%. Rhabdomyosarcomas are most common in young children. Embryonal rhabdomyosarcomas in children characteristically produce polypoid lesions in the base of the bladder, and is known as sarcoma botryoides. 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 consists of resection, radiation, and chemotherapy with single-agent (doxorubicin or ifosfamide). (See also Section I: “Bladder Cancer, General”; Section I: “Rhabdomyosarcoma, Pediatric [Sarcoma Botryoides].”)

REFERENCE

Rosser CT, et al. Clinical presentation and outcome of high-grade urinary bladder leiomyosarcoma in adults. Urology 2003;61:1151.

Stevens MC. Treatment for childhood rhabdomyosarcoma: The cost of cure. Lancet Oncol 2005;6(2):77–84.

BLADDER SMALL-CELL CARCINOMA (OAT CELL, SIGNET RING)

DESCRIPTION Neuroendocrine or small-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. Neuroendocrine tumor of the bladder is rare, with ~286 cases reported in the English literature. It can be seen alone or in combination with other tumor types, most frequently transitional cell carcinoma. Small-cell carcinoma of the bladder presents as any other bladder tumor, most frequently with hematuria. The diagnosis is made pathologically. The tumor usually presents as muscle-invasive disease (94% in one series), and often with metastatic disease (67% in same series). Most common sites of metastases are to 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.”)

SYNONYMS

- Small-cell carcinoma
- Neuroendocrine tumor
- Oat cell carcinoma

TREATMENT

- Partial or radical cystectomy
- Platinum-based chemotherapy has achieved partial regression.

REFERENCE

Sved P, et al. Small cell carcinoma of the bladder. BJU Int 2004;94:12–17.

BLADDER, TEARDROP

DESCRIPTION Diffuse pelvic pathology can compress the bladder into a teardrop configuration on various imaging studies, such as excretory urography or cystogram. Causes include pelvic lipomatosis, pelvic hematoma, pelvic adenopathy, and enlarged pelvic vasculature (usually caused by vena cava obstruction). Occasionally, a muscular patient with a hypertrophied iliopsoas muscle can exhibit this finding.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:287–288.

BLADDER TRABECULATION AND CELLULES

DESCRIPTION Trabeculation is a cystoscopic description of hypertrophy of smooth muscle bundles in the muscularis 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 dyssynergia. 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 mucosa 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.”)

REFERENCE

Bai SW, et al. The significance of bladder trabeculation in the female lower urinary system: An objective evaluation by urodynamic studies. Yonsei Med J 2005;46(5):673–678.

Sirosky MB, Babyan RK. Lower urinary tract symptoms. In: Siroksy MB, et al., eds. Handbook of Urology, 3rd ed. Philadelphia: Lippincott, 2004.

BLADDER, VILLOUS ADENOMA

DESCRIPTION This tumor has a histologic appearance identical to villous adenoma of the colon. It can also be seen in the urachus. Cystoscopically, it appears exophytic 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

Channer JL, et al. Villous adenoma of the bladder. J Clin Pathol 1993;46(5):450–452.

BLADDER WALL CALCIFICATION, DIFFERENTIAL DIAGNOSIS

DESCRIPTION Bladder wall calcification is a relatively uncommon finding. The differential includes:

- Amyloidosis
- Bilharzia (urinary schistosomiasis)
- Cyclophosphamide-induced cystitis
- Encrusted cystitis
- Mitomycin C intravesical treatment
- Tuberculosis
- Urothelial carcinoma

REFERENCE

Pollack HM, et al. Diagnostic considerations in urinary bladder wall calcification. AJR 1981;136(4): 791–797.

BLADDER WALL THICKENING, DIFFERENTIAL DIAGNOSIS

DESCRIPTION Bladder wall thickening can be seen on US, CT, or MRI. The differential includes:

- Bacterial/viral cystitis
- Bilharzial infection (urinary schistosomiasis)
- Bladder cancer (urothelial carcinoma, nonurothelial carcinoma)
- Bladder fistula (Crohn disease, diverticulitis)
- Hemorrhagic cystitis
- High-pressure storage/voiding (eg, bladder outlet obstruction, neurogenic bladder)
- Systemic lupus erythematosus
- Tuberculosis

REFERENCE

Wong-You-Cheong JJ, et al. Inflammatory and nonneoplastic bladder masses: Radiologic-pathologic correlation. Radiographics 2006;26(6): 1847–1868.

BLASTOMYCOSIS, GENITOURINARY

DESCRIPTION Blastomyces dermatitidis is endemic in the Ohio, Mississippi, and Missouri river basins. It is an opportunistic infection in immunocompromised 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. Prostatic abscess 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. Standard therapy is long-term amphotericin B for a total dose of 1–3 g.

REFERENCE

Wise GJ, Freyle J. Changing patterns in genitourinary fungal infections. AUA Update, Vol. XVI, Lesson 1, 1997.

BLEOMYCIN TOXICITY

DESCRIPTION Used in combination chemotherapy for testicular cancer as well as cervical, ovarian, squamous cell carcinoma, and lymphoma, induces single- and double-strand breaks in DNA called scission. Pulmonary fibrosis (fibrosing alveolitis) is a potentially lethal toxicity; it can develop 1–6 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 (nonproductive), dyspnea, pleuritic chest pain, fever, tachypnea, rales, lung restriction, and hypoxemia. Renal insufficiency is a risk factor for bleomycin toxicity (80% eliminated by the kidney).

TREATMENT

- Discontinue drug with suspected bleomycin-induced injury; steroids may help some cases.
- Attention to minimizing oxygen concentration and hydration status during surgery is essential.

REFERENCE

de Wit R, et al. Importance of bleomycin in combination chemotherapy for good-prognosis testicular non-seminoma: A randomized study of the European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group. J Clin Oncol 1997;15(5):1837–1843.

BLUE DIAPER SYNDROME

DESCRIPTION Defect in tryptophan absorption in which the urine contains indoles, giving it a blue color. Similar to Hartnup disease. Chronic course is usual. Hypoplasia of the optic disc and abnormal eye movements have also been reported.

SYNONYMS

- Familial hypercalcemia with nephrocalcinosis and indicanuria
- Tryptophan malabsorption

TREATMENT

Low-tryptophan diet; no treatment known for underlying defect

REFERENCE

Chen Y, et al. The ocular abnormalities of blue diaper syndrome. Metab Pediatr Systemic Ophthalmol 1991;14(3–4):73–75.

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 appendix testes or appendix epididymis. Should be sought during the evaluation of scrotal pain or swelling. The torsed appendix may swell to the size of the testicle itself. If torsion of the cord can be ruled out by palpation of the unequivocally normal testicle, appendiceal torsion can be observed. (See also Section I: “Torsion, Testis and Testicular Appendages.”)

REFERENCE

Dresner ML. Torsed appendage. Diagnosis and management: Blue dot sign. Urology 1973; 1(1):63–66.

BLUE NEVUS (MELANOSIS), UROLOGIC CONSIDERATIONS

DESCRIPTION Benign melanotic lesion of the prostate that must be differentiated from malignant melanoma. It is usually an incidental finding after TURP. In prostate, the term blue nevus has been used when melanin is confined to ovoid 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

Muzaffar S, et al. Melanosis of the prostate: A rare benign morphological entity. Br J Urol 1995;76(2): 265–266.

BOARI-OCKERBLAD FLAP

DESCRIPTION After appropriate bladder mobilization, a tonguelike flap of bladder based on the ipsilateral superior vesicle artery is incised. The base of the flap should be at least 4 cm, while the tip should be at least 3 cm. The tubularized flap is then anchored to the psoas minor tendon, and either direct or tunneled anastomosis with the ureter is then performed. Useful to reimplant the ureter when there is loss of the distal ureter.

REFERENCE

Kay R. Reimplantation of the ureter. In: Novick AC, et al., eds. Stewarts' Operative Urology, Baltimore: Williams & Wilkins, 1989:526–538.

BODY MASS INDEX (BMI), UROLOGIC CONSIDERATIONS

DESCRIPTION The BMI is defined as the weight (in kilograms) divided by the height (in meters2). 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 erectile dysfunction, with reduction of BMI correlating with increased 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 on line at: http://www.nhlbisupport.com/bmi/.

Classification of Overweight and Obesity by BMI

Obesity Class
BMI (kg/m2)
Underweight

<18.5
Normal

18.5–24.9
Overweight

25.0–29.9
Obesity
I
30.0–34.9
Obesity
II
35.0–39.9
Extreme obesity
III
40

REFERENCE

Esposito K, et al. Effect of lifestyle changes on erectile dysfunction in obese men: A randomized controlled trial. JAMA 2004;291:2978–2984.

Taylor EN, et al. Obesity, weight gain, and the risk of kidney stones. JAMA 2005;293:455–462.

BONE METASTASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Bone metastasis are a common problem in urologic malignancies. Prostate cancer has a predilection to metastasize to bone but bone metastasis from renal cell carcinoma, urothelial carcinoma, and adrenocortical carcinoma are also seen. An elevated alkaline phosphatase suggests bone lesions. The diagnosis often involves a radionucleotide bone scan with confirmatory imaging study and possibly a biopsy. Bone metastases are associated with pain (which may be severe), pathologic 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 radioisotopes such as strontium-89 are useful for palliation of more extensive bone metastasis. In prostate cancer in particular, bisphosphonate therapy is used to prevent progression and skeletal related complications and may be effective at preventing occurrence of bone metastases.

REFERENCE

Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res 2006;15;12(20 Pt 2):6243s–6249s.

BONE MINERAL DENSITY, UROLOGIC CONSIDERATIONS

DESCRIPTION Prolonged androgen deprivation therapy for prostate cancer is associated with decreased bone mineral density 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 bone mineral density during androgen ablation therapy. (See also Section II: “Osteoporosis and Osteopenia, Urologic Considerations.”)

Some recommend that bone mineral density should be monitored during androgen-deprivation therapy using bone mineral density scans (dual-energy x-ray absorptiometry or DEXA):

- T-score: The number of standard deviations (SDs) by which the patient’s bone mass falls above or below the mean peak bone mass for a 30-yr-old healthy adult. For every 1 SD decrease in T-score, relative risk of fracture increases ~1.5–2.5-fold
- WHO interpretation of T-scores: Normal: –1; Osteopenia: –1 to –2.5; Osteoporosis –2.5; Severe osteoporosis: –2.5 and 1 fracture

REFERENCE

Ryan CW, et al. Lifestyle factors and duration of androgen deprivation affect bone mineral density of patients with prostate cancer during first year of therapy. Urology 2007;70(1):122–126.

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 recurrent or metastatic disease in urologic malignancies (prostate, urothelial, renal, and adrenocortical carcinomas). A bone scan is generally performed by acquiring multiple images of the skeleton 3–4 hr after IV injection of 99mtechnetium-labelled 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 scan is extensively used in prostate cancer to detect and follow bone metastases. In prostate cancer patients with extensive bony metastasis, the bone scan may have a “super scan” appearance, in which the focal lesions coalesce to produce diffusely increased uptake. An increase in the contrast between bone and background soft tissue and faint or absent renal images are the typical appearances seen on a “super scan.”

REFERENCE

Coleman R, Rubens R. Radionucleotide bone scan. In: Abeloff, ed. Clinical Oncology, 3rd ed. New York: Churchill Livingstone, 2004.

BONNEY 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 symptomatically 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 elevation of the bladder neck. Bonney cautioned that the fingers must be carefully placed to avoid compressing the urethra in the midline.

Currently, the clinical utility has been questioned by many clinicians as a meaningful test.

REFERENCE

Miyazaki FS. The Bonney test: A reassessment. Am J Obstet Gynecol 1997;177(6):1322–1328; discussion 1328–1329.

BORS-COMARR CLASSIFICATION OF VOIDING DYSFUNCTION

DESCRIPTION Based on observations noted on spinal cord-injured patients. The system takes into account three main factors:

- Anatomic location of the lesion (upper motor neuron, lower motor neuron)
- Completeness of the lesion (partial vs. complete spinal cord injury)
- 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

REFERENCE

Pryse-Phillips W, Pryse-Phillips W. Companion to Clinical Neurology, 2nd ed. New York: Oxford, 2003.

BOSNIAK CLASSIFICATION OF RENAL CYSTS

DESCRIPTION Classification system to differentiate renal cystic masses visualized on CT as benign or malignant. Cysts are graded on scale from I–IV, with grade I having typical appearance of benign simple cyst, and grade IV having appearance of renal cell carcinoma. Classification is based on homogeneity and complexity of cystic fluid, presence or absence of septations, calcifications, or solid components; and the density of cystic fluid as determined by Hounsfield units. (See also Section II: “Renal Cysts,” Section II: “Renal Mass.”)

- Category I: Benign simple cysts; thin walls without septa, calcifications, or solid components; water density and no contrast enhancement. No further imaging needed.
- Category II: Benign cysts with a few thin septa; the wall or septa may contain fine calcification and sharp margins, are nonenhancing, and usually measure <3 cm.
- Category IIF: Well-marginated 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 lesions >3 cm. These require follow-up (designated by the “F” designation).
- Category III: Indeterminate cysts with thickened irregular or smooth walls or septa; enhancement present. 40–60% percent are malignant (cystic renal cell carcinoma and multiloculated cystic renal cell carcinoma). Other class III lesions are benign and include hemorrhagic cysts, infected cysts, and multiloculated cystic nephroma. Surgery is recommended, although additional imaging by MRI or with biopsy is supported by some clinicians.
- Category IV: Risk of malignancy is 85–100%. Characteristics of category III cysts, plus they contain contrast-enhancing soft-tissue components that are adjacent to and independent of the wall or septum. Surgery is recommended.

REFERENCE

Israel GM, Bosniak MA. Urology 2005;66(3):484–488.

BOURNE TEST

DESCRIPTION A diagnostic test for the detection of enterovesical or colovesical fistulas. The test consists of radiography of centrifuged urine samples obtained immediately after a barium enema. In one series of 10 patients, in 7 of the 10, the Bourne test was the only positive evidence of an otherwise occult colovesical fistula later proven at surgery.

REFERENCE

Lawrence C, et al. Image of the month. Bourne test, enterovesical fistulas. Gastroenterology 2003; 125(2):291, 641.

BOWENOID PAPULOSIS

DESCRIPTION Bowenoid papulosis is an uncommon skin lesion affecting the genitals, groin, and perianal areas of young, sexually active adult men and women. The histology appearance resembles Bowen disease. The natural history of the disease is unknown, 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 (averaging 4 mm in diameter), flat, reddish-violaceous or brown, often coalescent, and usually have a smooth, velvety 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 by excision, cautery, cryoablation, or laser surgery, much as ordinary warts, without the need for wide surgical margins. Alternatively, lesions may be treated for 3–5 wk with 5% 5-fluorouracil cream or imiquimod cream q.o.d.

REFERENCE

Habif TP. Bowenoid papulosis. In: Habif TP, ed. Clinical Dermatology: A Color Guide to Diagnosis and Therapy, 4th ed. St. Louis: Mosby, 2004:343.

BOYARSKY GUIDELINES FOR BPH

DESCRIPTION To provide reproducible guidelines for the severity of symptoms of prostatism, BPH, and LUTS, scored questionnaire formats have been developed. Traditional assessment tools include the Madsen-Iversen Point System and the Boyarsky Guidelines. These have been generally replaced by the AUA or I-PSS questionnaires, but are used in several ongoing follow-up studies of BPH therapies.

REFERENCE

Boyarsky S, et al. A new look at bladder neck obstruction by the Food and Drug Administration regulators: Guidelines for investigation of benign prostatic hypertrophy. Trans Am Assoc Genitourinary Surg 1976;68:29.

BOYCE NEPHROTOMY (ANATROPHIC NEPHROLITHOTOMY)

DESCRIPTION The longitudinal anatrophic nephrotomy takes advantage of a nearly avascular plane in the kidney (Brödel white line), which can be used to remove staghorn calculi (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 plain. Traditionally used for staghorn calculi.

REFERENCE

Straffon RA. Anatrophic nephrolithotomy. In: Novick AC, et al., eds. Stewart’s Operative Urology, Baltimore: Williams & Wilkins, 1989:191–197.

BRACHYTHERAPY SEED EMBOLUS

DESCRIPTION Brachytherapy is used to treat prostate cancer via image-guided implantation of radioactive seeds of iodine125 or palladium103. 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 iodine125 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. Two 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

Nguyen BD. Cardiac and hepatic seed implant embolization after prostate brachytherapy. Urology 2006;68(3):673.

BRAIN METASTASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Brain metastatic disease can be seen with several urologic malignancies, most commonly with renal cell carcinoma and germ cell tumors. 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 urologic tumors 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 high impact on quality of life, these often require prompt treatment usually via radiation therapy or surgical removal.

REFERENCE

Nguyen TD. Brain metastasis. Neurol Clin 2007; 25(4):1173–1192.

BRENNER TUMORS

DESCRIPTION These are tumors of variable malignant potential of the ovary. Extraovarian 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 stains for carcinoembryonic antigen (CEA). Theorized origin is from a metaplastic process of coelomic epithelium. Usually, surgical removal is used to assess malignant potential.

REFERENCE

Caccamo D, et al. Malignant Brenner tumor of the testes and epididymis. Arch Pathol Lab Med 1991; 115(5):524–527.

BRICKER URETERAL ANASTOMOSIS

DESCRIPTION A direct ureteral-to-small bowel end-to-side refluxing anastomosis incorporating full-thickness ureteral and intestinal wall. It is used in ileal conduit construction.

REFERENCE

McDougal WS. Use of intestinal segments and urinary diversion. In: Walsh PC, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998: 3137–3144.

BRIGHAM SLING (URETHROPEXY)

DESCRIPTION Used to treat stress incontinence in women. A combined endoscopic needle sling procedure that utilizes a rectus fascial strip placed at the bladder neck through a vaginal incision. The fascial sling is held in place with needles placed through the anterior abdominal wall, similar to the Stamey and Raz suspension needles. (See also Section I: “Incontinence, Urinary, Adult Female.”)

REFERENCE

Loughlin KR. The Brigham sling. Contemp Urol 1998;10:69–75.

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, and time were combined to form a 7-point scale. This scale has been revised several times; it is seldom used today.

REFERENCE

Brink CA, et al. A digital test for pelvic muscle strength in women with urinary incontinence. Nurs Res 1994; 43:352–356.

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. Disparate lesions are classified under a common category. The World Health Organization classification is used in most of the rest of the world.

REFERENCE

Ulbright TM. Neoplasms of the testes. In: Bostwick D, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

BRUNN BUDS AND NESTS (VON BRUNN NESTS)

DESCRIPTION Variant of bladder epithelium, noted in 80–90% of normal bladders. Brunn buds are an invagination of surface epithelium into the lamina propria. Brunn nests represent a further invagination within the lamina propria and are a more progressed form of a Brunn bud. Cystitis cystica is thought to result from a Brunn nest that closes over on itself, forming a cyst. May become involved with transitional cell carcinoma (TCC); controversy exists as to whether radical or conservative therapy is indicated if these lesions are involved by TCC.

REFERENCE

Dinney CP, et al. Management of transitional cell carcinoma involving von Brunn's nests. J Urol 1995;153:944–949.

BRUSHITE (CALCIUM MONOHYDROGEN PHOSPHATE)

DESCRIPTION A type of calcium phosphate calculus of the kidney. Brushite stones are particularly dense and are 2nd only to cysteine stones in their resistance to fragmentation.

Calcium phosphate is the most common type of stone seen in distal renal tubular acidosis (type 1). On metabolic evaluation, primary calcium phosphate stone formers tended to have higher urine volumes, and higher calcium and lower citrate excretion than do idiopathic calcium oxalate formers. (See also Section I: “Urolithiasis, Adult, General”; Section II: “Urolithiasis, Calcium Oxylate/Phosphate.”)

REFERENCE

Evan AP, et al. Crystal-associated nephropathy in patients with brushite nephrolithiasis. Kidney Int 2005;67(2):576–591.

BTA TESTING (BTA AND BTA STAT URINE TEST)

DESCRIPTION The BTA test (Bard; Redmond, Washington) is a latex agglutination assay that has recently been approved by the Food and Drug Administration. It qualitatively detects high-molecular-weight basement membrane complexes, present when tumor cells become invasive and undergo proteolytic degradation.

A comparison of BTA with bladder wash cytology reported a higher sensitivity of BTA (54% vs. 23%). However, BTA was associated with a high false-positive rate (specificity 9%). A multicenter trial demonstrated sensitivities of 40% and 16% for BTA and urine cytology, respectively.

The initial BTA test had two limitations: It is a latex agglutination test, and it yielded high false-positive rates. Consequently, the new BTA stat test was developed; it is a monoclonal antibody immunoassay that detects the presence of newly identified human complement factor H-related protein (hCFhrp). A study of BTA stat reported higher sensitivity compared with cytology. BTA stat has also had higher sensitivity compared with the BTA test, (58% vs. 44%). The specificity of BTA stat was reported as 72% for benign genitourinary disease and 95% in healthy volunteers. The main advantage of the BTA test is that it can simply be performed in an office setting and provides rapid results.

REFERENCE

Leyh H, et al. Comparison of the Bard BTA test with voided urine and bladder wash cytology in the diagnosis and management of cancer of the bladder. Urology 1997;50:49–53.

BULKING AGENTS, INJECTABLE

DESCRIPTION Injections of various agents (synthetic and natural) have been used in urology to treat conditions such as vesicoureteral reflux, intrinsic sphincter deficiency, and stress urinary incontinence. Some products common in the US are listed here. (See also Section I: “Incontinence, Urinary, Adult Male”; Section I: “Incontinence, Urinary, Adult Female”; Section I: “Vesicoureteral Reflux, Pediatric.”)

Material

Brand Name

Description

Polytetrafluoroethylene

PTFE (Teflon)

The small size of particles (90% <40 m) allows them to be phagocytosed, which can result in distant migration and granuloma formation. Not FDA approved for incontinence (migration risk).

Glutaraldehyde cross-linked bovine collagen

GAX-Collagen

Highly purified 35% suspension of bovine collagen (95% type I collagen and 1–5% type III 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

Durasphere

Nonresorbable pyrolytic carbon-coated zirconium beads are much larger (212–500 m) than either PTFE or silicone polymers and are transferred in a 2.8% -glucan water-based gel. Durasphere is more viscous than collagen, and its injection was more technically demanding.

Ethylene vinyl alcohol (EVOH)

Tegress

Permanently implanted nonpyrogenic, injectable bulking agent (EVOH dissolved in DMSO). The resulting mixture is 8% EVOH in DMSO. After injection into tissue, the DMSO diffuses away, resulting in the EVOH precipitating into a complex cohesive. spongiform mass. This phase transformation takes place rapidly (within 60 s), and this effect creates increased tissue bulk.

Silicone polymers

Macroplastique

Textured polydimethylsiloxane macro particles (>100 m) suspended in a bioexcretable carrier hydrogel of polyvinylpyrrolidone (povidone) in which the solid particle content is 33% of

the total volume.

Dextranomer microspheres

Deflux

Viscous gel of dextranomer microspheres (50 mg/mL) in a carrier gel of nonanimal stabilized hyaluronic acid, constituting a biocompatible and biodegradable implant. The dextranomer microspheres range from 80–250 microns (average 130 microns). The hyaluronic acid acts mainly as a carrier, leaving the dextranomer microspheres at the implant site.

REFERENCE

Wilson TS, et al. Management of intrinsic sphincteric deficiency in women. J Urol 2003;169(5): 1662–1669.

BULLOUS PEMPHIGOID

DESCRIPTION A dermatologic condition thought to be autoimmune related. The condition is more common in men and in patients >60 years of age. Although variable in clinical presentation, a preliminary nonbullous phase is usually characterized by severe pruritus and nonspecific skin changes, followed by formation of confluencing vesicles and marked erythema of the skin. Immunohistochemical evaluation of the skin biopsy shows IgG deposition along the skin basement membrane. Treatment is with steroids and immunosuppression.

REFERENCE

Kirtschig G, Khumalo NP. Management of bullous pemphigoid: Recommendations for immunomodulatory treatments. Am J Clin Dermatol 2004;5:319–326.

BLOOD UREA NITROGEN (BUN), INCREASED/DECREASED

DESCRIPTION Blood urea nitrogen (BUN) is a product of dietary protein metabolism. It is produced in the liver and cleared by the kidneys. The serum BUN level depends on both the rate of production and the rate of renal clearance. In renal failure, BUN and creatinine levels generally increase. Factors that might increase BUN include drugs (lithium, diuretics, aminoglycosides, corticosteroids), GI bleeding, prerenal azotemia, renal disease (diabetic nephropathy, pyelonephritis, glomerulonephritis), and obstructive nephropathy. Factors that lower BUN include liver disease, malnutrition and low-protein diets, 3rd-trimester pregnancy, celiac disease, and acromegaly. BUN along with sodium is thought to be responsible for the solute diuresis (postobstructive diuresis) that results after relief of renal obstruction.

REFERENCE

Loo MH, Vaughan ED. Obstructive nephropathy and postobstructive diuresis. AUA Update Series, Vol. 4, Lesson 9, 1985.

BURCH COLPOSUSPENSION

DESCRIPTION The paravaginal fascia is fixed to the Cooper ligament, usually through a Pfannenstiel incision and a retropubic exposure. It is used in treatment of stress incontinence in women.

REFERENCE

Burch JC. Urethrovaginal fixation to Cooper’s ligament for correction of stress incontinence, cystocele, and prolapse. Am J Obstet Gynecol 1961;81281–81290.

BUSCHKE-LOWENSTEIN TUMOR

DESCRIPTION Nonmalignant penile or perineal lesion, which may be large and exophytic. May cause urethral erosion and fistulas. Can be very locally invasive and mistaken grossly for squamous cell carcinoma. Microscopically, broad rete pegs, filled with benign squamous cells and surrounded by a layer of inflammatory cells, are noted. A possible role of human papilloma virus 6 and 11 in the development is theorized. Treatment is by local excision after proven diagnosis. (See also Section I: “Condylomata Acuminata (Venereal Warts)”; Section I: “Penis, Lesion.”)

SYNONYMS

- Verrucous carcinoma
- Giant condyloma acuminata

REFERENCE

Chu QD, et al. Giant condyloma acuminata (Buschke-Lowenstein tumor) of the anorectal and perianal regions. Analysis of 42 cases. Dis Colon Rectum 1994;37(9):950–957.

BYAR FLAPS

DESCRIPTION The penile prepuce is split dorsally and transferred ventrally, yielding redundant ventral skin to be used in 2nd-stage hypospadias repair.

REFERENCE

Duckett JW. Hypospadias. In: Walsh PC, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:2093–2119.

SHORT TOPIC SECTION C

CALCIFICATIONS, ABDOMINAL AND PELVIC

DESCRIPTION Abdominal and pelvic calcifications are a common finding on plain radiographs and CT. The differential is very broad and includes renal, ureteral and bladder calculi, vascular calcifications (arthrosclerosis and phleboliths), calcified tumors, lymph nodes, seminal vesicles, vas deferens, and infectious processes (TB).

REFERENCE

1. O'Connor OJ. Imaging of hematuria. Radiol Clin N Am 2008;46(1):113–132.

CALCIFICATIONS, BLADDER

DESCRIPTION Bladder calcifications on CT or plain radiograph:

- Intraluminal: Bladder calculi, 7% of bladder urothelial carcinomas may be calcified and appear as small stones, encrusted cystitis, foreign body, iatrogenic (post op 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

2. O'Connor OJ. Imaging of hematuria: Radiol Clin N Am 2008;46(1):113–132.

CALCIFICATIONS, RENAL

DESCRIPTION They may represent calcified renal calculi or calcified cystic or solid renal neoplasms. Renal cell carcinoma is detectable on plain radiography and calcified ~8–18% of the time. Other possible etiologies for renal calcifications include papillary tip calcifications, calcified renal pelvis transitional cell carcinoma, nephrocalcinosis, calcified renal artery, and tuberculosis.

REFERENCE

3. O’Connor OJ. Imaging of hematuria. Radiol Clin North Am 2008;46(1):113–132.

CALCINOSIS, IDIOPATHIC SCROTAL

DESCRIPTION Occurs in preexisting epidermal cysts or in the dermis without cysts. Usually affects young men. Multiple cysts (>50) are not uncommon. Calcifications range in size from a few millimeters to 3 cm. They may represent epidermal cysts that have, over time, lost their normal wall and calcified. Surgical excision is curative if symptomatic.

REFERENCE

4. Ro JY, et al. Penis and scrotum. In: Bostwick D, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

CALCIUM LOAD AND FAST STUDIES

DESCRIPTION Tests performed to evaluate hypercalciuria in stone-formers. One method is to place patients on a low-calcium, low-sodium diet for 1 wk. A fast is performed from 9 PM–9 AM. At 7 AM, the patient empties his bladder. This urine is discarded. 600 mL of distilled water is then consumed. Urine is collected from 7 AM–9 AM. At 9 AM, 1 g of calcium is consumed, and urine is collected from that point until 1 PM. Urine samples are analyzed for calcium, creatinine, and cAMP. Results can then differentiate between absorptive hypercalciuria, renal hypercalciuria, and hyperparathyroidism. On a normal diet, 24-hr urinary calcium levels are considered <300 mg/d (7.5 mmol/d) in men and <250 mg/d (6.25 mmol/d) in women. (See also Section I: “Urolithiasis, Adult, General”; Section I: “Urolithiasis, Calcium Oxylate/Phosphate”; Section II: “Hypercalcuria [Absorptive, Renal and Resorptive].”)

REFERENCE

5. Rivers K, et al. When and how to evaluate a patient with nephrolithiasis. Urol Clin North Am 2000; 27(2):203–213.

CALCIUM SUPPLEMENTATION AND UROLITHIASIS

DESCRIPTION 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-urine collection to identify those who will become or remain hypercalciuric while on calcium supplementation. In patients who are normocalciuric while receiving calcium citrate, no further intervention is necessary. In those patients found to be hypercalciuric, treatment with thiazide diuretics or slow-release potassium phosphate can be used.

REFERENCE

6. Curhan GC, et al. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. Ann Intern Med 1997;126(7):497.

CAMEY I AND II ORTHOTOPIC URINARY DIVERSION

DESCRIPTION In the Camey I surgery, a 40-cm segment of the midportion of the ileum is chosen for an orthotopic urinary diversion that can reach the urethra. A LeDuc antireflux ureteral ileal anastomosis is carried out on each end of the ileal 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 LeDuc ureteral anastomosis.

REFERENCE

7. Lilien OM, Camey M. 25-year experience with replacement of the human bladder (Camey procedure). J Urol 2002;167(2 Pt 2):1161.

CANAL OF NUCK HYDROCELE AND CYST (FEMALE HYDROCELE)

DESCRIPTION In the female, the labia majora are homologous to the scrotum in the male. The labia majora 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.

REFERENCE

8. Dietrich CS, et al. Surgical exposure and anatomy of the female pelvis. Surg Clin N Am 2008;88(2).

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 cause itching, burning, discharge, dryness, and dysuria in females (vulvovaginitis). Vesicopustules that enlarge and rupture and progresses to maceration and erythema. There are distinct red borders, often with satellite lesions with vaginal discharge being white and thick. Microscopic examination of scrapings or discharge with potassium hydroxide or Gram stain reveals hyphae/pseudohyphae. (For Systemic candida, see Section I: “Fungal Infections, Genitourinary.”)

TREATMENT

- Keep affected areas dry and exposed to air.
- Men: Topical Nystatin 100,000 U/d, miconazole cream QID
- Women vulvovaginitis: Oral fluconazole (single 150-mg dose) or topicals such as Nystatin 100,000–200,000 U/d for 1–2 wk.

Clotrimazole troches or cream 100 mg/d for 3–7 days, others.

More severe infections may require long-term ketoconazole

REFERENCE

9. Margesson LJ. Vulvar disease pearls. Dermatol Clin 2006;24(2):145–155.

CAPTOPRIL TEST

DESCRIPTION As a functional test for renovascular hypertension, PRA (plasma renin activity) is measured before and 1 hr after the administration of 25 mg of captopril. The test is considered positive if all of the following occur: Post-captopril PRA >12 ng/mL/hr, an absolute increase in PRA >10 ng/mL/hr, and a 400% increase in baseline PRA (150% increase if the baseline PRA was more than 3 ng/mL/hr). 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 light-sodium diet is necessary.

REFERENCE

Pickering TG, et al. Renovascular hypertension and ischemic nephropathy. In: Brenner BM, ed. The Kidney, 5th ed. Philadelphia: Saunders; 1996: 2106–2125.

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 5-hydroxyindoleacetic acid and argentaffin positive on special staining. Electron microscopy demonstrates granules similar to Kulchitsky cells. Primary treatment is surgical excision.

REFERENCE

Yang CH, et al. Primary carcinoid tumor of urinary bladder. Urology 1985;26(6):594–597.

CARCINOSARCOMA, BLADDER

DESCRIPTION Rare tumor exhibiting elements of epithelial and mesenchymal origin. These usually are bulky, fast growing, invasive tumors. Epithelial elements are typically transitional cell carcinoma, 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

REFERENCE

Orsatti G, et al. Carcinosarcoma of urothelial organs: Sequential involvement of urinary bladder, ureter, and renal pelvis. Urology 1993;41(3):289–291.

CARCINOSARCOMA, PROSTATE

DESCRIPTION Very rare tumor, similar to the carcinosarcoma of the bladder, these tumors are mixtures of epithelial and sarcomatous elements. The epithelial element in the prostate, however, is adenocarcinoma. Most differentiate from collision tumors, which are separate co-existing tumors of differing cell types. True carcinosarcomas have an intermixture of cells in the same tumor. Treatment is radical prostatectomy, if organ-confined.

REFERENCE

Nazzeer T, et al. Prostatic carcinosarcoma: Case report and review of literature. J Urol 1991;146(5): 1370–1373.

CARNEY SYNDROME

DESCRIPTION First described by Carney in 1977, this is a triad consisting of gastric leiomyosarcoma, extra-adrenal paraganglioma, and pulmonary chondroma. The syndrome is complete when 2 features are present. GI hemorrhage is a common presentation. It primarily affects young women, in whom elevated urinary catecholamines are found. Prognosis depends on malignant spread of tumors. Large-cell, calcifying Sertoli cell tumors are associated in male patients.

TREATMENT

- Surgical removal of sarcoma and paraganglioma
- Radiotherapy and chemotherapy for unresectable disease

REFERENCE

Lancha C, et al. A case of complete Carney's syndrome. Clin Nucl Med 1994;19(11):1008–1010.

CARUNCLE, URETHRAL

DESCRIPTION An inflammatory lesion of the distal female urethra that usually presents as an asymptomatic urethral mass in the postmenopausal woman. Usually reddish 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 I: “Urethra, Mass.”)

REFERENCE

Park DS, Cho TW. Simple solution for urethral caruncle. J Urol 2004;172(5 Pt 1):1884.

CASALE PROCEDURE

DESCRIPTION A variation of the Yang-Monti ileal tube, which is often too short to reach from the bladder to the skin surface. This procedure produces 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 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, Casale used an initial segment that is twice as long, partially split in the middle, and then opened in a spiral fashion on opposite sides to make a longer strip that can be tubularized in continuity. The long-term results of the Casale tube are comparable to those of the appendix and Yang-Monti tube in terms of durability, continence, and complication rate.

REFERENCE

Casale AJ. A long continent ileovesicostomy using a single piece of bowel. J Urol 1999;162(5): 1743–1745.

CAT-EYE SYNDROME

DESCRIPTION Rare, congenital syndrome with features of anal atresia, vertical iridochoroidal coloboma, congenital heart disease, urinary tract abnormalities, and mild to moderate mental retardation. The urologic abnormalities reported include renal hypoplasia, chronic pyelonephritis, horseshoe kidney, hydronephrosis, and vesicoureteral reflux, and an associated abnormality of chromosome 22. Close monitoring for possible pyelonephritis is warranted.

REFERENCE

Bellinghieri G, et al. Renal function in an adult female with cat-eye syndrome. Am J Nephrol 1994; 14(1):76–79.

CAUDA EQUINA SYNDROME

DESCRIPTION A term applied to the clinical picture resulting from compression of the cauda equina (or “horse tail”) formed by nerve roots caudal to the level of spinal cord termination. This includes perineal sensory loss, loss of anal and urethral sphincter control, and loss of erections. The most common causes include posterior, central lumbar disc herniation, spinal stenosis, tumor, and trauma. Cauda equina syndrome is present in 1–5% of all prolapsed lumbar disks. 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 damage often is permanent. On follow-up urodynamics an acontractile detrusor and variable EMG activity may persist.

REFERENCE

Mauffrey C, et al. Cauda equina syndrome: An anatomically driven review. Br J Hosp Med (Lond) 2008;69(6):344–347.

CAUDAL REGRESSION SYNDROME

DESCRIPTION First described by Duhamel in 1961, this syndrome is caused by disordered embryogenesis during the 4th–5th wk of gestation. It features a wide array of abnormalities centering on the anorectal, 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 is seen. These, in turn, are associated with voiding dysfunction. Vesicoureteral reflux is also quite common. Managing the myriad problems requires a multidisciplinary approach.

SYNONYMS

- Caudal dysplasia sequence
- VACTERL syndrome

REFERENCE

Boemers TM, et al. Urodynamic evaluation of children with the caudal regression syndrome (caudal dysplasia sequence). J Urol 1994;151:1038–1040.

CAVERNOSOGRAPHY

DESCRIPTION A test used to evaluate veno-occlusive leak in erectile 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 erection. Any visualized 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 crural veins.

REFERENCE

Hsu GL, et al. Penile venous anatomy: An additional description and its clinical implication. J Androl 2003;24(6):921–927.

CAVERNOSOMETRY

DESCRIPTION A test used to evaluate veno-occlusive leak in erectile dysfunction. Performed by 1st stimulating erection, either by saline infusion into the corpora or injection of a pharmacologic agent. Intracorporeal 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 infusion is indicative of veno-occlusive dysfunction.

REFERENCE

Vardi Y, et al. Cavernosometry: Is it a dinosaur? J Sex Med 2008 Apr;5(4):760.

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 ventral penile skin, as described by Thiersch. The penis is then buried in a mid-line scrotal incision. In the 3rd stage, the penis is freed from the scrotum, using scrotal skin to cover the ventrum of the penis, and the scrotum is primarily closed.

REFERENCE

Devine CJ, Devine PC. Operations for urethral stricture. In: Novick AC, et al., eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:650–680.

CECO URETEROCELE

DESCRIPTION A ureterocele is a congenital saccular dilatation of the terminal portion of the ureter. Cecoureteroceles are elongated beyond the ureterocele orifice by tunneling under the trigone and the urethra and represent a subtype of ureterocele.

REFERENCE

Smith EA, Parrott TS. The unsuspected cecoureterocele. J Urol 1994;152(1):182–184.

CELLO SCROTUM

DESCRIPTION A published factitious medical condition in which a cello player irritates the scrotum. Admitted as a “hoax” condition in 2009.

REFERENCE

Murphy E, Murphy JM. Cello scrotum confession. Murphy’s lore. BMJ 2009;338:b288.

CEREBRAL PALSY, UROLOGIC CONSIDERATIONS

DESCRIPTION Cerebral palsy is a broad term describing a generally nonprogressive brain dysfunction occurring perinatally (up to age 3 yr by some definitions) with the consequence 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 on 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 symptoms included incontinence (74%), frequency (56%), and urgency (37%). The most common urodynamic findings were detrusor overactivity (87% of those undergoing urodynamics), with 25% of these exhibiting apparent striated sphincter dyssynergia.

REFERENCE

Ozturk M, et al. Bladder and bowel control in children with cerebral palsy: Case-control study. Croat Med J 2006;47(2):264–270.

CERVICAL CANCER, UROLOGIC CONSIDERATIONS

DESCRIPTION Iatrogenic 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, as well as fistula, if combined with radiation. Radiation therapy also can be morbid, 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

Magerina JF. Complication of irradiation and radical surgery for gynecologic malignancies. Obstet Gynecol Surv 1993;48(8):571–575.

CHANCROID

DESCRIPTION An STD caused by Haemophilus ducreyi and relatively uncommon in the US but a common STD in developing countries. H. ducreyi is a gram-negative coccobacilli 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, nonindurated, purulent, and ragged with painful adenopathy in over 50%. Sites include the distal penis in men and labia and vagina in women. Diagnosis is based on clinical findings, but the CDC recommends culture of the organism 9 or PCR identification) or a rule out of other ulcer producing STD such as syphilis or herpes. Recommended treatment is a single does of azithromycin 1 g PO or ceftriaxone 250 mg IM.

REFERENCE

Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines, 2006. MMWR Recomm Rep. 2006;55(RR-11):1–94.

CHARGE ASSOCIATION

DESCRIPTION CHARGE refers to the association of coloboma, congenital heart disease, choanal atresia, retarded growth and development, structural brain abnormalities, and ear anomalies. Of urologic 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 for genital hypoplasia.

REFERENCE

Harvey AS, et al. CHARGE association: Clinical manifestations and developmental outcome. Am J Med Genet 1991;39:48–55.

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/andriamycin/cis platinum and gemcitabine/cisplatinum have significant nephrotoxicity, which can be problematic for older patients or patients with renal insufficiency or malignant ureteral obstruction. Bleomycin, used for nonseminomatous germ cell tumors as part of the bleomycin, etoposide, cisplatinum (BEP) regimen causes pulmonary toxicity. If postchemotherapy retroperitoneal lymphadenectomy is necessary, the anesthetist 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 metabolite, acrolein, which is excreted into the urine. Administering the agent Mesna decreases this toxicity. Cyclophosphamide also increases the risk of subsequent bladder cancer up to 9-fold. (See also Section II: “Bleomycin Toxicity.”)

REFERENCE

Baniel J, et al. Complications of post-chemotherapy retroperitoneal lymph node dissection. J Urol 1995;153:976–980.

Vlaovic R, Jewett AS. Cyclophosphamide induced bladder cancer. Can J Urol 1999;6:745.

CHLAMYDIA SEXUALLY TRANSMITTED DISEASE

DESCRIPTION Chlamydia is the most common bacterial STD in the world. Although often asymptomatic (up to 70% in women) it may cause urethritis, cervicitis, pelvic inflammatory disease in women, and prostatitis and epididymitis in men. In young sexually active males, it is the most common cause of epididymitis. Chlamydia trachomatis is an intracellular bacterium and does not grow in standard urine culture preparations. Nucleic acid amplification test by PCR of urine specimen is an effective diagnostic and screening tool. Alternatively, specialized cultures of urethral or cervical swabs can be performed. Treatment with azithromycin 1 g PO as a single dose or doxycycline 100 mg b.i.d. for 7 days is standard treatment. In pregnancy, erythromycin base 500 mg q.i.d. for 7 days is a safe alternative. Screening of sexual partners is recommended. (See also Section I: “Sexually Transmitted Diseases (STD), General.”)

REFERENCE

Watson EJ, et al. The accuracy and efficacy of screening tests for Chlamydial trachomatis: A systemic review. J Med Microbiol 2002;51:1021–1031.

CHRISTMAS TREE BLADDER

DESCRIPTION A radiologic change in the bladder wall caused by detrusor muscle hypotrophy and fibrosis as a result of detrusor-sphincter dyssynergia. Also called pinecone appearance.

REFERENCE

Nordling J, Olesen KP. Basic urographic and cystourethrographic patterns. In: Pollack HM, ed. Clinical Urography. Philadelphia: Saunders; 1990: 1935–1979.

CHRONIC KIDNEY DISEASE (CKD)

DESCRIPTION The National Kidney Foundation (NKF) has defined CKD as (1) evidence of kidney damage based on abnormal urine analysis results (eg, proteinuria, hematuria) or structural abnormalities observed on ultrasound images or (2) a GFR of <60 mL/min for 3 mo. The NKF has developed guidelines to further classify the progression of renal disease into 5 stages, from kidney disease with a preserved GFR to ESRD. This classification includes treatment strategies for each progressive level, as follows:

- Stage 1: Kidney damage with a normal GFR (90 mL/min). The action plan is diagnosis and treatment, treatment of comorbid conditions, slowing of the progressing of kidney disease, and reduction of cardiovascular disease risks.
- Stage 2: Kidney damage with a mild decrease in the GFR (60–90 mL/min). The action plan is estimation of the progression of kidney disease.
- Stage 3: Moderately decreased GFR (30–59 mL/min). The action plan is evaluation and treatment of complications.
- Stage 4: Severe decrease in the GFR (15–29 mL/min). The action plan is preparation for renal replacement therapy.
- Stage 5: Kidney failure. The action plan is kidney replacement if the patient is uremic.

REFERENCE

Levey AS, et al. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. 2003;139(2):137–147.

CHRONIC PELVIC PAIN SYNDROME (CPPS)

DESCRIPTION A term previously used exclusively in gynecology but is now being applied to men with chronic abacterial prostatitis. Nonbacterial prostatitis or CPPS occurs in men with no history of urinary tract infection and negative bacterial cultures of urine and prostatic fluid. The inflammatory type presents with GU or rectal pain or voiding symptoms; the prostatic fluid contains inflammatory cells. Men with the noninflammatory type, whose prostatic fluid has no leukocytes, have similar symptoms, but pelvic pain is usually the predominant complaint. (See Section I: “Prostatitis, Chronic, Nonbacterial, Inflammatory [NIH CP/CPPS III A]”; Section I: “Prostatitis, Chronic Nonbacterial, Noninflammatory [NIH CP/CPPS III B]”; Section II: “Pelvic Pain, Male.”)

TREATMENT

- Empiric 8–12-wk course of antibiotics
- Consider prostatic massage, if no response
- High-dose -blockers (Flomax, Cardura, Hytrin)
- Anti-inflammatory agents, lifestyle changes, stress reduction, holistic therapies
- Finasteride has shown promise in one study.
- Transurethral microwave thermotherapy (TUMT) as a last option

REFERENCE

Leskinen M, et al. Effects of finasteride in patients with inflammatory chronic pelvic pain syndrome: A double-blind, placebo-controlled, pilot study. Urology 1999;53(3):502–505.

CHRONIC PROSTATITIS SYMPTOM INDEX (CPSI)

DESCRIPTION An index developed by the National Institutes of Health comprised of 9 items that address 3 different aspects of the chronic prostatitis experience: Pain (location, severity, frequency), urinary function (irritative, obstructive), and quality of life (effect of symptoms on daily activities). 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, General;” Section VII: National Institutes of Health [NIH] Chronic Prostatis Symptom Index [CPSI].)

REFERENCE

Litwin M, et al. The National Institutes of Health Chronic Prostatitis Symptom Index: Development and Validation of a New Outcome Measure. J Urol 1999;162(2):369–375.

CHURG-STRAUSS SYNDROME

DESCRIPTION Also called allergic angiitis and granulomatosis, this is a vasculitis characterized by extravascular microscopic granulomas in the lungs, heart, GI tract, and skin. Histologically, necrosis and intense eosinophilic infiltration 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 involves corticosteroids with cytotoxic drugs are being investigated.

REFERENCE

Langford CA, Sneller MC. New developments in the treatment of Wegener's granulomatosis, polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome. Curr Opin Rheumatol 1997;9(1):26–39.

CHYLOCELE

DESCRIPTION Also called filarial hydrocele, chylocele is a cyst-like collection 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.

TREATMENT

- Vertical scrotal incision with complete excision of tunica vaginalis sac
- Orchiectomy and chordectomy for severe cases
- Medical treatment of filariasis (diethylcarbamazine, ivermectin, albendazole)

REFERENCE

DeVries CR. The role of the urologist in the treatment and elimination of lymphatic filariasis worldwide. BJU Int 2002;89(S1):37–43.

CHYLOUS ASCITES

DESCRIPTION An accumulation of milky lymphatic fluid in the peritoneal cavity; this fluid is rich in triglycerides and can be fatal. It is caused by leakage of lymphatics, usually from neoplastic (lymphoma and others) lesions, cirrhosis, congenital defects in children, infectious processes (TB, filariasis), heart failure, cardiomyopathy, nephrotic syndrome, and inflammatory processes (sarcoidosis, pancreatitis, radiation, retroperitoneal fibrosis). Postoperative causes include catheter placement for peritoneal dialysis, abdominal aneurysm resection and, in the urologic setting, after retroperitoneal lymph node dissection (RPLND). Inferior vena cava resection is also cited as a risk factor. Patients present with increasing abdominal girth. Paracentesis may be diagnostic and therapeutic, with peritoneal fluid triglyceride levels usually >200 mg/dL and a total protein content of 2.5–7.0 g/dL.

TREATMENT

- Conservative, using a high-protein and low-fat diet supplemented with medium-chain triglycerides (MCT). A low-fat diet with MCT supplements reduces the production and flow of chyle. MCT oil is given initially orally, at an adult dose of 1 tablespoon 3–4 times per day.
- Somatostatin and octreotide have also been reported to reduce lymphatic flow.
- TPN, peritoneovenous shunt, or surgery may be required if it fails to respond to conservative measures.

REFERENCE

Aalami OO. Chylous ascites: A collective review. Surgery 2000;128(5):761–778.

Baniel J, et al. Management of chylous ascites after retroperitoneal lymph node dissection for testicular cancer. J Urol 1993;150(5):1422–1424.

CIRCUMCISION, ADULT CONSIDERATIONS

DESCRIPTION Common reasons for adult circumcision in the US include phimosis, balanitis, condyloma, redundant foreskin, and elective issues. There is conflicting evidence regarding the impact on sexual function and erectile dysfunction; however, conclusive evidence shows that adult male circumcision reduces HIV acquisition by 50–60%, as recorded by 3 randomized trials performed in sub-Saharan Africa. The most common complication resulting in legal action is removal of too much prepuce in an adult, leading to painful erections and chordee. (See also Section I: “Phimosis and Paraphimosis.”)

REFERENCE

Fink K, et al. Adult circumcision outcomes study: Effect on erectile function, penile sensitivity, sexual activity and satisfaction. J Urol 2002;167(5):2113–2116.

CIRCUMCISION, PEDIATRIC CONSIDERATIONS

DESCRIPTION Removal of the foreskin has its benefits and complications. Meatal stenosis is a problem seen much more commonly in circumcised boys. Removal of too much foreskin, post-circumcision phimosis, and skin bridges are also risks. Circumcision is contraindicated when hypospadias is noted, and is indicated for phimosis and recurrent balanitis. Benefits include a decrease in UTIs in the 1st 6 mo of life. A decrease in risk of STDs such as HIV and penile cancer is likely. American Academy of Pediatrics policy currently recommends neonatal circumcision as optional. “Ritual” religious circumcision is associated with higher rates of neonatal UTI than is the formal surgical procedure. (See also Section I: “Phimosis and Paraphimosis.”)

REFERENCE

Elder JS. Circumcision. BJU Int 2007;99(6): 1553–1564.

Prais D, et al. Is ritual circumcision a risk factor for neonatal urinary tract infections? Arch Dis Child 20086 [Epub ahead of print].

CISPLATIN TOXICITY

DESCRIPTION Cisplatin is a very commonly used antitumor agent with significant adverse effects. Administered in urology for transitional cell 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

- Amifostine has been used to limit toxicity.
- Use of other platinum-based compounds may decrease toxicity while maintaining efficacy.

REFERENCE

Schellens JH, et al. Emerging drug treatments for solid tumors. Drugs 1996;51(1):45–72.

CLITOROMEGALY

DESCRIPTION Enlargement of the clitoris. When noted, the practitioner must consider the possibility of intersex issues. The condition may be so severe as to appear as a normal male penis, although chordee is also usually present. (See also Section I: “Disorders of Sexual Development [DSD]”; Section II: “Congenital Adrenal Hyperplasia.”) Virilization is most commonly secondary to congenital adrenal hyperplasia. The underlying cause must be addressed.

REFERENCE

Snyder HM. Intersex. Practical Cases in Urology, Series XIX, Course 4, 1996.

CLONIDINE SUPPRESSION TEST

DESCRIPTION A test sometimes used to rule out pheochromocytoma. Clonidine (0.3 mg) is administered and plasma norepinephrine levels are then measured. Those patients with essential hypertension with an elevation of norepinephrine levels will experience a 50% decrease in this catecholamine level. Patients with pheochromocytoma will not be suppressed. Patients should not be taking diuretics, -blockers, or tricyclic antidepressants; -blockers do not interfere with the test.

REFERENCE

Eisenhofer G, et al. Biochemical diagnosis of pheochromocytoma: How to distinguish true- from false-positive test results. J Clin Endocrinol Metab 2003;88(6):2656–2666.

CLOSTRIDIUM 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 the 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 leucocytosis is common. It is diagnosed by classic 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 t.i.d. or 250 mg q.i.d.) 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 q.i.d.

REFERENCE

Kelly CP, LaMont JT. Clostridium difficile: More difficult than ever. N Engl J Med 2008;59:1932.

CLOT RETENTION

DESCRIPTION The culmination of visible blood in the urine that has formed clots within the bladder. The presence of blood clots impede the outflow of urine via the urethra and result in urinary obstruction. If not addressed emergently, clot retention can lead to pain, vomiting, abdominal distension, hydroureteronephrosis, and bladder rupture.

TREATMENT

- Bedside insertion of urinary catheter for drainage and evacuation of blood clots
- May require operative cystoscopy and treatment of underlying cause of hematuria
- Correction of blood coagulation derangements

REFERENCE

Hicks D, Li C. Management of macroscopic hematuria in the emergency department. EMJ 2007;24: 385–390.

COBB COLLAR

DESCRIPTION Congenital narrowing of the bulbar urethra that can present with hematuria, UTI, or poor stream. Endoscopy and retrograde urethrogram reveal a bulbar urethral narrowing. The obstructing membrane is located just distal to the external sphincter and is reinforced by a fold extending from the verumontanum. Treatment is endoscopic resection.

SYNONYMS

- Moerman rings
- Congenital obstructive posterior urethral membrane

TREATMENT

Endoscopic resection

REFERENCE

Dewan PA, et al. Congenital urethral obstruction: Cobb's collar or prolapsed congenital obstructive posterior urethral membrane (COPUM). Br J Urol 1994;73(1):91–96.

COBRA HEAD SIGN

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

Nussbaum AR, et al. Ectopic ureter and ureterocele: Their varied radiographic manifestations. Radiology 1986;159:227.

COCCIDIOMYCOSIS, GENITOURINARY

DESCRIPTION Outbreaks of Coccidioides immitis infection are common when people are exposed to dust that contains the spore. An opportunistic infection more common in patients <5 and >50 yr, it is associated with AIDS, steroid use, and chemotherapy for malignancy. After pulmonary inoculation, the patient can develop erythema nodosum (valley bumps 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 coccidiomycosis may cause similar changes, as seen in renal TB (moth-eaten calyces, infundibular stenosis, ureteral stricture, and calcifications). Prostatic infection with occasional abscess and scrotal infections with fistulas have been reported. Epididymal and prostatic involvement can demonstrate necrotizing and nonnecrotizing granulomas.

Therapy includes up to 2 g of amphotericin, with 1 yr of ketoconazole (200 mg/d).

REFERENCE

Wise GJ, Freyle J. Changing patterns in genitourinary fungal infections. AUA Update, Vol. XVI, Lesson 1, 1997.

COHEN (“CROSS-TRIGONAL”) URETERAL REIMPLANTATION

DESCRIPTION Through a transvesical approach, the ureter is mobilized from its hiatus and delivered through a submucosal tunnel across the trigone. A cross-trigonal reimplantation is then carried out.

REFERENCE

Kay R. Reimplantation of the ureter. In: Novick AC, Streem SB, Pontes JE, eds. Stewart’s Operative Urology. Baltimore: Williams & Wilkins, 1989: 526–538.

COLLECTING SYSTEM DUPLICATION, COMPLETE

DESCRIPTION Duplicated collecting systems (also known as duplex collecting systems)can be defined as renal units containing 2 pyelocaliceal systems that are associated with a single ureter or with double ureters. The 2 ureters empty separately into the bladder or fuse to form a single ureteral orifice. Associated problems include upper-pole hydronephrosis from stenosis, ectopic insertion of the upper-pole ureter, ureterocele of the upper-pole ureter, and reflux involving the lower pole. Duplex collecting systems can be unilateral or bilateral andcan be associated with obstruction, reflux, and infection. Caused by early ureteral bud bifurcation or the occurrence of 2 ureteral buds from the Wolffian duct during renal embryogenesis.

REFERENCE

Glassberg KI, et al. Suggested terminology for duplex systems, ectopic ureters and ureteroceles. J Urol 1984;132(6):1153–1154.

COLON AND RECTAL CANCER, UROLOGIC CONSIDERATIONS

DESCRIPTION Colorectal cancer may present as locally invasive lesions that involve the bladder and/or prostate. En-bloc resection (pelvic exenteration) of the bladder and rectum/colon is sometimes indicated. In colorectal malignancies, a 7–12% incidence of locoregional extension into the adjacent organs has been reported, with the bladder as the most commonly involved organ. In women, the interposition 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, erectile and bladder dysfunction may occur secondary to disruption of the pelvic plexus up to 70% of the time. (See also Section I: Neurogenic Bladder, General; Section VII: TNM.)

REFERENCE

Calpista A, et al. Functional urological complications after colorectal cancer surgery. Pelviperineology 2007;26(1):38–40.

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 Bertin is located between the pyramids. (See also Section II: “Renal Pseudotumors.”)

REFERENCE

Redman JF. Anatomy of the genitourinary system. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

COMPARTMENT SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION Compartment syndrome, defined by the rise of 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 urethral and perineal surgeries. In abdominal compartment syndrome, a Foley catheter can provide continuous abdominal compartment pressure readings. (See also Section II: “Rhabdomyolysis.”)

REFERENCE

Bocca G, et al. Compartment syndrome, rhabdomyolysis and risk of acute renal failure as complications of the lithotomy position. J Nephrol 2002;15:183–185.

CONDYLOMATA LATA

DESCRIPTION Also called flat condyloma, these moist or mucous papules are found in the skin folds of syphilis patients and reflect the secondary stage of syphilis. They secrete serous fluid and can be covered by a layer of epidermal debris. They represent the hematogenous spread of spirochetes. (See also Section I: Syphilis.)

TREATMENT

- Single-dose of penicillin G (benzyl penicillin) 2.4 million units IM OR
- IM ceftriaxone 1,000 mg/d for 10 days OR
- Oral tetracycline 500 mg q.i.d. for 14 days OR
- Oral doxycycline 100 mg b.i.d. for 14 days

REFERENCE

Lautenschlager S. Cutaneous manifestations of syphilis: Recognition and management. Am J Clin Dermatol 2006;7(5):291–304.

CONGENITAL ADRENAL HYPERPLASIA

DESCRIPTION The adrenal cortex secretes 2 compounds, dehydroepiandrosterone and androstenedione, that require conversion to testosterone in peripheral tissues for their androgenic effects. Congenital adrenal hyperplasia (CAH) represents a group of autosomal-recessive, inherited metabolic errors, each characterized by a deficiency or total lack of a particular enzyme involved in the biosynthesis of cortical steroids, particularly cortisol. Steroidogenesis is then channeled 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 (>90%) and 11-hydroxylase deficiency (5–8%). The spectrum of presentation is substantial, resulting from the compound heterozygosity and multiple etiologies in this disease continuum. Phenotypic manifestations include ambiguous genitalia (CAH is the most common reason in newborns), clitoromegaly, labioscrotal fusion, and hypospadias. Clinical CAH subtypes include (1) salt wasters (virilization and aldosterone deficiency), (2) simple virilizers (virilization without salt wasting), and (3) nonclassic patients (no virilization or wasting). In the salt-wasting variant, symptoms begin weeks after birth with weight loss, failure to thrive, vomiting, dehydration, and life-threatening adrenal crisis. In virilizers, sexual precocity is the hallmark of disease. Diagnosis is often made from markedly elevated levels of serum 17-hydroxyprogesterone and progesterone (with 21-OH deficiency), but may also present as elevated 11-deoxycortisol and 11-DOC (with 11-OH deficiency). (See also Section I: “Disorders of Sexual Development [DSD]”; Section II: “11--Hydroxylase Deficiency and 21-Hydroxylase Deficiency.”)

Congenital Adrenal Hyperplasia: Features for Each Enzyme Defect

Feature	21-Hydroxylase Deficiency	11-Hydroxylase Deficiency	17-Hydroxylase Deficiency	3-Hydroxysteroid Deficiency	Lipoid Hyperplasia	Aldosterone Synthase Deficiency
Incidence	1:15,000	1:100,000	Rare			

Rare
Rare
Rare
Defective gene
CYP21
CYP11B1
CYP17
HSD3B2
StAR
CYP11B2
Chromosomal localization
6p21.3
8q24.3
10q24.3
1p13.1
8p11.2
8q24.3
Ambiguous genitalia
+ (female)
+ (female)
+ (male)
+ (male)
+ (male)
No

Absent puberty (female)
Mild in female
Absent puberty (female)

Acute adrenal insufficiency
+
Rare
No

+

++

Salt wasting only

Hormones:

Glucocorticoids

Reduced

Reduced

Reduced

Corticosterone normal

Reduced

Normal

Mineralocorticoids

Reduced

Increased

Reduced

Increased

Reduced

Reduced

Androgens

Increased

Increased

Reduced

Reduced (male)

Reduced

Normal

Increased (female)

Elevated hormonal metabolite
17-Hydroxy-progesterone
DOC, 11-deoxycortisol
Corticosterone, DOC
DHEA, 175-pregnenolone
None
Corticosterone, 18-OHB
Blood pressure
Decreased
Increased
Decreased
Increased
Decreased
Decreased
Potassium
Increased
Decreased
Increased
Decreased
Increased
Increased

DHEA, dehydroepiandrosterone; DOC, deoxycorticosterone; 18-OHB, 18-hydroxycorticosterone.

TREATMENT

- Monitor for severe, life-threatening salt wasting and dehydration in the 1st wk of life. Follow electrolytes.
- Monitor for adrenal crisis.
- Determination of etiology (measure 17-hydroxyprogesterone, ACTH, cortisol, 11-DOC, DHEA)
- Genetic analysis (karyotype, FISH for SRY region)
- Sex assignment. Girls with classic CAH typically undergo reconstructive surgery, usually clitoroplasty and vaginoplasty.

- Glucocorticoid replacement therapy: Hydrocortisone 12–18 mg/m2/d infants. In older children, dexamethasone 0.25–0.50 mg at bedtime. Stress dose increases for illness or surgery to avoid adrenal crisis.
- Mineralocorticoid replacement fludrocortisone 0.05–0.20 mg/d

REFERENCE

Diamond DA, et al. Recent advances in external genitalia. Pediatr Clin N Am 53 (2006) 449–464.

Merke DP, Bornstein SR. Congenital adrenal hyperplasia. Lancet 2005;365(9477):2125–2136.

CONGENITAL NEPHROSIS/NEPHROTIC SYNDROME

DESCRIPTION Congenital nephrotic syndrome is a rare condition affecting children from birth to the 3rd month 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 distention, anasarca, and malnutrition. Characteristic laboratory findings include proteinuria, hypoalbuminemia, and hyperlipidemia. Long-term survival is dependent on the correction of nutritional deficits and renal transplantation.

REFERENCE

Ramirez-Seijas F, et al. Congenital nephrotic syndrome. Intern Pediat 2000;15(2):121–122.

CONSTIPATION, UROLOGIC CONSIDERATIONS

DESCRIPTION Infrequent large bowel movements affect the urinary tract by increasing the risk of UTI, thus contributing to urinary incontinence and impairing the resolution of reflux in children. The exact pathophysiology is unclear, but a rectum distended with hard stool obviously displaces and distorts the bladder within the pelvis. Since the rectum and bladder share sacral nerve roots, overdistension of the rectum may interfere with bladder function at the spinal cord level. Urodynamic studies in children with functional constipation have revealed uninhibited contractions and small bladder capacity, both of which improve with improved bowel function. In addition, the same holding behavior that leads to functional constipation often alters bladder habits as well. Treatment of bowel dysfunction alone will resolve chronic recurrent UTI and urinary 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.

TREATMENT

- Diet changes
- Laxatives, stool softeners
- Toilet schedules

REFERENCE

Loening-Baucke V. Urinary incontinence and urinary tract infection and their resolution with treatment of chronic constipation of childhood. Pediatrics 1997;100:228.

CONTACT DERMATITIS

DESCRIPTION Contact dermatitis is caused by an external irritant or allergen, and the patient complains of itching and burning or stinging. The findings are inflammation, scaling, and crust formation. Extreme reactions can result in blistering and necrosis. Allergic agents typically induce dermatitis after repeated contact with the skin.

CAUSES

- Common irritant agents cause immediate symptoms and include industrial chemicals, soaps, cleansing products, spermicides and lubricants, perfumes, urogenital secretions, and feces.
- Sensitizing (allergic) agents for the genital skin include cleansing agents and disinfectants, lubricants and emollients, spermicides and other topical ointments, perfumes and fragrances, latex and other types of rubber, clothing, dyes, poison ivy (direct contact or indirect contact from the hand), metals such as nickel, and sanitary napkins.

TREATMENT

- Attempt to identify and remove the offending agent from contact with the skin.
- Topical corticosteroids, emollients, and antihistamines give symptomatic relief. Severe allergic contact dermatitis may require oral corticosteroids.
- Severe reactions (rarely) may require debridement and grafting.
- Patch testing of uninvolved skin to common antigens is often helpful.

REFERENCE

Buechner SA. Common skin disorders of the penis [review]. BJU Int 2002;90(5):498–506.

Burrows LJ, Shaw HA, Goldstein AT. The vulvar dermatoses. J Sex Med 2008;5(2):276–283.

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 medullary hypoxemia and direct cytotoxic effects of contrast material. Older agents are hyperosmolar and ionic 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: “Nephrogenic Systemic Fibrosis/Fibrosing Dermatopathy.”)

TREATMENT

- Preventative:
  - Avoid contrast material if possible; consider alternative imaging modalities such as US.
  - Avoid dehydration and NSAIDs, as both increase renal vasoconstriction.
  - IV saline or sodium bicarbonate (154 mEq/L in D5W, 3 mL/kg/hr 1 hr prior, 1 mL/kg/hr 6 hr following) surrounding contrasted study
  - Antioxidant acetylcysteine [600 mg PO b.i.d.] 1 day prior and following contrasted study
  - Use low- or iso-osmolal contrast agents.
- 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

Asif A, et al. Prevention of radiocontrast-induced nephropathy. Am J Kidney Dis 2004;44:12.

CORDONNIER AND NESBIT URETERAL ANASTOMOSIS

DESCRIPTION A direct ureteral colonic refluxing anastomosis incorporating full-thickness ureteral and intestinal wall.

REFERENCE

McDougal WS. Use of intestinal segments and urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3137–3144.

CORPORA AMYLACEA (CA)

DESCRIPTION Small, round, ovoid bodies, lamellar in structure, located in the alveoli of the prostate. Composed of lecithin, albumin, and nitrogenous substances, they may precipitate around sloughed and degenerated prostatic epithelial cells. Recently noted is a high prevalence of calcium phosphate in the form of hydroxyapatite. CAs become more common with age, and act as the nidus for the development of prostatic calculi formation. Although often observed histologically to be associated with inflammation, the contribution of CA to prostatitis-related symptoms of unknown etiology or to prostate carcinogenesis remains unclear.

REFERENCE

Sfanos KS, et al. Acute inflammatory proteins constitute the organic matrix of prostatic corpora amylacea and calculi in men with prostate cancer. Proc Natl Acad Sci U S A 2009;106(9):3443–3448.

CORTICAL NECROSIS, ACUTE (RENAL CORTICAL NECROSIS)

DESCRIPTION Acute cortical necrosis is a rare form of acute renal failure 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, placental abruption, peritonitis, transfusion reaction, pancreatitis, and toxins. (See also Section I: “Renal Failure, Acute.”)

REFERENCE

Wilck EJ, Gerard PS. Acute cortical necrosis. Urology 1997;49(3):116.

COSTOVERTEBRAL ANGLE TENDERNESS

DESCRIPTION Costovertebral angle (CVA) tenderness is a clinical sign elicited by percussion of the CVA and is 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 capsular distension resulting in innervation of afferent T11–L2 nerve roots. Common causes include pyelonephritis, perirenal abscess, urolithiasis, acute hydronephrosis, renal artery occlusion, and renal vein thrombosis. (See also Section I: “Flank Pain.”)

REFERENCE

Follin SA. Professional Guide to Signs & Symptoms, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

COUGH STRESS TEST

DESCRIPTION The cough stress test involves filling the patient's bladder to 300 mL or to subjective fullness, and then, while in an upright position, having the subject perform a series of forceful coughs. The external urethral meatus is observed during the coughs for gross urine loss. If urine loss 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.

REFERENCE

Swift S, Yoon E. Test-retest reliability of the cough stress test in the evaluation of urinary incontinence. Obstet Gynecol 1999;94(1):99–102.

COWPER DUCT CYST

DESCRIPTION The Cowper glands are paired periurethral structures located in the urogenital diaphragm and are drained by 2–3-cm long ducts that empty into the bulbous urethra through small, flush 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 irritative or obstructive urinary symptoms, particularly when there is a complaint of persistent post-void dribbling or incontinence. Urethrography and cystourethroscopy are the diagnostic studies of choice.

SYNONYMS

- Cowper syringocele
- Bulbourethral gland ductectasia

TREATMENT

Endoscopic unroofing of the syringocele (marsupialization) into the bulbar urethra

REFERENCE

Bevers F, et al. Cowper’s syringocele: Symptoms, classification and treatment of an unappreciated problem. J Urol 2000;163:782–784.

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 adenocarcinoma. However, local necrosis and tissue destruction may prevent exact localization of the site of origin. Combined surgical and radiation therapy has been employed.

REFERENCE

Mitsumori K, Elwell MR. Tumours of the male accessory sex glands. IARC Scientific Pub 1994;111: 431–449.

COWPERITIS (INFLAMMATION OF BULBOURETHRAL GLAND)

DESCRIPTION Normally, the bulbourethral glands are not palpable. One 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 exquisitely 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 tissue is compressed to detect tenderness or a mass.

REFERENCE

Chughtai B, et al. A neglected gland: A review of Cowper's gland. Int J Androl 2005;28(2):74–77.

CREATININE, SERUM, INCREASED/DECREASED

DESCRIPTION Serum creatinine represents the breakdown product of muscle creatine and is an ideal marker of glomerular filtration rate (GFR). 5–10% of excreted creatinine is secreted in the proximal tubule, rather than filtered through the glomerulus. Serum creatinine can estimate the GFR (eGFR) by 2 methods: The Modification Diet of Renal Disease (MDRD) or the Cockcroft-Gault formula. Increased levels can signify renal failure, renal infection, rhabdomyolysis, urinary tract obstruction, acute tubular necrosis, dehydration, eclampsia, drug toxicity, etc. Decreased levels may reflect female gender, advanced age, late stages of muscular dystrophy, or myasthenia gravis. (See also Section IV: “Urine Studies III Creatinine Clearance and Glomerular Filtration Rate.”)

REFERENCE

Rule AD, et al. Using serum creatinine to estimate glomerular filtration rate: Accuracy in good health and in chronic kidney disease. Ann Intern Med 2004;141(12):929–937.

CREDé MANEUVER

DESCRIPTION Used to facilitate voiding in those patients with decreased bladder tonicity and low outlet resistance. The maneuver involves placing the thumb of each hand over the left and right anterior superior iliac spine, and the fingers over the suprapubic area and pressing into the abdomen. Both hands are then pressed downward into the pelvis. It may not always be effective in emptying, as the external sphincter may contract during the maneuver.

SYNONYMS

Manual compression of bladder

REFERENCE

Barbalias GA, et al. Critical evaluation of the Crede' maneuver: A urodynamic study of 207 patients. J Urol 1993;130(4):720–723.

CRIBRIFORM CLEAR CELL HYPERPLASIA OF THE PROSTATE

DESCRIPTION This condition may be misdiagnosed as cribriform 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

Epstein J. Precursor lesions to prostatic adenocarcinoma. Virchows Arch 2009;454(1):1–16.

CRYPTOCOCCUS, GENITOURINARY

DESCRIPTION An opportunistic fungal infection, Cryptococcus neoformans 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 GU involvement are the prostate and kidney. The prostate may be a reservoir in patients with AIDS. Epididymis and penis have also been reported as sites. GU involvement is considered a manifestation of systemic disease. (See also Section I: “Fungal Infections, Genitourinary.”)

TREATMENT

- Systemic antifungal therapy with IV amphotericin B, flucytosine, fluconazole, or combination of drugs
- Surgical drainage of large abscesses may be considered.

REFERENCE

Traboulsi R, Kanafani ZA, Kanj SS. Fungal infections of the genitourinary tract [review]. J Med Liban 2004; 52(4):202–209.

CT SCAN, UROLOGIC CONSIDERATIONS

DESCRIPTION A CT the abdomen and pelvis can be performed with and without IV or PO contrast. Noncontrast studies are useful in the evaluation of urinary tract stones. IV contrast is useful to delineate vascular, renal, and collecting system anatomy. Delayed images (excretory phase) provide information on urinary tract drainage and urothelial anatomy. Protocols have been developed to delineate renal tumors, stones, urothelial tumors, and arterial supply by adjusting the presence of contrast and the timing of the study. Modern CT machines can provide detailed images quickly and efficiently, but the clinician must be aware of contrast complications and induced nephropathy (see also Section I: “Contrast Allergy and Reactions”; Section II: “Contrast Induced Nephropathy [CIN]”) and the increased risk of malignancy with repeat scans, especially in children.

REFERENCE

Blake MA, Kalra MK. Imaging of urinary tract tumors. Cancer Treat Res 2008;143:299–317.

Brenner DJ, Hall EJ. Computed tomography: An increasing source of radiation exposure. N Engl J Med 2007;357(22):2277–2284.

CULP-DEWEERD PYELOPLASTY

DESCRIPTION A spiral incision is carried out over the anterior and medial aspect of the pelvis and continued down across a point beyond the UPJ obstruction. The apex of the flap is brought down to the apex of the ureterotomy, where a 5-0 chromic stay suture is placed. The posterior and anterior anastomoses are completed with interrupt 5-0 chromic sutures. Used to treat UPJ obstruction.

REFERENCE

Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins; 1989:220–233.

CUNNINGHAM CLAMP

DESCRIPTION A clamp device designed to compress the penile 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 has a ratchet-type closure with foam padding and comes in small, medium, and large sizes. Inexpensive, it is the most commonly used clamp device.

REFERENCE

Moore K, et al. Assessing comfort, safety, and patient satisfaction with 3 commonly used penile compression devices. Urology 2004;63(1):150–154.

CYSTADENOCARCINOMA, GENITOURINARY

DESCRIPTION Commonly seen in other organ systems, such as the ovary, pancreas, appendix, and thyroid. In the GU system, cystadenocarcinoma is reported in testes, prostate, paratesticular structures, and kidney. Grossly, multilocular cystic masses are noted. Microscopically, cuboidal to columnar epithelium is seen lining the cysts. These cells can secrete serous or mucinous substances. Malignant cells will demonstrate multilayering of epithelium, nuclear atypia, and invasion of surrounding stroma. It is treated by primary surgical resection.

REFERENCE

Yu CC, et al. Papillary cystadenocarcinoma of the epididymis: A case report and review of the literature. J Urol 1992;147(1):1622–1625.

CYSTADENOMA, GENITOURINARY

DESCRIPTION A benign cystic epithelial-lined mass that has been described in the kidney, seminal vesicle, prostate, and epididymis, it occurs most commonly in the GI tract in the epididymis. It is often described as a papillary cystadenoma and represents benign epithelial hyperplasia. It usually causes very few symptoms. Lesions can be bilateral, and 2/3 may be associated with von Hippel-Lindau syndrome. Grossly, the lesion appears cystic. Microscopically, it demonstrates cells with clear, vacuolated cytoplasm arranged in glandular or papillary structures. It appears as a cystic to solid mass at the head of the epididymis on US. Treatment is observation or radical orchiectomy, if the diagnosis is in doubt.

REFERENCE

Choyke PL, et al. Epididymal cystadenomas in von Hippel-Lindau disease. Urology 1997;49(6): 926–931.

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. Urogenital findings include bilateral absence of the vas deferens, leading to infertility. Abnormal development of the mesonephric system, inguinal hernias, hydroceles, and undescended testes are also seen. Risk of testicular cancer may be increased. (See also Section I: “Vas Deferens, Congenital Absence.”)

REFERENCE

Milunsky JM, Milunsky A. Case report: Cystic fibrosis and embryonal carcinoma of the testes. Am J Med Sci 1996;311(4):191–192.

CYSTINOSIS

DESCRIPTION Although it may be confused with cystinuria, cystinosis is an autosomal recessive metabolic disorder demonstrating defective lysosomal transport of cystine. 3 types are described, based on the age at diagnosis: Infantile onset, adolescent onset, and adult onset. Patients with the infantile nephropathic form of cystinosis (the most common and the most severe) develop symptoms early in life and develop end-stage kidney failure by late childhood, if left untreated. The condition is characterized by the intracellular accumulation of excessive quantities of cystine. Daily excretion of cystine is only 5–10% of that found in cystinuria. Stone formation is rare. This condition has a varied range of severity, with severe forms progressing to ESRD. Medical management includes hydration, potassium, bicarbonate, vitamin D, and calcium supplementation. Cysteamine bitartrate (Cystagon) is a cysteine depleting medication. ESRD may require real transplantation.

REFERENCE

Gahl WA, Balog JZ, Kleta R. Nephropathic cystinosis in adults: Natural history and effects of oral cysteamine therapy. Ann Intern Med 2007;147(4):242–250.

CYSTITIS CYSTICA

DESCRIPTION Similar to von Brunn nests, which are areas of benign urothelium in the submucosa, except that in cystitis cystica the centers of the nests have undergone eosinophilic liquefaction (degeneration) to form small cystic mucin cavities; when intestinal metaplasia with gland formation is found it is described as cystitis glandularis. Both conditions are thought to be benign. Found in 60% of normal bladders at autopsy, cystoscopically they appear as small pearly white or yellowish lesions, usually <5 mm, but occasionally larger. No clear relation to malignant transformation is noted. There is no specific treatment; diagnosis is usually established by biopsy to rule out cancer.

REFERENCE

Alijani M, et al. An unusual case of cystitis cystica. BJU International 2002;89:634.

CYSTITIS, EOSINOPHILIC

DESCRIPTION A rare and severe form of allergic cystitis. Symptoms include hematuria, urgency, dysuria, and suprapubic discomfort. Urine analysis may show eosinophiluria. Cystoscopic findings may reveal raised plaques or ulcers that mimic CIS or invasive bladder cancer. Hydronephrosis may be seen on IVU or US. Bladder biopsy revealing eosinophilic infiltrate is pathognomonic. IVU or renal US may demonstrate hydronephrosis. Potential causes include allergies, including food (these patients are at increased risk); and parasitic infections; drugs, including methicillin, anthranilic acid, intravesical mitomycin, and thiotepa. 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 required. (See also Section II: “Cystitis Granulomatous.”)

TREATMENT

- Conservative medical management with oral antibiotics, antihistamines, and steroids
- A full allergy evaluation is required.

REFERENCE

Choe JM, et al. Intravesical thiotepa-induced eosinophilic cystitis. Urology 1995;46(5):729–731.

CYSTITIS, EMPHYSEMATOUS

DESCRIPTION A rare UTI with gas formation (bladder wall or lumen). Predominance of older women with diabetes. Presents with abdominal pain, dysuria, and pneumaturia; gas can be seen on imaging studies. E. coli and K. pneumoniae are most common pathogens and medical management is similar to acute complicated pyelonephritis.

REFERENCE

Thomas AA, et al. Emphysematous cystitis: A review of 135 cases. BJU Int. 2007;100(1):17–20.

CYSTITIS FOLLICULARIS

DESCRIPTION Cystitis follicularis (also called bacteriuric bumps or follicular cystitis) is characterized by the formation of lymphoid follicles in the lamina propria of the trigonal region of the bladder. It is caused by repeated or chronic UTIs. It may appear grossly as punctate, yellow submucosal nodules. It is not associated with malignancy, and treatment of the underlying infection is curative.

REFERENCE

McIntire M, et al. Cystitis follicularis in bladder washings: Report of 2 cases and review of the literature. Diagn Cytopathol 2007;35(8):537–538.

CYSTITIS GLANDULARIS AND CYSTITIS GLANDULARIS OF INTESTINAL TYPE

DESCRIPTION Similar to von Brunn nests, which are areas of benign urothelium in the submucosa, except that these transitional cells have undergone glandular metaplasia. It is usually only detected microscopically, but occasionally can appear as a grossly visible lesion and may appear papillary. Typical cystitis glandularis is the most common form. Diffuse cystitis glandularis of the intestinal type is seen in chronically irritated bladders, and is associated with an increased risk of bladder cancer (adenocarcinoma) and may be associated with pelvic lipomatosis. No specific treatment except follow-up due to cancer risk.

REFERENCE

Eble JN, Young RH. Carcinoma of the urinary bladder: A review of its diverse morphology. Semin Diagn Pathol 1997;14(2):98–108.

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 allergic cystitis in patients who often have a significant allergic history. It mimics other forms of intractable 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 after the use of intravesical BCG for bladder cancer as a thickened, edematous bladder with erythematous plaques, ulcerations, and submucosal hemorrhage. Microscopy reveals fibrosis and inflammatory cells with extensive eosinophil infiltration of bladder wall. Patients present with frequency, dysuria, and hematuria.

TREATMENT

- Condition is usually benign with self-limited course
- Optimal management unclear; usually NSAIDs, steroids, and antihistamines.

REFERENCE

Ladocsi LT, et al. Eosinophilic granulomatous cystitis in children. Urology 1995;46(5):732–735.

Littleton R, et al. Eosinophilic cystitis: An uncommon form of cystitis. J Urol 1982;127(1):132–133.

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 urethritis, polypoid ureteritis, and polypoid pyelitis when present in the urethra, ureter, and renal pelvis, respectively; these are clinically and diagnostically similar lesions. Clinical settings for this diagnosis include evaluation of gross hematuria, bladder and/or urethral stones, prostate cancer with radiation therapy, history of urothelial carcinoma treatment, long-term urinary stents, and colovesical fistulas. Proper diagnosis relies on low-power microscopic identification of the reactive process with an inflamed background that is edematous or densely fibrous with predominantly simple, nonbranching, broad-based fronds of relatively normal-thickness urothelium. If the tissue is examined at higher power, some fronds may appear to resemble a urothelial neoplasm. Treatment is directed at the inciting cause.

REFERENCE

Lane Z, Epstein JI. Polypoid/papillary cystitis: A series of 41 cases misdiagnosed as papillary urothelial neoplasia. Am J Surg Pathol 2008;32(5):758–764.

CYSTITIS, RADIATION

(See Section I: “Cystitis, Hemorrhagic Infectious, Noninfectious, Radiation.”)

CYSTITIS, VIRAL

DESCRIPTION Viruses are increasingly recognized as the cause of lower UTIs—especially hemorrhagic cystitis among immunocompromised patients—and usually affect children or immunocompromised adults. Viral cystitis is caused most commonly by viremic spread to bladder of adenovirus, papovavirus, or influenza A. BK virus, adenovirus, and cytomegalovirus are predominant pathogens involved in hemorrhagic cystitis after stem cell and solid organ transplantation, and their early diagnosis and treatment may prevent significant morbidity. These can produce clinically significant symptoms, such as dysuria, hematuria, and frequency. Standard urine culture is negative. Urine analysis may show WBCs and RBCs. Cytology may be suspicious for malignancy, with abnormally large cells having prominent nuclei. The diagnosis of viral lower UTI is based on molecular techniques, and real-time polymerase chain reaction is often the method of choice because it allows for quantification of viral load. (See also Section I: “Cystitis, Hemorrhagic”; Section II: “BK Virus, Urologic Considerations.”)

TREATMENT

- Usually self-limited
- In immunosuppressed patients, the use of antiviral agents (cidofovir, vidarabine, ribavirin) administered PO, IV, or intravesically is recommended.

REFERENCE

Paduch DA. Viral lower urinary tract infections. Curr Urol Rep 2007;8(4):324–335.

CYSTOCELE GRADING

DESCRIPTION The grading and evaluation of cystoceles have evolved from the Baden-Walker to the current Pelvic Organ Prolapse Quantification (POPQ) systems. Although the 2 systems are widely used in research, the POPQ is more time-intensive and informative. The classic Baden-Walker grading system was 1st described in 1968. The POPQ was later developed in 1996. (See also Section I: “Pelvic Prolapse [Cystocele and Enterocoele].”)

Baden-Walker Grading

1st degree:

Descensus of the anterior vaginal wall halfway to the hymen

2nd degree:

Descensus to the level of the hymen

3rd degree:

Descensus to outside the hymen

POP-Q Staging

Stage 0:

No descensus of pelvic structures during straining

Stage I:

Descensus >1 cm above the hymenal ring

Stage II:

Descensus between +1 and –1 cm of the hymen

Stage III:

Prolapse >1 cm beyond hymenal ring

Stage IV:

Complete vaginal eversion

REFERENCE

Bump RC, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 1996;175(1): 10–17.

CYSTOGRAM, INDICATIONS AND TECHNIQUE

DESCRIPTION A cystogram is an x-ray examination of the urinary bladder that can show the bladder's position, shape, presence of reflux, and filling defects. A catheter is inserted into the bladder and is used to fill the bladder with a contrast agent under gravity drainage. Typically, 300 mL of contrast is utilized depending on the patient's anatomy. Fluoroscopic images are then taken of the opacified bladder in the AP and oblique views. A cystogram can provide information regarding bladder perforation, reflux, diverticula, fistulas, foreign bodies, stones, and sometimes bladder tumors. A post-drainage view is important to evaluate residual volume and to ensure no missed contrast extravasation behind the bladder. Common indications for cystography include abdominal/pelvic trauma, infection, fistula, reflux, and incontinence. Cystography has been largely replaced by the use of the CT cystogram.

REFERENCE

Cass AS. Diagnostic studies in bladder rupture. Indications and techniques. Urol Clin N Am 1989; 16(2):267–273.

CYSTOMETROGRAM

DESCRIPTION The cystometrogram evaluates the filling and/or storage phases of detrusor function. Catheters to measure the vesical pressure and abdominal pressure and to fill the bladder with saline, water, or CO2 are utilized. The bladder filling rate is 25–100 mL/min. Simultaneous measurements of pressure and volume are recorded, and a curve is created. Variables observed are compliance, contractility, sensation, and capacity. During filling, the bladder volumes are recorded at (1) the 1st sensation of filling, (2) sensation of urgency to void, and (3) sensation of maximum capacity. Coughing and the Valsalva maneuver should be utilized to uncover involuntary contractions. Abnormalities that may be detected include altered sensation, changes in detrusor compliance, disorders of detrusor contractility, and/or presence of involuntary detrusor contraction or detrusor areflexia.

REFERENCE

Steers WD, et al. Voiding function and dysfunction. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

CYSTOSARCOMA PHYLLODES, PROSTATE

DESCRIPTION A tumor type commonly seen in breast but rarely in prostate, it can present with voiding symptoms. Grossly, the tumor is unusually soft, cystic, and spongy. Microscopically, elongated cells with spindle-shaped nuclei and scant pale cytoplasm are seen. It can range from benign to malignant; the treatment is surgical resection.

REFERENCE

Cacic M, et al. Cystosarcoma phyllodes of the prostate. Scand J Urol Nephrol 1996;30(6):501–502.

CYTOKERATIN STAINING

DESCRIPTION Commonly used in prostate cancer diagnosis (ie, to differentiate PIN from basal cell hyperplasia or distinguish various forms of acinar proliferations that are not cancer on needle biopsy) 343E12, which detects basal cell–specific cytokeratin, is commonly used. If basal cell staining is present, this helps to rule out carcinoma; it is also used to examine lymph nodes or periprostatic 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 micrometastasis to lymph nodes. Its utility in prostate cancer metastasis is being investigated. (See also Section II: “Immunohistochemical Staining, Urologic Considerations.”)

REFERENCE

Moul JW, et al. Immunohistologic detection of prostate cancer pelvic lymph node micrometastases: Correlation to preoperative serum prostate-specific antigen. Urology 1994;43(1):68–73.

CYTOLOGY, PROSTATE

DESCRIPTION Examination of cells, usually obtained by fine-needle aspiration, for the detection of malignancy. Characteristics that can be determined include DNA ploidy status, cell cycle distribution, and cytologic grade. Its advantages over standard pathologic techniques include 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 cytopathologist to ensure reliability.

REFERENCE

Paz-Bouza JI, et al. Transrectal fine needle aspiration biopsy of the prostate combining cytomorphologic, DNA ploidy status and cell cycle distribution studies. Pathol Res Pract 1994;190(7):682–689.

CYTOLOGY, URINARY

DESCRIPTION Microscopic examination of the urine, usually performed for the detection of malignant cells during follow-up of TCC. Criteria for malignancy include increased cytoplasmic-to-nuclear ratio, eccentric nucleus, nuclear pleomorphism and irregularity, hyperchromasia, chromatin clumping, nuclear crowding and overlapping, prominent nucleoli, mitotic figures, lack of cytoplasmic vacuolization, and loss of cell cohesion. Highly accurate (95%) in high-grade carcinoma and CIS but less (10–50%) accurate in low-grade bladder cancer, it is also useful in detecting unresected residual tumor, and may predict future tumor recurrence after transurethral resection.

REFERENCE

Hudson MA, Catalona WJ. Urothelial tumors of the bladder, upper tracts and prostate. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

CYTOMEGALOVIRUS, UROLOGIC CONSIDERATIONS

DESCRIPTION Cytomegalovirus (CMV) is the most important infectious threat to renal transplant recipients. Risk factors include the serologic status of donor and recipient, as well as the immunosuppressive regimen utilized. Other effects include voiding dysfunction by invading peripheral nerves. CMV cystitis has been reported to occur in AIDS, and it is one of the TORCH infections that can cause fetal malformations. CMV has been associated with perinatal renal vein thrombosis, and it can be a cause of virally induced hemorrhagic cystitis.

Ganciclovir has been effective in transplant patients.

REFERENCE

Miles BJ, et al. The urological manifestations of the acquired immunodeficiency syndrome. J Urol 1989;142(3):771–773.

CYTOXAN (CYCLOPHOSPHAMIDE) TOXICITY

DESCRIPTION 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, diarrhea, alopecia, and lethargy. However, Cytoxan has unique toxicities, including the development of hemorrhagic cystitis and secondary cancers such as transitional cell carcinoma of the bladder and leukemia. Acrolein, a metabolite of Cytoxan, is the main cause of acute hemorrhagic cystitis (and thought to be the cause of long-term increased risk of urothelial carcinoma in patients treated with Cytoxan). Hemorrhagic cystitis can be prevented by administering Mesna at the time of Cytoxan readministration; Mesna binds the toxic metabolite acrolein. (See also Section I: “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 when present.
- Hydration

REFERENCE

Hu R, et al. Severe hemorrhagic cystitis associated with prolonged oral cyclophosphamide therapy: Case report and literature review. Rheumatol Int 2008. Epub ahead of print.

SHORT TOPIC SECTION D

DAVIS INTUBATED URETEROTOMY

DESCRIPTION An incision is carried out over the strictured UPJ, and a nephrostomy is placed through a lower pole calyx. A stenting catheter is passed through the cortex of the kidney, down the ureter, and into the bladder. The stent can be removed after a minimum of 6 wk, after which time the ureterostomy catheter is removed. An antegrade nephrostogram is done to ensure patency of the ureter, after which the nephrostomy catheter is removed.

REFERENCE

1. Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:220–233.

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 stratification:

- Low risk: Minor surgery, <40 yrs, no risk factors
- Moderate risk: Minor surgery with additional risk factors or patients 4O–60 yr with no additional risk factors OR patients 40–60 yr with no additional risk factors
- High risk: Patients >60 yr OR patients 40–60 yr with additional risk factors
- Highest risk: Patients with multiple risk factors

RECOMMENDATIONS

- Transurethral or low-risk minor procedures: Early and frequent ambulation only
- Major open procedures: Heparin 5,000 U SQ q12h start post op OR Enoxaparin 40 mg SQ/daily (if CrCL <30 mL/min 30 mg) OR intermittent pneumatic compression
- Active bleeding: Compression stockings and/or intermittent pneumatic compression
- Laparoscopic/robotic surgery: Early and frequent ambulation; with risk factors, one or more of the above medical or mechanical prophylaxis
- Selected very high-risk patients: Consider postdischarge enoxaparin or warfarin.

REFERENCE

Best Practice Statement 2008: Prevention of Deep Vein Thrombosis in Patients Undergoing Urologic Surgery. Available at: www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm. Accessed August 2009.

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 value ranges differ by age and sex. Common clinical reasons to measure these levels include female virilism, hirsutism, precocious puberty, congenital adrenal hyperplasia, 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.

DHEA (ng/mL)
DHEA-S (g/mL)
Child
1–3
N/A
Male
1.7–9.5
80–560
Female
2–10
35–430

REFERENCE

3. Baulieu E, et al. Dehydroepiandrosterone (DHEA), DHEA sulfate, and aging: Contribution of the DHEAge Study to a sociobiomedical issue. Proc Natl Acad Sci U S A 2000;97(8):4279–4284.

DELAYED NEPHROGRAM

DESCRIPTION In most imaging studies, contrast is typically appreciated within a few minutes of injection. In a delayed nephrogram, contrast appearance in the kidney is delayed. The most common cause is intraluminal obstruction of the collecting system by calculus, tumor, or clot. Other causes are:

- Extraluminal obstruction of the collecting system by extrinsic mass
- Intrarenal obstruction, usually by precipitated substances in the tubules, such as Tamm-Horsfall protein
- Azotemia
- Hypotension
- Renal vein thrombosis
- Rarely, acute renal failure

REFERENCE

4. Friedenberg RM. Excretory urography in the adult. In: Pollack HM, et al., eds. Clinical Urography, 1st ed. Philadelphia: Saunders, 1990.

DEMENTIA AND VOIDING DYSFUNCTION

DESCRIPTION Dementia represents a debilitating neurologic cognitive disability seen in patients with Alzheimer, Parkinson, and Lewy body disease. These patients typically develop lower urinary tract symptoms of urgency, frequency, and urge incontinence. The incontinence may be a result of urgency and/or functionality. The more advanced the dementia and lack of mobility, the greater the role of functional incontinence. These patients are very difficult to manage successfully and require significant ancillary care. Incontinence in these patients is typically caused by detrusor hyperreflexia from upper motor neuron lesions.

TREATMENT

- Anticholinergic medication
- -Blocker medication
- Behavioral modifications
- Underlying cause of dementia

REFERENCE

5. Ransmayr GN, et al. Lower urinary tract symptoms in dementia with Lewy bodies, Parkinson disease, and Alzheimer disease. Neurology 2008;70(4):299–303.

DENT DISEASE

DESCRIPTION Dent disease is characterized by hypercalciuria, nephrocalcinosis, kidney stones, renal failure, and rickets. It is a disorder of the proximal tubules with X-linked recessive inheritance. Symptomatic disease is almost exclusively confined to males. Typical childhood presentation is polyuria, microscopic hematuria, asymptomatic proteinuria, or urolithiasis. Treatment is focused on reducing the hypercalcuria. (See Section II: “Hypercalcuria [Absorptive, Renal, and Resorptive].”)

REFERENCE

6. Stechman MJ, et al. Genetic causes of hypercalciuric nephrolithiasis. Pediatr Nephrol 2008; Epub ahead of print.

DENYS-DRASH SYNDROME (DDS), UROLOGIC CONSIDERATIONS

DESCRIPTION A rare disorder consisting of congenital nephropathy, Wilms tumor, and intersex disorders (male pseudohermaphroditism) resulting from WT-1 gene mutations on chromosome 11p13. Patients develop hypertension, ESRD, and gonadoblastomas in their dysgenetic gonads. Also called Drash syndrome.

TREATMENT

- Early prophylactic bilateral nephrectomy
- Gonadectomy
- Chemotherapy based on National Wilms Tumor protocol
- Renal transplantation after 2 yr of disease free on dialysis

REFERENCE

7. Shapiro O, et al. Mixed gonadal dysgenesis and Denys-Drash syndrome: urologists should screen for nephrotic syndrome. Can J Urol 2007;14(6): 3767–3769.

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 excoriations, 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 examination. Diagnosis is made by the presence of IgA deposits in the upper papillary dermis seen on direct immunofluorescence of a skin biopsy specimen. The mainstays of treatment are dapsone and a gluten-free diet.

REFERENCE

8. Alonso-Llamazares J, et al. Clinical, pathologic, and immunopathologic features of dermatitis herpetiformis: Review of the Mayo Clinic experience. Int J Dermatol 2007;46(9):910–919.

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 obese 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 fungus 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; talcum, cornstarch, or other desiccant powders to keep the area dry
- Topical antifungals (powders, creams, lotions, solutions) such as terbinafine (Lamisil), clotrimazole (Lotrimin), econazole (Spectazole), ciclopirox (Loprox), others)

REFERENCE

9. Nadalo D, et al. What is the best way to treat tinea cruris? J Fam Pract 2006;55(3):256–258.

DERMOID CYST, TESTICULAR

DESCRIPTION Dermoid 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 enucleation.

REFERENCE

Viganò P, et al. 7-year history of an intratesticular mass: Patient description and review of the literature about dermoid cysts of the testis. Urol Int 2006;77(3):281–283.

DESMOPLASTIC SMALL ROUND CELL TUMOR

DESCRIPTION Rare, usually very aggressive tumor that typically presents in the abdominal cavity but sometimes involves 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. The cause is theorized reciprocal translocation between chromosomes 11 and 22. Surgical resection and multidrug chemotherapy have been employed with poor success.

REFERENCE

Furman J, et al. Urogenital involvement by desmoplastic small round-cell tumor. J Urol 1997;158:1506–1509.

DE TONI-FANCONI-DEBRE SYNDROME

DESCRIPTION Syndrome of multiple defects of tubular function, characterized by aminoaciduria, phosphaturia, glycosuria, osteomalacia, 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 deficits (especially potassium)
- Correction of acidosis with bicarbonate or citrate
- Replacement of phosphate loss with isoionic neutral phosphate solution
- Encouragement of liberal calcium intake with added vitamin D

REFERENCE

Ogier H, et al. De Toni-Fanconi-Debre syndrome with Leigh syndrome revealing severe muscle cytochrome C oxidase deficiency. J Pediatr 1988;112(5):734–739.

DETRUSOR INSTABILITY (DI)

DESCRIPTION Involuntary or uninhibited contraction of the detrusor muscle of the bladder (as seen with multichannel urodynamics) that lacks a neurologic cause. Clinically, DI usually presents as a persistent sensation of urinary urgency accompanied by frequency and nocturia with or without urge incontinence. (See also Section I: Overactive Bladder.)

SYNONYMS

- Detrusor hyperreflexia (neurologic cause)
- Detrusor overactivity (unknown/unspecified cause)
- Overactive bladder

TREATMENT

- Behavior modification: Fluid restriction, timed voiding, pelvic floor exercises
- Anticholinergic/antimuscarinic therapy
- Intravesicular therapy: Hydrodistention, botulinum toxin type A
- Sacral neuromodulation
- Surgical treatments: Ileovesicostomy, augmentation cystoplasty, cystectomy

REFERENCE

Vasavada SP, et al. Evaluation and management of refractory overactive bladder. Curr Urology Rep 2006;7:370–375.

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 indicative 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 by both low- and high-dose dexamethasone, then a cortisol-secreting adrenocortical 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 the correct dose of dexamethasone will suppress ACTH—and thus cortisol release in normal subjects—whereas patients with corticotrophic adenomas will not suppress below a specified cutoff. Traditionally, high-dose dexamethasone has been used to suppress pituitary sources of ACTH and thus serum cortisol levels to help distinguish Cushing disease from the ectopic ACTH syndrome. 2 mg of dexamethasone is given q6h for 48 hr, after which urinary cortisol is measured. Suppression of basal urinary cortisol levels (measured in the initial screening) by 90% is the commonly quoted cutoff for this test. It is advised that high-dose dexamethasone suppression be used more as a confirmatory test, if at all, for the diagnosis of Cushing disease.

REFERENCE

Gross BA, et al. Diagnostic approach to Cushing disease. Neurosurg Focus 2007;23(3):E1.

DIABETES INSIPIDUS, UROLOGIC CONSIDERATIONS

DESCRIPTION Diabetes insipidus (DI) may cause polyuria. DI is distinguished as neurogenic and nephrogenic. Of urologic interest, the IVP can show marked hydronephrosis, dilated ureters, and megacystis secondary to the great increase in urine flow. Signs include hypernatremia and hyperosmolarity. The condition is diagnosed by the inability to concentrate urine despite water deprivation and administration of ADH. Neurogenic DI is caused by the loss of ADH secretion from trauma, tumor, or for iatrogenic reasons. Nephrogenic DI can be idiopathic, due to medications, or a result of obstructive uropathy.

TREATMENT

- Neurogenic: Replace ADH.
- Nephrogenic:
  - Remove the underlying cause
  - Chlorothiazide with low-sodium diet.

REFERENCE

Garofeanu CG, et al. Causes of reversible nephrogenic diabetes insipidus: A systematic review. Am J Kidney Dis 2005;45(4):626–637.

DIETL CRISIS

DESCRIPTION The most severe manifestation of nephroptosis, originally described by Jozef Dietl in 1864. Classically, colicky flank pain, nausea, chills, tachycardia, oliguria, and transient hematuria or proteinuria was described. Hydronephrosis secondary to vascular obstruction of the ureter is the postulated cause. Physical examination reveals an enlarged, tender kidney. Nephroptosis was thought to be a relatively common condition in women in the early 20th century.

TREATMENT

- Manual reduction of the ptotic kidney was initially used.
- Nephropexy has been used for nephroptosis and was one of the most commonly performed operations of the early 20th century; uncommon procedure today.

REFERENCE

Moss S. Floating kidneys: A century of nephroptosis and nephropexy. J Urol 1997;158:699–702.

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

Hardy R, Austin J. DMSA renal scans and the top-down approach to urinary tract infection. Pediatr Infect Dis J 2008;27(5):476–477.

DIURETIC RENOGRAM

DESCRIPTION A noninvasive nuclear medicine study that provides functional information regarding upper urinary tract obstruction (sometimes referred to as “Lasix renogram”). This test is most commonly utilized to determine obstruction in the setting of hydronephrosis. A tubular agent is preferred, therefore MAG3 is widely used for its high extraction fraction, rapid parenchymal transit, low radiation absorbed dose, and excellent imaging properties. The recommended dose of furosemide (Lasix) in adults is 40 mg IV. In the standard protocol, Lasix is injected when the collecting system appears to be full (usually 15–20 min after tracer injection, called F + 20). In patients with equivocal results, a 2nd study with administration of Lasix 15 min before tracer injection (called F – 15) is performed to maximize the diuretic stress, which improves the sensitivity and specificity and reduces the chances of equivocal outcome. Quantitative parameters like time to peak (TTP), 20 min to peak activity ratio (20/MAX), pelvic T1/2 clearance time, and parenchymal transit time (PTT) are calculated.

REFERENCE

Foda M, et al. A prospective randomized trial comparing 2 diuresis renography techniques for evaluation of suspected upper urinary tract obstruction in children. J Urol 1998;159(5): 1691–1693.

DOPPLER, PENILE

DESCRIPTION Currently, the most widely utilized method to measure arterial flow and prove arterial insufficiency as an etiology in impotence. It allows visualization of individual arteries and measurement of flow. Performed in the flaccid and erect states (after the intracavernosal injection of vasoactive agents). An increase in mean arterial diameter of >75% of the flaccid value and a mean peak flow velocity of >25 cm/s after vasoactive agent injection is used to determine adequate arterial capacity. A wide variability in some patients has been shown, however.

REFERENCE

Bertolotto M. Penile sonography. Eur Urol 1999;540: 7–12.

DOWN SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION Also known as trisomy 21, the findings of this commonly seen trisomy include brachycephalic skull; congenital nasal hypoplasia; broad, short hands; and GU anomalies in the form of undescended testicles and a small penis. Males affected are hypogonadal with a smaller than average phallus. Approximately 1/4 will have cryptorchidism. Microscopic renal cysts, usually of the glomerular space, can also occur.

REFERENCE

Rabinowitz R. General consideration of congenital anomalies. In: Gillenwater JY, Grayhack JT, Howards SS, Duckett JW, eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

DRIBBLING, POST-VOID

DESCRIPTION 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 urethral diverticulum in women. In men, it is a complaint associated clinically with BPH following radical prostatectomy and stricture disease.

REFERENCE

Ablove T. Post void dribbling: Incidence and risk factors. Neurourol urodyn. 2009; epub ahead of print.

DROMEDARY HUMP

DESCRIPTION A normal anatomic variant of the left kidney consisting of a bulge of normal tissue that mimics a tumor. Dromedary humps arise from the superolateral aspect of the left kidney secondary to molding by the spleen. It is usually mistaken for tumors on IVP or kidney tomograms. Other imaging, such as CT, MRI, or renal US can be used to rule out a tumor. Appropriately named after the dromedary camel.

REFERENCE

Dyer R, et al. Classic signs in uroradiology. Radiographics 2004;24:S247–S280.

DROOPING LILY SIGN

DESCRIPTION Excretory urographic description for the lower-pole moiety in a duplicated collecting system. The nonfunctioning upper pole produces a mass effect that pushes the lower pole downward. The lower-pole ureter tends to be orthotopic, whereas the upper pole is typically ectopic.

REFERENCE

Amis ES, Newhouse JH. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:263.

DRUG ERUPTION, FIXED

DESCRIPTION This sharply localized dermatitis characteristically recurs at the same site each time the offending drug is administered (penis is most common site), with an acute phase followed by desquamation and hyperpigmentation. Symptoms usually appear after 6 hr, although lesions can occur 24–48 hr later. A macrophage migration inhibition factor (MIF) assay is essential for diagnosis.

Common medications responsible include phenolphthalein, trimethoprim-sulfamethoxazole, antipyrine, quinine, tetracycline, salicylates/NSAIDS, and hydroxyzine hydrochloride. Discontinuation of the drug causing the reaction results in complete resolution of the fixed drug eruption. Supportive topical therapy (steroids) is used, as needed.

REFERENCE

Cohen HA, et al. Fixed drug eruption of the penis due to hydroxyzine hydrochloride. Ann Pharmacother 1997;31(3):327–329.

DYSFUNCTIONAL VOIDING

DESCRIPTION Syndrome wherein external sphincter dyssynergia is noted in the absence of an identifiable neurologic cause. Occurring in children, it is theorized to be psychogenic in origin and is usually brought to attention through UTIs or secondary enuresis. 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 or EMG readings during urodynamics. (See also Section II: “Hinman Syndrome [Hinman-Allen Syndrome;” Section II: “Nonneurogenic Neurogenic Bladder];” Section II: “Occult Neuropathic Bladder.”)

SYNONYMS

- Hinman-Allen syndrome
- Hinman syndrome
- Nonneurogenic neurogenic bladder

TREATMENT

- Combination of medications, behavioral therapy, and intermittent catheterization
- Surgery for diversion may be required to protect upper tracts.

REFERENCE

Yang CC, Mayo ME. Morbidity of dysfunctional voiding syndrome. Urology 1997;49(3):445–448.

DYSGERMINOMA

DESCRIPTION Malignant tumor of the ovary, which is roughly the counterpart of seminoma of the testes, occurring in children and young women. It is occasionally seen in gonadal dysgenesis or testicular feminization syndrome. Patients may present with pelvic mass or abdominal pain. Pure dysgerminomas do not secrete tumor markers such as AFP or hCG.

TREATMENT

- Surgical resection for local disease
- Radiation therapy or chemotherapy for advanced disease

REFERENCE

Berek JS. Ovarian cancer. In: Hacker NF, et al., eds. Essentials of Obstetrics and Gynecology, 2nd ed. Philadelphia: Saunders, 1992.

DYSRAPHISM, SPINAL

DESCRIPTION Most common cause of neurogenic bladder dysfunction in childhood, dysraphism is defined as failure of closure of the vertebral canal during embryonic development, leading to spinal cord dysfunction. The most common dysraphism, myelodysplasia, includes meningoceles, myelomeningoceles, and lipomeningoceles. Reflux, continence, sexuality, and bowel function are often important issues with these patients. Many rarer forms also exist, including tight filum terminale, dermoid cysts, and aberrant nerve roots with varying levels of resulting dysfunction. (See also Section II: “Myelodysplasia [Myelomeningocele], Urologic Considerations”; Section III: “Tethered Cord Syndrome.”)

REFERENCE

Bauer SB. Neurogenic dysfunction of the lower urinary tract in children. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998.

SHORT TOPIC SECTION E

ECCHYMOSIS, FLANK

DESCRIPTION The presence of ecchymosis in the flank region (Grey-Turner sign) is a physical sign of retroperitoneal bleeding. Common associations may include renal trauma, ruptured abdominal aortic aneurysm, and acute pancreatitis.

REFERENCE

1. Bonani M, et al. Images in emergency medicine. Cullen’s sign and Grey-Turner’s sign. Ann Emerg Med 2008;51(4):448–458.

ECHINOCOCCUS, RENAL

DESCRIPTION Renal hydatid disease is a parasitic tapeworm infestation that results in renal cysts that occupy space and cause local mass symptoms. This is a parasitic infection caused by the larval stage of the cestode Echinococcus granulosus. 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, curvilinear 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 cysts

TREATMENT

- Surgical excision of intact cyst, with care not to spill or rupture cyst
- Medical treatment (mebendazole) is reserved for surgically unfit patients

REFERENCE

2. Angulo J, et al. Renal echinococcosis: Clinical study of 34 cases. J Urol 1997;157(3):787–794.

EDEMA, LOWER EXTREMITY, UROLOGIC CONSIDERATIONS

DESCRIPTION Edema of the lower extremity can present bilaterally or unilaterally and can have many urologic implications, depending on the clinical presentation. Unilateral edema in the peri- or postoperative period may be a manifestation of deep venous thrombosis or an expected result after lymphadenectomy. Bilateral edema may be a result of underlying congestive heart failure or generalized anasarca. Postoperative fluid management should be closely monitored with this finding. In endemic regions, filariasis may present with significant bilateral lower extremity edema.

CAUSES

- Anasarca
- Congestive heart failure
- Deep venous thrombosis
- Filariasis
- IVC thrombosis/obstruction
- Lymphadenectomy (retroperitoneal, pelvic, inguinal)
- Superficial thrombophlebitis
- Urinary obstruction/retention

REFERENCE

3. Ely J, et al. Approach to leg edema of unclear etiology. J Am Board Fam Med 2006;19(2):148–160.

EDWARD SYNDROME

DESCRIPTION Also known as trisomy 18, in the majority of the cases malformations such as ventricular septal defect, horseshoe kidneys, esophageal atresia, omphalocele, facial clefts, diaphragmatic hernias, and genital hypoplasia can be found. High incidence of urologic abnormalities is noted. Horseshoe kidney and hydronephrosis are seen in about 50%, with hypospadias and cryptorchidism also common. Up to 90% of patients die within the 1st yr, usually secondary to cardiopulmonary problems. Uterine and vaginal abnormalities are common in females.

REFERENCE

4. Surányi A, et al. Unusual clinical history of a male infant with Edwards syndrome. Pathol Oncol Res 2009;15(1):147–152.

EJACULATION, PAINFUL

DESCRIPTION The incidence of pain associated with or immediately after ejaculation is 1–9.7%. Can be iatrogenic, 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 genitalia that are responsible for semen transport during ejaculation.

CAUSES

- Prostatitis
- BPH
- Ejaculatory duct obstruction by calculi
- Postoperative (prostatectomy)
- Antidepressants
- Pudendal neuropathy

TREATMENT

- -Adrenoreceptor inhibitors
- Rule out and treat ejaculatory duct obstruction
- Pudendal nerve injection with bupivacaine/triamcinolone
- Pudendal nerve release

REFERENCE

5. Ilie C, et al. Painful ejaculation. BJU Intern 2007; 99(6):1335–1339.

EJACULATORY ANHEDONIA

DESCRIPTION A rare condition, affecting males predominantly, in which ejaculation occurs without an accompanying sense of orgasmic pleasure. Most common causes are psychogenic in origin or related to SSRI antidepressants usage.

REFERENCE

6. Lue TF, et al. Summary of the recommendations on sexual dysfunctions in men. J Sex Med 2004; 1(1),6–23.

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, Müllerian and Wolffian duct cysts; ejaculatory duct stenosis; or atresia. Acquired causes include infection, calculus, trauma, or prior instrumentation. Physical examination is usually normal, with the occasional palpable midline mass or dilated seminal vesicles. Semen analysis shows low volume, acidic pH, absent fructose, and failure to coagulate. Transrectal ultrasonography (TRUS) demonstrates a cystic midline structure within the prostate, with dilated seminal vesicles. When TRUS is equivocal, additional tests include TRUS-guided seminal vesicle aspirate (demonstrates abundant spermatozoa) or vasography. (See also Section II: “Vasography, Technique and Indications.”)

Treatment is through transurethral resection of ejaculatory duct, in which the ejaculatory duct cyst is unroofed by transurethral resection at the level of the verumontanum, until efflux from the ducts is seen.

REFERENCE

7. Fisch H, et al. Management of ejaculatory duct obstruction: Etiology, diagnosis, and treatment [review]. World J Urol 2006;24(6):604–610.

ELECTROEJACULATION

DESCRIPTION Procedure for obtaining sperm for assisted reproductive techniques in patients who cannot ejaculate on their own, such as spinal cord injury patients, typically used after failure of vibratory penile 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 erection and ejaculation in >80% of patients. Rectosigmoidoscopy is performed before and after the procedure to rule out rectal injury. Blood pressure monitoring is essential during the procedure for patients who may have autonomic dysreflexia.

REFERENCE

8. Snksen J, Ohl DA. Penile vibratory stimulation and electroejaculation in the treatment of ejaculatory dysfunction. Int J Androl 2002;25(6):324–332.

ELECTROMYOGRAPHY, EXTERNAL SPHINCTER

DESCRIPTION Generally, electromyography is the measurement of bioelectric potentials generated by the depolarization of muscle. During urodynamics, the activity of the external sphincter can be monitored by transperineal needle electrodes or surface electrodes. During filling, there should be increases in activity, which will reach maximum near capacity. During voiding, there should be sudden and persistent cessation of sphincter activity. When empty, baseline sphincter activity recurs. 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, voluntary contraction of the pelvic floor with the Valsalva maneuver, and dysfunctional voiding, among others. May also be used as biofeedback therapy for dysfunctional voiding.

REFERENCE

9. Steers WD, et al. Voiding function and dysfunction. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

ELEJALDE SYNDROME

DESCRIPTION Also known as acrocephalopolydactylous dysplasia, this exceedingly rare autosomal recessive syndrome is characterized by craniosynostosis and fibroblast hyperproliferation in organs such as skin, liver, kidney, and pancreas. High birth weight, craniofacial dysmorphism, polydactyly, hepatomegaly, splenic abnormalities, hypertrophic kidneys, and renal cysts are also common features.

REFERENCE

Silhánová E, et al. 2006. Elejalde syndrome: A case report. Am J Med Genet Part A 140A:2223–2226.

ELEPHANTIASIS, SCROTUM

DESCRIPTION Also called elephantiasis scroti, this is the end result of longstanding lymphatic obstruction in which the scrotum and penis can become massively enlarged and debilitating. Usually associated with filariasis, which is uncommon in the US. 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 Genitalia [Peno-Scrotal Edema];” Section II: “Filariasis, Urologic Considerations.”)

TREATMENT

- Drug therapy for any infectious etiology
- Surgery for resection of redundant scrotum with flap coverage of testes

REFERENCE

Apesos J, Anigian G. Reconstruction of penile and scrotal lymphedema. Ann Plast Surg 1991; 27(6):570–573.

ELIMINATION SYNDROME: DYSFUNCTIONAL, OF CHILDHOOD

DESCRIPTION Nonneurogenic voiding dysfunction symptoms in childhood are believed to arise from behavioral issues that affect toilet training and delay the maturation of urinary control, and this broad array of conditions are collectively termed dysfunctional elimination syndrome (DES). DES also embraces the concept that functional GI disorders impact lower urinary tract function. DES symptoms are attributable to detrusor overactivity, infrequent voiding syndrome, and functional GI disturbances. DES includes a wide spectrum of disease conditions. At one extreme are patients with non-neurogenic neurogenic bladder (Hinman syndrome) who have severe uropathologic changes due to severe urinary retention, VUR, hydronephrosis, and renal scarring. On the end of the spectrum are those patients with significant clinical symptoms without pathologic changes, such as enuresis, urinary incontinence, urge syndrome, post-void dribbling, and primary bladder neck dysfunction. DES is strongly associated with VUR and recurrent UTI. Functional bowel dysfunction associated with DES includes constipation and fecal soiling.

REFERENCE

Feldman AS, Bauer SB. Diagnosis and management of dysfunctional voiding. Curr Opin Pediatr 2006;18(2): 139–147.

ENCOPRESIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Children who are incontinent of stool, even with minor fecal soiling, usually have significant constipation. Occult pathology of the bowel or nervous system must 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.

TREATMENT

- Diet changes
- Laxatives, stool softeners
- Toilet schedules

REFERENCE

O'Regan S, et al. Constipation, bladder instability, urinary tract infection syndrome. Clin Nephrol 1985;23:152.

ENCRUSTED CYSTITIS AND PYELITIS

DESCRIPTION Inflammatory ulcerating condition of the bladder and pelvicaliceal system characterized by encrustation with calcium deposits (struvite and apatite calculi). Commonly, the presence of alkaline urine, infection by urea-splitting Corynebacterium group D2 bacterium, and recent history of a urologic procedure in a immunocompromised host (eg, renal transplant) is found. Clinical manifestations of encrusted cystitis are often fever, 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-wall edema of the bladder and/or pyelocaliceal system. Calcifications seldom appear on plain abdominal radiographs unless in association with staghorn calculi. The endoscopic appearance is of calcified white 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 or sheep blood agar.

TREATMENT

- Treat Corynebacterium infection according to sensitivity.
- Acidify urine through irrigation (eg, Suby's solution G, Thomas C24) or PO acetohydroxamic acid
- Remove calcified plaques where bacteria harbor: TUR, endoscopic

REFERENCE

Meria P, et al. Encrusted cystitis and pyelitis. J Urol 1998;160(1):3–9.

ENDOCARDITIS (SBE) PROPHYLAXIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Based on the latest American Heart Association guidelines on the prevention of infectious endocarditis (IE) published in October 2007, antibiotic prophylaxis solely for the prevention of IE is NOT recommended for GU procedures. The AHA guidelines concluded that bacteremia resulting from random daily activities are much more likely to cause IE than bacteremia associated with GU procedures.

REFERENCE

Wilson W, et al. Prevention of infective endocarditis. Circulation 2007;116(15):1736–1754.

ENDOCERVICOSIS, BLADDER

DESCRIPTION This rare mucinous analogue of endometriosis histologically demonstrates glandular lesions involving the bladder, with prominent endocervical-like epithelium. It is a benign condition only reported in women. Patients are presumed to have an underlying malignancy and are usually treated surgically. Patients present with irritative voiding symptoms and pelvic pain. Transurethral resection or partial cystectomy is curative, and close follow-up is recommended.

REFERENCE

Rodriguez R, Alfert H. Endocervicosis of the bladder: A rare mucinous analogue of endometriosis. J Urol 1997;157(4):1355.

ENDOMETRIOID CARCINOMA, PROSTATE

DESCRIPTION This term has been replaced by ductal carcinoma of the prostate. The lesion originates from periurethral prostatic ducts and may grow into an exophytic urethral lesion around the verumontanum. Early presentation is hematuria and obstructive symptoms. A mixture of cribriform and papillary structures is seen on microscopy, resembling endometrial adenocarcinoma of the uterus. It accounts for 0.5% of prostatic adenocarcinomas. Serum PSA levels and DRE at the time of diagnosis tend to underestimate disease. Patients often present with advanced disease, and it runs an aggressive course, sharing a similar prognosis as Gleason score 8 acinar adenocarcinoma and also sharing similar cribriform morphologic features.

SYNONYMS

- Ductal carcinoma of the prostate
- Endometrioid carcinoma
- Endometrial carcinoma

TREATMENT

Similar to high-grade acinar adenocarcinoma of prostate, with perhaps slightly worse prognosis

REFERENCE

Brinker DA, et al. Ductal adenocarcinoma of the prostate diagnosed on needle biopsy: Correlation with clinical and radical prostatectomy findings and progression. Am J Surg Path 1999;23(12):1471.

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 third of ureter. 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 hematuria” is uncommon.

Diagnosis is through IVP/CT urography and urine analysis, laparoscopy to inspect the pelvis and obtain tissue biopsy, or cystoscopy or ureteroscopy to evaluate hematuria and obtain biopsy.

TREATMENT

- Hormonal therapy with oral contraceptives, danocrine, or GNRH agonists
- Surgery when medical treatment fails
- Partial cystectomy, ureterolysis, ureteric reimplantation or stenting may be performed.

REFERENCE

Umar SA, et al. Endometriosis of the ureter J Urol. 2008;179(6):2412.

EPCA-2 (EARLY PROSTATE CANCER ANTIGEN)

DESCRIPTION A nuclear matrix protein that shows promise as a new serum-based biomarker of prostate cancer, which is postulated to have better sensitivity and specificity than PSA. Leman and colleagues demonstrated that it may differentiate between organ-confined and extracapsular disease, and it may be utilized for post-prostatectomy monitoring. As of publication date, not yet FDA approved.

REFERENCE

Leman ES, et al. EPCA-2: A highly specific serum marker for prostate cancer. Urology 2007;69: 714–720.

EPIDERMOID CYST, TESTICLE

DESCRIPTION Epidermoid cysts account for ~1% of testicular tumors. Producing keratinizing, stratified, squamous cell-lined cysts supported by fibrous tissue, these cysts are considered special cases of teratoma, but are not truly considered a teratoma since only a single germinal layer and not the required 2 layers is represented. Benign in behavior; scrotal US is suggestive of the diagnosis but not usually definitive.

TREATMENT

- Inguinal orchiectomy
- Some advocate organ-sparing surgery if the diagnosis is definitively proven by frozen section.

REFERENCE

Heidenreich A, et al. Organ preserving surgery in testicular epidermoid cysts. J Urol 1995;153(4): 1147–1150.

EPIDIDYMIS, METASTASIS TO

DESCRIPTION Extremely 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 as an incidental finding on orchiectomy for prostate cancer. 4 mechanisms for spread have been proposed, including direct extension, retrograde venous extension, retrograde lymphatic extension, and arterial embolism.

REFERENCE

Powell BL, et al. Secondary malignancies of the penis and epididymis: A case report and review of the literature. J Clin Oncol 1985;3:110–116.

EPIDIDYMIS, OBSTRUCTION

DESCRIPTION A cause of obstructive azoospermia. Most common cause is vasectomy, which results in a fixed obstruction and elevated vessel pressures resulting, in the blowout of the epididymal tubules. Other causes include trauma, congenital malunion of the vas and epididymis, infection, inflammatory damage to the epididymis, and idiopathic. Epididymovasostomy is the treatment of choice. (See also Section I: Infertility, Urologic Considerations; Section II: Azoospermia.)

REFERENCE

Kim ED, et al. Pathological epididymal obstruction unrelated to vasectomy: Results with microsurgical reconstruction. J Urol 1998;160(6, Part 1): 2078–2080.

ERECTILE DYSFUNCTION INVENTORY OF TREATMENT SURVEY (EDITS)

DESCRIPTION A validated satisfaction questionnaire for both patient (11 items) and partner (5 items) based on their subjective evaluation of the treatment for erectile dysfunction (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 functioning.

REFERENCE

Althof SE, et al. EDITS: Development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. Urology 1999;53(4):793–799.

ERYSIPELAS, EXTERNAL GENITALIA

DESCRIPTION Superficial bacterial infection of the dermis with marked dermal lymphatic involvement. The irritation afflicts extremes of ages, 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 peau d'orange appearance. The clinician must differentiate erysipelas from cellulitis and Fournier gangrene (exclusion of this diagnosis is a priority in all cutaneous infections of the external genitalia). It is usually caused by Group A hemolytic streptococcus (eg, S. pyogenes), or rarely S. aureus.

TREATMENT

- Mild infection: PO penicillin, macrolides, or clindamycin
- Severe infection: Parenteral penicillin or vancomycin

REFERENCE

Link RE. Cutaneous disease of the external genitalia. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007:419–420.

ERYTHEMA MULTIFORME, EXTERNAL GENITALIA

DESCRIPTION Erythema multiforme (EM) is a common acquired blistering skin condition that affects all age groups, ethnicities, and sex. 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 mucoepithelial 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 bulls-eye, commonly occurring on the hands. Painful rash is characteristic, and macules, papules, urticaria, vesicles, bullae, purpura or petechiae are pleomorphic. In EM major, large tracts of skin and oral mucosa may be denuded, along with conjunctivitis, and GU 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: Wet compress with topical astringent, topical acyclovir (for HSV-related EM)
- EM major (Stevens-Johnson syndrome): Hospitalization required, nutrition, hydration, aggressive topical nursing care equivalent to burns treatment

REFERENCE

Fine J-D. Blistering diseases. In: Kerdel FA, FJimenez-Acosta, eds. Dermatology: Just the Facts. New York: McGraw-Hill, 2003:143–145.

ERYTHRASMA

DESCRIPTION Superficial, asymptomatic skin infection by a diphtheroid Corynebacterium minutissimum. Physical examination reveals sharply delineated, round to oval patches with scales in the intertriginous regions. Wood's lamp examination reveals coral-red fluorescence. Histologically, only the stratum corneum is affected, with all other layers normal. More common in tropical climates. Treatment is antibiotic therapy (topical 2% erythromycin or tetracycline for 14 days).

REFERENCE

Ro JY, Amin MB, Ayala AG. Penis and scrotum. In: Bostwick J, et al., eds. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

EXCRETORY UROGRAM: INTRAOPERATIVE (SINGLE-SHOT IVP)

DESCRIPTION The preferred imaging study for renal trauma is contrast-enhanced CT, and the indications for intraoperative excretory urography is uncommon. However, a “single-shot” IVP may be performed in a setting in which renal trauma is suspected during abdominal exploration for a trauma patient too unstable for CT. A single film is shot on the operative table at 10 min after administration of 2 mL/kg of IV contrast. An abnormal or inconclusive study should prompt renal exploration to complete staging of the renal injury and perform appropriate repairs; a properly performed study can potentially reduce the need for renal exploration by 32%. The study is also valuable in confirming the presence of a normal contralateral renal unit before renal exploration.

REFERENCE

Jankowski JT, Spirnak JP. Current recommendations for imaging in the management of urologic traumas. Urol Clin N Am 2006;33(3):365–376.

Morey AF, et al. Single shot intraoperative excretory urography for the immediate evaluation of renal trauma. J Urol 1999;161(4):1088–1092.

EXPRESSED PROSTATIC SECRETIONS (EPS)

DESCRIPTION EPS represents prostatic fluid expressed after vigorous prostatic massage. Evaluation of this fluid is part of the Stamey test used in the evaluation of prostatitis. Note that prostate massage is contraindicated in the setting of acute bacterial prostatitis. The WBC count in an EPS for a diagnosis of chronic bacterial prostatitis (NIH category II) is >10 WBCs/hpf (40× objective) or clumping of WBCs with the presence of oval fat bodies and a positive EPS bacterial culture. NIH category III prostatitis is divided into IIIa and IIIb, based on whether greater or fewer than 10 WBCs are seen on microscopic examination of the EPS, respectively. The pH of prostatic fluid increases with infection (6.5–>8.0).

REFERENCE

Nickel JC, et al. How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome? J Urol 2006;176(1):119–124.

EXSTROPHY-EPISPADIAS COMPLEX

DESCRIPTION Exstrophy-epispadias complex (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 to 1 in 50,000 live births, with a male preponderance. The risk of recurrence in a family is 1 in 100. The condition is believed to be due to failure of the cloacal membrane to be reinforced by in growth of mesoderm, therefore preventing the medial migration of mesenchymal tissues and lower abdominal wall development. The defective 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, Exstrophy, Bladder [Classic Exstrophy].”)

TREATMENT

- Immediate at birth: Prevent irritation/trauma to exposed mucosal surfaces (eg, Saran 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 urethral closure, with osteotomy. Epispadias repair between 6–12 mo. Reconstruction of continent bladder neck and ureteric reimplantation, usually at age 4–5 yr.
- Single-stage reconstruction

REFERENCE

Eeg K, Khoury A. The exstrophy-epispadias complex. Curr Urol Rep 2008 9;9(2):158–164.

EXTRAGONADAL GERM CELL TUMORS (EGCT)

DESCRIPTION Rare entity representing 3–5% of all germ cell tumors. There is a clinical association with Klinefelter syndrome, and testicular US is necessary to exclude primary tumor. Primary EGCT are located in the midline generally, in decreasing frequency: Mediastinum, retroperitoneum, pineal/suprasellar region, and the sacrococcygeal region. All tumor types are reported, with nonseminomatous being most common. They can present with wide local invasion and advanced metastasis with few symptoms. Management of EGCT parallels that of metastatic testicular GCT, however EGCT have a worse prognosis.

TREATMENT

- Surgical excision, if feasible
- Chemotherapy, irradiation, or combination

REFERENCE

Scholz M, et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: Results from an international analysis. J Clin Oncol 2002;20(7): 1864–1873.

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 metachronous GU (most commonly bladder) or GI (most commonly colon) malignancy. Differential diagnoses include Squamous cell carcinoma in situ or malignant melanoma.

TREATMENT

- Surgical excision with wide margin, Moh's microsurgical excision, or radiation
- Screen for occult GU and GI malignancy

REFERENCE

Smoller BR. Paget's disease. In: Morgan MB, et al. eds. Deadly Dermatologic Diseases: Clinicopathologic Atlas and Text. New York: Springer, 2007:43–50.

SHORT TOPIC SECTION F

FABRY DISEASE/SYNDROME

DESCRIPTION Fabry disease consists of multiple cutaneous angiokeratomas, corneal opacification, and progressive renal insufficiency. Symptoms of severe burning pain in the extremities usually begin in the 1st decade, and can cause febrile episodes. The skin lesion is known as angiokeratoma corporis diffusum. Cardiovascular effects include coronary artery disease and congestive heart failure. Renal failure leads to uremia and hypertension in the 3rd–5th decades. This is an X-linked disorder that affects the lysosomal enzyme -galactosidase gene.

TREATMENT

- Enzyme replacement therapy with agalsidase-
- Renal replacement therapy

REFERENCE

1. Mehta A, et al. Fabry disease defined: Baseline clinical manifestations of 366 patients in the Fabry Outcome Survey. Eur J Clin Invest 2004;34(3):236–242.

FAMILIAL TESTOTOXICOSIS

DESCRIPTION Cause of isosexual precocity 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. Hyperplasia of Leydig cells is noted on biopsy. Testolactone, a competitive inhibitor of aromatase, has been used in combination with spironolactone with some success.

REFERENCE

2. Aziz AA, et al. Testotoxicosis: Gonadotrophin-independent male sexual precocity. Postgrad Med J 1992;68(797):225–228.

FANCONI SYNDROME

DESCRIPTION An acquired or inherited disorder characterized by abnormalities of renal proximal tubular function, including glucosuria, phosphaturia, aminoaciduria, and bicarbonate wasting. The aminoaciduria is generalized, and defects in uric acid, water, potassium, and sodium absorption can also occur. The basic abnormality is unknown. Acquired disease is caused by 6-mercaptopurine or outdated tetracycline, renal transplantation, multiple myeloma, amyloidosis, intoxication with heavy metals or other chemical agents, and vitamin D deficiency. Inherited (usually seen with other disorders) form presents in infancy with proximal tubular acidosis, hypophosphatemic rickets, hypokalemia, polyuria, and polydipsia. In the nephropathic form, failure to thrive and growth retardation are common, with progressive renal failure. Diagnosed by demonstrating the abnormalities of renal function.

TREATMENT

- Sodium bicarbonate for acidosis
- Renal transplantation has been successful.

REFERENCE

3. Bickel H, Manz F. Hereditary tubular disorders of the Fanconi type and the idiopathic Fanconi syndrome. Prog Clin Biol Res 1989;305:111–335.

FATTY CASTS

DESCRIPTION Fatty casts contain fat globules embedded within tubular epithelial casts. Polarized light microscopy may reveal a “Maltese 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 embolism syndrome.

REFERENCE

4. Schrier RW. Clinical evaluation. In: Diseases of the Kidney and Urinary Tract. Philadelphia: Lippincott Williams & Wilkins; 2007:294.

FECALURIA

DESCRIPTION The presence of fecal matter passed from the urethra, suggestive of a fistula tract between the urinary and intestinal tract. Etiologies include pathologic processes such as Crohn disease, diverticulitis, or cancer, or iatrogenic causes such as perineal surgery, radiation, or trauma to the region. Initial evaluation may include barium enema and CT urogram to help delineate the location of fistula tract.

REFERENCE

5. Diverticular disease. In: Townsend CM, et al., eds. Sabiston Textbook of Surgery, 18th ed. Philadelphia: Saunders, 2007.

FEMALE HYPOACTIVE SEXUAL DESIRE DISORDER

DESCRIPTION Female sexual dysfunction has been extensively defined in the DSM-IV manual and subsequently summarized as absent or diminished feelings of sexual interest or desire, absent sexual thoughts or fantasies, and a loss of motivation to become sexually aroused. Prevalence ranges from 39–43% in recent studies.

CAUSES

- Hormonal: Hypothalamic/pituitary dysfunction, menopause, chronic oral contraceptive pills
- Musculogenic: Hyper- or hypotonicity of pelvic floor
- Neurogenic: Spinal cord injury, nervous system disorders (DM, CVA)
- Psychogenic: Relationship problems, poor body image/self-esteem, mood disorders
- Vasculogenic: Poor 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

6. Frank JE, et al. Diagnosis and treatment of female sexual dysfunction. Am Fam Physician 2008; 77(5):635–642.

FEMINIZING GENITOPLASTY

DESCRIPTION Surgical treatment of ambiguous genitalia may be indicated in the genetic female with virilization of external genitalia for psychosocial development. Common cause of virilization in the female newborn is congenital adrenal hyperplasia (CAH). Feminizing genitoplasty may be performed early in infancy to facilitate gender-appropriate upbringing, or delayed until adolescence when the patient can participate in consent. Extensive counselling of parents of any intersex infant is critical before considering genitoplasty. Goals of surgery are to create external genitalia with an esthetic female appearance, and permit sexual function and, if possible, fertility. (See also Section I: “Disorders of Sexual Development [DSD].”)

REFERENCE

7. Schober JM. Feminization (surgical aspects). In: Stringer MD, Oldham KT, Mouriquand PDE, eds. Pediatric Surgery and Urology: Long-term Outcomes. New York: Cambridge, 2006:595–611.

FERTILE EUNUCH DISEASE/SYNDROME

DESCRIPTION Also called isolated LH deficiency, patients have eunuchoid proportions with variable degrees of virilization and, often, gynecomastia. Large testes and ejaculate containing a few sperm are present. Plasma FSH levels are normal, but both serum LH and serum testosterone concentrations are low normal. Testosterone replacement is standard; hCG therapy may be useful.

REFERENCE

8. McClure RD. Male infertility. In: Tanagho EA, McAninch JW, eds. Smith's General Urology, 14th ed. Norwalk, CT: Appleton & Lange, 1995.

FIBROEPITHELIAL POLYP

DESCRIPTION The most common benign ureteral tumor, arising from the upper third of the ureter, these polyps resemble a smooth nodule or may be pedunculated. Histologically, a central fibrous core surrounded by normal or hyperplastic urothelium is seen. Patients present with flank pain and hematuria, usually as a young adult. Radiographically, smooth filling defects are seen. Hydroureteronephrosis can be seen, as well as ureteral intussusception. They can recur locally.

TREATMENT

Ureteroscopic resection, open ureterotomy with polypectomy, or partial ureterectomy, if the diagnosis can be confirmed preoperatively

REFERENCE

9. Sun Y, et al. Is endoscopic management suitable for long ureteral fibroepithelial polyps? J Endourol 2008;22(7):1459–1462.

FIBROUS HAMARTOMA OF INFANCY

DESCRIPTION Uncommon subcutaneous proliferative lesion, usually found in the shoulder and axillary regions during the 1st or 2nd of life; also reported to occur in the genital region and should be in the differential diagnosis of genital masses. Histologically, it demonstrates mature adipose tissue, scattered mesenchymal cells, and bundles of fibrous tissue. Local excision is curative.

REFERENCE

Stock JA, et al. Fibrous hamartoma of infancy: A report of 2 cases in the genital region. Urology 1995; 45(1):130–131.

FIBROUS PSEUDOTUMOR OF TESTICULAR TUNIC

DESCRIPTION Reactive, benign process of the tunica vaginalis in which multiple firm nodules occur in the tunica or within it. Presents as testicular masses, sometimes associated with trauma or hydrocele. It may be difficult to distinguish from malignant processes. Histologically, the lesion can demonstrate granulation tissue, fibroblastic proliferation, and nodules of hyalinized tissue. Orchiectomy is usually necessary to confirm the diagnosis.

SYNONYMS

- Fibrous pseudotumors
- Multiple fibromas of the tunica vaginalis testes
- Reactive periorchitis

TREATMENT

Orchiectomy usually necessary to confirm diagnosis

REFERENCE

Parker PM. Benign fibrous pseudotumor of tunica vaginalis testis. Urology 2006;68(2):427:e17–e19.

FILARIASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Filariasis is transmitted by mosquitoes, most commonly Wuchereria bancrofti, which is found in many 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 (fever, headache, myalgia, and lymphadenitis). In lymphatic disease, manifestations usually occur 3 mo to 1 yr after acquisition. Occasionally, moderate lymphadenopathy, particularly involving the inguinal lymph nodes, occurs. Inflammation of the lymphatics of the extremities and genitalia leads to retrograde adenolymphangitis. Epididymitis, orchitis, and funiculitis can also occur, along with fever, chills, and other nonspecific systemic symptoms. Lymphatic dysfunction, with resulting chronically progressive edema of the limbs and genitalia, is relatively infrequent in children. Elephantiasis 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 assays are not available, and in elephantiasis the microfilariae may no longer be present. Eosinophilia of 25% frequently occurs in early disease. (See also Section I: “Edema, External Genitalia [Peno-Scrotal Edema].”)

TREATMENT

- Diethylcarbamazine citrate is the drug of choice. The late obstructive phase of the disease is not affected by chemotherapy.
- Ivermectin, an investigational drug in the US, 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.
- Chyluria originating in the bladder responds to fulguration; chyluria originating in the kidney is much more difficult to correct.

REFERENCE

AAP 1997 Red Book: Report of the Committee on Infectious Diseases, 24th ed. Elk Grove, IL: American Academy of Pediatrics, 1997.

FINE NEEDLE ASPIRATION (FNA) OF PROSTATE

DESCRIPTION In the detection of prostatic carcinoma, FNA cytology of the prostate has largely been 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.

REFERENCE

Hautmann SH, Conrad S, Henke RP, et al. Detection rate of histologically insignificant prostate cancer with systematic sextant biopsies and fine needle aspiration cytology. J Urol 2000;163:1734–1738.

FISH: URINARY FLUORESCENT IN SITU HYBRIDIZATION (UROVYSION TEST)

DESCRIPTION Cytogenetic studies describe frequent alterations in chromosomes 1, 3, 4, 7, 8, 9, 11, 17, etc., in urothelial cancers. 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 specimens with probes for chromosome 3, 7, 17, and 9p21, and allows observation of the cells under a fluorescence microscope. Reported sensitivity of UroVysion test is higher for higher-grade tumors (83–97%) and CIS (almost 100%), than 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 urothelium that is at risk of malignant transformation.

REFERENCE

Lokeshwar VB, et al. Bladder tumor markers beyond cytology: International Consensus Panel on bladder tumor markers. Urology 2005;66(6, Suppl 1):35–63.

FISTULA, ENTEROVESICAL

DESCRIPTION An abnormal fistulous communication between the bowel (such as colovesical fistula) and urinary bladder due to various inflammatory and neoplastic causes. Usually presents with fecaluria, pneumaturia, and/or recurrent UTI. Gouverneur syndrome is the “classic” presentation of vesicoenteric fistula: Suprapubic pain, urinary frequency, dysuria, and tenesmus. Causes include inflammatory processes (diverticulitis, Crohn disease), neoplasia (bladder or colonic malignancy), and radiation. Diagnosis may require the use of 1 diagnostic modality, such as endoscopy (colonoscopy, cystoscopy), contrast imaging (cystography, contrast enema), and CT. Oral activated charcoal and urinary straining on a stone filter may be useful, as well as the Bourne test (see Section II: “Bourne Test.”)

TREATMENT

- Surgical resection of fistulous tract with or without fecal and urinary diversion
- Fecal and urinary diversion
- Conservative management

REFERENCE

Kavanagh D, et al. Diagnosis and treatment of enterovesical fistulae. Colorectal Dis 2005;7(3): 286–291.

FISTULA, RECTOURETHRAL

DESCRIPTION An abnormal communication between the urethra and rectum, almost exclusively in males due to anatomic reasons. May present with passage of urine in the stools. Causes include iatrogenic (transurethral instrumentation and surgery, radical prostatectomy, cryosurgery or radiotherapy of prostate), trauma, inflammatory bowel disease, pelvic infection, or congenital malformations. Diagnosis may require the use of 1 diagnostic modality, such as endoscopy (proctosigmoidoscopy, cystoscopy), contrast imaging (urethrocystography, contrast enema), CT or MRI with endorectal coil.

TREATMENT

- Surgical excision of fistulous tract, urethral repair, tissue interposition, and rectal closure with possible use of advancement flaps or vascularized flaps
- Posterior trans-ano-sphincteric, transperineal, transanal, transabdominal approaches described
- Possible vascularized flaps include dartos flap, scrotal myocutaneous flap, island groin flap, gracilis flap, and omental flap.
- Proximal bowel diversion usually recommended
- Fecal and urinary diversion
- Conservative management

REFERENCE

Gupta G, et al. Surgical management of rectourethral fistula. Urology. 2008;71(2):267–271.

FISTULA, URETEROARTERIAL

DESCRIPTION May present with microscopic hematuria, intermittent gross hematuria, or torrential hemorrhage in extremis. Risk factors include prior pelvic surgery, chronic indwelling ureteric stents, pelvic irradiation, and arterial disease. Rarely, this is the etiology for hematuria, but should be considered for persistent 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 uretero-pyelography, and angiography may be nonspecific but aid in planning reconstructive options. Removal of stents 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
  - Ureteric reconstruction by uretero-ureterostomy, cutaneous ureterostomy, transverse ureteroureterostomy, or ureteric ligation with nephrostomy
- In the actively bleeding patient, immediate surgical intervention or angiographic occlusion

REFERENCE

Krambeck AE, et al. Ureteroiliac artery fistula: Diagnosis and treatment algorithm. Urology 2005;66:990–994.

FISTULA, VESICOCUTANEOUS

DESCRIPTION An abnormal communication between the urinary bladder and skin of the anterior abdominal wall or groin. The fistulous tract that exists after placement of suprapubic catheter is the most commonly seen. Causes include urinary diversion (suprapubic catheterization); infected urachal remnant; radiation; dehiscence of urinary bladder repair, usually in association with complex pelvic and bowel surgery; and others (bladder calculus, inguinoscrotal hernia). Diagnosis is made by cystoscopy and CT contrast imaging.

TREATMENT

- Surgical excision of fistulous tract and repair
- Conservative management

REFERENCE

Kobori Y, et al. Vesicocutaneous fistula caused by giant bladder calculus. Urol Res 2007;35(3):161–163.

FISTULA, VESICOUTERINE

DESCRIPTION Rare, usually caused by simultaneous injury to uterus and bladder. Urinary incontinence is present if the cervical os is incompetent. The lesion occasionally presents with Youseff syndrome, which describes menouria (urine in menses), cyclic hematuria with apparent amenorrhea, infertility, and urinary incontinence in patient with prior low-segment caesarean section, which is the most common cause. Other causes include uterine rupture during obstructed labor tearing the posterior bladder wall, placenta percreta, and others (IUD, brachytherapy, traumatic bladder catheterization). Differential diagnosis includes vesicovaginal fistula, ureterovaginal fistula, and endometriosis of bladder. Diagnosis is made by cystography, cystography, and contrast CT or MRI of the pelvis, which helps exclude concomitant ureteric injury.

TREATMENT

- Prolonged bladder drainage with or without fulguration of fistula tract, and await spontaneous resolution. Option of hormonal induction of menopause to help induce involution of uterus.
- Surgical management:
  - Hysterectomy and bladder repair, if fertility not desired
  - Uterus-sparing surgery if fertility preferred

REFERENCE

Rao MP, et al. Post caesarean vesicouterine fistulae-Youssef syndrome: Our experience and review of published work. ANZ J Surg 2006; 76(4):243–245.

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 continuous urinary incontinence, with prior history of recent pelvic or gynecologic surgery or other causes.

CAUSES

- Iatrogenic obstetric and gynecological surgery
- Pelvic malignancy
- Irradiation
- Inflammatory: Pelvic and abdominal infections
- Trauma
- Foreign body

DIAGNOSIS

- Pelvic examination, “3-sponge test” with instillation of colored fluid in bladder.
- Cystoscopy with cystography and/or retrograde pyelography
- Contrast imaging (eg, IVP, CT urography)

TREATMENT

VVF and UVF should be considered an urgent gynecologic and urologic event. Early delineation of the fistula and anatomy is vital. UVF should be managed early by reimplantation of ureter. Consider early primary repair of VVF. Even small VVFs seldom close spontaneously with simple bladder drainage by Foley catheter, so advocate early repair rather than delay. If diagnosis has been delayed by several weeks, then it is prudent to delay repair to 3 mo. Principles of VVF repair include:

- Good preoperative planning and demarcation of fistula
- Approaches: Transvaginal, transabdominal
- Excise diseased tissue, layered closure with interrupted absorbable sutures
- Consider vascularized tissue interposition, especially when quality of tissue healing is expected to be compromised (eg, previous failed repair, post-irradiation, diabetes, infection)
- Martius labial rotation flap, pedicled muscle flap, peritoneal flap, omental flap
- Adequate bladder drainage

REFERENCE

Chapple C, Turner-Warwick R. Vesico-vaginal fistula. BJU Int 2005;95(1):193–214.

FITZ-HUGH-CURTIS SYNDROME

DESCRIPTION Perihepatic inflammation and right upper-quadrant pain found in a small segment of patients with pelvic inflammatory disease (PID). PID is a polymicrobial, ascending, post-coital infection of the upper genital tract usually associated with gonorrhea, Chlamydia, Haemophilus, or Streptococcus. Fitz-Hugh-Curtis is believed to occur from transperitoneal or vascular dissemination of PID organisms, often suggesting a profound pathologic inoculation. The diagnosis is confirmed by laparoscopic visualization of filmy perihepatic adhesions.

REFERENCE

Torrealday S, et al. Benign gynecologic conditions. Surg Clin N Am 2008;88:245–264.

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. Flank “bulge” is not a true hernia and is believed to be due to laxity of the transversus and oblique abdominal wall muscles, caused by injury to the intercostal nerves, in particular the 11th intercostal, and accentuated in part by unopposed contraction of contralateral musculature. About 15% of patients develop flank bulge after a retroperitoneal flank incision. Care should be taken to avoid injury to the intercostal nerves during incision and closure.

TREATMENT

- Flank hernia: Generally should be repaired with or without mesh, unless patient is asymptomatic or infirm, in which case a corset can be offered
- Flank bulge: Repair seldom needed except for cosmesis

REFERENCE

Gardner GP, et al. The retroperitoneal incision. An evaluation of postoperative flank “bulge.” Arch Surg 1994;129(7):753–756.

FLUORESCENT CYSTOSCOPY

DESCRIPTION Drugs for fluorescence diagnosis, such as 5-ALA and hexaminolevulinate (Hexvix), are placed intravesically where they preferentially stain malignant or premalignant tissue and emit a red fluorescence when excited by visible violet light. Fluorescent cystoscopy (93%) sensitivity is superior to white-light cystoscopy (73%). It is limited by specificity, which is equivalent to or poorer than white-light cystoscopy. Consider fluorescent cystoscopy to enhance the diagnosis of patients with positive cytology, and for surveillance of high-risk bladder cancers/CIS. At publication, Hexvix is approved in Europe but not in the US.

REFERENCE

Jocham D, et al. Photodynamic diagnosis in urology: State-of-the-art. Eur Urol 2008;53(6):1138–1150.

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 ureterotomy and a 5-0 chromic stay suture is placed. Interrupted 5-0 chromic sutures are used to complete the anastomosis. Used for UPJ repair.

REFERENCE

Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, et al. eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:220–233.

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. Amazonian parasitic catfish (Candiru) and leeches have also been reported to enter the urethra while bathing in a river. Symptoms include urethral pain, dysuria, urinary retention, hematuria, frequency, painful voiding, weak stream, and sepsis. (See also Section II: “Bladder Filling Defect.”)

TREATMENT

- Urethral foreign body: Endoscopic retrieval may be easier by 1st pushing back into bladder; alternatively, urethrotomy, especially when periurethral abscess is present
- Bladder foreign body: Endoscopic retrieval; open vesicostomy.

REFERENCE

Van Ophoven A, DeKernion JB. Clinical management of foreign bodies of the genitourinary tract. J Urol 2000;164(2):274–287.

FOSSA NAVICULARIS DIVERTICULUM

DESCRIPTION First described by Guérin (1864), this diverticulum is partially separated from the urethra by a septum. On 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 urethra being formed by the urethral folds. 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.

REFERENCE

Seskin FE, Glassberg KI. Lacuna magna in 6 boys with post-void bleeding and dysuria: Alternative approach to treatment. J Urol 1994;152(3): 980–982.

FOWLER-STEPHENS ORCHIOPEXY

DESCRIPTION This procedure is used to treat intra-abdominal testes. It entails ligating the spermatic vessels and allows the testes to survive from the vasal and cremasteric collaterals. The operation was originally described as a 2-stage procedure in which the vessels are divided, and then 6 mo later the testes are brought down to the scrotum, after collaterals have become well developed. It is now commonly performed using laparoscopy.

REFERENCE

Esposito C, et al. Long-term outcome of laparoscopic Fowler-Stephens orchiopexy in boys with intra-abdominal testis. J Urol 2009;181(4): 1851–1856.

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 bilateral macro-orchidism are also seen. Measurement of testis size in mentally retarded males has been suggested as a simple screening test for this condition.

REFERENCE

Hagerman RJ. Fragile X syndrome. Molecular and clinical insights and treatment issues. West J Med 1997;166(2):129–137.

FRALEY SYNDROME

DESCRIPTION A condition in which vascular obstruction of the superior infundibulum might lead to hydrocalyx, bleeding, and intermittent flank pain infection. Vessels causing obstruction may be arteries, veins, or both. Impaired drainage on delayed films or isotope renography must be confirmed before surgery. On US, diuretics will accentuate the caliectasis. Surgery provides relief.

REFERENCE

Fraley EE. Vascular obstruction of superior infundibulum causing nephralgia: A new syndrome. N Engl J Med 1966;275:1403.

FRENCH CATHETER SCALE

DESCRIPTION Used to measure the outer diameter of catheters, cystoscopes, and other endoscopes. The diameter in millimeters of the instrument is determined by dividing 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

Bedside procedures. In: Gomella LG, Haist SA, eds. Clinicians Pocket Reference, 11th ed. New York: McGraw-Hill, 2007.

FREQUENCY, URINARY

DESCRIPTION An entirely subjective symptom, 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 one of many complaints included in the nonspecific, nondiagnostic symptom complex known as lower urinary tract symptoms or LUTS. Frequency is further categorized as one of the storage symptoms (experienced during the bladder filling phase or storage phase of micturition), as opposed to the voiding or postmicturition symptoms.

REFERENCE

Wein A, et al. The standardization of terminology in lower urinary tract function: Report from the standardization sub-committee of the international continence society. Urology 2003;61:37–49.

FREQUENCY-DYSURIA SYNDROME

DESCRIPTION Occurring in children and women, this is also called “urethral syndrome.” Patients present with complaints of frequency and dysuria, but evaluation finds no infectious, anatomic, functional, or physiologic abnormalities. Because this term is so nonspecific, it is not a currently accepted meaningful term for diagnosis or treatment planning. In childhood, hypercalciuria was theorized and in adults, fastidial organisms were once thought to be the cause. (See also Section II: Urethral Syndrome.)

REFERENCE

Brock JW III. The frequency and frequency dysuria syndromes of childhood: Hypercalciuria as a possible etiology. Urology 1994;44(3):411–412.

Gillespie WA, et al. Microbiology of the urethral (frequency and dysuria) syndrome. A controlled study with 5-year review. Br J Urol 1989;64(3):270–274.

FUHRMAN NUCLEAR GRADING CLASSIFICATION, RENAL CELL CARCINOMA

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, uniform nuclei with minute or absent nucleoli. Grade 2 is slightly irregular nuclei about 15 m, with nucleoli visible at 400×. Grade 3 is more irregular nuclei, 20 m, with nucleoli visible at 100×. Grade 4 is similar to grade 3, with bizarre feature noted.

REFERENCE

Eble JN. Neoplasms of the kidney. In: Bostwick D, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

FUNGURIA

DESCRIPTION Funguria (sometimes called candiduria due to the frequent finding of Candida species) refers to fungus in the urine (fungal UTI of the 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 (such as Aspergillus sp., Fusarium, others). Associated predisposing factors include catheters, antibiotics, diabetes mellitus, hospitalization, and immunocompromised states. Urinary colonization is usually asymptomatic, whereas invasive fungal infection of bladder may have irritative voiding symptoms. Fungal infection of the kidney is often hematogenous 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, Genitourinary”; Section II: “Bezoars, Genitourinary.”)

TREATMENT

- Remove predisposing factors
- Asymptomatic candiduria rarely requires antifungal therapy (unless in the setting of neutropenia, neonates, or urinary tract instrumentation):
  - Fluconazole, 200–400 mg (3–6 mg/kg) daily for several days if urinary tract instrumentation is planned.
- Symptomatic cystitis: Fluconazole 200 mg (3 mg/kg) daily for 2 wk or amphotericin B 0.3–0.6 mg/kg for 1–7 days; or flucytosine 25 mg/kg q.i.d. for 7–10 days. Amphotericin B bladder irrigation is recommended only for fluconazole-resistant organisms (eg, C. krusei and C. glabrata).

Symptomatic infections should be treated.

- Bezoars should be removed (see also Section II: “Bezoars”).

REFERENCE

Pappas PG, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48:503.

FUNICULITIS

DESCRIPTION Inflammation of the spermatic cord; the entire spermatic cord is subject to inflammatory diseases, usually as a result of trauma or pyogenic bacteria (termed funiculitis), and this condition is occasionally seen with scrotal inflammation or epididymitis. Parasitic infections (filariasis, schistosomiasis) can also induce inflammatory changes in the cord (see also Section I: “Spermatic Cord Mass”).

REFERENCE

Sabiston D. Textbook of Surgery, 15th ed. Philadelphia: Saunders, 1997.

SHORT TOPIC SECTION G

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 ethical or religious objections to IVF and prefer fertilization in vivo rather than in vitro. Technique involves inducing superovulation, aspirating the ovarian follicles vaginally under US guidance, and identifying eggs. Sperm is collected and capacitated. During laparoscopy, sperm and eggs are mixed and transferred into one of the fallopian tubes, allowing in vivo fertilization. A 20–30% pregnancy rate per cycle is reported. Limitations of GIFT are that patients must have normal fallopian tubal function and the procedure requires general anesthesia and laparoscopy.

REFERENCE

1. DeUgarte CM, et al. Assisted reproductive technologies: In vitro fertilization & related techniques. In: DeCherney AH, Nathan L, eds. Current Diagnosis & Treatment Obstetrics & Gynecology, 10th ed. New York: McGraw-Hill, 2006.

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 varied in appearance and malignant potential, with prognosis and behavior depending on histology. The cause is unknown, but it has been reported to have a genetic predisposition. Treated by surgical resection.

REFERENCE

2. Koike K, et al. Adult-type ganglioneuroblastoma in the adrenal gland treated by a laparoscopic resection: report of a case. Surg Today 2003;33(10):785–790.

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

3. Gupta R, Dinda AK. Ganglioneuroma of the adrenal gland: A rare case. Indian J Pathol Microbiol 2007; 50(4):782–784.

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 ureteric bud from the mesonephric duct that leads to persistence of the Gartner duct, often with cystic dilation. The Gartner duct is associated with Müllerian duct developmental anomalies and with abnormal ureteric development, such as ureteric ectopia. Abnormal development of the ureter also results in the maldevelopment, ectopic kidney, or absence of the ipsilateral kidney. The usual presentation is an anterior vaginal wall mass with ipsilateral renal dysgenesis with or without urinary incontinence. Differential diagnoses include ectopic ureterocele, urethral diverticulum, urethral tumor, Skene gland cyst or abscess, and vaginal wall cysts or tumors. Diagnosis is by voiding cystourethrography, cystourethroscopy, and retrograde pyelography (maldevelopment of the bladder neck and hemitrigone; ureteric ectopia or ureteric dysgenesis) and renal and bladder US (a cystic lesion behind bladder is suggestive of Gartner duct cyst and ipsilateral renal agenesis or ectopic kidney). Treated surgically, depending on anatomic anomalies, including transvaginal or transabdominal excision of the Gartner duct and closure of any associated urinary fistula; reconstruction of bladder neck and urethra; reimplantation of ipsilateral and/or contralateral ureter; or removal of nonfunctioning renal unit and ectopic ureter.

REFERENCE

4. Dwyer PL, Rosamilia A. Congenital urogenital anomalies that are associated with the persistence of Gartner’s duct: A review. Am J Obstet Gynecol 2006;195:354–359.

GENITAL PIERCING, UROLOGIC CONSIDERATIONS

DESCRIPTION Urologists must be familiar with complications from genital piercing. In males, piercings include the penile glans, shaft, urethra, scrotum, and combinations of these. Clitoral and labial piercings 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
- Priapism
- Paraphimosis
- Recurrence of condyloma acuminatum
- Urethral fistula
- Hypertrophic scarring, keloid
- Trauma during intercourse: To partner or self

REFERENCE

5. Anderson W, et al. The urologist’s guide to genital piercing. BJU Int 2003;91(3):245–251.

GERM CELL APLASIA (SERTOLI 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 fine-needle aspiration of the testis. 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.

REFERENCE

6. Odabas O, et al. Assessment of the testicular cytology by fine-needle aspiration and the imprint technique: Are they reliable diagnostic modalities? Br J Urol 1997;79(3):445–448.

GIBBON CLASSIFICATION OF VOIDING DYSFUNCTION

DESCRIPTION Historic classification based in large part on the system proposed by Bors-Comarr. 5 categories are proposed to be important: (1) Full general and neurologic diagnosis, (2) state of the bulbocavernosus and anal reflexes in cord injuries, (3) presence or absence of reflex detrusor contractions, (4) urodynamic findings, and (5) failure of storage, emptying, or control when dealing with incontinence.

REFERENCE

7. Gibbon NOK. Nomenclature of neurogenic bladder. Urology 1976;8:423.

GIBSON INCISION

DESCRIPTION A curvilinear incision is made starting 2–3 cm medial to the anterior superior iliac spine, running parallel to the inguinal ligament down to 2–3 cm superior and just lateral to the pubic tubercle. The external and internal obliques and the transversalis muscle are bluntly opened along their fibers. After transecting the transversalis fascia, the peritoneum is swept medially to expose the ureter at its midsection. Useful for distal ureteral stones and renal transplant.

REFERENCE

8. Montague DK. Surgical incisions. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:15–40.

GIL-VERNET ORTHOTOPIC URINARY DIVERSION

DESCRIPTION A continuous segment of terminal ileum, cecum, and ascending colon are 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.

REFERENCE

9. Benson MC, Olsson CA. Continent urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:3190–3245.

GIL-VERNET URETERAL REIMPLANTATION

DESCRIPTION Through a transvesical approach, the ureters are dissected free from their hiatus. The principle involves advancing the ureters across the trigone to the midline such that both ureteral orifices are juxtaposed. A single incision is made in the trigone mucosa, which will serve to join traction sutures from each ureter that are anchored in the midline.

REFERENCE

Atala A, Keating MA. Vesicoureteral reflux and megaureter. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:1882–1896.

GITTES NEEDLE URETHROPEXY

DESCRIPTION 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 proline suture is used to suspend the bladder neck on both sides, and the vaginal sutures eventually cut through the wall and become buried in scar. Used to treat stress incontinence.

REFERENCE

Benson JT, et al. Evaluation of a minimal-incision pubovaginal suspension as an adjunct to other pelvic-floor surgery. Obstet Gynecol 1990;75(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 radical prostatectomy, even when present in a small percentage of total tumor volume, has prognostic significance. Its presence is associated with biochemical recurrence and adverse pathologic features such as seminal vesicle invasion, extraprostatic extension, and positive surgical margins.

REFERENCE

Harnden P, et al. Should the Gleason grading system for prostate cancer be modified to account for high-grade tertiary components? A systematic review and meta-analysis. Lancet Oncology 2007;8(5):411–419.

Sim HG, et al. Tertiary Gleason pattern 5 in Gleason 7 prostate cancer predicts pathological stage and biochemical recurrence. J Urol 2008;179: 1775–1779.

GLEASON GRADING SYSTEM, PROSTATE CANCER

DESCRIPTION A widely accepted system to describe the aggressiveness of prostatic 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 summated to give the Gleason score (or Gleason sum). Gleason system, the most prevalent and the 2nd most prevalent pattern (if at least 5% of the tumor) are added together to obtain a Gleason score (e.g., Gleason grade 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 this separation usually distinguishes 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 cancers 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 one should be able to draw an imaginary circle around each of them. Cribriform glands may also be Gleason pattern 3, with these glands being slightly larger than benign glands and having regular outer contours. They resemble intraductal cribriform carcinoma of the breast. Cribriform pattern 3 must be separated from cribriform pattern 4, intraductal 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 lumen formation, or cribriform. Fused glands are chains, nests, or masses of glands that are no longer completely separated by intervening stroma. Fused glands contain rare 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 “hypernephromatoid” pattern described by Gleason is an uncommon variant of fused glands and resembles renal cell carcinoma. Cribriform glands of pattern 4 are either large cribriform glands (cribriform sheets) or small cribriform glands with irregular infiltrating borders. The small cribriform glands with irregular infiltrating borders of pattern 4 must be distinguished from cribriform pattern 3, in which the small cribriform 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 comedonecrosis 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 comedonecrosis is present. Separating poorly defined pattern 4 glands from cords 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 8–10, all of which are poorly differentiated.

REFERENCE

Egevad L, et al. Gleason Grading of prostate carcinoma. Available at: www.pathology2.jhu.edu/gleason/patterns.cfm.

Harnden P, et al. Should the Gleason grading system for prostate cancer be modified to account for high-grade tertiary components? A systematic review and meta-analysis. Lancet Oncology 2007;8(5):411–419.

GLEASON GRADING SYSTEM, MODIFIED

DESCRIPTION The International Society of Urologic Pathology held a consensus conference in 2005 at which the “old Gleason grading system” for prostatic carcinoma from 1966 underwent its 1st major revision. With this modified grading system, a shift of the most frequent Gleason scores from 6–7a (3 + 4) in biopsy specimens and an increased degree of agreement between specimens 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 pT3–4. 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 of >20% had higher scores (7b or higher). Cancers with tumour infiltration of <1 mm in 1 of 12 cores and PSA <10 ng/mL were mainly low grade (Gleason scores 6 and 7a) and may correspond to so-called insignificant carcinoma of the prostate. Using the modified Gleason system, grade, stage, tumor extent, and serum PSA show good correlations and characterize the difference between low- and high-grade malignancy of the prostate.

REFERENCE

Helpap B, Egevad L. Modified Gleason grading. An updated review. Histol Histopathol 2009;24(5): 661–666.

GLENN-ANDERSON URETERONEOCYSTOSTOMY

DESCRIPTION Through a transvesical approach, the ureter is mobilized from its hiatus and advanced toward the bladder neck through a submucosal tunnel, where it is reimplanted. Used to reimplant ureter in reflux or resection of ureter.

REFERENCE

Kay R. Reimplantation of the ureter. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989: 526–538.

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 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

Gusmano R, et al. Glomerulocystic kidney disease. Nephrol Dial Transplant 2002;17:813–818.

GLOMERULOSCLEROSIS

DESCRIPTION An accumulation of homogenous eosinophilic material in the glomerulus, made up of plasma proteins that have exuded 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 endothelial or capillary wall injury and the end result of various forms of glomerular damage.

REFERENCE

Alpers CE. The kidney. In: Kumar V, Abbas AK, Fausto N, eds. Robbins and Cotran: Pathologic Basis of Disease, 7th ed. Philadelphia: Elsevier Saunders, 2005.

GLUCAGON STIMULATION TEST

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 (catecholamines only modestly elevated). 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. A rise in plasma norepinephrine to greater than 3-fold or greater than 2000 pg/mL is diagnostic of pheochromocytoma.

REFERENCE

Guber HA, et al. Evaluation of endocrine function. In: McPherson RA, Pincus MR, eds. Henry's Clinical Diagnosis and Management by Laboratory Methods, 21st ed. China: Saunders Elsevier, 2007.

GLYCOSURIA, RENAL

DESCRIPTION Normal urine contains small amounts of glucose. Increased amounts represent either inefficient handling by the tubule or hyperglycemia. Diabetes is the most common cause of glycosuria. Causes of primary glucosuria are either intestinal glucose-galactose 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 causative. Glycosuria may also be part of Fanconi syndrome or RTA.

REFERENCE

Brodehl J, Demar BS, Hoyer PF. Renal glucosuria. Pediatr Nephrol 1987;1(3):502–508.

GOLDSTEIN TEST

DESCRIPTION Intraoperative diagnostic pneumoperitoneum, also known as Goldstein test, is done in the setting of pediatric open inguinal hernia repair. To prevent unnecessary contralateral inguinal exploration, the test is performed by introducing a soft rubber catheter through the ipsilateral hernia sac. Air is insufflated into the peritoneal cavity, distending it, and the contralateral groin is palpated for crepitus. The presence of crepitus constitutes a positive test and necessitates repair of metachronous hernia. Currently, this practice has been largely supplanted by the use of laparoscopy.

REFERENCE

Haynes JH. Inguinal and scrotal disorders. Surg Clin N Am 2006;86(2):371–381.

GOLDSTON 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 triads with a double band of fibrous tissue without bile ducts. The brain shows the Dandy-Walker malformation, which is the cystic dilation of the 4th ventricle, secondary to obstruction of the foramina of Luschka and Magendie. Renal replacement therapy, as indicated, and hydrocephalus requiring a shunt are standard treatments.

REFERENCE

Gloeb DJ, et al. The Goldston syndrome: Report of a case. Pediatr Pathol 1989;9(3):337–343.

GONADAL DYSGENESIS, MIXED

DESCRIPTION Gonadal dysgenesis syndromes include Turner syndrome (45,XO), 46XX "pure" gonadal dysgenesis, mixed gonadal dysgenesis (45,XO/46,XY), partial gonadal dysgenesis (aka, dysgenetic male pseudohermaphroditism), and bilateral vanishing testis syndrome. It is the second most common cause of ambiguous genitalia in the newborn after CAH. Mixed gonadal dysgenesis is characterized by unilateral testis, 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. Usual karyotype is 45,XO/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 fallopian tubes, but with varying degrees of phallic development, labioscrotal fusion, and undescended testis. Increased risk exists of gonadoblastoma (incidence 20%) in either dysgenetic testis or streak gonad (more frequently testis), as well as an increased risk of Wilms tumor. Clinical diagnosis is at 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 gonadectomy (if male, consider prophylactic gonadectomy versus bringing testis down to scrotum for purpose of screening of gonadoblastoma).
- Screen for Wilms tumor.
- Initiate appropriate sex and growth hormone replacement.

REFERENCE

Kolon TF. Disorders of sexual development. Curr Urol Rep 2008;9(2):172–177.

GONADAL DYSGENESIS, PURE

DESCRIPTION 46 XX “pure” gonadal dysgenesis (“bilateral streak gonads”) is closely related to Turner syndrome, except that it lacks the somatic stigmata associated with Turner syndrome. Patients present with amenorrhea and lack of pubertal development. Evaluation reveals normal female external genitalia and Müllerian ducts, absent Wolffian ducts, normal height, sexual infantilism, bilateral streaked gonads, and 46,XX karyotype. A streak gonad is dysgenetic and resembles ovarian stromal tissue, but no germ cells are present. This is an autosomal recessive trait with no increased risk of gonadoblastoma (unlike in mixed gonadal dysgenesis). It is treated with cyclic estrogen and progesterone replacement. (See also Section I: Disorders of Sexual Development [DSD]; Section II: Gonadal Dysgenesis, Mixed.)

REFERENCE

Kolon TF. Disorders of sexual development. Curr Urol Rep 2008;9(2):172–177.

GONADOBLASTOMA

DESCRIPTION Rare tumor comprising 0.5% of all testes tumors that occurs almost always in gonadal dysgenesis (intersex disorders). This is abenign tumor that has the potential for malignant transformation. Patients present either with a palpable mass or virilization secondary to androgen production. It has 2 distinct cell types: large germ cells (similar to dysgerminoma and seminoma) and small cells resembling immature Sertoli or granulosa cells. Tubules microscopically contain PAS-positive staining Call-Exner bodies. Upregulation of the TSPY gene is implicated in this tumor. (See also Section II: Turner Syndrome.)

SYNONYMS

- Tumors of dysgenetic gonads
- Mixed germ cell tumor
- Gonadocytoma

TREATMENT

- With an intersex disorder or Turner syndrome: Prophylactic removal of the dysgenic gonad prior to developing gonadoblastoma
- Radical orchiectomy with possible contralateral orchiectomy secondary to high incidence of bilaterality

REFERENCE

Brant WO, et al. Gonadoblastoma and Turner syndrome. J Urol 2006;175(5):1858–1860.

GOODPASTURE SYNDROME

DESCRIPTION Characterized by a triad of pulmonary hemorrhage, iron deficiency anemia, and glomerulonephritis, representing <1% of all cases of GN. Anti-GBM antibody deposition in the lungs and kidneys 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 production
- Renal replacement therapy for ESRD

REFERENCE

Shah MK, Hugghins SY. Characteristics and outcomes of patients with Goodpasture's syndrome. South Med J 2002;95(12):1411–1418.

GOODWIN URETERAL ANASTOMOSIS

DESCRIPTION Through a transcolonic approach, a nonrefluxing anastomosis is performed by raising a tunnel of mucosa 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 colonic mucosa while incorporating some muscularis for security.

REFERENCE

McDougal WS. Use of intestinal segments and urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3137–3144.

GORLIN SYNDROME

DESCRIPTION Autosomal dominant cancer condition characterized by increased risk of multiple basal cell carcinomas. Features include disorders of the skin, skeletal, eye, nervous system, and endocrine glands. The lesions are sensitive to ionizing radiation.

SYNONYMS

- Nevoid basal cell carcinoma syndrome
- Basal cell nevus syndrome

REFERENCE

Mitchell G, Farndon PA, Brayden P, et al. Genetic predisposition to cancer: The consequences of a delayed diagnosis of Gorlin syndrome. Clin Oncol (R Coll Radiol) 2005;17(8):650–654.

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 20% 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: Urolithiasis, Uric Acid.)

TREATMENT

- Alkalinization of urine and increasing urine output help prevent stones.
- Allopurinol or following a low-purine diet will decrease serum urate levels.

REFERENCE

Liebman SE, Taylor JG, Bushinsky DA. Uric acid nephrolithiasis [review]. Curr Rheumatol Rep 2007;9(3):251–257.

GOUVERNEUR SYNDROME

DESCRIPTION Classic presentation of vesicoenteric fistula, with suprapubic pain, urinary frequency, dysuria, and tenesmus.

REFERENCE

Vidal Sans J, et al. Review of 31 vesicointestinal fistulas: Diagnosis and management. Eur Urol 1986;12(1):21–27.

GRANULOMA INGUINALE (DONOVANOSIS)

DESCRIPTION Ulcerative disease of the genitals with significant locoregional lymphadenopathy, caused by Klebsiella granulomatis. Ulceration at site inoculation may be on the genitals or extragenital sites, and prominent lymphadenopathy often results in further skin ulceration over the nodes. Untreated, it results in lymphedema and genital mutilation. (See also Section I: Sexually Transmitted Disease.)

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. Azithromycin is therapy of choice.

REFERENCE

O'Farrell N. Donovanosis. Sex Transm Infect 2002; 78:452–457.

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

Chan YF, et al. Juvenile granulosa cell tumor of the testis: Report of 2 cases in newborns. J Pediatr Surg 1997;32(5):752–753.

GRATIFICATION DISORDER

DESCRIPTION Also known as infantile masturbation, usually peaks at 4 yr but can be seen as early as 3 mo 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

Yang ML, et al. Masturbation in infancy and early childhood presenting as a movement disorder: 12 cases and review of the literature. Pediatrics 2005;116:127–1432.

GRIESS TEST

DESCRIPTION Detects the presence of nitrite in urine, which is formed when bacteria reduce the normally present nitrate. With a lower sensitivity and specificity than microscopy and culture, this test in combination with leukocyte esterase has been used to screen asymptomatic patients. Microscopy is indicated for the higher-risk population for UTI.

REFERENCE

Schaeffer AJ. Urinary tract infections. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

GRISS SEX FUNCTION INDEX

DESCRIPTION Golombok-Rust Inventory of Sexual Satisfication (GRISS) is 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 subscales of erectile dysfunction, orgasmic disorders, vaginismus, and male and female nonsensuality. It may be used in individuals undergoing marital or sex therapy.

REFERENCE

Wiegel M, et al. Sexual dysfunction In: Barlow D, et al., eds. Assessment and Treatment Planning for Psychological Disorders. New York: Guilford Press, 2002.

GROIN HERNIA, PEDIATRIC

DESCRIPTION The most common surgery in the pediatric age group. Most hernias in this population are indirect and congenital. The incidence is higher in preterm births, with a male to female ratio of 6:1. The hernia is formed from the persistence of the processus vaginalis and can present as a communicating hydrocele, hydrocele of the cord, simple hydrocele, or incarceration and strangulation of intraperitoneal contents. Surgical repair is usually indicated.

REFERENCE

Warner BW. Pediatric surgery. In: Townsend CM, et al., eds. Sabiston Textbook of Surgery, 18th ed. Philadelphia: Saunders, 2008.

GUILLAIN-BARRé (TRANSVERSE MYELITIS) SYNDROME: UROLOGIC CONSIDERATIONS

DESCRIPTION Also known as acute inflammatory demyelinating polyneuropathy, an inflammatory demyelinating disorder of the autonomic and peripheral nervous system. It is thought to be triggered by a bacterial or viral antigen, causing the immune system to cross-react and attack self 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 urge and stress incontinence to urinary retention.

TREATMENT

- Manage lower urinary tract dysfunction (CIC, anticholinergics, etc.)
- Plasmapheresis
- IV immunoglobulin

REFERENCE

Ganesan V, Borzyskowski M. Characteristics and course of urinary tract dysfunction after acute transverse myelitis. Dev Med Child Neurol 2001;43(7):473–475.

GUN SHOT WOUND, BLADDER

DESCRIPTION The urinary bladder, due to its location deep in bony pelvis, is less associated with penetrating trauma than most of GU organs. Penetrating bladder trauma is associated with significant nonurologic injuries and mortality. Injuries should be explored primarily and closed, and external drainage should be implemented. (See also Section I: Bladder Trauma.)

REFERENCE

Pérez Fentes DA, et al. Gunshot bladder trauma: Case report and literature review. Actas Urol Esp 2006; 30(9):947–953.

GUN SHOT WOUND, EXTERNAL GENITALIA

DESCRIPTION The genitalia have several characteristics that are somewhat protective against sustained injury. Characteristics such as the laxity 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 copious 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.”)

REFERENCE

Phonsombat S, et al. Penetrating external genital trauma: A 30-year single institution experience. J Urol 2008;180(1):192–195.

GUN SHOT WOUND, KIDNEY

DESCRIPTION The kidney is subject to the majority of external injuries in the GU system. Hematuria is a good indicator of injury but its amount or absence does not eliminate renal injury nor 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 pulsatile perirenal hematoma. Relative indications include urinary extravasation, nonviable 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 for the Kidney.”)

REFERENCE

Voelzke BB, McAninch JW. Renal gunshot wounds: clinical management and outcome. J Trauma 2009;66(3):593–600.

GUN SHOT WOUND, URETER

DESCRIPTION Penetrating injury to the ureter occurs in <4% of penetrating cases. In civilian gunshot injury, there is a high risk of associated injuries (ie, small bowel > large bowel, kidney, and bladder), and mortality approaches up to 1/3 of patients. The path of the bullet may not only directly injure the ureter but may also indirectly injure the blood supply, resulting in ureteral necrosis. Patients should be imaged for any degree of hematuria or a wound pattern that may suggest trauma to ureter. Open exploration should be preformed and debridement of the ureter back to a bleeding edge with a primary anastomosis (if possible) should be performed. (See also Section I: “Ureter, Trauma.”)

REFERENCE

Akay AF, et al. Gunshot injuries of the ureter: One centre’s 15-year experience. Acta Chir Belg 2006;106(5):572–577.

SHORT TOPIC SECTION H

HAILEY-HAILEY DISEASE (BENIGN FAMILIAL PEMPHIGOID)

DESCRIPTION Autosomal dominant skin disease arising from mutations of the ATP2C1 gene. The appearance begins as a flaccid 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 perianal areas). Lesions heal without scarring. Treatment involves antibiotics for superinfection, steroids, and dermabrasion.

REFERENCE

1. McKibben J, Smalling C. Hailey-Hailey. Skin Med 2006;5(5):250–252.

HALD-BRADLEY CLASSIFICATION OF VOIDING DYSFUNCTION

DESCRIPTION Based on the anatomic location of the neurologic lesion, voiding dysfunction is broken down into 5 classes: (1) Suprasacral, (2) suprasacral spinal, (3) infrasacral, (4) peripheral autonomic neuropathy, and (5) muscular lesions. Examples include coordinated voiding with hyperreflexia in suprasacral lesions, whereas muscular lesions may be a decompensated bladder from longstanding bladder outlet obstruction.

REFERENCE

2. Hald T, Bradley WE. The neurogenic bladder. In The Urinary Bladder, Neurology and Urodynamics. Baltimore: Williams and Wilkins, 1982.

HAND FOOT SYNDROME

DESCRIPTION Many oncologic medications have ben 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. Symptoms include tingling or burning, redness, flaking, swelling, and small blisters and sores on the palms of the hands or soles of the feet. Some patients experience eventual skin hardening.

SYNONYMS

- Palmar-plantar erythrodysesthesia (PPE)
- Plantar-palmar toxicity
- Palmoplantar keratoderma

TREATMENT

- Reduce exposure of hands and feet to friction and heat.
- Stopping the medication temporarily reduces the symptoms. The drug can often be restarted at a lower dose.

REFERENCE

3. Hutson TE, et al. Targeted therapies for metastatic renal cell carcinoma: An overview of toxicity and dosing strategies. Oncologist 2008;13(10): 1084–1096.

HAUTMANN 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 is arranged into an M or W shape. The limbs are sutured to each other with absorbable suture material to form a broad ileal plate. A preselected segment is anastomosed to the urethra, and the ureters are implanted in a LeDuc fashion. The plate is then closed into a pouch and anastomosed to the urethra.

REFERENCE

4. Hautmann RE, et al. The ileal neobladder. J Urol 1988;139(1):39–42.

HEIKEL-PARKKULAINEN REFLUX CLASSIFICATION SYSTEM

DESCRIPTION Described by Heikel and Parkkulainen in 1966, this system is used to grade vesicoureteral reflux based on ureteral diameter and pelvicaliceal dilatation. It gained much popularity in Europe. Later, features of this system were used to create the International Classification System, which is now the standard.

REFERENCE

5. Heikel RE, Parkkulainen KV. Vesico-ureteric reflux in children: A classification and results of conservative treatment. Ann Radiol 1966;9:37.

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 tumor, in which case US is helpful. Causes include trauma, infection, bleeding disorders, tumor, and rarely uremia. (See also Section I: “Scrotum and Testicle, Mass”; Section I: “Scrotum and Testicle, Trauma.”)

TREATMENT

- Conservative management if patient asymptomatic and diagnosis confirmed. Often, diagnosis by surgical exploration

REFERENCE

6. Leibovitch I, et al. Chronic hematocele complicating renal failure and hemodialysis. J Urol 1991; 146(1):162–164.

HEMATURIA, 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 RBCs 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 hypoxic changes secondary to the vasoconstriction of the splanchnic and renal vessels or to constriction of the efferent glomerular arteriola resulting in increased filtration pressures in the kidney. The hematuria should be distinguished from myoglobinuria and hemoglobinuria.

SYNONYMS

- Sports hematuria
- Athletically induced hematuria

TREATMENT

- The hematuria should be self-limited and provoked by strenuous exercise.
- Co-existing urologic pathology should be ruled if history or physical exam is suspicious.

REFERENCE

7. Abarbanel J, et al. Sports hematuria. J Urol 1990;7143:65887–65890.

HEMATURIA-DYSURIA SYNDROME

DESCRIPTION Hematuria-dysuria syndrome is the most common reported complication of gastrocystoplasty. The syndrome of dysuria and hematuria is defined as 1 or a combination of the following symptoms: Bladder spasm or suprapubic, penile or periurethral pain, coffee brown or bright red hematuria without infections, skin irritation or excoriation, and dysuria without infections.

REFERENCE

8. Chadwick PJ, et al. Long-term follow-up of the hematuria-dysuria syndrome. J Urol 2000;164(3 Pt 2): 921–923.

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. Recent literature has suggested that this syndrome is not a distinct clinicopathologic entity. A concerted medical and psychological approach is advocated.

REFERENCE

9. Hall R, Lailis A, Rapoport A. Hematuria-loin pain syndrome: Its existence as a discrete clinicopathological entity cannot be supported. Clin J Pain 1997;13(2):171–177.

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 <0.60 is seen in males who failed in vitro fertilization. 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

Yao YQ, et al. The factors affecting sperm binding to the zona pellucida in the hemizona binding assay. Hum Reprod 1996;11(7):1516–1519.

HEMORRHAGE, POSTOPERATIVE, UROLOGIC 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 dilation, 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

Srivastava A, et al. Vascular complications after percutaneous nephrolithotomy: Are there predictive factors. Urology 2005;66:38–40.

HEMOSIDERIN, URINARY

DESCRIPTION Hemosiderin occurs when hemoglobin is reabsorbed by the proximal tubular cells and then catabolized into ferritin and hemosiderin. Urinary hemosiderin can occur up to 2 days after an acute hemolytic episode, and is also demonstrated in chronic hemolytic states and hemochromatosis.

REFERENCE

McPherson R, Threatte G. Urine and other body fluids. In: McPherson RA, Pincus MR, eds. Henry's Clinical Diagnosis and Management by Laboratory Methods, 21st ed. Philadelphia: Saunders, 2006.

HENOCH-SCHöNLEIN PURPURA

DESCRIPTION A form of purpura with an underlying pathologic feature of vasculitis, affecting mainly small blood vessels. The disease is predominately seen in children. Clinically, the purpuric skin lesions are typically located on the lower extremities. However, the hands, arms, and trunk can be affected. Joint pain, abdominal pain, and GI bleeding may be present. Hematuria denotes a renal lesion, which is usually reversible. 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 sometimes IgG. Lab tests reveal high ESR and normal to high platelet counts. If renal involvement is not severe, the disease will subside without sequelae within 6 wk.

TREATMENT

- Currently no effective treatment is available.
- Immunosuppressive (steroids, cytotoxics) drugs have shown some success in nephropathies caused by that disorder.

REFERENCE

Assadi F. Childhood Henoch-Schönlein nephritis: A multivariate analysis of clinical features and renal morphology at disease onset. Iran J Kidney Dis 2009;3(1):17–21.

HEPATITIS A & B (HAV/HBV), UROLOGIC CONSIDERATIONS

DESCRIPTION HAV and HBV both belong to a family of 5 hepatropic viruses. HAV is a picornavirus and is mostly enterically transmitted by fecal–oral routes. Transmission has been noted in men who have sex with men and with oral–anal contact regardless of sexual preference. No significant transmission occurs through semen or vaginal secretions, but transmission through blood products is rare but possible. Extrahepatic manifestations include vasculitis, cardiac abnormalities, Guillain-Barré (transverse myelitis), and renal failure. HBV is a double-shelled hepadnavirus and is mostly transmitted parenterally, which can take place from mother to fetus, through blood products, and through cutaneous and mucosal exposure to infectious blood or bodily fluid. Unlike HAV, HBV has a chronic phase that may lead to hepatocellular carcinoma.

REFERENCE

Curry M, Chopra S. Acute viral hepatitis. In: Mandell et al., eds. Principles and Practice of Infectious Diseases, 6th ed. Philadelphia: Churchill Livingstone, 2005.

HEPATORENAL SYNDROME

DESCRIPTION Known as progressive oliguric renal failure complicating the course of end-stage liver disease, the cause is thought to be functional, due perhaps to discharge of the sympathetic nervous system and/or metabolic imbalances, including endothelin and nitric oxide. The prognosis usually involves recovery of renal function and for survival overall. Urine is characteristically hyperosmolar, with a high creatine-to-plasma ratio and a very low sodium concentration.

TREATMENT

- A transjugular intrahepatic portosystemic shunt has been attempted.
- Orthotopic liver transplantation

REFERENCE

Epstein M. Hepatorenal syndrome: Emerging perspectives. Semin Nephrol 1997;17(6):563–575.

HEREDITARY LEIOMYOMA RENAL CELL CARCINOMA (HLRCC) SYNDROME

DESCRIPTION HLRCC syndrome is manifested by uterine leiomyomas, multiple cutaneous leiomyomas, and renal cell carcinoma (papillary cell carcinoma). The disorder results from an autosomal dominant germline mutation encoding for fumarate hydratase. The renal tumors have been found to be aggressive, leading early metastases and death.

TREATMENT

- Early diagnosis and close follow-up
- Nephrectomy (partial or radical) when indicated

REFERENCE

Hayedeh G, et al. Hereditary leiomyomatosis and renal cell carcinoma syndrome: A case report. Dermatology Online J 2008;14(1):16.

HERNIA UTERINE INGUINALE

DESCRIPTION A cause of male pseudohermaphroditism, thought to be due to an isolated defect in the production of Müllerian inhibition substance or the response to MIF. This is a rare syndrome of Müllerian ducts persistence. Affected males are not ambiguous at birth and generally present later, most commonly with an inguinal hernia on 1 side and an impalpable contralateral testes. Hernia sac may contain uterus. Karyotype is 46,XY. The gonadal tissue is exclusively testicular. Both Wolffian and Müllerian duct derivatives are present, with a vas and epididymis alongside an ipsilateral uterus, fallopian tube, and upper vagina. Testes have malignant potential. No uterine or vaginal malignancies have been reported.

TREATMENT

- Sex assignment as male
- Primary or staged orchidopexy
- Müllerian structures do not require removal, as the vas may be damaged.

REFERENCE

Snyder HM. Intersex. Practical Cases in Urology. Series XIX, Course 4, 1996.

HIDRADENITIS SUPPURATIVA (ACNE INVERSA), UROLOGIC CONSIDERATIONS

DESCRIPTION A chronic suppurative disease of the apocrine gland–bearing areas of the body, such as the axilla, buttocks, and groin. Not primarily infectious; caused by plugging of the follicles. Secondary infection can occur after the follicle plugs, with resultant inflammatory response. Lesions resemble boils and can resolve without scarring but more typically result in fibrosis, keloids, and sinus tract formation. Mild cases resemble simple boils (furunculosis). Diagnosed primarily 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 genital 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 intralesional corticosteroids may be effective.
- Surgical excision and plastic repair of the affected areas may be necessary.

REFERENCE

Goldberg JM, et al. Advanced hidradenitis suppurativa presenting with bilateral vulvar masses. Gynecol Oncol 1996;160(3):494–497.

HINMAN SYNDROME (HINMAN-ALLEN SYNDROME)

DESCRIPTION 1st described in 1937 by Hinman and Bauman, this is a syndrome of vesicourethral dysfunction (dysfunctional voiding) that can produce signs of recurrent UTIs, vesical trabeculation, poor emptying, and hydronephrosis and possibly progress to renal failure. Hinman syndrome is thought to occur from bladder sphincteric dysfunction with no signs of neurologic cause and may begin in the neonate or in the child around the time of toilet training.

SYNONYMS

Nonneurogenic neurogenic bladder

TREATMENT

- Early intervention
- Clean intermittent catheterization (CIC)
- Cutaneous vesicostomy

REFERENCE

Mosawi AJ. Identification of nonneurogenic neurogenic bladder in infants. Urology 2007; 70:356–357.

HISTOPLASMOSIS, GENITOURINARY

DESCRIPTION Histoplasma capsulatum grows in soil enriched by bird guano, with outbreaks reported in caves, construction sites, and on bird farms. Disseminated virulent disease is seen in AIDS, children, and immunosuppressed individuals. GU involvement is a manifestation of systemic disease and can result in sloughed papilla, prostatic obstruction, or prostatic abscess. Epididymitis can resemble sperm granulomas. Up to 7% can experience adrenal insufficiency from adrenal destruction.

TREATMENT

2 g of amphotericin B with maintenance therapy with itraconazole to prevent relapse.

REFERENCE

Wise GJ, Freyle J. Changing patterns in genitourinary fungal infections. AUA Update, Vol. XVI, Lesson 1, 1997.

HIV NEPHROPATHY

DESCRIPTION HIV nephropathy (HIVAN) is the most common cause of chronic renal failure among HIV seropositive patients. It can occur in both the chronic and acute 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

- Highly active antiretroviral therapy
- Steroids
- ACE inhibitor

REFERENCE

Audard B, et al. HIV-related nephropathies associated with changes in blood and kidney tissue virus load. Kidney Int 2008;73:651–655.

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-Sternberg 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 renal cell carcinoma patients has been proposed. Treatment with radiation for Hodgkin may predispose to bladder cancer. 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: “Lymphoma, Urologic Considerations.”)

REFERENCE

Jones MW. Primary Hodgkin’s disease of the urinary bladder. Br J Urol 1989;63(4):438.

HODGSON TYPE I, II, III HYPOSPADIAS REPAIR

DESCRIPTION Type I: Chordee is repaired. A longitudinal tube 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: Hodgson 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 prepuce 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 neourethral is created, based on preputial and shaft skin.

REFERENCE

Devine CJ, Horton CE. Repair of hypospadias and epispadias. In: Novick AC, et al., eds. Stewart’s Operative Urology. Baltimore: Williams & Wilkins, 1989:689–714.

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 GU abnormalities, such as an increased frequency of ureteral duplication, reflux, and dysplasia. Usually asymptomatic, horseshoe kidney may be associated with urolithiasis and UPJ obstruction. Radiographic diagnosis can be made with IVP or CT, which reveals deviation of the axis of the kidneys. 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 I: “Renal Fusion Anomalies.”)

TREATMENT

- Pyeloplasty and ureteral implantation may be required for proven UPJ obstruction or severe reflux, respectively.
- Can affect management of many other disease conditions, such as neoplasm, aortic aneurysm, and transplantation

REFERENCE

O’Brien J, et al. Imaging of horseshoe kidneys and their complications. J Med Imaging Radiat Oncol 2008;52(3):216–226.

HORTON-DEVINE “FLIP-FLAP” HYPOSPADIAS REPAIR

DESCRIPTION The distal ventral skin over the urethra is mobilized, and the distal urethra is also mobilized. Parallel incisions are made in the glans to create a urethral plate, and the proximal flap is flipped over and sutured onto the urethral plate. The wings of the glans are then approximated over this distal repair.

REFERENCE

Devine CJ, Horton CE. Repair of hypospadias and epispadias. In: Novick AC, et al., eds. Stewarts Operative Urology. Baltimore: Williams & Wilkins, 1989:689–714.

HOUNSFIELD UNITS

DESCRIPTION Named after Hounsfield, the inventor of the CT scanner, this 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 –100 to 0 HU, while water with electrolytes is slightly above 0 HU. Soft tissue is in the range of 35 HU.

REFERENCE

Miraldi F. Imaging principles in computed tomography. In: Haaga JR, et al., eds. Computed Tomography of the Whole Body, 1st ed. St. Louis: Mosby, 1983.

HPC-1 (HEREDITARY PROSTATE CANCER 1 LOCUS)

DESCRIPTION A locus found on chromosome 1q24–25, which has been potentially linked to inherited prostate cancer. Families in which this altered gene is found were determined to have a lower age at diagnosis, a higher grade of cancer, and more cases of advanced disease than normal.

REFERENCE

Gronberg H, et al. Characteristics of prostate cancer in families potentially linked to the hereditary prostate cancer 1 (HPC1) locus. JAMA 1997;278(15): 1251–1255.

HPV (HUMAN PAPILLOMA VIRUS), UROLOGIC CONSIDERATIONS

DESCRIPTION This family of viruses, with double-stranded DNA, causes various warts, papillomas, and cervical cancer. Types 6, 11, 42, and 44 are associated with condyloma acuminatum. Types 16, 18, 31, 33, 35, and 39 have an association with cancer. Types 6 and 11 have been associated with Buschke-Lowenstein tumor. Subclinical condyloma can be detected with application of 5% acetic acid and inspection with a magnifying glass. HPV is associated also with Bowenoid papulosis and Squamous cell carcinoma of the penis and urethra. Bladder cancer association is controversial. (See also Section I: “Condylomata Acuminata [Venereal Warts]”; Section I: “Penis, Lesion, General”; Section II: “Buschke-Lowenstein Tumor.”)

TREATMENT

- Podophyllin or trichloroacetic acid for condyloma
- Laser therapy is also effective.

REFERENCE

Abol-Enein H. Infection: Is it a cause of bladder cancer? Scand J Urol Nephrol Suppl 2008; (218):79–84.

Kayes O, et al. Molecular and genetic pathways in penile cancer. Lancet Oncol 2007;8(5):420–429.

HUNNER ULCER

DESCRIPTION Cystoscopic finding of ulceration of the bladder mucosa in patients with interstitial cystitis, this fulfills 1 of the NIH criteria for IC. Found in a variable number of patients with IC, it was 1st described by Hunner in 1918, when he noted the ulcer in association with the constellation of clinical findings of IC. (See also Section I: “Interstitial Cystitis.”)

REFERENCE

Koziol JA, et al. Discrimination between the ulcerous and the non-ulcerous forms of interstitial cystitis by noninvasive findings. J Urol 1996;155(1):87–90.

HUTCH DIVERTICULUM

DESCRIPTION Herniation of the bladder mucosa through the weakest point of the hiatus, in the detrusor above the intramural ureter, producing Hutch diverticulum and reflux. The condition is usually due to a chronic increase in intravesical pressure as a result of bladder outlet obstruction. (See also Section I: “Vesicoureteral Reflux, Adult”; Section I: “Vesicoureteral Reflux, Pediatric.”)

REFERENCE

Hutch JA, et al. The bladder musculature with special reference to the uretero vesical junction. J Urol 1961;85:531.

HYDATID CYST (HYDATID DISEASE)

DESCRIPTION Infection occurs after ingestion of the dog parasite, Echinococcus granulosus (tapeworm). Sheep are the intermediate hosts. Cases occur in the Middle East, Australia, and Argentina. The hydatid is the larval form of E. granulosus, and the cysts represent a thick parasitic membrane that is enveloped in fibrous tissue. The cysts are fluid filled and contain the parasites. They grow slowly over many years and typically involve the kidney (2% incidence with echinococcus), with cases of seminal vesical involvement also reported. 3% affect the kidneys. Large cysts form that can be asymptomatic or present with flank pain. Renal cysts may cause pressure and chronic pain but do not affect renal function. They may rupture, causing new metastatic cysts. A peripheral eosinophilia is seen with a positive hydatid complement-fixation test. X-rays and CT show a thick-walled, fluid-filled spherical cyst with a calcified wall. (See also Section III: “Echinococcus, Renal.”)

TREATMENT

- Medical therapy is with albendazole.
- Where surgical excision is indicated, cysts can be 1st sterilized with formalin or alcohol. Praziquantel is also recommended preoperatively or if cyst contents are spilt (which can cause systemic anaphylaxis).

REFERENCE

Kaya K, et al. Isolated renal and retroperitoneal hydatid cysts: A report of 23 cases. Trop Doct 2006;36(4):243–246.

HYDROCALYCOSIS

DESCRIPTION A relatively rare cystic dilation of a major calyx. A calyceal diverticulum is distal to a minor calyx, whereas the hydrocalyx is a dilation of a major calyx. Caused by a congenital anomaly secondary to acquired intrinsic obstruction from a parapelvic cyst or crossing vessel causing infundibular stenosis. Differential diagnoses includes megacalycosis, ureteral obstruction and hydronephrosis, calyceal clubbing due to pyelonephritis or medullary necrosis, renal TB, or calyceal diverticulum. Patients may complain of flank pain, hematuria, or infection. Dismembered pyeloplasty or percutaneous treatment of the narrowed infundibulum is curative.

REFERENCE

Craver R, et al. Renal hypertrophic infundibular stenosis. Fetal Pediatr Pathol 2004;23(4):285–292.

HYDROCELE OF THE SPERMATIC CORD

DESCRIPTION A loculated fluid collection along the spermatic cord, the process is caused by a failure of the process vaginalis to close during development. The hydrocele can be in communication with the peritoneum at the internal inguinal ring (funicular) or may be encysted, where the fluid collection does not communicate with peritoneum or the tunica vaginalis. Patients usually present with groin swelling and should be evaluated with US, which will exhibit an oval anechoic mass in the groin along the spermatic cord and above and separated from the testis and the epididymis. (See also Section I: “Hydrocele, Adult and Pediatric”; Section I: “Spermatic Cord Mass.”)

REFERENCE

Rathaus V, et al. US features of spermatic cord hydrocele in children. Br J Radiol 2005;74:818–820.

HYMENAL SKIN TAGS

DESCRIPTION A polypoid lesion of the hymenal ring. A normal variant and rarely symptomatic (ie, bleeding, irritation), treatment involves observation or excision when symptomatic or to exclude malignancy.

REFERENCE

Rink R, Kaefer M. Surgical management of intersexuality, cloacal malformation and other abnormalities of the genitalia in girls. In: Wein AJ, et al. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007.

HYPERCALCEMIA, UROLOGIC CONSIDERATIONS

DESCRIPTION In urology, generally the result of metastatic lesions to bone, hydrochlorothiazide therapy, hyperparathyroidism, or chronic renal failure. Symptoms include anorexia, weakness, somnolence, polyuria, and coma. This condition may also occur as a paraneoplastic syndrome from renal cell carcinoma and can lead to hypercalciuria, 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.
- Mithramycin, steroids, and etidronate disodium have also been used.

REFERENCE

Assadi F. Hypercalcemia: An evidence-based approach to clinical cases. Iran J Kidney Dis 2009;3(2):71–79.

HYPERCALCURIA (ABSORPTIVE, RENAL, AND RESORPTIVE)

DESCRIPTION Hypercalciuria is the most commonly encountered 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 mEq sodium) is a urinary calcium level of >4 mg/kg/d or with a urinary level >200 mg calcium/liter of urine. Hypercalcuria consists of several types:

- Absorptive hypercalciuria. Caused by the intestinal hyperabsorption of calcium. Hypercalciuria results from the increased filtered load and reduced renal tubular reabsorption of calcium, caused by parathyroid suppression. Absorptive hypercalciuria Type I is a severe, uncommon form; Type II is mild–moderate and the most common form of this condition. Type III, sometimes called renal phosphate leak, is uncommon.
- Renal hypercalciuria. Also called renal leak, this is caused by impairment in the renal tubular reabsorption of calcium. There may be excessive mobilization of calcium from bone and an enhanced intestinal absorption of calcium because of the parathyroid hormone excess and the stimulation of the renal synthesis of 1,25–(OH)2D. Unlike primary hyperparathyroidism, serum calcium is normal and the hyperparathyroidism is secondary.
- Resorptive hypercalciuria. The hypercalciuria is due to primary hyperparathyroidism with excessive resorption of bone resulting from hypersecretion 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 hypercalcuria, calcium load usually consists of 1 g of oral calcium gluconate.

Hypercalciuria Type

Urinary Calcium on 400-mg Calcium Diet (Normal = <200 mg/24 h)

Fasting Calcium/Creatinine Ratio (Normal = <0.11)

Post-calcium Load Calcium/Creatinine Ratio (Normal = <0.20)

Normal

Normal

Normal

Normal

Absorptive type I

High

Normal
High
Absorptive type II
Normal
Normal
High
Absorptive type III (renal phosphate leak)
High
High
High
Renal calcium leak
High
High
High
Resorptive (hyperparathyroidism)
High
High
High

Leslie SW. Hypercalcuria http://www.emedicine.com/med/TOPIC1069.HTM, Accessed May 13, 2009.

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 osteopenia.
- 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 hypocalciuric action and the high cost and inconvenience of alternative therapy (sodium cellulose phosphate).
- Absorptive hypercalciuria type I:
  - Thiazide does not correct the basic, underlying physiologic defect in absorptive hypercalciuria.
  - Potassium supplementation (as potassium citrate), should be employed when using thiazide therapy to prevent hypokalemia and hypocitraturia (eg, trichlormethiazide 4 mg/d

and potassium citrate 15–20 mEq b.i.d.)

– Amiloride 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 amiloride.

– Thiazides may lose their hypocalciuric effect over time and cause hypokalemia, hypocitraturia, and increased uric 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 in absorptive hypercalciuria type I. Low calcium intake (400–600 mg/d) and high fluid intake (sufficient for a minimum urine output >2 L/d) is helpful. Normo-calciuria can be restored by dietary calcium restriction alone, and increased urine volume has been shown to reduce urinary saturation of calcium oxalate.

• Absorptive hypercalciuria type III (renal phosphate leak) is treated with slow-release neutral potassium phosphate (UroPhos-K) that corrects the hyperphosphatemia.

• Renal hypercalcuria:

– Thiazide diuretic augments calcium reabsorption in the distal tubule, causes extracellular volume depletion, and stimulates proximal tubule reabsorption of calcium. Agents include hydrochlorothiazide 50 mg b.i.d., chlorthalidone 50 mg/d, or indapamide 1.25 mg/d, trichlormethiazide (Naqua) 2–4 mg/d, and indapamide (Lozol) 1.25–2.5 mg/d. Potassium supplementation (~40 mEq/d) is required to prevent hypokalemia and attendant hypocitraturia. Potassium citrate has been shown to be effective in averting hypokalemia and in increasing urinary citrate when administered to patients with calcium nephrolithiasis taking thiazide.

– Triamterene is contraindicated because of the risk of triamterene renal stone formation

• Resorptive hypercalciuria: Parathyroidectomy is the optimum treatment.

REFERENCE

Pak CY. Pharmacotherapy of kidney stones. Expert Opin Pharmacother 2008;9(9):1509–1518. Review.

HYPERCARBIA DURING LAPAROSCOPY

DESCRIPTION Carbon dioxide (CO_2) is the most abundantly used insufflant in the US for laparoscopic surgery. CO_2 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 hypercarbia 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 CO_2 levels. Rarely a CO_2 gas embolism may occur.

REFERENCE

Bandi G, Gomella LG. Basic principles of laparoscopy: Transperitoneal, extraperitoneal and hand-assisted techniques. In: Graham S, Keane T, eds. Glenn’s Operative Urology, 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2009.

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 peaked T waves, long PR interval, long QRS complex, and absent P wave.

TREATMENT

- Monitor patient on ECG if symptomatic or if K+ is >6.5 mEq/L; discontinue all K+ intake, including IV fluids; order a repeat stat K+ to confirm.
- Pseudohyperkalemia should be ruled out. If doubt exists, obtain a plasma K+ in a heparinized tube; the plasma K will be normal if pseudo-hyperkalemia is present.
- Rapid correction: These steps only protect the heart from K+ shifts, and total body K+ must be reduced by 1 of the treatments shown under slow correction:
  - Calcium chloride, 500 mg, slow IV push
  - Alkalinize with 50 mEq (1 amp) Na bicarbonate (causes intracellular K+ shift)
  - 50 mL D50W, IV push, with 10–15 units regular insulin, IV push (causes intracellular K+ shift)
- Slow correction:
  - Sodium polystyrene sulfonate (Kayexalate) 20–60 g PO with 100–200 mL of sorbitol or 40 g Kayexalate with 40 g sorbitol in 100 mL water given as an enema. Repeat doses q.i.d. as needed.
- Dialysis (hemodialysis or peritoneal):
  - Correct underlying cause, such as stopping K-sparing diuretics, ACE inhibitors, mineralocorticoid replacement for hypokalemia

REFERENCE

Fluids and electrolytes. In: Gomella LG, Haist SA, eds. Clinician’s Pocket Reference, 11th ed. New York: McGraw-Hill, 2007.

HYPERNATREMIA, UROLOGIC CONSIDERATIONS

DESCRIPTION Hypernatremia 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+ loss results in low total body Na. Due to renal (diuretics, osmotic diuresis due to glycosuria, mannitol, postobstructive diuresis, etc.) or extrarenal (sweating, GI [vomiting, NG suction], respiratory) losses.
- Excess water loss (isovolemic hypernatremia): Total body Na+ remains normal, but total body water is decreased. Caused by diabetes insipidus (central and nephrogenic), excess skin losses, respiratory loss, others.
- Excess sodium (hypervolemic hypernatremia): Total body Na+ increased. Caused by iatrogenic Na+ administration (ie, hypertonic dialysis, hypertonic saline enemas, Na-containing medications) or other exogenous sources (seawater ingestion, salt tablets) or adrenal hyperfunction (Cushing syndrome, hyperaldosteronism).

TREATMENT

- Check the serum Na+ levels frequently while attempting to correct hypernatremia:
  - Hypovolemic hypernatremia. Determine if the patient's volume is depleted by determining if orthostatic hypotension is present; if volume is depleted, rehydrate with NS until patient is hemodynamically stable, then administer hypotonic saline (1/2NS).
  - Euvolemic/isovolemic (no orthostatic hypotension): Calculate the volume of free water needed to correct the Na+ to normal as follows:

Body water deficit = Normal total water Current TBW

where

Normal TBW = 0.6 × Body weight in kg

  - Give free water as D5W, 1/2 the volume in the 1st 24 hr and the full volume in 48 hr. (Caution: The rapid correction of the Na+ level using free water (D5W) can cause cerebral edema and seizures.)
  - Hypervolemic hypernatremia: Avoid medications that contain excessive Na+ (carbenicillin, etc.). Use furosemide along with D5W.

REFERENCE

Fluids and electrolytes. In: Gomella LG, Haist SA, eds. Clinician's Pocket Reference, 11th ed. New York: McGraw-Hill, 2007.

HYPEROXALURIA, UROLOGIC CONSIDERATIONS

DESCRIPTION The greatest significance of hyperoxaluria is the increased risk of urolithiasis, which is more significant than calcium in the formation of most kidney stones. Oxylate and calcium form an insoluble compound that can result in urolithiasis. The normal upper level of urinary oxalate excretion is 40 mg (440 mol)/24 hr. Hyperoxaluria is caused by dietary excess, bowel disorders such as extensive ileal resection, and primary hyperoxaluria. Primary hyperoxalurias are disorders associated with a congenital defect in the oxylate pathway. (See also Section I: “Urolithiasis, Calcium Oxylate/Phosphate.”):

- Enteric hyperoxaluria: Accounts for a relatively small number of cases of hyperoxaluria (5%). Caused by chronic diarrhea and malabsorption (colitis or jejunoileal bypass), throughthe reduced GI calcium availability to bind oxylate and keep it from being absorbed systemically.
- Dietary hyperoxaluria: Caused by increased intake of foods high in oxalates (eg, nuts, chocolate, tea, spinach, rhubarb, beets, wheat bran, strawberries, and other plant products). Reduced dietary calcium intake can also result in hyperoxaluria due to reduced intestinal binding of oxalate and increased oxylate absorption.
- Idiopathic: The most common cause; may be due to increased dietary absorption or due to increased intrinsic production of oxylate, with some suggestions of a genetic predisposition.
- Primary hyperoxaluria type I (also called glycolic aciduria): A form of primary hyperoxaluria caused by an enzymatic deficiency of glyoxylate carboligase transmitted as an autosomal recessive trait. Caused by a deficiency of the peroxisomal liver-specific alanine-glyoxylate aminotransferase (AGT) gene. Pyridoxine (vitamin B6) is a cofactor in this pathway that normally converts glyoxylic acid to glycine. With a block in this conversion, because of deficiency or absence of this enzyme, high levels of glycolic and oxalic acids result that are converted to oxalate that is then excreted in the urine. This causes extensive nephrocalcinosis with kidney failure common in childhood. Most patients die at <30 yr. The condition often presents with stone disease in childhood. Type I can be associated with ESRD secondary to stones and interstitial deposits of calcium oxalate.
- Primary hyperoxaluria type II: Less common than type I hyperoxaluria, this entity is caused by deficiency of D-glyceric dehydrogenase 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.
- Other: Increased hepatic conversion, due to pyridoxine deficiency, type I glycol ingestion, and methoxyflurane anesthesia

TREATMENT

- Primary hyperoxaluria: Oral phosphates and dietary oxylate restriction are usually unsuccessful. Increase urine flow. Prescribe high-dose pyridoxine (vitamin B6) 150–500 mg/d. Liver–kidney transplantation is often required at end stage.
- Enteric hyperoxaluria: Calcium citrate without vitamin D, potassium citrate 40–60 mEq/d in divided doses (increases urinary pH and citrate). Dietary restriction of oxalate with low fat and reduced meat protein diet.
- Idiopathic hyperoxaluria: Increase urine flow. Avoid excess Vitamin C (can be converted to oxylate). Prescribe high-dose pyridoxine (vitamin B6) 150–500 mg/d.

REFERENCE

Parks JH, Coe FL. Pathogenesis and treatment of calcium stones. Semin Nephrol 1996;16(5): 398–411.

HYPERPARATHYROIDISM, UROLOGIC CONSIDERATIONS

DESCRIPTION Hyperparathyroidism can cause a variety of urologically related conditions and problems, includingnephrolithiasis, hypercalciuria, nephrocalcinosis, chronic renal insufficiency, and abnormalities in renal tubular function (decreased concentrating ability). Also associated in the MEN1 syndrome. About 5% of new stone formers have hyperparathyroidism, whereas up to 20% of patients with hyperparathyroidism will have stones (most common calcium oxylate). These patients usually exhibit elevated serum and urine calcium with an inappropriately normal or elevated serum PTH level and elevated calcitriol level. Treatment is through parathyroidectomy and workup for MEN when appropriate. (See also Section II: “Hypercalcuria and Multiple Endocrine Neoplasia.”)

REFERENCE

Jabbour N, et al. The natural history of renal stone disease after parathyroidectomy for primary hyperparathyroidism. Surg Gynecol Obstet 1991; 172(1):25–28.

HYPERSPERMIA AND HYPOSPERMIA

DESCRIPTION Hyperspermia is a poorly studied condition characterized by an excessive volume of ejaculate defined in studies as >5.5–6.5 mL/semen analysis. Hypospermia is generally defined as a total ejaculate of <1.5 mL. (See also Section II: “Semen Analysis, Abnormal Findings and Terminology”; Section II: “Semen Analysis, Technique and Normal Values.”)

REFERENCE

Cooke S, et al. Hyperspermia: The forgotten condition? Human Reprod 1995;10(2):367–368.

HYPERTENSION, UROLOGIC CONSIDERATION

DESCRIPTION Primary hypertension is the most common form of this disease, but when significant findings on evaluation are present or if the hypertension is refractory to intensive multiple-drug therapy or requires hospitalization, a secondary cause should be sought. Common urologic considerations are primary aldosteronism, CAH, Cushing syndrome, pheochromocytoma, and renovascular disease. Workup entails physical exam, endocrinologic workup, and imaging.

REFERENCE

Victor G. Arterial hypertension. In: Goldman L, ed. Cecil Medicine, 23rd ed. Philadelphia: Saunders, 2007.

HYPOCITRATURIA

DESCRIPTION Citrate is a urinary inhibitor of crystal formation. Hypocitraturia is defined as urinary citrate excretion of <320 mg/d, but the absolute value can vary. It is a common cause of calcium urolithiasis, because citrate combines with calcium to form a nondissociable soluble complex with less calcium to combine with oxalate. Citrate also inhibits crystal agglomeration, in which individual calcium oxalate crystals combine to form a stone. Hypocitruria may develop from distal renal tubular acidosis (type I), chronic diarrhea, thiazide use, very high animal protein diet, and gastrocystoplasty, or it may be idiopathic.

TREATMENT

- Correction of acidosis in RTA
- Replacement therapy with potassium citrate (powder: 1 packet in water after meals and at bedtime; adjust dose to urinary pH; solution: 15– 30 mL after meals and at bedtime; adjust dose based on urinary pH)

REFERENCE

Bek-Jenson, H, et al. Is citrate an inhibitor of calcium oxalate crystal growth in high concentrations of urine? Urol Res 1996;24(2):67–71.

HYPOKALEMIA, UROLOGIC CONSIDERATIONS

DESCRIPTION Hypokalemia (K+ of <3.6 mEq/L [mmol/L]) can result from excessive upper GI losses, diarrhea, diuretic therapy, steroid administration, and hyperaldosteronism. Metabolic alkalosis is often associated and causes an intracellular redistribution of potassium. Other high-renin states, such as renin-secreting tumors, have been reported as a cause. A serum K+ level of 2 mEq/L (mmol/L) probably represents a deficit of at least 200 mEq (mmol) in a 70-kg adult; to change K+ from 3 mEq/L (mmol/L) to 4 mEq/L (mmol/L) takes about 100 mEq (mmol) of K+ in a 70-kg adult.

TREATMENT

- Treat underlying cause.
- Hypokalemia potentiates the cardiac toxicity of digitalis. In the setting of digoxin use, hypokalemia should be aggressively treated.
- Treat hypomagnesemia if present. It will be difficult to correct hypokalemia in the presence of hypomagnesemia.
- Rapid correction: Give KCl IV. Monitor heart with replacement at >20 mEq/hr; IV KCI can be painful and damaging to veins:
  - Patient <40 kg: 0.25 mEq/kg/hr × 2 hr
  - Patient >40 kg: 10–20 mEq/hr × 2 hr
  - Severe [<2 mEq/L (mmol/L)]: Maximum 40 mEq/hr IV in adults. In all cases, check a stat K+ following each 2–4 hr of replacement.
- Slow correction: Give KCl PO:
  - Adult: 20–40 mEq b.i.d. or t.i.d.
  - Pediatric patients: 1–2 mEq/kg/d in divided doses. Potassium supplementation either with PO or IV forms

REFERENCE

Fluids and electrolytes. In: Gomella LG, Haist SA, eds. Clinician’s Pocket Reference, 10th ed. New York: McGraw-Hill, 2007.

HYPONATREMIA, UROLOGIC CONSIDERATIONS

DESCRIPTION Hyponatremia is a 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 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, RTA, GI losses, and mineralocorticoid insufficiency. (See also Section I: “TUR [Transurethral Resection] Syndrome.”)

Tumor Type
IHC Stains Positive
IHC Stains Negative
Other Staining (+) Positive (–) Negative
Prostate adenocarcinoma
AMACR, PSA, PSAP, PSMA
Loss of basal cells (negative for keratin 903 (also called high-molecular-weight cytokeratin 34e12) & nuclear 63

Prostate neuroendocrine (small cell)
Chromogranin neuron-specific enolase (NSE), synaptophysin, and myoglobulin
CD3e, CD20, leukocyte common antigen, and CD99

RCC chromophobe
Keratin AE1/AE3, E-cadherin, EMA, CK 7
Vimentin, CD 10, RCC Ag, GSTalpha
Colloidal iron (+), PAS ()
RCC conventional (clear cell and its variants)
RCC Ag, vimentin, CD 10, PLAP, keratin AE/AE3, EMA, GSTalpha
CEA, inhibin, CK 7, CK 20, CD 117
Oil red O (+)
RCC papillary
Keratin AE1/AE3, CK 7, vimentin, AMACR, EMA
CK 19
Mucin (), PAS (+)
Renal metanephric adenoma

Keratin AE1/AE3, Leu 7 EMA, vimentin
CEA, CD 10, HMB-45, chromogranin
PAS (), oil red O ()
Renal oncocytoma
Keratin AE1/AE3, CD 117 (c-Kit)
CK 7, vimentin, RCC Ag
Colloidal iron ()
Testis, choriocarcinoma
B-hCG, CEA, keratin AE1/AE3, EMA, inhibin

Testis, embryonal carcinoma
Keratin AE1/AE3, PLAP, OCT 4, CD 30
EMA, CEA, vimentin, c-kit

Testis, seminoma
PLAP, OCT 4, c-Kit, keratin AE1/AE3
AFP, inhibin, EMA, CD 30
PAS (+)
Testis, yolk sac carcinoma
PLAP, AFP, keratin AE1/AE3, 1-antitrypsin
CD 30, EMA

Urothelial carcinomas (bladder, ureter, etc.)
CK 7, CK 10, uroplakin, P 53, CEA, thrombomodulin
Vimentin, CA 125

AFP, -fetal protein; AMACR, -methyl acetyl CoA racemase; CD, cluster designation; CEA, carcinoembryonic antigen; CK, cytokeratin; EMA, epithelial membrane antigen; hCG, human chorionic gonadotropin; HMB-45, melanoma antigen; IHC, immunohistochemical stain; PAS, periodic acid Schiff; RCC, renal cell carcinoma

TREATMENT

- Treat the underlying cause.
- Therapy is based on determination of volume status. Evaluate volume status by physical exam: HR and BP lying and standing after 1 min, skin turgor, and edema, and by determination of the plasma osmolality. It is not necessary to treat hyponatremia from pseudo-

hyponatremia (increased protein or lipids) or hypertonic hyponatremia (hyperglycemia); treat underlying disorder (see above):

– Life-threatening (seizures, coma): 3–5% NS can be given in the ICU setting. Attempt to raise the Na to at least 125 mEq/L with 3–5% NS.

– Isovolemic hyponatremia (SIADH): Restrict fluids (1,000–1,500 mL/d). Demeclocycline can be used in chronic SIADH.

– Hypervolemic hyponatremia: Restrict Na and fluids (1,000–1,500 mL/d). Treat with furosemide.

– Hypovolemic hyponatremia: Give D5NS or NS.

REFERENCE

Fluids and electrolytes. In: Gomella LG, Haist SA, eds. Clinician's Pocket Reference, 11th ed. New York: McGraw-Hill, 2007.

SHORT TOPIC SECTION I

IC (INTERSTITIAL CYSTITIS) SYMPTOM INDEX

DESCRIPTION Also called the Oleary-Sant Symptom Index, this is a validated questionnaire for patients with IC to measure urinary and pain symptoms. It is based on 4 questions that are graded from 0–5, with 5 being the most severe. It is frequently used with the IC problem index.

REFERENCE

1. O'Leary MP, et al. The interstitial cystitis symptom index and problem index. Urology 1997;49(5A Suppl):58–63.

ICE WATER TEST

DESCRIPTION Performed after standard cystometrogram, 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/suprasacral lesions have a positive test (ie, Parkinson, MS, CVA). Patients with lower motor neuron lesions almost never have a positive test.

REFERENCE

2. Petersen T, et al. The ice-water test in detrusor hyper-reflexia and bladder instability. Br J Urol 1997;79(2):163–167.

IMMUNOHISTOCHEMICAL STAINING, UROLOGIC CONSIDERATIONS

DESCRIPTION The following are common markers and patterns of immunohistochemical and other staining patterns commonly used in urologic pathology.

REFERENCE

3. Bostwick D, et al. Immunohistochemistry of the prostate and bladder, testis, and renal tumors. In: Dabbs D, ed. Diagnostic Immunohistochemistry. Philadelphia: Churchill Livingstone; 2002:407–434.

4. Liu, et al. Immunohistochemical analysis of chromophobe renal cell carcinoma, renal oncocytoma, and clear cell carcinoma: An optimal and practical panel for differential diagnosis. Arch Pathol Lab Med 2007;131(8):1290–1297.

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 hydrocolpos or mucocolpos that may obstruct the urinary tract. At puberty, females may present with primary amenorrhea and cyclic abdominal pain. Treatment is surgical if it causes symptoms.

REFERENCE

5. Katz V, Lentz G. Congenital abnormalities of the female reproductive system. In: Katz VL, ed. Comprehensive Gynecology. St. Louis: Mosby, 2007.

IN VITRO FERTILIZATION (IVF) AND EMBRYO TRANSFER

DESCRIPTION Currently IVF is used for women with nonfunctioning oviducts, severe endometriosis, and in couples with male factor infertility or unexplained infertility. In most clinics, the female patient undergoes ovarian 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 oocyte, the eggs are incubated and placed in culture media. Sperm from the male is then integrated into the culture media after being separated from the semen. After about 48–96 hr, 1–4 splitting embryos are placed in the uterus via transcervical injection.

REFERENCE

6. Lobo R. Infertility: Etiology, diagnostic evaluation management, prognosis. In: Katz VL, ed. Comprehensive Gynecology, 5th ed. St. Louis: Mosby, 2007.

INCONTINENCE (URINARY) WITH ORGASM

DESCRIPTION Coital urinary incontinence can be divided into 2 forms: Incontinence at penetration and incontinence during orgasm. Both may be caused by pelvic floor dysfunction, but more specifically, incontinence during orgasm has been associated with detrusor overactivity, whereas incontinence during penetration can be associated with stress incontinence. The term climacturia is used mostly when referring to males who have incontinence associated with orgasm; this condition is seen mostly after radical prostatectomy.

REFERENCE

7. Serati M, et al. Female urinary incontinence during intercourse: A review on an understudied problem for women's sexuality. J Sex Med 2009;6(1):40–48.

INCONTINENCE IMPACT QUESTIONNAIRE (IQ-7)

DESCRIPTION One of several validated scales available to assist in evaluating the severity of urinary incontinence.

REFERENCE

8. Lentz G. Urogynecology physiology of micturition, diagnosis of voiding dysfunction and incontinence: Surgical and nonsurgical treatment. In: Katz VL, ed. Comprehensive Gynecology, 5th ed. St. Louis: Mosby, 2007.

INDEVUS 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).

REFERENCE

9. Zinner N, et al. The overactive bladder-symptom composite score: A composite symptom score of toilet voids, urgency severity and urge urinary incontinence in patients with overactive bladder. J Urol 2005;173(5):1693–1643.

INDIANA POUCH

DESCRIPTION A urinary reservoir is created from the right colon, and the ileal cecal apparatus is used as a continent catheterizable limb. Originally described by Gilchrist et al. in 1950, the pouch was modified by Rowland and co-workers at the University of Indiana. Modifications included detubularizing the colon with subsequent closure in a Heinecke-Mikulicz configuration, strengthening of the ileocecal valve with imbricating sutures (which are performed on the ileal limb), and a tunneled ureterocolonic anastomosis.

REFERENCE

Bihrle R. The Indiana pouch continent urinary reservoir. Urol Clin N Am 1997;24(4):773–779.

INFERTILE MALE SYNDROME

DESCRIPTION Syndrome caused by mutations in the androgen receptor gene, leading to partial androgen insensitivity. Described as phenotypically normal males with azoospermia or oligospermia, and high/normal serum gonadotropins and testosterone.

REFERENCE

Aiman J, et al. Androgen insensitivity as a cause of infertility in otherwise normal men. N Engl J Med 1979;300:223–227.

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 (Crohn disease), malabsorption syndromes leading to nephrolithiasis, and pyoderma gangrenosum of the genitalia.

REFERENCE

Stenson P. Inflammatory bowel disease In: Goldman L, ed. Cecil Medicine 23rd ed. Philadelphia: Saunders, 2007.

INFUNDIBULAR STENOSIS, DIFFERENTIAL DIAGNOSIS

DESCRIPTION Narrowing of the renal infundibulum caused by intrinsic or extrinsic compression. Both retroperitoneal malignancy and fibrosis are extrinsic causes; intrinsic conditions include renal calculi, TB, chronic scarring from renal surgery (ie, PCNL) and neoplasm. The condition can be rarely caused by a crossing segmental artery. Differential diagnosis includes hydronephrosis, polycalycosis, and infundibular stenosis.

REFERENCE

Pieretti-Vanmarcke R, et al. Megacalycosis: A rare condition. Pediatr Nephrol 2009;24(5):1077–1079.

INFUNDIBULOPELVIC DYSGENESIS

DESCRIPTION This is an obstructive process secondary to narrowing of the infundibulopelvic system that produces various congenital anomalies such as hydrocalycosis, calyceal diverticula, ureteropelvic junction stenosis, and multicystic kidney.

REFERENCE

Uhlenhuth E, et al. Infundibulopelvic dysgenesis: A spectrum of obstructive renal disease. Urology 2007;35:334–337.

INGUINAL HERNIA, ADULT, UROLOGIC CONSIDERATIONS

DESCRIPTION A direct hernia is the most common inguinal hernia in adult males. It occurs when there is a protrusion of intra-abdominal contents in an area called the Hesselbach triangle (rectus abdominis muscle, inferior epigastric artery, inguinal ligament). Untreated 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 a patent processus vaginalis.

REFERENCE

Jeyarajah R, et al. Abdominal hernias and gastric volvulus In: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia: Saunders, 2006.

INGUINAL HERNIA, PEDIATRIC, UROLOGIC CONSIDERATIONS

DESCRIPTION Typically, an indirect hernia is the most common type of inguinal hernia in the pediatric population. During embryologic development, the spermatic cord and testis descend through the anterior abdominal wall to the inguinal canal through the projection of the process vaginalis. If the process vaginalis persists, an indirect inguinal hernia may form and is always associated with a hydrocele.

REFERENCE

Jeyarajah R, et al. Abdominal hernias and gastric volvulus In: Sleisenger & Fordtran’s Gastrointestinal and Liver Disease, 8th ed. Philadelphia: Saunders, 2006.

INSECT BITE, PENIS AND SCROTUM

DESCRIPTION Insect bites and stings are typically acute processes with rapid onset of symptomatologies, including pain and 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 imperative to rule out pathologic events such as testicular torsion or cancer.

REFERENCE

Moran ME, et al. Venomous bites to the external genitalia: An unusual cause of acute scrotum. J Urol 1992;147(4):1085–1086.

INTERNATIONAL GERM CELL CANCER COLLABORATIVE GROUP (IGCCCG)

DESCRIPTION Effective chemotherapy regimens for germ cell tumors resulted in the development of prognostic groups for patients with metastatic disease. With good-risk disease, the goal is to minimize the toxicity of current regimens, while preserving the high cure rates. In patient with high-risk disease, investigational studies have been designed to improve long-term response rates. In the IGCCCG staging system, patients are divided into good-, intermediate-, and poor-risk groups, based upon primary site of the germ cell tumor, sites of metastasis, and serum tumor markers. Within each risk group, criteria differ for seminomas and nonseminomatous germ cell tumors. Survival in >5200 patients is correlated with risk status: Good-risk disease, 91% 5-yr survival; intermediate-risk disease, 79% 5-yr survival; poor-risk disease, 48% 5-yr survival. (See also Section I: “Testis, Cancer, General”; Section I: “Testis, Nonseminomatous Germ Cell Tumors, General”; Section I: “Testis, Seminoma.”)

SEMINOMA: GOOD RISK

All of the following:

- Any primary site
- No nonpulmonary visceral metastases
- Normal serum AFP

SEMINOMA: INTERMEDIATE RISK

All of the following:

- Any primary site
- Nonpulmonary visceral metastases present
- Normal serum AFP

NONSEMINOMATOUS GERM CELL TUMORS: GOOD RISK

All of the following;

- Testicular or retroperitoneal primary tumors
- No nonpulmonary visceral metastases
- Serum AFP <1,000 ng/mL, -hCG <5,000 mlU/mL, and LDH <1.5× upper limit of normal

NONSEMINOMATOUS GERM CELL TUMORS: INTERMEDIATE RISK

All of the following:

- Testicular or retroperitoneal primary tumors
- No nonpulmonary visceral metastases
- Intermediate level of any of the following: AFP 1,000–10,000 ng/mL OR -hCG 5,000–50,000 mlU/mL, or LDH 1.5–10 × upper limit of normal

NONSEMINOMATOUS GERM CELL TUMORS: POOR RISK

Any of the following:

- Mediastinal primary OR
- Nonpulmonary visceral metastases, OR
- Serum AFP >10,000 ng/mL, OR
- Serum -hCG >50,000 mlU/mL, OR
- LDH >10 × upper limit of normal

REFERENCE

International Germ Cell Consensus Classification: A prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol 1997;15(2):594–603.

INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)

DESCRIPTION A patient self-scoring instrument used for assessment of symptoms severity in men with lower urinary tract symptoms. The symptoms are scored from mild (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 II: “AUA Symptom Index for BPH” and the IPSS Appendix VII.)

REFERENCE

Hakenberg OW, et al. Does evaluation with the International Prostate Symptom Score predict the outcome of transurethral resection of the prostate? J Urol 1997;158(1):94–99.

INTERSTITIAL NEPHRITIS

DESCRIPTION Acute interstitial nephritis is most commonly caused by drugs, but autoimmune diseases (eg, lupus) and a variety of infections (streptococcal, legionella) can also be the cause. Many drug-related causes have been described, but the most common are penicillins, cephalosporins, NSAIDs, ciprofloxacin, rifampin, sulfonamides, allopurinol, cimetidine, and indinavir. Nonspecific symptoms and signs, along with acute renal dysfunction include nausea, vomiting, and malaise. Urine analysis reveals WBCs, RBCs, WBC casts. Proteinuria is usually absent or mild (<1 g/d). With drug-related interstitial nephritis, allergic-type reactions may be present, such as rash, fever, and eosinophilia. Diagnosis can only be confirmed on renal biopsy. Chronic interstitial nephritis is typically caused by long-term exposure to medications such as analgesics, anticonvulsants, and Chinese herbal medications; heavy metal exposure; chronic obstruction; and other causes. Presentation is insidious with hypertension, inability to concentrate urine, acidosis, and anemia being the more common symptoms. Treatment involves stopping offending medication or treating the underlying 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.

REFERENCE

Reid TG. Interstitial nephritis. In: Domino FJ, ed. The 5-Minute Clinical Consult, 17th ed. Philadelphia: Lippincott, 2009.

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

DESCRIPTION An assisted reproductive technique (ART) in which a single spermatozoon is injected into the cytoplasm of an ovum. This technique is typically utilized in males with severe oligospermia or azoospermia, as the cost is high.

REFERENCE

Lobo R. Infertility: Etiology, diagnostic evaluation, management, prognosis. In: Katz VL, ed. Comprehensive Gynecology, 5th ed. St. Louis: Mosby, 2007.

INTRAOPERATIVE FLOPPY IRIS SYNDROME (IFIS)

DESCRIPTION The triad of intraoperative observations of flaccid iris stroma that undulates and billows in response to ordinary intraocular fluid currents, a propensity for the floppy iris to prolapse toward the phacoemulsification tip and incisions, and progressive intraoperative pupil constriction. This syndrome has been associated with -blocker therapy in men with BPH, especially tamsulosin and is due to relaxation of the dilator muscle. Discontinuation of tamsulosin appears to be unpredictable and may not reliably reduce the severity. To mitigate the intraopterative problems, pharmacological and mechanical strategies are used.

REFERENCE

Friedman AH. Tamsulosin and the intraoperative floppy iris syndrome. JAMA. 2009;301(19):2044–2045.

INTRAUTERINE INSEMINATION (IUI)

DESCRIPTION An assisted reproductive technique (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 and also cervical stenosis or “hostile cervical mucous” in females.

REFERENCE

Lobo R. Infertility: Etiology, diagnostic evaluation, management, prognosis. In: Katz VL, ed. Comprehensive Gynecology, 5th ed. St. Louis: Mosby, 2007.

INTRINSIC SPHINCTER DEFICIENCY (ISD)

DESCRIPTION ISD is 1 of many components that contribute to stress urinary incontinence and is defined as the loss of coaptation and compression of the urethra along its length. Its etiology is usually multifactorial. ISD may occur simultaneously with urethral hypermobility, but should be differentiated, as the latter is an anatomic cause of stress urinary incontinence and not synonymous with ISD.

CAUSES

- Complete loss of urethral tone (catheter trauma, surgical trauma)
- Pudendal nerve dysfunction and denervation of the mid-urethral complex (external sphincter)
- Estrogen deficiency (resulting in mucosal changes effecting coaptation)
- Diabetes (autonomic dysfunction of smooth and nonstriated skeletal muscle)
- Parity (pudendal neuropathy and pelvic floor destruction)

TREATMENT

- Periurethral bulking agents (collagen, Coaptite)
- Native suspension procedures (Burch, MMK, vaginal-obturator shelf, paravaginal)
- Prosthetic suspension devices (tension-free vaginal tape, suprapubic arc sling, artificial sphincter)

REFERENCE

Staskin D, et al. Genuine stress incontinence: Theories of etiology and surgical correction. Urol Clin N Am 2002;29:527–535.

INVERTED PAPILLOMA, BLADDER

DESCRIPTION An uncommon tumor of the urinary tract characterized by proliferating urothelium arranged as inverting cords and nests with an intact overlying urothelium. Inverted papilloma is thought to be a benign lesion but because of reports of multiplicity, recurrence, and associated transitional cell carcinoma, its management has been controversial.

REFERENCE

Ho H, et al. Inverted papilloma of urinary bladder: Is long-term cystoscopic surveillance needed? A single center’s experience. Urology 2006;68:333–336.

INVERTED PAPILLOMA, URETER AND RENAL PELVIS

DESCRIPTION Considered 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 tumors. Papillary fronds project opposite into the mucosa, appearing as smooth-surfaced, pedunculated, or sessile lesions of urothelium. There is a strong male predominance (91%). The lesions are typically small (<3 cm), pedunculated, and polypoid. Muscularis invasion is not seen microscopically. Inverting cords and nests 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 transitional cell carcinoma. Diagnosis is by ureteroscopy for direct visualization and biopsy. Treatment has been nephroureterectomy; however, local excision is possible, but careful follow-up for other sites of cancer is essential.

REFERENCE

Chiura AN, et al. Upper urinary tract inverted papillomas. Urology 1998;52(3):514–516.

IRS (INTERGROUP RHABDOMYOSARCOMA STUDY) CLINICAL CLASSIFICATION

DESCRIPTION A generally accepted classification and staging system used in the IRS. (See Section I: “Rhabdomyosarcoma, Pediatric [Sarcoma Botryoides].”):

- Group I: Localized disease, completely removed, regional nodes not involved
- A: Confined to muscle or organ of origin
- B: Contiguous involvement, with infiltration outside the muscle or organ of origin; this group includes both gross impression of complete removal and microscopic confirmation of complete removal
- Group II:
- A: Grossly removed tumor with microscopic residual disease; no evidence of gross residual tumor; no evidence of regional node involvement
- B: Regional disease, completely removed (regional nodes involved and/or extension of tumor into an adjacent organ; no microscopic residual disease)
- C: Regional disease with involved nodes, grossly removed, but with evidence of microscopic residual disease
- Group III: Incomplete removal or biopsy with gross residual disease
- Group IV: Distant metastatic disease present at onset

REFERENCE

Andrassy RJ, et al. Conservative surgical management of vaginal and vulvar pediatric rhabdomyosarcoma: A report from the Intergroup Rhabdomyosarcoma Study III. J Pediatr Surg 1995;30:1034.

SHORT TOPIC SECTION J

JACK STONES

DESCRIPTION A term that refers to irregular, spiculated calcium oxylate stones, resembling children’s jacks, which are sometimes seen in the bladder.

REFERENCE

1. Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:224.

JARISCH-HERXHEIMER REACTIONS

DESCRIPTION Originally 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 spirochete 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, hypotension, 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- antibodies or steroids.

REFERENCE

2. Pound MW, May DB. Proposed mechanisms and preventative options of Jarisch-Herxheimer reactions. J Clin Pharm Ther 2005;30:291–295.

JEUNE SYNDROME (ASPHYXIATING THORACIC DYSPLASIA)

DESCRIPTION A form of lethal, short-limbed dwarfism with features that include constriction of the upper thorax and polydactyly. It has autosomally recessive inheritance. Of urologic interest, renal dysplasia, sometimes leading to end-stage renal disease, is associated with the condition.

REFERENCE

3. Ring E, et al. Retrospective diagnosis of Jeune’s syndrome in 2 patients with chronic renal failure. Child Nephrol Urol 1990;10(2):88–91.

JOINT REPLACEMENT, UROLOGIC CONSIDERATIONS

DESCRIPTION Prophylaxis is no longer routinely indicated for patients receiving orthopedic pins, plates, and screws or even total joints. Antimicrobial prophylaxis is intended 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 BOTH sets of criteria in the table here. For patients NOT meeting both these criteria, antimicrobial prophylaxis still may be indicated to reduce the risk of other infections. (Based on AUA Guidelines Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis.)

Increased Risk of Hematogenous Total Joint Infection

Increased Risk of Bacteremia Associated with Urologic Procedures

Patients during the first two years after prosthetic joint replacement

Any stone manipulation (includes shock-wave lithotripsy)

Immunocompromised patients with prosthetic joint replacements:

Any procedure with transmural incision into urinary tract (does not include simple ligation with excision or percutaneous drainage procedure)

- Inflammatory arthropathies (e.g., rheumatoid arthritis, systemic lupus erythematosus)

Any endoscopic procedures of upper tract (ureter and kidney)

- Drug-induced immunosuppression

Any procedure that includes bowel segments

- Radiation-induced immunosuppression

Transrectal prostate biopsy

Patients with prosthetic joint replacements and comorbidities:

Any procedure with entry into the urinary tract (except for urethral catheterization) in individuals with higher risk of bacterial colonization:

- Previous prosthetic joint infections
- Indwelling catheter or intermittent catheterization
- Malnourishment
- Indwelling ureteral stent
- Hemophilia
- Urinary retention
- HIV infection
- History of recent recurrent urinary tract infection or prostatitis
- Diabetes
- Urinary diversion
- Malignancy

TREATMENT

Recommended antimicrobial regimens:

– A single systemic 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 in patients allergic to ampicillin) plus gentamicin 1.5 mg/kg IV 30–60 min preoperatively.

– For some procedures, additional or alternative agents may be considered for prophylaxis against specific organisms and/or other infections.

REFERENCE

4. Wolf J, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2007;179: 1379–1390.

JUVENILE GANGRENOUS VASCULITIS, SCROTAL (PYODERMA GANGRENOSUM)

DESCRIPTION A variant of scrotal gangrene of unknown etiology, which is thought to be a variant of pyoderma gangrenosum. The lesions usually occur in healthy individuals <30 yr old, following an upper respiratory infection. The lesions can present with scrotal itching or stinging, with 1 skin lesions. Laboratory findings can show an increased ESR with normal microbiologic tests. Biopsy of the lesions reveals mostly neutrophilic dermal infiltrate and fibrinoid necrosis of small blood vessels without vasculitis. Treatment is systemic corticosteroids. The condition is often self-limited.

REFERENCE

5. Caputo R. Juvenile gangrenous vasculitis of the scrotum: Is it a variant of pyoderma gangrenosum? J Am Acad Dermatol 2006;55(2 Suppl):S50–S53.

JUXTAGLOMERULAR CELL TUMOR, KIDNEY

DESCRIPTION Rare but important benign renal mass caused by the secretion of renin. The ultimate cause is surgically curable hypertension. Patients (typically young females) present with severe diastolic hypertension, hypokalemia, and elevated plasma renin levels. CT, renal angiography, and renal vein sampling may be helpful in localization. Partial nephrectomy or enucleation is the treatment of choice.

REFERENCE

6. Remynse LC, et al. Juxtaglomerular cell tumor with elevation of serum erythropoietin. J Urol 1989; 142(6):1560–1562.

SHORT TOPIC SECTION K

KALLMANN SYNDROME

DESCRIPTION Also known as hypogonadotropic hypogonadism with anosmia, caused by failure of GnRH secretion by the hypothalamus, leading to testicular failure. KAL1, encoding the extracellular glycoprotein anosmin-1, 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 X chromosome, and has variable inheritance and penetrance. Anosmia, cleft palate, renal anomalies, microphallus, cryptorchidism, blindness, and deafness are also associated. Testes are also small. Delayed puberty is often a presenting sign.

TREATMENT

- Androgens can virilize but will not promote spermatogenesis.
- hCG with FSH and LH may help fertility.

REFERENCE

1. Dodé C, Hardelin JP. Kallmann syndrome. Eur J Hum Genet 2009;17(2):139–146.

KAPOSI SARCOMA, UROLOGIC CONSIDERATIONS

DESCRIPTION A tumor of reticuloendothelial system that presents as a raised, painful papule or ulcer with a bluish hue. In the U.S., it is seen most commonly in association with AIDS. Most common site in the GU system is the penis, with a much higher incidence in homosexual males. It may cause urethral obstruction. (See also Section I: “HIV/AIDS, Urologic Considerations.”)

TREATMENT

- Radiation or penectomy (partial or total) aimed at palliation
- Proximal urethrostomy for obstruction not responsive to other treatment

REFERENCE

2. Angulo JC, et al. Kaposi’s sarcoma of the penis as an initial urological manifestation of AIDS. A report of 2 cases. Urol Int 1991;46(2):235–237.

KARTAGENER SYNDROME (IMMOTILE CILIA SYNDROME)

DESCRIPTION Also called primary ciliary dyskinesia syndrome, this syndrome is characterized by situs inversus, chronic sinusitis, otitis media, airway disease, and immotile sperm leading to infertility. The absence of the inner and outer dynein arm 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.

REFERENCE

3. Haddad G, Kashgarian M. Primary ciliary dyskinesia (immotile cilia syndrome). In: Kliegman R, et al., eds. Nelson Textbook of Pediatrics, 18th ed. Philadelphia: Saunders, 2007.

KEGEL EXERCISES

DESCRIPTION 1st described by Arnold Kegel in 1948, these exercises can be used as treatment for urinary incontinence. Modern cure/improvement rates range from 50–80%. The usual regimen consists of multiple contractions the of pubococcygeus, muscle, 3 times a day. (This is the muscle group that stops the flow of urination voluntarily. However, patients should not make it a habit of starting and stopping the stream as this can cause more harm. Start with 10 repetitions of 3 second contractions done 3 times a day.) Biofeedback, electrical stimulation, and cystometry are adjuncts to the Kegel exercise that seem to increase efficacy.

REFERENCE

4. Bump RC, et al. Assessment of Kegel pelvic muscle exercise performance after brief verbal instruction. Am J Obstet Gynecol 1991;165(2):322–327.

KELAMI CLASSIFICATION SYSTEM (MODIFIED)

DESCRIPTION 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 30°; grade 2, curvature of 30–60°; and grade 3, 60° curvature. (See also Section I: “Penis, Curvature and/or Pain.”)

REFERENCE

5. Usta MF, et al. Relationship between the severity of penile curvature and the presence of comorbidities in men with Peyronie’s disease. J Urol 2004;171(2 Pt 1):775–779.

KELLY CYSTOCELE REPAIR

DESCRIPTION This procedure was initially described in 1912 for the repair of a cystocele and not incontinence. Through a midline vaginal incision, the lateral tissues were reapproximated with silk or linen with bites of 1.5 cm of tissue.

REFERENCE

6. Raz S, et al. Vaginal reconstructive surgery for incontinence and prolapse. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:1066–1094.

KERR KINKS

DESCRIPTION Kinking of the renal pelvis due to a deformity of the pyelocalyceal system, caused by traction of a strictured infundibulum and parenchymal fibrosis of a tuberculous kidney. The deformity leads to obstruction and dilatation of areas not directly affected by tuberculous ulcerations and eventual pressure atrophy of renal tissue.

REFERENCE

7. Barrie HJ, Kerr WK, Gale GL. The incidence and pathogenesis of tuberculous strictures of the renal pelvis. J Urol 1967;98:584.

KIBRICK TEST

DESCRIPTION A test designed to evaluate circulating immune factors, as an aid to diagnosing causes of infertility. Dilutions of serum from both partners are combined with semen samples in a medium with an agglutinating gelatin. Agglutination will occur if antibodies in the serum are reactive against the sperm. Controls are usually also run with the samples to prevent errors.

REFERENCE

8. Ainmelk Y, et al. Primary infertility: Correlation between sperm migration test and humoral immunity. Int J Fertil 1982;27(1):52–55.

KIDNEY, METASTASIS TO

DESCRIPTION Kidney metastases may present as a renal mass and grossly appear as renal primary neoplasm. Discovered most often at autopsy, with an incidence of about 7% in autopsy series. 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.

REFERENCE

9. Belldegrun A, deKernion JB. Renal tumors. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998.

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 rarely is 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, vaginal atresia, and duplicated female urethra. Treatment is unnecessary unless disease is present. (See also Section I: Renal Ectopia and Renal Fusion Anomalies.)

REFERENCE

Bernik TR, et al. Ectopic supernumerary kidney, a cause of para-aortic mass: Case report and review. Am Surg 2001;67(7):657–659.

KLINEFELTER SYNDROME

DESCRIPTION A syndrome characterized by small, firm testes, gynecomastia, and elevated urinary gonadotropins; it is present in 1 out of 600 male births. Usually presents as incomplete virilization, infertility, or rarely as male pseudohermaphroditism. Mental retardation and low bone mineral density are associated. A testicular biopsy usually shows sclerosis of tubules. The condition is caused by a nondisjunction of the meiotic 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: “XXY Syndrome.”)

REFERENCE

Paduch DA, et al. New concepts in Klinefelter syndrome. Curr Opin Urol 2008;18(6):621–627. Review.

KOCK POUCH AND HEMI-KOCK NEOBLADDER

DESCRIPTION A Kock continent catheterizable urinary reservoir (pouch) is created from 70–80 cm of small bowel. The mid 45-cm portion is folded into a U-shaped configuration and opened along its antimesenteric border, and the adjoining edges of the U are sutured together. The resulting U patch is folded again from top to bottom to form a reservoir. The 17-cm end limbs are intussuscepted and stapled to create nipple valves at each end. The ureters are anastomosed in the proximal afferent limb, where the nipple prevents reflux and the efferent limb is used to create a continent stoma, which is catheterized to empty the pouch.

The hemi-Kock neobladder is an orthotopic neobladder constructed based on the theme of the Kock pouch. In this diversion, a single intussuscepted ileal nipple valve is used to create a nonrefluxing ureteroileal anastomosis. The remainder of the pouch is made from a detubularized ileum, which is configured into a pouch and anastomosed to the urethra. Not currently a recommended form of urinary diversion due to complications related to intussuscepted nipple valves.

REFERENCE

Hautmann RE, et al. Urinary diversion. World Health Organization (WHO) Consensus Conference on Bladder Cancer. Urology 2007;69(1 Suppl):17–49. Review.

SHORT TOPIC SECTION L

LABIAL ADHESIONS AND FUSION

DESCRIPTION Complete (fusion) or partial adherence 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 found at birth, and occurs in prepubescent girls and postmenopausal women. Fecal soiling as an infant, vulvovaginitis, eczema, dermatitis, and sexual abuse may be inciting factors. It may cause voiding dysfunction in severe cases, with resulting hydroureteronephrosis.

SYNONYMS

- Acquired postinflammatory cohesion of the labia minora
- Vulvar fusion
- Synechiae of the vulva

TREATMENT

- Conjugated estrogen cream locally applied
- Surgical treatment for severe cases

REFERENCE

1. Berkowitz CD, et al. Labial fusion in prepubescent girls: A marker for sexual abuse? Am J Obstet Gynecol 1987;156(1):16–20.

LACTATE DEHYDROGENASE (LDH), UROLOGIC CONSIDERATIONS

DESCRIPTION LDH is a cellular enzyme useful in monitoring the treatment of germ cell tumors. It tends to have a low specificity (further impaired in smokers), and therefore must be correlated with other clinical findings and lab markers (ie, -fetoprotein and -hCG). Some correlation has been made between LDH and tumor bulk. LDH can also be elevated in cases of liver involvement by other tumors such as renal cell carcinoma.

REFERENCE

2. Weissbach L, et al. The value of tumor markers in testicular seminomas. Results of a prospective multicenter study. Eur Urol 1997;32(1):16–22.

LAPIDES CLASSIFICATION OF VOIDING DYSFUNCTION

DESCRIPTION A historic system for categorizing neurogenic voiding dysfunction into 5 areas:

- Sensory neurogenic bladder: Interrupted afferent bladder sensation can lead to chronic bladder distension and deterioration. Common processes include diabetes mellitus, tabes dorsalis, and pernicious anemia.
- Motor paralytic bladder: Destruction of parasympathetic motor innervation to the bladder results in painful overdistension initially and inability to initiate and maintain micturition. Common processes include pelvic surgery or trauma and possibly herpes zoster.
- Uninhibited neurogenic bladder: Injury to the corticoregulatory tract of the sacral spinal cord (micturition reflex center) leads to frequency, urgency, and urge incontinence. Common processes include cerebrovascular accident, brain or spinal cord tumor, Parkinson disease, and demyelinating disease.
- Reflex neurogenic bladder: Complete interruption of sensory and motor pathways between the sacral spinal cord and brainstem 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

3. Voiding dysfunction: Diagnosis, Classification and management. In Gillenwater JY. Adult and Pediatric Urology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2002.

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), postaxial polydactyly, central obesity, mental retardation, and hypogenitalism. 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. Undescended or maldescended testes can be present neonatally in up to 25% of males.

SYNONYMS

- Bardet-Biedl syndrome: More general, including all of the above description
- Laurence-Moon syndrome: Much rarer; differs with the above description, including progressive spastic paraparesis and distal muscle weakness but without polydactyly

REFERENCE

4. Beales PL, et al. Bardet-Biedl syndrome: A molecular and phenotypic study of 18 families. J Med Genet 1997;34(2):92–98.

LAZY BLADDER SYNDROME (NURSE'S BLADDER)

DESCRIPTION First described by Swenson in 1962, this condition occurs when children exhibit holding behavior and void very infrequently. Thought to be caused by the continuous 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 VCUG shows a large smooth-walled bladder, and US of the upper tract is usually normal. Urodynamic studies show large bladders with decreased sensation during bladder filling, low pressures, and large post-void residuals. Timed voiding schedules, antibiotic suppression, biofeedback bladder training, and intermittent catheterization are all options for treatment.

REFERENCE

5. Bauer SB, et al. The unstable bladder of childhood. Urol Clin N Am 1980;7:321.

LEADBETTER-CLARKE URETERAL ANASTOMOSIS

DESCRIPTION A nonrefluxing anastomosis is created by making a longitudinal incision through the taenia, just outside the mucosa. The ureter is laid over the mucosa and a small buttonhole is made through the mucosa to anastomose the spatulated end of the ureter. The taenia is closed over the ureter.

REFERENCE

6. Kay R. Reimplantation of the ureter. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989: 526–538.

LEADBETTER-POLITANO URETERONEOCYSTOSTOMY

DESCRIPTION Through a transvesical exposure, the ureter is mobilized from the bladder wall and surrounding peritoneum. A new ureteral hiatus is created 2–3 cm above the old hiatus. The ureter is then delivered behind the entire bladder, through the new hiatus and tunneled submucosally toward the old hiatus, where it is reimplanted.

REFERENCE

7. Kay R. Reimplantation of the ureter. In: Novick AC, Streem SB, Pontes JE, et al., eds. Stewart’s Operative Urology. Baltimore: Williams & Wilkins, 1989: 526–538.

LEAK POINT PRESSURE (LPP)

DESCRIPTION The LPP, also known as the Valsalva leak point pressure, is the pressure required to cause urinary leakage in the absence of a bladder contraction. An LPP of <60 cm H_2O suggests significant intrinsic sphincter deficiency. If the LPP is 60–90, it suggests mild sphincter deficiency. Sphincter deficiency is minimal or absent with an LPP >90 cm H_2O. Performed during cystometric evaluation, the bladder is filled and the standing patient is asked to Valsalva until leakage occurs. The lowest pressure that results in leakage is the LPP.

REFERENCE

8. Webster GD, Kreder KJ. Neurologic evaluation. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998.

LEBAG NEOBLADDER

DESCRIPTION This is a modification of the Mainz I 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 staplers to create a broad intestinal plate, which is then converted into a pouch with a ureterocolonic and urethral anastomosis.

REFERENCE

9. Pannek J, Senge T. History of urinary diversion. Urol Int 1998;60(1):1–10.

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. The ureter is pulled through this opening and laid in the mucosal incision. The mucosa is then sutured to the side of the ureter.

REFERENCE

Evangelidis A, et al. Evaluation of ureterointestinal anastomosis: Wallace vs Bricker. J Urol 2006; 175(5):1755–1758.

LEIOMYOMATOSIS, HEREDITARY

DESCRIPTION Familial cancer syndrome of a triad of cutaneous leiomyomas, uterine leiomyomas, and type 2 papillary renal cell carcinoma (RCC). Renal tumors tend to be solitary and unilateral and are likely to be aggressive; collecting duct RCCs have also been observed. The lesions are usually seen in women 20–35 yr old.

Given their aggressive nature, the prompt surgical resection of renal tumors is recommended.

REFERENCE

Coleman JA. Familial and hereditary renal cancer syndromes. Urol Clin N Am 2008;35(4):563–572.

LEOPARD SYNDROME

DESCRIPTION An autosomal dominant condition similar to Noonan syndrome, except for multiple lentigines (macule pigment accumulation within the dermis and epidermis). LEOPARD syndrome is the mnemonic for lentigines, ECG abnormalities, ocular hypertelorism/obstructive cardiomyopathy, pulmonary valve stenosis, abnormalities of genitalia in males, retardation of growth, and deafness. Cardiomyopathy is an important feature because it is associated with significant mortality. Genital hypoplasia in males, including a small penis and small, often undescended testicles, is the most common association. Hypospadias and delayed puberty may also be found.

SYNONYMS

- Multiple lentigines syndrome
- Progressive cardiomyopathic lentiginosis

TREATMENT

Orchiopexy, repair of hypospadias

REFERENCE

Coppin BD, Temple IK. Multiple lentigines syndrome (LEOPARD syndrome or progressive cardiomyopathic lentiginosis). J Med Genet 1997;34(7):582–586.

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/feet, and inability to maintain a stable erection due to inadequate arterial flow to the penis (hypogastric arterial obstruction). Gradual occlusion allows for collateral circulation; therefore, acute symptoms are unlikely. The condition is also known as

SYNONYMS

Gradual thrombotic obliteration of the abdominal aorta and iliac arteries

TREATMENT

Bypass graft from the aorta to iliac or common femoral arteries.

REFERENCE

Krotovsky GS, et al. Surgical treatment and prevention of vasculopathic impotence in conjunction with revascularization of the lower extremities in Leriche's syndrome. J Cardiovosc Surg 1991;32(3):340–343.

LESCH-NYHAN SYNDROME

DESCRIPTION First described in 1964 as an X-linked recessive disorder associated with failure to form hypoxanthine phosphoribosyltransferase, this disorder is caused by loss of function of the enzyme Hpoxanthine guanine posphoribosyl-transferase. Manifestations are hyperuricemia and uric acid lithiasis, choreoathetosis, mental retardation, spastic cerebral palsy, and self-mutilation of fingers and lips by biting. Allopurinol is the main urologic intervention to reduce hyperuricemia.

REFERENCE

Nyhan WL, Wong DF. New approaches to understanding Lesch-Nyhan disease. N Engl J Med 1996;334(24):1602–1604.

LEUKEMIA, UROLOGIC CONSIDERATIONS

DESCRIPTION Leukemic infiltration of the testicle can be seen in children with acute lymphoblastic leukemia (ALL). The typical presentation is testicular enlargement, typically bilateral. Open testicular biopsy, bilaterally, should be performed along with bone marrow and CSF analysis for tumor recurrence. Orchiectomy is not indicated for leukemic infiltration. Testes were once a common site of relapse, but with current intensive chemotherapy regimens, the testicular relapse rate is <5%. No strong evidence suggests an increase in birth defects in the children of leukemia survivors. Patients treated with cyclophosphamide-containing regimens are at risk for hemorrhagic cystitis and long-term urothelial tumors. (See also Section I: “Cystitis, Hemorrhagic [Infectious, Noninfectious].”)

TREATMENT

- If the testicle 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 hypogonadotropic hypogonadism and low testosterone with azoospermia.

REFERENCE

Pui CH, Rivera GK. Acute lymphoblastic leukemia. In: Rudolph AM, ed. Rudolph’s Pediatrics, 19th ed. Norwalk, CT: Appleton & Lange, 1991.

LEUKOPLAKIA, PENIS

DESCRIPTION Solitary or whitish plaques with hyperkeratosis, parakeratosis, and hypertrophy of the squamous rete pegs, with edema and lymphocytic infiltration. The condition often involves the penile meatus and has been associated with in situ squamous cell carcinoma and verrucous carcinoma.

TREATMENT

- Eliminate chronic irritation
- Circumcision
- Surgical excision with periodic biopsy of incompletely excised lesions

REFERENCE

Bissada NK. Conservative extirpative treatment of cancer of the penis. Urol Clin N Am 1992;19(2): 283–290.

LEUKORRHEA

DESCRIPTION Generally refers to nonmalodorous, mucousy, white or yellowish vaginal discharge in the absence of any pathologic cause. The quantity and quality vary among individuals, and mild irritative symptoms can be normal. Leukorrhea is also seen during infancy secondary to maternal estrogens, as well as during puberty secondary to estrogen surges. Reassurance is all that is necessary if the cervical and vaginal exam is normal, vaginal pH is normal (<4.5), and there are normal findings on microscopy and a negative amine test. (See also Section II: “Vaginosis”; Section III: “Vaginal Discharge Algorithm.”)

REFERENCE

Anderson AU, et al. Are vaginal symptoms ever normal? A review of the literature. MedGenMed 2004;22:49.

LICH-GREGOIR URETERAL REIMPLANTATION

DESCRIPTION This extravesical, less invasive repair does not disrupt the ureteral trigonal continuity. A 4–5-cm trough is created by dissecting the detrusor of the mucosa, and the mobilized ureter is placed in the trough with the detrusor closed over it.

REFERENCE

Kay R. Reimplantation of the ureter. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989: 526–538.

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, lymphocytes, 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

- Spontaneous healing is common.
- Oral histamines
- Topical antipruritics and topical corticosteroids may be helpful.

REFERENCE

Davis DA, Skidmore RA, Woosley JT. Lichen nitidus. Urology 1996;47(4):573.

LICHEN PLANUS, PENIS

DESCRIPTION An uncommon pruritic inflammation of the skin, which typically occurs on the penile glans. Benign, it is characterized by pruritic, violaceous, and flat-topped papules. Histologically, there can be seen 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, Bowen disease, psoriasis, Zoon balanitis, and squamous cell carcinoma.

There is no specific treatment; symptomatic relief is obtained through antihistamines, ataractics, and topical lotions.

REFERENCE

Varghese M, Kindel S. Pigmentary disorders and inflammatory lesions of the external genitalia. Urol Clin N Am 1992;19(1):111–121.

LICHEN SCLEROSIS ET ATROPHICUS

DESCRIPTION An uncommon cutaneous disorder with a female predominance. Early lesions are characterized as either 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. Extragenital areas (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 has been reported to occur.

SYNONYMS

- Lichen sclerosis
- The late stage evolves into balanitis xerotica obliterans

TREATMENT

- Circumcision
- Topical treatments for nongenital areas

REFERENCE

Lipscombe TK, et al. A study of clinical and aetiological factors and possible associations of lichen sclerosus in mates. Australia J Dermatol 1997;38(3):132–136.

LICHEN SIMPLEX CHRONICUS (LICHEN SIMPLEX COMPLEX)

DESCRIPTION Localized chronic pruritus with patches of dermatitis, resulting from chronic scratching/rubbing. Common sites are the perineum, thigh, scrotum, and vulva. The tesions appear as multiple oval plaques that become thickened and scaly. There is a whitish gray discoloration caused by lichertification and maceration. The skin may become more susceptible to secondary infection and allergic contact dermatitis. Etiologies include contactants (irritant and allergic), infection, and underlying dermatoses. Microscopically, the lesions resemble chronic dermatitis with hyperkeratosis and parakeratosis. Diagnosis is usually clinical, but biopsy may be necessary.

SYNONYMS

Circumscribed neurodermatitis.

TREATMENT

- Break the scratch-itch cycle.
- Stop all irritants.
- Sitz baths or soaks
- Open wet compresses to affected areas
- Systemic antipruritics and/or sedating medications may be necessary to lessen the itching.
- Topical and occasionally systemic steroids are necessary.

REFERENCE

Margesson LJ. Vulvar disease pearls. Dermatol Clin 2006;24(2):145–155.

Weyers W, et al. Lichen amyloidosus: A consequence of scratching. J Am Acad Dermatol 1997;37(6):923–928.

LIFE EXPECTANCY, UROLOGIC CONSIDERATIONS

DESCRIPTION Life expectancy is commonly used by urologists when determining therapy for localized prostate cancer, as age directly influences choice of treatment.

Current Age	Life Expectancy (yr) Male	Life Expectancy (yr) Female
65	16.67	19.5
66	15.96	18.72
67	15.27	17.95
68	14.59	17.19
69	13.93	16.45
70	13.27	15.72
71	12.64	15.01
72	12.01	14.31
73	11.41	13.62
74	10.81	

12.95
75
10.24
12.29
76
9.68
11.64
77
9.14
11.01
78
8.62
10.4
79
8.11
9.8
80
7.62
9.22
81
7.15
8.65
82
6.7
8.11
83
6.26
7.59
84
5.84
7.09
85
5.45
6.62
86

5.08
6.17
87
4.73
5.74
88
4.4
5.33
89
4.09
4.96
90
3.8
4.6

REFERENCE

Social Security Administration. Available at: www.socialsecurity.gov. Accessed August 13, 2009.

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 circumscribes the homogenous, sharply marginated fat. It is benign and must be distinguished from liposarcoma, angiolipoma, and cystic teratoma, usually by CT. Treatment is by surveillance, unless symptomatic. (See also Section II: “Bladder Mass.”)

REFERENCE

Berens BM, Azarvan A. Bladder outlet obstruction due to pelvic lipoma: Computerized tomography, magnetic resonance imaging and radiographic evaluation. J Urol 1991;145(1):138–139.

LIPOMA, SPERMATIC CORD

DESCRIPTION Benign lobulated preperitoneal fat that can project down the cord. Accounts for up to 90% of spermatic cord tumors and is most commonly seen in adults. Histologic variants include angiolipoma, fibrolipoma, fibromyxolipoma, myxolipoma, and myxoid myolipoma. The lesion can present as a mass, and must be distinguished from adenomatoid tumor, leiomyoma, fibroma, liposarcoma, leiomyosarcoma, and fibrosarcoma. (See also Section I: “Spermatic Cord Mass.”) Complete excision at time of surgery is recommended.

REFERENCE

Lioe TF, Biggart JD. Tumours of the spermatic cord and paratesticular tissue. A clinicopathological study. Br J Urol 1993;71(5):600–606.

LIPOMATOSIS, PELVIC

DESCRIPTION First described in 1959 as an overgrowth of fat in the perirectal and perivesical regions that can cause compression of the lower urinary tract and lead to uremia. 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. On a plain abdominal x-ray, it presents with radiolucency of the perivesical areas. On cystography, a full bladder has an abnormal shape (banana shape) and position (superiorly as well as anteriorly). Pelvic lipomatosis has been associated with a higher incidence of hypertension. Cystoscopy should be performed, as there are reports of associated cystitis glandularis. Surgical removal of the fat (difficult and feasible in select few patients) may be possible. For those patients with obstructive uropathy, treatment options include ureteral stenting, nephrostomy tubes, ureteral reimplantation, or urinary diversion. Pelvic exploration is done with caution as the normal anatomic planes are disrupted by the infiltrating fat.

REFERENCE

Trilla Herrera E, et al. Pelvic lipomatosis: Clinical review and report of four new cases. Actas Urol Esp 2000;24(5):423–428.

LIPOMENINGOCELE, UROLOGIC CONSIDERATIONS

DESCRIPTION A meningocele associated with an overlying lipoma. This condition belongs to the family of occult spinal dysraphisms 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 absent perineal sensation, back pain, secondary incontinence (incontinence after initial period of dryness), recurrent UTIs, or fecal soiling. In children <3 yr old, urodynamic testing may be normal but it is usually abnormal in children >3 yr.

Address urinary symptoms as appropriate after urodynamic testing, and refer to a neurosurgeon for evaluation of tether release to prevent further injury and growth.

REFERENCE

Rendeli C, Ausili E, Tabacco F. Urodynamic evaluation in children with lipomeningocele: Timing for neurosurgery, spinal cord tethering and follow-up. J Urol 2007:177(6):2319–2324.

LIVER METASTASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION The liver is a primary site for many malignant neoplasms, including those arising in the GU tract. Transitional cell carcinoma, renal cell carcinoma, 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 urobilinogen levels on urine analysis.

TREATMENT

- Evaluate and treat primary tumor.
- Segmental resection or locally ablative therapies may be appropriate.

REFERENCE

Campbell SC, Novick AC, Bukowski MD. Renal tumors. In: Wein et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

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 (Escherichia coli, Klebsiella, Aerobacter aerogenes, 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 II: “Pyelonephritis, Acute.”)

SYNONYMS

- Acute lobar nephronia
- Acute focal bacterial nephritis

TREATMENT

- IV antibiotics
- Radiologic surveillance: CT or US

REFERENCE

Papanicolaou N, Pfister RC. Acute renal infections. Radiol Clin N Am 1996;34(5):965–995.

LORD PROCEDURE

DESCRIPTION Described in 1964 as a bloodless operation for the treatment of hydroceles using a trans-scrotal incision to deliver the hydrocele from the scrotum. The testes are extruded, and the tunica vaginalis is plicated with no resection of the hydrocele sac. Not suitable for thick-walled or multiloculated hydroceles due to the amount of bundled residual tissue. A Penrose drain is recommended.

REFERENCE

Oesterling JE. Scrotal surgery. In: Glenn JF, ed. Urologic Surgery, 4th ed. Philadelphia: JB Lippincott, 1991:924–926.

LOWE SYNDROME

DESCRIPTION Also called oculocerebrorenal syndrome, it was first described in 1952 as an X-linked recessive disorder manifested by congenital cataracts, hypotonia, developmental delay, poor growth, and renal tubular dysfunction. Proteinuria and aminoaciduria are present by 1 yr of age, with gradual progression of Fanconi syndrome (typically failure to reabsorb water, electrolytes, bicarbonate, glucose, calcium, phosphorus, and small molecules). Polyuria, metabolic acidosis, hypophosphatemia with rickets, hypercalciuria, and sodium and potassium wasting can occur, leading eventually to end-stage renal disease. Nephrolithiasis has been reported due to the hypercalciuria. Vitamin D supplements and surveillance for nephrolithiasis are recommended.

REFERENCE

Sliman GA, et al. Hypercalciuria and nephrocalcinosis in the oculocerebrorenal syndrome. J Urol 1995; 153(4):1244–1246.

LOWER URINARY TRACT SYMPTOMS (LUTS)

DESCRIPTION Historically, urinary tract symptoms in older men were referred to as prostatism. Since these symptoms may not be gender-specific, use of this term is no longer recommended. Prostatism also implies that the symptoms have a prostatic origin; however, even in men, the symptoms may not be caused by prostatic disease. Since voiding symptoms are neither pathognomonic for benign prostatic hypeplasia (BPH) nor specifically related to diseases of the prostate, a more accurate expression is the term lower urinary tract symptoms (LUTS). Historically, bladder outlet obstruction (BOO), LUTS, and hyperplasia of the prostate have been considered to be almost synonymous; however, an increasing number of studies demonstrate that the correlations between these parameters are weak, and symptoms may originate outside the lower urinary tract (ie, polyuria as a cause of urinary frequency). Traditionally, LUTS has been divided into obstructive and irritative symptoms. Recently, it has been suggested that these effects are more appropriately termed voiding symptoms and storage symptoms, respectively.

- Voiding symptoms: Weak stream, abdominal straining, hesitancy, intermittency, incomplete bladder emptying, dribbling, and dysuria
- Storage symptoms: Frequency, nocturia, urgency, incontinence, and bladder pain

(See also Section I: “Bladder Outlet Obstruction and Prostate, Benign Hyperplasia/Hypertrophy (BPH)”; Section II: “Voiding Symptoms, Definitions [International Continence Society Definitions].”)

REFERENCE

Jepsen JV, Bruskewitz RC. Office evaluation of men with lower urinary tract symptoms. Urol Clin N Am 1998;25(4):545–554.

LUB SYNDROME

DESCRIPTION Very rare, incomplete androgen insensitivity of karyotype XY with testes but ambiguous genitalia. Nonfertile, with elevated testosterone and LH levels, these children are usually raised as female and early gonadectomy and feminizing genitoplasty is performed in infancy. (See Section I: “Disorders of Sexual Development [DSD].”)

REFERENCE

Snyder HM. Management of ambiguous genitalia in the neonate. In: Snyder NM, ed. Urologlic Surgery in Neonates and Young Infants, 19th ed. Philadelphia: Saunders, 1988:346–348.

LYME DISEASE, UROLOGIC CONSIDERATIONS

DESCRIPTION Lyme disease is caused by the spirochete Borrelia burgdorferi and is a multisystem inflammatory disorder. Urinary dysfunction is rarely reported but has been linked to detrusor hyperreflexia or, less commonly, hyporeflexia. Detrusor external sphincter dyssynergia has not been described. The urinary tract may be part of the neuro-borreliosis phase or the spirochete may directly invade the urinary tract.

SYNONYMS

- Neuroborreliosis
- Bannwarth syndrome
- Acrodermatitis chronica atrophicans

TREATMENT

- Therapy is aimed at stage of dissemination and symptomatology; 1st-line therapy is doxycycline 100 mg b.i.d. or amoxicillin 500 mg q.i.d. for 10–15 days; a longer course and IV antibiotics are required for more severe disease.
- Conservative bladder management including CIC guided by urodynamic evaluation

REFERENCE

Chancellor MB, et al. Urinary dysfunction in Lyme disease. J Urol 1993;149(1):26–30.

LYMPHADENOPATHY, PELVIC AND RETROPERITONEAL

DESCRIPTION Abnormally enlarged lymph nodes seen on abdominal imaging including CT, MRI, and sometimes US. Enlargement is generally identified when the nodes are multiple or >2–3 cm. If needed, biopsy can be performed by laparotomy, laparoscopy, or percutaneous techniques. (See also Section I: “Retroperitoneal Masses and Cysts.”)

CAUSES

- Systemic malignancies (ie, lymphoma)
- Infectious disease (ie, TB)
- Pelvic malignancy, including prostate cancer, transitional cell carcinoma, and testicular and penile cancer

REFERENCE

Ferri FF. 2008 Ferri’s Clinical Advisor: Instant Diagnosis and Treatment, 1st ed. Philadelphia: Mosby Elsevier, 2008.

LYMPHANGIOGRAM, PEDAL

DEFINITION

Contrast injection into lymphatic channels on the dorsum of foot to visualize retroperitoneal lymph nodes. This technique has been largely replaced by CT, but it can be used to assess the retroperitoneal lymph nodes in patients with testicular and prostatic cancer. Its major advantage over CT scan is the detection of architectural changes in nonenlarged lymph nodes. It is time-consuming, invasive, does not opacify sentinel nodes, cannot differentiate between malignant and nonmalignant changes, and may cause fibrosis of lymph nodes due to reaction to the contrast medium.

REFERENCE

Pollack H. Tumors of the testis and testicular adnexa. In: Pollack H, ed. Clinical Urography. Philadelphia: Saunders, 1990:1424–1428.

LYMPHANGIOMA, BLADDER

DEFINITION

This rare bladder lesion presents with hematuria, and several cases are reported in children. Treatment is by partial cystectomy. The lesion is composed of multiple small cystic cavities filled with proteinaceous material, typical of cavernous lymphangiomas.

REFERENCE

Bolkier M, et al. Lymphangioma of bladder. J Urol 1983;129(5):1049–1050.

LYMPHANGIOMA, RENAL

DESCRIPTION A rare tumor, with 1/3 occurring in children and 2/3 in adults. The lesion appears as a solitary encapsulated mass with multiple cysts. Microscopy reveals benign endothelial cells with septa, which may contain smooth muscle. If within the renal sinus, the mass may cause obstruction.

REFERENCE

Bostwick DG. Neoplasms of the kidney. In: Bostwick DG, Eble JN, eds. Urological Surgical Pathology. St. Louis: Mosby, 1997:110.

LYMPHANGIOMA, SCROTAL

DESCRIPTION Congenital malformations of the intrascrotal lymphatic system, which may form cystic masses. These lymphangiomas are benign tumors, occurring mostly in children. They are found relatively infrequently in the scrotum. Treatment consists of surgical excision; unless completely removed, recurrences are common.

REFERENCE

MacMillan RW, et al. Scrotal lymphangioma. Urology 1984;23(1):79–80.

LYMPHOMA, UROLOGIC CONSIDERATIONS

DESCRIPTION Lymphoma can involve any part of the urinary tract, but is more commonly seen in the testicle and kidney:

- Lymphoma represents a common cause of testicular cancer in older men. It may be a local tumor growth or a late manifestation of widespread disease. >50% of testicular tumors in men >60 are lymphomas; these must be differentiated from seminoma. In adults, most are diffuse, large B-cell lymphomas; children can have Burkitt lymphoma involving the testicle.
- Bladder involvement is usually secondary to systemic disease and is present in 13% of patients dying of non-Hodgkin lymphoma. Primary bladder lymphoma occurs almost exclusively in females. Lesions may be sessile or polypoid and should be differentiated from chronic inflammatory bladder involvement, 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 prostatitis with follicular hyperplasia, neuroendocrine prostate cancer, and granulomatous prostatitis.
- Adrenal involvement is present in up to 25% dying of systemic disease. The adrenals are a rare primary site of disease, with bilateral, clinical, adrenal involvement in 18% of non-Hodgkin lymphoma and 9% of Hodgkin lymphoma. (See also Section II: “Hodgkin Lymphoma, Urologic Considerations.”)

TREATMENT

- Testicular lymphomas are usually managed by radical orchiectomy followed by systemic chemotherapy, depending on the extent of the disease. For stage I disease, 5-yr survival is >60%; if advanced, survival at 5 yr is <20%.
- Primary bladder lymphoma treated with radiation has reasonably good response rates. If the bladder site is part of systemic manifestation, systemic therapy is used.
- Prostatic lymphoma carries a poor prognosis, regardless of primary site; most die in <24 mo. Systemic therapy with TUR is used for obstructive symptoms.

REFERENCE

In: Bostwick DG, Eble JN, eds. Urological Surgical Pathology. St. Louis: Mosby, 1997:401, 403,627–629.

LYMPHORETICULAR MALIGNANT NEOPLASM, PENIS

DESCRIPTION Rarely, lymphoreticular malignancies (ie, 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 combined with local low-dose radiation.

REFERENCE

Begun FP, et al. Leukemia of the penis. J Urol 1989;142(1):123–124. Review.

LYMPHOVASCULAR INVASION, UROLOGIC CONSIDERATIONS

DESCRIPTION Lymphovascular invasion describes an important feature for many aspects of urologic oncology, because it is an adverse prognostic indicator transitional cell carcinoma (TCC) of the bladder and upper tracts, prostate cancer, and testicular cancer. In upper-tract TCC, 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 retroperitoneal and/or systemic failure.

REFERENCE

Sheinfeld J, Bartsch G, Bosl GJ. Surgery of testicular tumors. In: Wein et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

LYNCH SYNDROME

DESCRIPTION An autosomal dominant genetic syndrome caused by mutations in mismatch-repair enzymes, most commonly MSH2 and MLH1. This creates DNA microsatellite instability and increases the risk of colon and endometrial malignancy. An increased risk of upper-tract transitional cell carcinoma is also observed.

SYNONYMS

- Hereditary nonpolyposis colorectal cancers
- Hereditary 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 cytologies, upper endoscopy, and US of the endometrium)

REFERENCE

George P, Silvia J. In: Ferri FF, ed. 2008 Ferri's Clinical Advisor: Instant Diagnosis and Treatment, 1st ed. Philadelphia: Mosby Elsevier, 2008.

SHORT TOPIC SECTION M

MACE PROCEDURE

DESCRIPTION The Malone antegrade continence enema (MACE) procedure is performed mostly in children with complex constipation or fecal incontinence secondary to neurogenic dysfunction. Using the appendix, a continent catheterizable colonic stoma is made. Antegrade enemas delivered by this route produce complete colonic emptying and minimize fecal soiling.

REFERENCE

1. Malone PS, Ransley PG, Kiely EM. Preliminary report: The antegrade continence enema. Lancet 1990; 336(8725):1217–1218.

MACRO-ORCHIDISM

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 infiltration, carcinoma in situ, or as part of a fertility workup. MO may be related pathogenically to some hormonal regulation mechanism or to a higher seminiferous tubule sensitivity to FSH.

REFERENCE

2. Martinez-Garcia F, et al. Macro-orchidism: New pathogenetic and histopathologic aspects. Espanol Urol 1994;47(1):59–65.

MADSEN-IVERSEN SYMPTOM SCORE

DESCRIPTION Self-administered questionnaires have been used as an investigational tool for the evaluation of bladder outlet obstruction. The Madsen-Iversen score has been generally replaced by the AUA and I-PSS scoring systems, but this system is still widely reported for ongoing clinical studies and has high correlation with other indices.

REFERENCE

3. Barry MJ, et al. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversen, Boyarsky, and Maine Medical Assessment Program symptom indexes. J Urol 1992;148:1558–1563.

MAG3 RENAL SCAN

DESCRIPTION A nuclear medicine study is used to evaluate renal function and the presence of obstruction. MAG3 (technetium99m-mercaptoacetyltriglycine) is a nuclear isotope secreted by the renal tubules. Multiple images are taken over time to give anatomic details, including scarring and function of the kidney. A split differential function between the 2 kidneys is obtained. Commonly, furosemide is administered to induce diuresis, and the time for the kidney to clear 1/2 of the tracer is calculated (t½). A t½ of 0–10 min indicates nonobstructive drainage, 10–20 min is indeterminate, and >20 min is consistent with obstruction.

REFERENCE

4. Hubert, KC, Palmer, JS. Current diagnosis and management of fetal genitourinary abnormalities. Urol Clin N Am 2007;34(1):89–101.

MAGPI HYPOSPADIAS REPAIR

DESCRIPTION The acronym MAGPI stands for meatal advancement and glanuloplasty procedure. 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 glans is reapproximated ventrally, which, in effect, advances the meatus.

REFERENCE

5. Duckett JW. MAGPI (meatoplasty and glanuloplasty) a procedure for subcoronal hypospadias. 1981. J Urol 2002;167(5):2153–2158.

MAINZ I, II, III POUCH URINARY DIVERSION

DESCRIPTION The Mainz I (ileocecal pouch) is an orthotopic pouch created by opening the cecum and 2 limbs of distal ileum; the limbs are then sutured to create a broad intestinal plate. After a tunneled ureterocolonic anastomosis is made, the cecal portion of the plate is anastomosed to the male urethral stump and the plate is closed into a sphere. The Mainz II (sigma rectum pouch) is an augmented valved rectum created by making a 10–12-cm rectosigmoid opening. The sigmoid colon is configured into a U shape, and the medial plate is closed. Ureters 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 pouch made exclusively of colon (transverse-ascending colon pouch or transverse-descending colon pouch) with the efferent segment created from a tapered bowel segment embedded in the pouch wall.

REFERENCE

6. Bader P, et al. Urinary diversions: Which one is right for which patient? Urologe A 2009;48(2):127–136.

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.

REFERENCE

7. Long JP Jr., Althausen AF. Malacoplakia: A 25-year experience with a review of the literature. J Urol 1989;141(6):1328–1331.

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 urologic practice settings.

REFERENCE

8. Lue TF, Broderick GA. Evaluation and nonsurgical management of erectile dysfunction and premature ejaculation. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

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 lower urinary tract symptoms. It provides more in-depth assessment of ejaculatory function than previous measures of sexual dysfunction, mainly 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

9. Rosen RC, et al. Development and validation of four-item version of Male Sexual Health Questionnaire to assess ejaculatory dysfunction. Urology. 2007;69(5):805–809.

MALROTATED KIDNEY

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.

REFERENCE

Graham SD, Glenn JF, Keane TE. Glenn's Urologic Surgery 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2004.

MARSHALL-MARCHETTI-KRANTZ (MMK) CYSTOURETHROPEXY

DESCRIPTION A surgical procedure for the treatment of stress incontinence in women, it is performed through a Pfannenstiel incision. The retropubic space is exposed and the urethra, vaginal wall, bladder neck, and bladder are identified. The original description reports placement of a 3 paired No. 1 catgut suture to attach the paraurethral anterior vaginal wall to the back of the symphysis pubis, with the most proximal suture being at the bladder neck. The procedure can be performed laparoscopically.

REFERENCE

Parnell JP 2nd, et al. Primary management of urinary stress incontinence by the Marshall-Marchetti-Krantz vesicourethropexy. J Urol 1982;127(4):679–682.

MARTIUS GRAFT

DESCRIPTION A surgical technique used to repair urinary-vaginal fistulae. The flap is a well-vascularized fat pad from the labia major 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 sutured to the bladder or urethral wall at the site of the fistula repair. It serves as a barrier between suture layers to prevent recurrent fistula formation.

SYNONYMS

- Martius labial pedicle graft
- Martius labial fat pad repair
- Martius flap

REFERENCE

Rangnekar NP, Imdad N, Kaul SA, et al. Role of the Martius procedure in the management of urinary-vaginal fistulas. J Am Coll Surg 2003;191(3): 259–263.

MATHIEU HYPOSPADIAS REPAIR

DESCRIPTION A ventral flap is mobilized based on the Dartos blood supply, and it is transposed over the urethral plate to advance the meatus. The lateral wings of the glans are approximated over the repair.

REFERENCE

Minevich E, et al. Mathieu hypospadias repair: Experience in 202 patients. J Urol 1999;162(6):2141–2142.

MATURATION ARREST

DESCRIPTION The term maturation arrest has been used to describe testicular biopsies in cases of infertility. Two forms of maturation arrest have been described: Spermatogenic arrest and spermatocytic (meiotic) arrest. The arrest is most frequently observed at the primary spermatocyte level. Reversible arrest at that level can be due to heat, infections, and hormonal and nutritional factors. Irreversible arrest at the primary spermatocyte or spermatid level has a genetic origin due to chromosomal anomalies. The dysfunction occurs in somatic and germ cells.

REFERENCE

Martin-du Pan RC, Campana A. Physiopathology of spermatogenic arrest. Fertil Steril 1993;60(6):937–946.

MAYER-ROKITANSKY-KUSTER-HAUSER SYNDROME

DESCRIPTION A congenital absence of the vagina, with some form of abnormal or absent uterus. The diagnosis is usually made when amenorrhea is noted in a normal pubertal female. Renal and skeletal anomalies are a common association. The defect involves mesodermal development and the mesonephric kidney, the latter resulting in abnormalities in the paramesonephros (uterus and vagina) and in the metanephric kidney.

REFERENCE

Griffin JE, Edwards C, Madden JD, et al. Congenital absence of the vagina. The Mayer-Rokitansky-Kuster-Hauser syndrome. Ann Intern Med 1976;85(2):224–236. Review.

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 features, such as cytoplasmic-nuclear-nucleolar morphology, mitotic activity, and tumor invasiveness, are all used to assign grade.

REFERENCE

Kozlowski JM, Grayhack JP. Carcinoma of the prostate. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 2nd ed. St. Louis: Mosby, 1991.

MCCUNE-ALBRIGHT SYNDROME

DESCRIPTION A syndrome characterized by a classic triad of fibrous dysplasia (cystic bone lesions), precocious puberty, and cutaneous pigmentation. Association with various endocrine abnormalities is common.

SYNONYMS

- Polyostotic fibrous dysplasia
- Osteitis fibroso cystica

TREATMENT

- Hyperthyroidism surgery
- Adrenalectomy

REFERENCE

Giovannelli G, Bernasconi S, Banchini G. McCune-Albright syndrome in a male child: A clinical and endocrinologic enigma. J Pediatr 1978;92:220.

MCGUIRE URINAL

DESCRIPTION An external male urine collection device consisting of a reusable latex urinal sheath that is either self-contained or attached directly to a leg bag. It is often supported by fabric suspensions in a jock-strap type fashion.

REFERENCE

Tanagho EA, Bella AJ, Lue TF. Neuropathic bladder disorders. In: Tanagho EA, McAininch JW, eds. Smith's General Urology, 17th ed. New York: McGraw-Hill, 2007.

MEATAL STENOSIS, URETHRAL, FEMALE

DESCRIPTION Distal urethral (meatal) stenosis is a recognized entity. Females with this condition present clinically with complaints ranging from UTI to enuresis. Distal urethral stenosis may be associated with the roentgenologic appearance of a prominent, collar-like vesical neck, which reflects generalized detrusor hypertrophy. When treatment is deemed necessary, the distal urethra is calibrated with bougies. (See also Section III: “Urethra, Meatus, Normal Caliber.”)

REFERENCE

Perlmutter AD, et al. Urethral meatal stenosis in female children simulating bladder-neck obstruction. J Pediatr 1966;69(5):739–743.

MEATAL 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 meatus. Meatal stenosis is usually not apparent until the child is toilet trained. Strength and/or 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. Meatoplasty is the corrective procedure for those requiring surgical correction. (See also Section II: “Calibration, Meatus and Urethra.”)

REFERENCE

Brem J, Jaffee SR. Hidden meatal stenosis in male infants and children. Am Fam Physician (GP) 1970;2(2):72–73.

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 reliable diagnostic accuracy. For this reason, appropriate prenatal counseling is advocated for those at high risk.

REFERENCE

Sepulveda W, Sebire NJ, Souka A, et al. Diagnosis of the Meckel-Gruber syndrome at eleven to fourteen weeks' gestation. Am J Obstet Gynecol 1997;176(2):316–319.

MEDIAN BAR

DESCRIPTION Median bar refers to prostatic posterior commissural hyperplasia, an acinar hyperplasia involving the posterior vesical lip 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

Randall A. Surgical Pathology of Prostatic Obstruction. Baltimore: 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 outgrows of epithelium after primary closure of urethral folds, or that they arise from epithelial remains caused by incomplete closure of the folds. Cysts can be found anywhere from the distal penis to anus at the midline. They are usually asymptomatic until adulthood, when they can be traumatized or secondarily infected, producing swelling, tenderness, and purulent discharge. Treatment is simple excision followed by primary closure.

REFERENCE

Krauel L. Median raphe cysts of the perineum in children. Urology 2008;71(5):830–831.

MEDULLARY CYSTIC KIDNEY

DESCRIPTION A form of progressive renal disease with up to 75% of cases having medullary cysts, although it is primarily a tubulointerstitial disease. Juvenile nephronophthisis and medullary cystic disease are similar anatomically and clinically, but they have different modes of transmission and different clinical presentations. Juvenile nephronophthisis usually is inherited as an autosomal recessive trait (onset age: 6–20 yr), and medullary cystic disease typically is inherited as an autosomal dominant trait that presents after the 3rd decade. Patients present with polyuria and polydipsia due to salt wasting, a concentrating defect, anemia, and profound growth retardation. Juvenile nephronophthisis often is associated with disorders of the retina (ie, retinitis pigmentosa), skeletal abnormalities, hepatic fibrosis, and Bardet-Biedl syndrome (obesity, mental retardation, polydactyly, retinitis pigmentosa, and hypogenitalism). On US or CT, the medullary cysts can be seen with parenchyma and may appear hyperechogenic due to tubulointerstitial fibrosis.

SYNONYMS

- Juvenile nephronophthisis
- Uremic medullary cystic disease
- Salt-losing enteropathy
- Uremic sponge kidney

TREATMENT

Sodium replacement initially, with dialysis and transplantation later. The transplant graft appears to be resistant to the disease.

REFERENCE

Bernstein J, Gardner KD Jr. Familial juvenile nephronophthisis: Medullary cystic disease. In: Edelman CM Jr., ed. Pediatric Kidney Disease. Boston: Little, Brown, 1979:580.

MEGA PREPUCE

DESCRIPTION Also known as megameatus intact-prepuce variant, this is a variant of hypospadias in which the ventral prepuce is intact. It is normally discovered following a dorsal slit at the time of circumcision. Associated anomalies include chordee, penoscrotal inversion, bifid scrotum, and cryptorchidism.

TREATMENT

Abort circumcision, apply Vaseline gauze to incision and refer the patient to a pediatric urologist

REFERENCE

Mesrobian HO. Urologic problems of the neonate: An update. Clin Perinatol 2007;34(4):667–679.

MEGACALYCOSIS

DESCRIPTION A nonobstructive enlargement of the calyces due to a congenital malformation of the renal papillae. There is no dilation of the renal pelvis, and no evidence of ureteropelvic junction obstruction. Found almost exclusively in males, it often presents in children due to a UTI workup or in adults with hematuria and renal calculi. The clinician must differentiate between hydronephrosis and UPV obstruction.

TREATMENT

None necessary. A diuretic renogram fails to demonstrate any obstruction.

REFERENCE

Gittes RF, Talner MB. Congenital megacalyces vs obstructive hydronephrosis. J Urol 1972;108:833.

MEGACYSTIS, CONGENITAL

DESCRIPTION A dilated, thin-walled bladder with a wide and poorly developed trigone. Because of the laterally displaced ureters, vesicoureteral reflux is commonly seen. Bladder contractility is normal, but most urine refluxes retrograde into the collecting system. Correction of the reflux often restores normal bladder dynamics. It is most often diagnosed on prenatal US. It is associated with megacystis- microcolon-intestinal hypoperistalsis syndrome, a rare congenital disorder characterized by a dilated, nonobstructive urinary bladder and hypoperistalsis of the GI tract.

TREATMENT

Correction of vesicoureteral reflux after 6 mo of age

REFERENCE

Frimberger D, Kropp BP. Bladder anomalies in children. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

MEGACYSTIS-MEGAURETER SYNDROME

DESCRIPTION The term megacystis-megaureter describes the radiologic appearance of a large-capacity, thin-walled bladder and massive primary vesicoureteral reflux. The pathophysiology of these massively dilated ureters and the large-capacity bladder is the constant recycling of large volumes of refluxed urine. Bladder contractility is normal, even with a poorly developed trigone. Surgical correction of the reflux usually leads to a normal voiding pattern. (See also Section I: “Vesicoureteral Reflux, Pediatric.”)

TREATMENT

Correction of the reflux surgically should lead to a normal voiding pattern.

REFERENCE

Burbige KA, Lebowitz RL, Colodny AH, et al. The megacystis-megaureter syndrome. J Urol 1984; 131(6):1133–1136.

MEGALOURETHRA

DESCRIPTION Megalourethra is an extremely rare congenital deficiency of the mesodermal tissues of the phallus can best be described as a urethral diverticulum that affects the entire penile urethra. Two types have been described, scaphoid and fusiform. Scaphoid megalourethras are more common and have an absence of corpus spongiosum, whereas fusiform megalourethras lack both spongiosum and corpora cavernosa. Often associated with lethal congenital anomalies, fusiform megalourethras 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 mesenchymal defect similar to the pathophysiology of prune belly syndrome (PBS). Many other conditions are associated, such as PBS, renal agenesis, hypospadias, cryptorchidism, and others. For PBS, urethrostomy may be needed secondary to bladder outlet obstruction 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.

REFERENCE

Vaghefi H, et al. Two extremes of the megalourethra spectrum. Urology 2006;67:614–616.

MELANOMA, ADRENAL

DESCRIPTION Primary malignant melanoma of the adrenal gland is an established entity. It originates in the adrenal medulla from cells derived from the neural crest. Because of the high frequency of metastatic involvement of the adrenal by cutaneous and ocular melanomas, diagnosis can be difficult. Primary adrenal melanoma is a highly malignant tumor of middle age that often manifests as a painful flank mass. Distant lymph node metastases can be seen as a presenting sign. Treatment is not effective, with a mortality rate approaching 100% within 2 yr.

REFERENCE

Dao AH, Page DL, Reynolds VH, et al. Primary malignant melanoma of the adrenal gland. A report of two cases and review of the literature. Am Surgeon 1990;56(4):199–203.

MELANOMA, GENITOURINARY

DESCRIPTION Malignant melanoma of the GU tract is rarely a primary disease. However, lesions of the penis and urethra 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 die of metastatic disease within 2 yr.

REFERENCE

Stein BS, Kendall AR. Malignant melanoma of the genitourinary tract. J Urol 1984;132(5):859–868.

MELANOMA, URETHRAL

DESCRIPTION A malignant degeneration of melanocytes and nevus cells, primary malignant melanomas are rare. The urethra is the preferred site of the urinary tract and accounts for ~4% of urethral 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 urethral tumors, but melanuria is sometimes seen. It may be confused with urethral polyps, caruncles, mucosal prolapse, chancre, or more common malignant urethral tumors. It is most commonly unifocal. These are usually deeply invasive; local extension is common and inguinal lymph node metastases are present at diagnosis in 1/2 of the cases. Most patients do not survive >3 yr.

TREATMENT

- Limited data are available; most are treated with radical surgery and frequently bilateral lymph node dissection.
- Chemotherapy, immunotherapy, radiotherapy, or a combination of all 3 is experimental.

REFERENCE

Oliva E, Quinn TR, Amin MB, et al. Primary malignant melanoma of the urethra: A clinicopathologic analysis of 15 cases. Am J Surg Pathol 2000;24(6): 785–796.

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. Neurogenic function progressively deteriorates. A colorless and friable hair is characteristically found. There tends to be a high incidence of GU anomalies, including bladder diverticula, UTI, ureteropelvic junction obstruction, vesico-ureteral reflux, and cryptorchidism.

TREATMENT

- Parental copper therapy
- Bladder diverticula generally are treated with clean intermittent catheterization, as well as open cutaneous vesicostomy. Excision of the bladder diverticula is hazardous because of the generally poor health of these patients.

REFERENCE

Oshio, T, et al. Urologic abnormalities in Menkes' kinky hair disease: Report of three cases. J Pediatr Surg 1997;32(5):782–784.

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 dyspareunia (~40%), itching, and vaginal dryness (~55%) occur secondary to reduced estrogen and androgen secretions. A change in the pH of vaginal fluid from acidic to neutral occurs 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.
- 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.

REFERENCE

Lobo RA. Menopause: Endocrinology, consequences of estrogen deficiency, effects of hormone replacement therapy, treatment regimens. In: Katz VL, et al. Comprehensive Gynecology, 5th ed. Philadelphia: Mosby Elsevier, 2007.

MESOTHELIOMA, BENIGN, TESTICULAR TUNIC

DESCRIPTION Both a benign papillary and nonpapillary (adenomatoid tumor) variety exist. The nonpapillary tumor is the most common tumor of the epididymis and cord. Both arise from the tunica vaginalis and are usually seen in young men 20–50 yr of age. The most common clinical presentation is associated with a painless scrotal mass or hydrocele.

REFERENCE

Bostwick DG. Spermatic cord and testicular adnexa. In: Bostwick DG, Eble JN, eds. Urological Surgical Pathology. St. Louis: Mosby, 1997.

MESOTHELIOMA, MALIGNANT, TESTICULAR TUNIC

DESCRIPTION Mesothelioma is a rare tumor (<100 cases reported), affecting the serosal surface of pleura, pericardium, peritoneum, and tunica vaginalis (an extension of the peritoneum). It usually presents as an incidental finding at the time of hydrocele surgery. It most commonly presents in the 5th–7th decades, although it has been reported in a patient 10 yr old. Patients typically present with a hydrocele, but the initial physical exam rarely suggests malignancy. Metastatic spread occurs early via the lymphatic system to the paraaortic, inguinal, and supraclavicular nodes. The tumor spreads less commonly via the bloodstream to the lungs and liver. In the absence of metastatic spread, aggressive local surgery seems to yield the best results. The role of adjuvant chemotherapy and radiotherapy is less clear.

REFERENCE

Eden CG, Bettochi C, Coker CB, et al. Malignant mesothelioma of the tunica vaginalis. J Urol 1995;153[3 Pt 2]:1053–1054.

METABOLIC SYNDROME, UROLOGIC CONSIDERATIONS

DESCRIPTION An increasingly more prevalent disease affecting ~22% of American adults, metabolic syndrome is characterized by having any three of the following: Abnormal waist circumference, hypertriglyceridemia, low HDL, hypertension, or abnormal fasting glucose parameters. Sexual dysfunction can occur, including hypogonadism and erectile dysfunction. Many patients have a low urinary pH, thus increasing the risk of uric acid stones. Subclinical Cushing syndrome accounts for 3–5% of metabolic syndrome and should be in the differential diagnosis.

SYNONYMS

- Syndrome X
- Insulin resistance syndrome
- Obesity dyslipidemia syndrome

TREATMENT

- Lifestyle modifications with dietary changes, increased physical activity, and smoking cessation
- Consider bariatric surgery in the management of obesity.
- Pharmacologic therapy aimed at hypertension, hyperlipidemia, other
- Testosterone for hypogonadism may have protective cardiovascular effects
- Oral hydration and urine alkalinization can be considered for uric acid stone formers.

REFERENCE

Fagan M, Gopalakrishnan G. Metabolic syndrome. In: Ferri FF, ed. Ferri's Clinical Advisor 2008, 1st ed. Philadelphia: Mosby Elsevier, 2008.

METANEPHRIC ADENOFIBROMA

DESCRIPTION A pediatric benign 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 renal cell carcinoma. 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.

REFERENCE

Shek TWH, et al. Metanephric adenofibroma: Report of a case and review of the literature. Am J Surg Pathol. 1999;23:727–733.

METANEPHRIC ADENOMA

DESCRIPTION A recently recognized renal tumor originally described in 1980; it bears 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 5th–6th decades of life, and the lesion is often discovered incidentally. An association with polycythemia has been reported in 12% of the cases. These adenoma are typically unilateral and 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 renal cell carcinoma on imaging studies.

REFERENCE

Hartman DJ, MacLennan GT. Renal metanephric adenoma. J Urol 2007:178(3):1058.

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 functional steroids, thereby lessening the severity of symptoms. Metapyrone blocks the conversion of 11-deoxycortisol to cortisone. It is a diagnostic test for hypothalamic-pituitary ACTH function:

- Day 1: Control period: Collect 24-hr urine to measure 17-hydroxycorticosteriods or 17-ketogenic steroids.
- 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 metyrapone with milk or snack. (Adult: 750 mg PO q4h for 6 doses; Pediatric: 15 mg/kg q4h 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 metyrapone is a 2–4-fold increase in 17-OHCS excretion; drug interactions with phenytoin, cyproheptadine, and estrogens may lead to subnormal response.

REFERENCE

Scott HW Jr., Orth DN. Hypercortisolism. In: Surgery of the Adrenal Glands. Philadelphia: JB Lippincott, 1990.

MEYER-WEIGERT LAW

DESCRIPTION In cases in which separate ureteric buds on the same mesonephric duct form a completely duplicated collecting system, separate investigators (Weigert and then Meyer) noted that there exists a consistent relationship between the upper and lower pole orifices as they relate to one another on the trigone. The caudad, or distally placed, orifice actually drains the upper-pole moiety; whereas the cranial, or superior, 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

Schlussel RN, Retik AB. Anomalies of the ureter. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:1817–1819.

MICHAELIS-GUTMANN BODIES

DESCRIPTION Michaelis-Gutmann bodies are the pathognomic finding in the benign inflammatory process known as malacoplakia. Light microscopy demonstrates a granulomatous inflammatory process, characterized by the accumulation of large mononuclear cells with abundant granular cytoplasm and PAS-positive calcific intracytoplasmic inclusions (so-called Michaelis-Gutmann bodies). On electron microscopy, such inclusions appear as concentric lamellated structures with a mineralized core.

REFERENCE

Lambird PA, Yardley JH. Urinary tract malakoplakia: Report of a fatal case with ultrastructural observations of Michaelis-Gutmann bodies. Johns Hopkins Med J 1970;126(1):1–14.

MICROLITHIASIS, TESTIS

DESCRIPTION Testicular microlithiasis is an uncommon condition characterized by the presence of calcifications within degenerating seminiferous tubules. A review of scrotal sonograms in adults revealed the incidence of bilateral testicular microlithiasis to be 0.6%. Although the condition is considered benign, microlithiasis has been described in association with various testicular neoplasms. Testicular microlithiasis may be differentiated from tumorous calcifications by a combination of physical exam, tumor marker levels, and US. Currently, no particular etiologic relationship has been documented between testicular microlithiasis and testis tumor.

REFERENCE

Miller RL, Wissman R, White S, et al. Testicular microlithiasis: A benign condition with a malignant association. J Clin Ultrasound 1996;24(4):197–202. Review.

MICROPAPILLARY BLADDER CANCER

DESCRIPTION A variant of bladder cancer first described in 1994. The histologic features closely resemble papillary serous carcinoma of the ovary. It accounts for 0.7–2.2% of all urothelial tumors and is nearly always associated with an advanced stage of disease and aggressive clinical course. A recent review of 100 consecutive patients at MD Anderson Cancer Center indicated an average age of 64.7 yr, with a male-to-female ratio of 10:1. 5 and 10-yr survivals of 51% and 24%, respectively. Intravesical therapy appears to be ineffective. Radical cystectomy provides a chance of cure in these patients. (See also Section I: “Bladder Cancer, General.”)

TREATMENT

- Expeditious radical cystectomy in patients with surgically resectable disease

REFERENCE

Kamat AM, et al. Micropapillary bladder cancer: A review of the University of Texas MD Anderson Cancer Center experience with 100 consecutive patients. Cancer 2007;110(1):62–67.

MILK OF CALCIUM, URINARY TRACT

DESCRIPTION The crystallization of calcium salts without actual stone formation. These usually accumulate in simple renal cysts or calyceal diverticula. On US, it is an echogenic focus or layer within the cyst. On IVP, it appears as a crescent-shaped density whose meniscus may adjust relative to patient positioning.

TREATMENT

Endoscopic, percutaneous, or ablative procedures may be performed if clinically indicated (ie, pain, infection).

REFERENCE

Sidhu R, Bhatt S, Dogra VS. Renal colic. Ultrasound Clin 2008;3:159–170.

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 hypercalciuria. The associated vomiting and dehydration can produce further volume contraction and alkalosis.

TREATMENT

- Withdrawal of milk and alkali, with gentle hydration to lower serum calcium
- Vigorous hydration can result in rebound hypocalcemia due to the chronic suppression of the parathyroid glands.

REFERENCE

Smith SG. Milk-alkali syndrome. In: Dambro M, ed. Griffith's 5-Minute Clinical Consult. Philadelphia: Lippincott Williams & Wilkins, 1999:686.

MITROFANOFF 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 continent apparatus to be used in continent colonic urinary diversions.

REFERENCE

Benson MC, Olsson CA. Continent urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3190–3245.

MIXED EPITHELIAL STROMAL TUMOR OF THE KIDNEY (MESTK)

DESCRIPTION MESTK 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, MESTK is well-circumscribed but unencapsulated, and cystic on a cut surface. Microscopically, it is composed both of epithelial structures similar to renal tubules and stroma comprising nonspecific spindle cells. The differential diagnosis for these tumors includes cystic nephroma and cystic partially differentiated nephroblastoma.

REFERENCE

Michal M, et al. Mixed epithelial and stromal tumors of the kidney. A report of 22 cases. Virchows Arch 2004;445(4):359–67. Epub 2004 20.

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 papule. 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, thighs and pubic areas. Lesions usually persist for ~2 mo, but the disease may last 6–9 mo and even longer in patients with impaired cell-mediated immunity. Diagnosis is usually clinical, but brick-shaped virions can sometimes be seen under negative-stain electron microscopy. Henderson-Paterson bodies are characteristically seen on pathology. (See also Section I: “Sexually Transmitted Diseases [STD], General.”)

TREATMENT

- Observation is reasonable for nongenital lesions.
- Curettage is useful for treating a few lesions; scarring may develop.
- Liquid nitrogen therapy, cantharidin 0.7%, tretinoin 0.025% gel or 0.1% cream; laser therapies are also common.

REFERENCE

Damon I. Other poxviruses that infect humans: Parapoxvirus, molluscum contagiosum, and tanapox. In: Mandell GL, et al., eds. Mandell, Douglas, & Bennett’s Principles and Practice of Infectious Diseases, 6th ed. Philadelphia: Elsevier, 2005.

MONFORT TECHNIQUE

DESCRIPTION A type of abdominal wall reconstruction in patients with prune belly syndrome. This technique utilizes an elliptical incision that preserves the umbilicus and thickens and strengthens the anterior abdominal wall. Full-thickness resection of skin from the central abdomen 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.

REFERENCE

Monfort G, Guys JM, Bocciardi A, et al. A novel technique for reconstruction of the abdominal wall in the prune belly syndrome. J Urol 1991;146(2):639–640.

MONTI PROCEDURE

DESCRIPTION Also known as the Monti ileovesicostomy, a technique most often used in children to create a continent catheterizable stoma. A short segment of bowel (2–3 cm of ileum) is incised 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.

REFERENCE

Cain MP, et al. Initial experience using a catheterizable ileovesicostomy (Monti procedure) in children. Urology 1998;52(5):870–873.

MORRIS SYNDROME

DESCRIPTION An intersex 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

Hyun G, Kolon TF. A practical approach to intersex in the newborn period. Urol Clin N Am 2004;31(3):435–443.

MOSKOWITZ VAGINAL PROLAPSE REPAIR

DESCRIPTION Through a transabdominal exposure, the procedure entails closing the cul-de-sac through placement of a series of purse-string sutures. The procedure was initially described to treat rectal prolapse by securing the rectum to the fixed vagina, and the same logic has been used to correct vaginal prolapse by fixing it to the rectum. Unfortunately, the rectum is not well anchored. (See also Section I: “Pelvic Prolapse [Cystocele and Enterocoele].”)

REFERENCE

Raz S, Stothers L, Chopra A. Vaginal reconstructive surgery for incontinence and prolapse. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998: 1066–1094.

MOSTOFI (WHO) GRADING SYSTEM, PROSTATE CANCER

DESCRIPTION Traditional prostate cancer grading system, generally replaced by the Gleason grading system:

- Grade I: Well differentiated, with slight nuclear anaplasia
- Grade II: Moderately to poorly differentiated, with moderate nuclear anaplasia
- Grade III: Poorly differentiated, with marked nuclear anaplasia, or undifferentiated carcinoma

SYNONYMS

World Health Organization Grading System

REFERENCE

Mostofi FK. Grading of prostatic carcinoma. Cancer Chemother Rep 1975;59[Pt I]:111–117.

MUCORMYCOSIS, GENITOURINARY

DESCRIPTION A fungal infection that usually affects immunocompromised patients. Patients receiving hemodialysis and deferoxamine 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

Wise GJ, Freyle J. Changing patterns in genitourinary fungal infections. AUA Update Series, Vol. XVI, Lesson 1, 1997.

MUIR-TORRE SYNDROME

DESCRIPTION An autosomal dominant skin condition characterized by tumors of the sebaceous gland or keratoacanthoma associated with 1 visceral malignancies including colorectal, endometrial, urologic, and upper GI. Usually considered a subtype of hereditary nonpolyposis colorectal cancer syndrome; ~25% of the visceral cancers are associated with the urogenital tract, the most common of which are transitional cell carcinomas.

REFERENCE

Ponti G, et al. Muir-Torre syndrome. Lancet Oncol 2005;6:980–987.

MULBERRY STONES

DESCRIPTION A term that refers to the surface appearance of irregular calcium oxylate stones often seen in the bladder.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little-Brown, 1991:224.

MüLLERIAN DUCT REMNANTS AND SYNDROME

DESCRIPTION Refers to the persistence of the Müllerian duct structures (uterus, fallopian tubes) in the genotypically and phenotypically normal male. The remnants persist due to the absence of Müllerian inhibiting substance. Patients present with cryptorchidism and hernia, and the persistent Müllerian structures are found within the hernia sac.

SYNONYMS

- Prostatic utricular cyst
- Müllerian duct cyst

REFERENCE

Buchloz NP, et al. Persistent Müllerian duct syndrome. Eur Urol 1998;34:230–232.

MULTILOCULAR CYSTIC NEPHROMA (MULTIOCULAR CYST)

DESCRIPTION A round, well-encapsulated multilocular cystic mass whose septa are composed of well-differentiated tissues, without blastemal 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 Wilms tumor on the malignant end. Grossly, multilocular cystic nephroma and CPDN look identical. The contents of the cysts consist of either clear to 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 3 mo–2 yr (2:1 male-to-female) and in adulthood (8:1 female-to-male). 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 IV urography, CT, or MRI. The nephromas contain noncommunicating cysts with thin septa separating the cysts. On US, multiple anechoic spaces are seen, separated by hyperechoic septa. CT reveals a well-marginated, rounded or polycyclic 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
- Focal polycystic kidney
- Multicystic or cystic adenoma

TREATMENT

- Partial nephrectomy or radical nephrectomy is indicated.
- Follow-up is required because of local recurrence.

REFERENCE

Stamatiou K, Polizois K, Kollaitis G, et al. Cystic nephroma: A case report and review of the literature. Cases J 2008;1(1):267.

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 urologic interest because of the possibility of adrenal involvement, hyperparathyroidism, renal stones, and hyperlactatemia:

- MEN I (Wermer syndrome): Autosomal dominant condition with neuroendocrine parathyroid, pancreas, duodenal, and pituitary lesions. Cutaneous tumors may also 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. Pituitary lesions may cause hyperprolactinemia and ACTH-producing lesions.
- MEN II (Sipple syndrome): Autosomal dominant:
  - Type IIA triad: Pheochromocytoma, medullary carcinoma of the thyroid, parathyroid adenoma
  - Type IIB: Pheochromocytoma, 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 neuroma syndrome).

REFERENCE

Callender GG, et al. Multiple endocrine neoplasia syndromes. Surg Clin N Am 2008;88(4):863–895.

MULTIPLE MYELOMA, UROLOGIC CONSIDERATIONS

DESCRIPTION A malignant proliferation of plasma cells derived from a single clone. The cause is unknown. The classic triad involves marrow plasmacytosis, lytic 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 likely 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. Glomerular, tubular, 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.

REFERENCE

Sakhuja V, et al. Renal involvement in multiple myeloma: A 10-year study. Ren Fail 2000;22(4):465–477.

MUMPS ORCHITIS

DESCRIPTION Mumps is a single-stranded RNA (paramyxo) virus. After the prodromal period, one or both parotid glands begin to enlarge. Mumps orchitis follows the development of parotitis by 4–7 days, with about 20% 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, scrotal support, analgesics) with resolution in about 7 days. Unilateral testicular atrophy occurs in 60%. Impaired fertility can affect up to 13%, but sterility is rare. (See also Section I: “Orchitis, General.”)

REFERENCE

Masarani M, et al. Mumps orchitis. J R Soc Med 2006;99(11):573–575.

MURCS ASSOCIATION (MüLLERIAN DUCT, RENAL, AND CERVICAL VERTEBRAL DEFECTS)

DESCRIPTION MURCS association consists of a nonrandom 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 Sprengel deformity, upper limb defects, and moderately frequent rib anomalies. It is the 2nd most frequent cause of primary amenorrhoea after Turner syndrome.

REFERENCE

Braun-Quentin C, et al. MURCS association: Case report and review. J Med Genet 1996;33(7):618–620.

MUSTARDé HYPOSPADIAS REPAIR

DESCRIPTION A more extensive Mathieu technique in which the ventral flap is tubularized to form a neourethra and then transposed distally. The glans wings are again approximated over the neourethra.

REFERENCE

Belman AB. The modified Mustardé hypospadias repair. J Urol 1982;127(1):88–90.

MYCOPLASMA GENITALIUM INFECTION

DESCRIPTION Mycoplasma genitalium is a common organism that resides within the genital tracts of both men and women. However, it may be a cause of chronic prostatitis in men or urgency and frequency in women. Identifying and culturing this organism is difficult. Initial treatment includes doxycycline 100 mg b.i.d. for 2 wk or azithromycin 1 g in a single dose.

REFERENCE

Moi H, et al. Mycoplasma genitalium is associated with symptomatic and asymptomatic non-gonococcal urethritis in men. Sex Transm Infect 2009;85(1):15–18.

MYCOPLASMA HOMINIS, URINARY TRACT INFECTION

DESCRIPTION Mycoplasma hominis commonly resides in the genital tracts of both men and women. This organism is often found in women with bacterial vaginosis. It is generally susceptible to tetracycline and quinolones.

REFERENCE

Kenny GE. Genital mycoplasmas: Mycoplasma genitalium, Mycoplasma hominis, and Ureaplasma species. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Bennett, & Dolin: Principles and Practice of Infectious Diseases, 6th ed. Philadelphia: Elsevier, 2005:2280–2282.

MYOCUTANEOUS FLAPS

DESCRIPTION Myocutaneous flaps, such as rectus flap, gracilis flap, or tensor fascia flap, can be utilized during urologic reconstructive surgery. Common applications are for skin coverage during ilioinguinal node dissections for penile cancer, closure of urinary fistulae, and reconstruction after Fournier gangrene:

- Rectus abdominis flap: The blood supply of the rectus abdominis is the superior and deep inferior epigastric vessels. The deep superior epigastric vessels are not utilized as a vascular pedicle for the free flap because of their smaller caliber and a greater amount of skin can be transferred by relying on the interior epigastric pedicle.
- Gracilis flap: The origin of the gracilis muscle is the ischium and inferior ramus of the pubis and the insertion is the medial tibia. The gracilis muscle is 4–8 cm wide and is harvested from the inner thigh. It can be utilized either as a muscle flap or myocutaneous flap and leaves the patient without any functional deficit. The nerve supply to the gracilis muscle is a branch of the obturator nerve, and its blood supply is a single artery from the profunda femoral system.
- Tensor fascia lata flap: The tensor fascia lata can be harvested from the lateral aspect of the upper leg. The vascular pedicle is comprised of the transverse branch of the lateral circumflex femoral artery, and the sensory supply is the lateral femoral cutaneous nerve of the thigh, which originates from T12. A skin island of up to 15 centimeters can be harvested and leaves the patient without any functional deficit.

REFERENCE

Smith HO, et al. The rectus abdominis myocutaneous flap: Modifications, complications, and sexual function. Cancer 1998;83(3):510–520.

MYOFASCIAL PELVIC PAIN SYNDROME (MPPS)

DESCRIPTION MPPS is a disorder in which pelvic pain is attributed to short, tight, tender pelvic floor muscles, usually with hypersensitive trigger points. Pelvic floor trigger points refer pain to the vagina, vulva, perineum, rectum, and bladder. Pain can be also be referred to the thighs, buttocks, or lower abdomen. Irritative symptoms (eg, urinary urgency, vulvovaginal burning, rectal fullness) may be more prominent than pain. The diagnosis is clinical. Treatment is customized and based on reducing the response of the trigger point. Stress reduction (meditation, relaxation exercises), physical therapy (stretch/massage), heat, ice, or NSAIDs are recommended for mild cases. Pelvic floor physical therapy (manual myofascial release, stretching, and strengthening) is useful for many patients. More severe cases may require trigger point injections (bupivacaine), gabapentin, or botulinum toxin if muscle spasm can be identified. (See also Section I: “Pelvic Pain, Female.”)

REFERENCE

Srinivasan AK, et al. Myofascial dysfunction associated with chronic pelvic floor pain: Management strategies. Curr Pain Headache Rep 2007;11(5):359–364.

MYOGLOBIN NEPHROTOXICITY

DESCRIPTION Renal failure associated with the excessive deposit of myoglobin into the serum following massive muscle necrosis/rhabdomyolysis. Renal failure is initiated by acute tubular obstruction, and necrosis is caused by free chelatable iron and ischemia. Granular casts are found in the urine. Renal failure is initially manifested by oliguria and followed later by a polyuric state. (See also Section II: “Myoglobinuria and Rhabdomyolysis.”)

TREATMENT

- Myoglobin nephrotoxicity is prevented by maintaining fluid balance through the use of diuretics and hydration, using isotonic saline initially.
- If renal failure develops, fluid retention should be avoided by limiting infusion rates.
- In polyuric states, vigilant replacement of electrolytes is required.

REFERENCE

Melli G, et al. Rhabdomyolysis: An evaluation of 475 hospitalized patients. Medicine (Baltimore) 2005;84(6):377–385.

MYOGLOBINURIA

DESCRIPTION First 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, toxins, malignant hyperthermia, and other causes, and imparts a cola-like color to the urine. Diagnosis is made by electrophoresis separation and radioimmunoassay of urinary myoglobin. Serum creatinine kinase is elevated, and there is an absence of red cells in the urine. (See also Section II: “Myoglobin Nephrotoxicity and Rhabdomyolysis.”)

CAUSES

- Diabetic acidosis
- Fluid/electrolyte imbalance
- Infectious myositis
- Ischemia
- Malignant hyperthermia
- Neuroleptic malignant syndrome
- Rhabdomyolysis
- Toxins
- Trauma

TREATMENT

- Remove the causative agent.
- Protect against renal failure through correction of electrolyte imbalances, alkalinization of urine with sodium bicarbonate, hydration, and diuretics.

REFERENCE

Melli G, et al. Rhabdomyolysis: An evaluation of 475 hospitalized patients. Medicine (Baltimore) 2005;84(6):377–385.

SHORT TOPIC SECTION N

NAGAMATSU INCISION

DESCRIPTION A dorsolumbar incision is made over either the 11th or 12th rib, which is resected. After rib removal, the diaphragm and pleura are retracted superiorly, and the kidney and the adrenal may be exposed.

REFERENCE

1. Montague DK. Surgical incisions. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:15–40.

NATIONAL INSTITUTES OF HEALTH (NIH) CHRONIC PROSTATITIS SYMPTOM INDEX (CPSI)

DESCRIPTION The CPSI is a validated and reproducible measure of outcomes for men with prostatitis. With 9 questions, it captures the 3 domains of the prostatitis experience: Pain, urinary function, and quality of life. While not a diagnostic aid, it is useful for both research studies and clinical practice, in initially assessing patients, subsequently following their progress, and providing specific treatment. (See Section VII.)

REFERENCE

2. Litwin MS, et al. The National Institutes of Health chronic prostatitis symptom index: Development and validation of a new outcome measure. J Urol 1999;162:369–375.

NCCN (NATIONAL COMPREHENSIVE CANCER NETWORK) GUIDELINES

DESCRIPTION The NCCN is a nonprofit alliance of NCI-designated Comprehensive Cancer Centers devoted to improving care for cancer patients. This includes the development of treatment guidelines for most cancers, including GU cancers such as prostate, bladder, kidney, and testes. Useful treatment algorithms are available on their site. Registration (no charge) required.

REFERENCE

Online at: www.nccn.org.

NECROSPERMIA

DESCRIPTION A condition in which the sperm are both nonmotile and nonviable. The etiology of this condition is variable.

REFERENCE

4. Chavez-Badiola A, et al. Necrospermia, antisperm antibodies, and vasectomy. Fertil Steril 2008; 89(3):723.e5–7.

NELSON SYNDROME

DESCRIPTION The development of pituitary tumors (usually a chromophobe adenoma) seen in 10–20% of patients originally treated with bilateral adrenalectomy for Cushing disease. Believed to be caused by a lack of hypothalamic/pituitary feedback and resultant high levels of ACTH and related compounds, patients must be followed with ACTH levels and imaging of the sella turcica.

TREATMENT

- Surgical excision
- Radiation therapy
- Prophylactic pituitary radiotherapy (shown to reduce the incidence of Nelson syndrome by 50%)

REFERENCE

5. Kasperlik-Zalusica AA. Early diagnosis of Nelson syndrome. J Mol Neurosci 1996;7(2):87–90.

NEPHRITIS, RADIATION

DESCRIPTION Renal dysfunction occurs if 23 Gy of radiation therapy is administered to both kidneys during a period of 5 wk. Histologic exam shows hyalinized glomeruli, atrophic tubules, interstitial fibrosis, and hyalinization of the media of renal arterioles. Radiation-induced renal ischemia causes tubulointerstitial damage, which may take months to manifest. Acute radiation nephritis presents with rapidly progressing azotemia, moderate to malignant hypertension, anemia, and proteinuria. More than 50% of patients progress to chronic renal failure. Malignant hypertension may follow unilateral radiation and resolve with nephrectomy. This entity has essentially vanished due to refinement in radiation therapy techniques.

REFERENCE

6. Kelly CJ, Neilson EG. Tubulointerstitial diseases. In: Brenner BM, ed. The Kidney, 5th ed. Philadelphia: Saunders, 1996:1655–1679.

NEPHROGENIC ADENOMA AND METAPLASIA

DESCRIPTION A rare lesion occurring in the bladder; histologically, it resembles primitive renal collecting tubules. It is a metaplastic response of urothelium to trauma, infection, radiation therapy, or chronic immunosuppression. Edema and inflammatory cell infiltration are common, but little nuclear atypia or mitotic activity is demonstrated. It is more common in men and is associated with symptoms of dysuria and urinary frequency. Treatment involves transurethral resection of the tumor, with extensive fulguration of the tumor base and frequent follow-up cystoscopies and repeat resection, as needed, to control symptoms.

REFERENCE

7. Navarre RJ Jr. , Loening SA, et al. Nephrogenic adenoma: A report of nine cases and review of the literature. J Urol 1982;127:775.

NEPHROGENIC SYSTEMIC FIBROSIS/FIBROSING DERMATOPATHY (NSF/NFD)

DESCRIPTION NSF is a scleroderma-like skin disease that affects patients with renal insufficiency. There is a strong association between the development of NSF and exposure to gadolinium contrast agents used in performing MRI. The skin lesions begin as patches, plaques, or papules, then coalesce to form a woody skin appearance. The skin thickening can limit joint motion. There is no known effective treatment.

REFERENCE

8. Kurtkoti J, et al. Gadolinium and nephrogenic systemic fibrosis: Association or causation. Nephrology 2008;13:235–241.

NEPHRONOPHTHISIS (JUVENILE, INFANTILE, AND ADOLESCENT)

DESCRIPTION A group of four diseases, known as the juvenile nephronophthisis–renal medullary cystic disease complex, that result in end-stage renal disease (ESRD). Nephronophthisis is the most common cause of tubointerstitial nephropathy in children, and is inherited in an autosomal recessive pattern mapped to chromosome 2. Three subtypes of nephronophthisis exist, based on the age of onset of ESRD. Juvenile nephronophthisis is the most common (1 in 50,000 births), with a median onset of 13 yr; infantile nephronophthisis usually causes ESRD by 5 yr; and adolescent nephronophthisis has a mean onset of 19 yr. The disease presents as failure to thrive, azotemia, polyuria, and polydipsia. Hypertension is less common. Microscopically, it resembles an interstitial nephritis with cysts. US reveals muddling of corticomedullary junction and small reniform kidneys with cysts found at the corticomedullary junction. Retinitis pigmentosa hepatic fibrosis and Bardet-Biedl syndrome are associated. Renal replacement therapy, as needed, is the treatment of choice. Extrarenal involvement is described and can involve the retina, liver, and brain. (See also Section I: “Medullary Cystic Kidney Disease.”)

REFERENCE

9. Saunier S, et al. Nephronophthisis. Curr Opin Gen Dev 2005;15:324–331.

NEPHROPATHY, ANALGESIC

DESCRIPTION A chronic interstitial nephritis seen in patients who consume large quantities of analgesics over many years. They usually suffer from chronic headaches or low back pain and have consumed a mixture of analgesics, including acetaminophen, aspirin, and NSAIDs. 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 dramatically 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. IVP shows the ring sign, which refers to the contrast agent surrounding sloughed papilla, although the current use of IVP is limited due to contrast load. Renal US shows small kidneys, with irregular thinning of the renal cortex. Renal biopsy shows interstitial infiltrates and fibrosis. Noncontrast CT shows bilateral reduced renal size, bumpy renal contours, 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 transitional cell carcinoma of the urinary tract. Cessation of drug use can lead to stabilization of renal function.

REFERENCE

Mihatsch MJ, et al. Obituary to analgesic nephropathy—an autopsy study. Nephrol Dial Transplant 2006;21(11):3139–3145.

NEPHROPATHY, ISCHEMIC

DESCRIPTION Ischemic nephropathy is described as a deterioration in 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 acute renal failure, or flash pulmonary edema. Numerous tests are used to define the presence, size, 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

Chonchol M, Linas S. Diagnosis and management of ischemic nephropathy. Clin J Am Soc Nephrol 2006;1:172–181.

NEPHROPATHY, MEMBRANOUS

DESCRIPTION Renal disease that manifests with nephrotic syndrome. Affecting mainly middle-aged adults, it can progress to either spontaneous remission or end-stage renal disease (ESRD). It is the most common cause of nephrotic syndrome in nondiabetic adults. Proteinuria with microscopic hematuria is often present; massive proteinuria, hypertension, and impaired renal function on presentation, and male gender, are all poor prognostic factors. Believed to be related to in situ formation of immune complexes, it is most commonly idiopathic, but may be secondary to diseases (malignancy, infection, systemic lupus erythematosus [SLE]) or drug use (gold, penicillamine). Immunofluorescence often reveals deposits of IgG and complement. Treatment is based on the risk of progression associated with proteinuria (low risk <4 g/protein/d; moderate 4–8 g/protein/d; high risk >8 g/protein/d, lasting >3 mo or associated with a reduce creatinine clearance). Low-risk patients are at high likelihood of spontaneous remission and are treated with nonimmunosuppressive therapy, including ACE inhibitors or angiotensin II receptor blockers. In high-risk disease, cyclophosphamide and chlorambucil, both given with glucocorticoids, are effective in inducing remission of proteinuria and preventing progression to ESRD. Other agents reported include cyclosporine and tacrolimus (plus low-dose prednisone 10 mg/d max). (See also Section I: “Nephrotic Syndrome.”)

REFERENCE

Glassock RJ. Diagnosis and natural course of membranous nephropathy. Semin Nephrol 2003; 23(4):324–332.

NEPHROPATHY, MINIMAL CHANGE

DESCRIPTION A common cause of 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 hypertension. RBCs 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, neoplasm, 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

Waldman M, et al. Adult minimal-change disease: Clinical characteristics, treatment, and outcomes. Clin J Am Soc Nephrol 2007;2(3):445–453.

NEPHROPATHY, OBSTRUCTIVE

DESCRIPTION Obstructive nephropathy occurs when renal deterioration 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 fibrosis. The tubular injury in obstructive nephropathy is caused initially by the increased intratubular pressure and later by atrophy induced by reduced perfusion, inflammation, and 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. With total obstruction of the ureter, relatively complete recovery of glomerular filtration rate can be achieved within 1 wk, whereas after 12 wk, little or no recovery is seen. (See also Section I: “Hydronephrosis/Hydroureteronephrosis [Dilated Ureter/Renal Pelvis], Adult.”)

REFERENCE

Better OS, et al. Studies on renal function after relief of complete unilateral ureteral obstruction of three months duration in man. Am J Med 1973;54(2):234–240.

NEPHROPATHY, URATE

DESCRIPTION A disorder in which an abrupt deterioration in renal function occurs due to the renal tubular deposition of urate and uric acid crystals. Chronic renal injury from uric acid deposition is most often associated with gout and is uncommon today. Two forms are recognized, acute and chronic. Acute urate nephropathy occurs almost exclusively in the setting of malignancies, such as leukemias 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 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 elevated serum urate levels and renal failure, such as trauma with rhabdomyolysis. (See also Section I: “Urolithiasis, Uric Acid”; Section II: “Gout, Urologic Considerations; Tumor Lysis Syndrome [TLS].”)

TREATMENT

- Prevention is the key, using xanthine oxidase inhibition with allopurinol and alkaline diuresis prior to initiation of chemotherapy.
- Alkalinization of urine in the acute tumor lysis syndrome is not possible in the setting of brisk diuresis.
- Rasburicase (Elitek) is recombinant urate oxidase that converts uric acid to water-soluble allantoin.
- Occasionally, dialysis is required to correct azotemia and reduce urate levels.

REFERENCE

Conger JD. Acute uric acid nephropathy. Med Clin N Am 1990;74:859–871.

NEPHROPTOSIS

DESCRIPTION Nephroptosis, also referred to as floating kidney or renal ptosis, is a condition in which the kidney drops into the pelvis when the patient stands up. It tends to be more common in women and is thought to be caused by a lack of perirenal fat. Patients are usually asymptomatic but colicky type pain can be attributed to this conditions, similar to a Dietl crisis. The pain is classically relieved by lying down. Imaging can demonstrate the renal descent and aid in diagnosis. Conservative management had been the mainstay of treatment, although laparoscopic nephropexy is now recommended for symptomatic patients. (See also Section II: “Dietl Crisis.”)

REFERENCE

Barber NJ, Thompson PM. Nephroptosis and nephropexy-hung up on the past? Eur Urology 2004;46:428–433.

NESBIT CHORDEE REPAIR

DESCRIPTION A surgical procedure in which 1 transverse ellipses are removed from the longer convex side, and the ellipses are closed transversely, which results in shortening of the longer side.

REFERENCE

Montague DK. Correction of chordee. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:822–825.

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 (oat) cell carcinomas, medullary carcinoma of the thyroid, Merkel cell tumor, cutaneous neuroendocrine carcinoma, pancreatic islet cell tumors, and pheochromocytoma. Small (oat) cell carcinomas have been described most often in the prostate and bladder. Prostate cancer with neuroendocrine differentiation is considered a variant of Gleason 5 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 I: Pheochromocytoma; Section II: “Multiple Endocrine Neoplasia [MEN I, MEN II];” “Prostate Cancer, Small Cell [Neuroendocrine].”)

REFERENCE

Helpap B. Morphology and therapeutic strategies for neuroendocrine tumors of the genitourinary tract. Cancer 2002;95(7):1415–1420.

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 long areas of stenosis that are generally best treated with revascularization rather than angioplasty. In addition, a 30-fold increase in the incidence of neurofibromatosis in patients with Wilms tumor has been reported.

REFERENCE

Saborio P, et al. Genetic renal disease. Curr Opin Pediat 1998;10:174–183.

NEVES-ZINCKE CLASSIFICATION

DESCRIPTION A largely historic classification system for describing the level of tumor thrombus associated with a renal mass. The categories are: Renal vein, 2 cm above the renal vein, infrahepatic >2 cm but below the intrahepatic vena cava, intrahepatic but below the diaphragm and atrial above the diaphragm. (See also Section I: “Renal Cell Carcinoma with Tumor Thrombus.”)

REFERENCE

Neves RJ, Zincke H. Surgical treatment of renal cancer with vena cava extension. BJU 1987;59(5):390–395.

NMP-22 TESTING

DESCRIPTION Nuclear matrix protein (NMP-22) has been found to serve as a urinary marker for transitional cell carcinoma. The NMP-22 test (Matritech, Inc., Newton, MA) is a quantitative immunoassay that measures nuclear matrix protein-22. The addition of NMP-22 testing to cytology may increase the sensitivity for recurrence detection in patients with superficial transitional cell bladder cancer. Patients with positive NMP-22 findings developed significantly more recurrences compared with those with negative NMP-22 findings in several studies.

REFERENCE

Gupta NP, et al. Nuclear matrix protein 22 as adjunct to urine cytology and cystoscopy in follow-up of superficial TCC of urinary bladder. Urology 2009;73(3):592–596.

NOCTURNAL ERECTIONS, NORMAL AND ABNORMAL

DESCRIPTION Nocturnal erections occur at night during REM sleep. The number of erections peak during puberty. Various criteria exist for what is considered normal erectile activity at night, but normal is usually 4–5 erectile episodes 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 70% at both base and tip. (See also Section II: “Nocturnal Penile Tumescence Testing.”)

REFERENCE

Lue TF, Broderick GA. Evaluation and nonsurgical management of erectile dysfunction and premature ejaculation. In: Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007:765.

NOCTURNAL PENILE TUMESCENCE TESTING

DESCRIPTION Nocturnal penile tumescence (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 erotically induced erections. (See also Section II: “Nocturnal Erections, Normal and Abnormal.”)

REFERENCE

Greenstein A, et al. Are consecutive nightly recordings required for valid evaluation of sleep-associated erections? Int J Impot Res 2007;19(2):196–199.

NOCTURNAL POLYURIA

DESCRIPTION Nocturnal polyuria (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 >1/3 of total 24-hr urine output between midnight and 8 AM (normal physiologic response is reduced urine output at night). A voiding diary (frequency volume chart or FVC) that records time and volume of each void over a 24-hr period for 7 days establishes if the patient is polyuric or nonpolyuric. True polyuria is present throughout the 24-hr period, whereas nocturnal polyuria is confined to elevated night-time output. Altered sleep patterns caused by frequent trips to the bathroom can cause problems staying alert at work, major depression, and hypertension. Although traditional therapies in men have been directed toward medical or surgical treatment, NP does not respond well to these standard interventions. (See also Section II: “Polyuria and Voiding Diary [Frequency Volume Chart, FVC].”)

TREATMENT

- Lifestyle changes: Limiting fluids in the late afternoon and evening, such as coffee, soft drinks, or tea.
- Taking diuretics early in the day
- Desmopressin mimics the action of vasopressin in reducing nocturnal urine production.

REFERENCE

Kujubu DA, Aboseif SR. An overview of nocturia and the syndrome of nocturnal polyuria in the elderly. Nat Clin Pract Nephrol 2008;4(8):426–435.

NOMOGRAMS, UROLOGIC

DESCRIPTION Nomograms are mathematical tools that allow for the prediction of various outcomes. Validated nomograms have been developed for all major urologic cancers, as well as for some benign urologic diseases. Useful online prediction tools are available from Memorial Sloan Kettering Cancer Center (http://www.mskcc.org/mskcc/html/5794.cfm) for prostate, bladder, and kidney cancer. Manual algorithms can be found in Section VII: “Kattan Nonograms.”

REFERENCE

Kattan MW, Scardino PT. Evidence for the usefulness of nomograms. Nat Clin Pract Urol 2007;4(12):638–639.

NONARTERITIC ANTERIOR ISCHEMIC OPTIC 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 phosphodi-esterase inhibitors sildenafil, vardenafil, and others. The mechanism and exact nature of this association is still under investigation.

REFERENCE

Seftel AD, et al. Office evaluation of male sexual dysfunction. Urol Clin N Am 2007;34:463–482.

NON-SACRAL NEUROMODULATION

DESCRIPTION Neuromodulation involves the use of electrical current to alter physiologic properties. This technology has been applied to lower urinary tract voiding 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 sacral nerve roots as well, including the pudendal, dorsal genital, and posterior tibial nerves.

REFERENCE

Bennett RC, et al. Nonsacral neuromodulation. In: Goldman HB, Vasavada SP, eds. Female Urology: A Practical Clinical Guide. Totowa, NJ: Humana Press, 2007.

NOONAN SYNDROME

DESCRIPTION This autosomal dominant syndrome consists of multiple congenital anomalies, including characteristic facial features, short stature, and chest deformity. 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 close follow-up. Growth hormone replacement may have value in treating short stature.

REFERENCE

Noonan JA. An update and review for the primary pediatrician. Pediatrics 1997;33:549.

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 bony metastasis and bisphosphonate therapy. Typical reference ranges are (BCE = bone collagen equivalent): Normal adult male 21–83 nM BCE/mM creatinine; adult female premenopausal: 17–94 nM BCE/mM creatinine; postmenopausal 26–124 nM BCE/mM creatinine. A decrease of 30–40% from the NTx baseline after 3 mo of therapy is typical for treatment with bisphosphonate.

REFERENCE

Rubin CT, Rubin JE. Biology, physiology, and morphology of bone. In: Harris ED, Budd RC, Genovese MC, et al., eds. Kelley's Textbook of Rheumatology, 7th ed. Philadelphia: Saunders, 2005.

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 nephrectomy, autotransplantation, renocaval reimplantation, and venolysis have been employed. Gore-Tex graft renal vein interposition and anterior nephropexy have been successful.

REFERENCE

Wang L, et al. Diagnosis and surgical treatment of nutcracker syndrome: A single-center experience. Urology 2009;73(4):871–876.

SHORT TOPIC SECTION O

OBTURATOR NERVE INJURY, INTRAOPERATIVE

DESCRIPTION The obturator nerve, which provides motor innervation of medial thigh adductor muscles, can be injured in surgeries involving pelvic lymphadenectomy, such as prostatectomy and cystectomy. Additionally, excessive hip flexion or cautery injury during surgery can cause neurapraxia of the obturator nerve. Postoperatively, EMG can be helpful in making the diagnosis. Symptoms include gait disturbance, pain, or anesthesia along the nerve's sensory distributions along the inner thigh and scrotum. The incidence of intraoperative obturator nerve injury is not well documented but thought to be rare. When transection of the obturator nerve is identified intraoperatively, surgical repair may be done by end-to-end anastomosis or grafting when achieving tension-free anastomosis is not possible. Nerve transection can be repaired with end-to-end approximation of nerve edges with four 6–0 to 10–nylon or Prolene epineural stitches, using magnification if possible. Efforts must be made to align the nerve fibers prior to approximation. A nerve wrap/protector, which is expensive, helps the healing process when applied to the new anastomosis. If the nerve is frayed and grossly devitalized, efforts can be made to trim both segments sharply. In the event of a significant gap, nerve-grafting techniques can be performed at a later date using a sural nerve (which is a nonessential nerve) graft.

REFERENCE

1. Spaliviero M, et al. Laparoscopic injury and repair of obturator nerve during radical prostatectomy. Urology 2004;64(5):1030.

OBTURATOR REFLEX, UROLOGIC CONSIDERATIONS

DESCRIPTION Stimulation of the obturator nerve during surgical procedures (eg, transurethral resection of 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. The response can usually be prevented by muscle-paralyzing anesthetic agents.

REFERENCE

2. Jones JS, Campbell SC. Non-Muscle-Invasive Bladder Cancer (Ta, T1, and CIS). In: Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

OLIGOASTHENOTERAT-OSPERMIA

DESCRIPTION Oligoasthenoteratospermia describes very generalized abnormalities in sperm concentration, motility, and morphology. The cause of these combined defects in sperm parameters are commonly caused by the effects of a varicocele (most commonly cited cause), cryptorchidism, and other transient insults such as heat, drugs, or environmental toxins. Trichomonas has been implicated in some studies. Treatment involves the removal of potentially offending spermatotoxins and a repeat semen analysis in 3 mo. No good data exist on the use of agents such as bromocriptine, clomiphene citrate, human chorionic gonad tropin (hCG), or tamoxifen. (See also Section I: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Terminology;” “Semen Analysis, Technique, and Normal Values.”)

REFERENCE

3. Cavallini G, et al. A study to sustain the hypothesis of the multiple genesis of oligoasthenoteratospermia in human idiopathic infertile males. Biol Reprod 2008;79(4):667–673.

OLIGOSPERMIA

DESCRIPTION Oligospermia occurs when sperm density is <20 million/mL or with a total count of <50 million sperm. Severe oligospermia occurs if counts are <10 million/mL, and may be due to hormone deficiency. A count of <20 million/mL is associated with substantially decreased fertility rates. (See also Section I: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Terminology”; “Semen Analysis Technique, Normal Values.”)

REFERENCE

4. Grimes DA. Oligozoospermia, azoospermia, and other semen-analysis terminology: The need for better science. Fertil Steril 2007;88(6):1491–1494.

OMPHALOCELE-EXSTROPHY OF THE BLADDER—IMPERFORATE ANUS-SPINA BIFIDA DEFECTS (OEIS) COMPLEX

DESCRIPTION This complex represents the most severe end of a spectrum of birth defects, the exstrophy-epispadias sequence, which, in order of increasing severity, includes phallic separation with epispadias, pubic diastasis, vesical exstrophy of the bladder and cloacal exstrophy, and OEIS complex. The incidence of the OEIS complex is rare (1 of 200,000–400,000 pregnancies). Exstrophy of the cloaca includes the persistence and exstrophy of a common cloaca that receives ureters, ileum, and a rudimentary hindgut and is associated with failure of fusion of the genital tubercles and pubic rami; incomplete development of the lumbosacral vertebrae with spinal dysraphism; imperforate anus; cryptorchidism and epispadias in males; anomalies of the Müllerian duct derivatives in females; and a wide range of urinary tract anomalies including renal defects. Omphalocele (a defect in the umbilical ring, through which the peritoneum and an amnion-covered sac herniate) is common, and most patients have a single umbilical artery. The etiology of the OEIS complex is still unclear; single defects in blastogenesis and mutations in homeobox genes, such as HLXB9, have been suggested as responsible. Although often fatal, extensive surgical reconstruction has been successful.

REFERENCE

5. Keppler-Noreuil K. Prenatal ascertainment of OEIS complex/cloacal exstrophy: 15 new cases and literature review. Am J Med Genet A 2007 15;143A(18):2122–2128.

OPITZ-FRIAS SYNDROME

DESCRIPTION Also called the G syndrome (named for one of the first patients), this condition is due to a defect of midline development, characterized by numerous congenital abnormalities, especially of the face. Many patients have hypertelorism and posteriorly rotated ears; hypospadias is almost always present. Other manifestations include cleft lip and palate, high tracheal bifurcation, duodenal stricture, imperforate anus, lung hypoplasia, and cardiac abnormalities. Inheritance is autosomal dominant with incomplete penetrance. Carriers show minimal abnormalities. It is more common in males, and perinatal mortality is around 30%.

REFERENCE

6. Conlon BJ, O'Dwyer TH. The G syndrome, Opitz oculo-genital-laryngeal syndrome, Opitz BBB/G syndrome, Opitz-Frias syndrome. J Laryngol Otol 1995;109(3):244–246.

ORAL-FACIAL-DIGITAL (OFD) SYNDROME

DESCRIPTION At least 11 different types of oral-facial-digital (OFD) syndromes have been described. OFD type I is an X-linked dominant condition characterized by malformations of the face, oral cavity, and digits with polycystic kidney disease and variable involvement of the CNS. Facial milia, orofacial defects such as cleft palate, hand deformities, including shortening of the phalanges, and CNS defects are noted. Of urologic interest, renal cystic disease is found that resembles autosomal dominant polycystic kidney disease in appearance and course. Liver and pancreatic cysts may be observed. Polycystic kidney disease occurs in fewer than 50% of individuals with OFD type 1; the exact frequency is unknown. Renal cysts can develop from both tubules and glomeruli. The age of onset is most often in adulthood, but renal cysts in children have been described. End-stage renal disease has been reported in affected girls and women ranging in age from 11–70 yr. Recently it has been emphasized that the risk for significant renal disease may be greater than previously reported. Close monitoring of renal function if renal cystic disease present and renal replacement therapy, as needed.

REFERENCE

7. Toprak O, et al. Oral-facial-digital syndrome type 1, Caroli’s disease and cystic renal disease. Nephrol Dialys Transplant 2006;21(6):1705–1709.

ORCHITIS, GRANULOMATOUS

DESCRIPTION This condition encompasses a group of disorders that have similar clinical and pathologic findings. It is usually of sudden clinical onset during the 6th–7th decade of life. The patient may complain of a painful and swollen scrotum, and occasionally fever and/or skin changes may be present. Often, the diagnosis is rendered postoperatively after inguinal orchiectomy is performed for presumed malignancy and histology shows chronic inflammation with granuloma. The most common cause is Mycobacterium tuberculosis. Less commonly, brucellosis, actinomycosis, and sarcoidosis is found. The condition can be a rare complication of intravesical bacillus calmette-Guérin therapy for urothelial cancer. If TB is suspected, anti-tubercular chemotherapy is warranted, with operative treatment for medical failures. For other causes, medical and/or surgical therapy can be utilized.

REFERENCE

8. Harving SS, et al. Granulomatous epididymo-orchitis, a rare complication of intravesical bacillus Calmette-Guérin therapy for urothelial cancer. Scand J Urol Nephrol 2009;24:1–3.

ORGASMIC PAIN (PAINFUL EJACULATION)

DESCRIPTION Pain associated with ejaculation and orgasm is widely underreported. The nature, duration, and location of the pain can vary widely between patients. The exact cause of the pain is unknown but can be related to previous surgery (including radical prostatectomy), ejaculatory duct stones, pudendal nerve neuropathy, and antidepressant medications. Treatments include the use of conservative measures, anti-inflammatory medications, -blockers, topiramate, steroid injections, relief of seminal duct obstruction, and surgical interventions such as neurolysis and fasciotomy of Alcock canal. (See also Section I: “Ejaculatory Disturbances [Delayed, Decreased, or Absent].”)

REFERENCE

9. Ilie CP, et al. Painful ejaculation. BJU Int 2007;99:1335–1339.

OSSIFYING RENAL TUMOR OF INFANCY

DESCRIPTION Rare, calcified tumor of infancy, usually resembling a renal pelvis calculus. Occurs usually in 1st yr of life, with gross hematuria as the most common presenting symptom. Anatomic and histologic origins are unclear but are thought to be of urothelial origin. Lesions are apparently benign, with no reported cases of recurrence or metastasis. Surgical enucleation with renal-sparing procedure is the treatment, with careful follow-up using renal sonograms, as necessary.

REFERENCE

Steffens J, et al. Ossifying renal tumor of infancy. J Urol 1993;149(5):1080–1081.

OSTEITIS PUBIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Osteitis pubis is a noninfectious inflammation of the pubic symphysis that is characterized by sclerosis and bony changes. It can cause significant pelvic and abdominal pain. Various urologic procedures can result in osteitis pubis, in particular the Marshall-Marchetti-Krantz procedure; sling procedures utilizing permanent bone anchors have also been known to cause this condition. NSAIDs and physical therapy are the main treatment. Postoperative pubic osteomyelitis (usually due to Pseudomonas or Staphylococcus spp.) requires aggressive therapy and possible removal of the sling material or bone anchors.

REFERENCE

Chapple CR. Retropubic suspension surgery for incontinence in women In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

OSTEOPOROSIS AND OSTEOPENIA, UROLOGIC CONSIDERATIONS

DESCRIPTION Osteoporosis and osteopenia are conditions of decreased bone mineral density that lead to an increased risk of fracture. Although traditional emphasis has been placed on diagnosing osteoporosis in women, as the male population ages, increased numbers of men are at risk for developing skeletal fractures. In addition, more men are being placed on long-term androgen-deprivation therapy (orchiectomy of LHRH analogue) as treatment for prostate cancer, which further increases the risk for osteopenia and osteoporosis. A dual-energy x-ray absorptiometry (DEXA) scan can be used prior to treatment to measure bone mineral density. Central DEXA is the gold standard and measures the spine and hip bone mineral density. The T-score is the number of SDs by which the patient's bone mass falls above or below the mean peak bone mass for a 30-yr-old healthy adult. For every 1 SD decrease in T-score, relative risk of fracture increases ~1.5–2.5-fold. According to the National Osteoporosis Foundation, a normal T-score is >–1, osteopenia is –1 to –2.5, and osteoporosis is <–2.5. Further, it is recognized that, in addition to cancer treatment–induced bone loss, many men may suffer skeletal-related events (SREs) as a consequence of bony metastatic disease. Improving bone mineral density may also decrease SREs (radiation for bone pain or to treat pathologic fractures or spinal cord compression, pathologic fractures, spinal cord compression, and vertebral body collapse or surgery to bone).

TREATMENT

- Calcium: 1,200 mg/d calcium from foods (dairy, green leafy vegetables) or supplements
- Vitamin D: At least 400–800 IU/d from foods (fatty fish and oils, liver, fortified milk) with sun exposure of 30 min/d or supplements
- Exercise to include weight-bearing
- Stop smoking; limit alcohol and caffeine
- Consider bisphosphonates:
  - Alendronate (Fosamax, Fosamax Plus D):
    In men with osteoporosis, bisphosphonates are not FDA approved for metastases
  - Risedronate (Actonel) for men with osteoporosis
  - Pamidronate (Aredia) for men with Paget disease, hypercalcemia of malignancy, malignant myeloma
  - Zoledronic acid (Zometa); approved for bony mestatisis but not male osteoporosis
  - Zoledronic acid (Reclast); 5 mg/yr in men with Paget disease

- Denosumab (injectable monoclonal antibody to RANK ligand, an osteoclast regulator) under study to reduce treatment-related osteoporosis.

REFERENCE

Diamond TH, et al. Osteoporosis in men with prostate carcinoma receiving androgen-deprivation therapy: Recommendations for diagnosis and therapies. Cancer 2004;100:892–899.

Online guidelines. Available at: http://www.nof.org/professionals/Clinicians_Guide.htm. Accessed 5/24/09.

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.

REFERENCE

Coleman RL, Gershenson DM. Neoplastic diseases of the ovary: Screening, benign and malignant epithelial and germ cell neoplasms, sex-cord stromal tumors. In: Katz VL, et al., eds. Comprehensive Gynecology, 5th ed. St. Louis: Mosby, 2007.

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. Symptoms may begin weeks to 5 yr postoperatively.

TREATMENT

- Hormonal manipulation can be used as treatment.
- Excision of the ovarian remnant is the most widely accepted treatment method.
- Surgery is associated with an 8–10% recurrence rate.

REFERENCE

Lafferty HW, et al. Ovarian remnant syndrome: Experience at the Jackson Memorial Hospital, University of Miami, 1985 through 1993. Am J Obstet Cynecol 1996;174:641.

OVARIAN VEIN SYNDROME

DESCRIPTION Ureteral obstruction, usually right-sided, occurring secondary to occlusion by dilated ovarian veins. The ovarian veins lie adjacent to the ureters, and dilation of these veins, especially during pregnancy, is thought to result in ureteral obstruction. The obstruction is usually seen around the L3–L4. Symptoms include chronic flank pain, but colicky pain has also been found. The symptoms can also begin several days prior to menses and then regress. Diagnosis can be made by IV urogram, retrograde ureteropyelogram, and simultaneous angiography. Ureterolysis and ovarian vein resection can be performed using open or laparoscopic techniques.

REFERENCE

Sato F, et al. Retroperitoneoscopic treatment of ovarian vein syndrome. J Laparoendosc Adv Surg Tech A 2008;18(5):739–742.

OXYLATE-ASSOCIATED RENAL DISEASE

DESCRIPTION Hyperoxaluria 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: “Hyperoxaluria,” for the causes of increased urinary oxylate.)

TREATMENT

- Pyridoxine supplements (200–400 mg/d) for primary hyperoxaluria
- Oral hydration; low-oxalate, low-fat diet for enteric hyperoxaluria
- Pyridoxine and thiazides for idiopathic hyperoxaluria

REFERENCE

Danpure CJ. Molecular and cell biology of primary hyperoxaluria type I. Clin Invest Med 1994;72:725.

Scheinman JI. Primary hyperoxaluria: Therapeutic strategies for the 90s. Kidney Int 1991;40:389–399.

SHORT TOPIC SECTION P

P53, UROLOGIC CONSIDERATIONS

DESCRIPTION The p53 gene produces a nuclear phosphorylation protein that has a tumor-suppression function. Loss of wild-type p53 is the most common genetic abnormality associated with TCC. 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 increased probability of biochemical relapse and is found in a higher percentage of hormone-refractory cancers.

REFERENCE

1. Minimo C, et al. Grading of upper urinary tract transitional cell carcinoma by computed DNA content and p53 expression. Urology 1997:50:869.

PAD TESTING

DESCRIPTION Used as a clinical tool to assess the severity of urinary incontinence, often in association with a micturition diary. The pad test provides a gross/semiquantitative measurement of urine loss over a given period of time. Several types have been described, but none has met with widespread approval. One technique has a patient take Pyridium 200 mg t.i.d. and then change pads every 6 hr for a 24-hr period. The amount of staining is an estimate of incontinence. Another approach is to weigh the pads (1 g = 1 mL urine).

REFERENCE

2. Ryhammer AM, Djurhuus JC, Laurberg S. Pad testing in incontinent women: A review. Int Urogynecol J Pelvic Floor Dysfunct 1999;10(2):111–115.

PAGANO URETERAL ANASTOMOSIS

DESCRIPTION A 4–5-cm linear incision is made through the taenia of the colon, and the mucosa is dissected from the submucosa to the level of the mesentery. The ureters are pulled through the lateral muscular wall and implanted distally into the mucosa. The serosa is reapproximated while incorporating mucosa in the midline.

REFERENCE

3. Pagano F. Ureterocolonic anastomosis: Description of a technique. J Urol 1980;123(3):355–356.

PAGE KIDNEY

DESCRIPTION This condition was first described in 1939, 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 renin secretion from the compromised kidney and decreased renin production from the contralateral renal unit result. Diagnosis can be made with US, CT, or MRI, demonstrating a surrounding hematoma or fibrous 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 reabsorption of the hematoma.

REFERENCE

4. Sterns RH, et al. “Page kidney.” Hypertension caused by chronic subcapsular hematoma. Arch Intern Med 1985;145(1):169–171.

PAGET DISEASE, ANOGENITAL/EXTRAMAMMARY

DESCRIPTION Extramammary Paget disease is an adenocarcinoma of the epidermis that can exist in numerous areas, including the penis, scrotum, bladder, vulva, perianal area, umbilicus, axilla, and conjunctiva. An underlying adnexal neoplasm is associated half the time with an increased risk of other malignancies. Generally considered an adenocarcinoma that occurs in apocrine gland areas of the body, the mammary type originates from lactiferous ducts and extends into epidermis. The anogenital type is usually slow growing and resembles dermatitis clinically, rarely involving the penile or scrotal skin. Often associated with underlying carcinoma such as bladder, prostate, and urethral cancers. Typically presents in the 60s or 70s with lesions that appear as crusted, indurated, erythematous to whitish patches. Histologically, the intraepithelial neoplastic cells contain mucin and are PAS positive. Differential diagnosis includes squamous cell carcinoma in situ and malignant melanoma. The lesions originate from pluripotent cells in epidermis that formed apocrine glands and may also result from extracutaneous adenocarcinoma that spread into the epidermis. Excision of skin lesion and evaluation for underlying malignancy should be performed.

REFERENCE

5. Balducci L, et al. Extramammary Paget’s disease: An annotated review. Cancer Invest 1988;6:293.

PAGET DISEASE, BONE

DESCRIPTION This condition affects up 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 1/3 of Paget disease cases have monostotic 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 lysis due to osteoclastic reabsorption 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 trabecular 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 or Medications.") Calcitonin is reserved for those intolerant of bisphosphonates.

REFERENCE

6. Ralston SH, et al. Pathogenesis and management of Paget's disease of bone. Lancet 2008;12;372(9633):155–163.

PAINFUL BLADDER SYNDROME (PBS)

DESCRIPTION The International Continence Society (ICS) defines PBS as suprapubic pain related to bladder filling, accompanied by other symptoms such as increased day- and nighttime 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 modifications, behavioral changes, and nonprescription medications, followed by intravesical therapy and prescription medications. Patients who fail these therapies can move to more invasive therapies including hydrodistention, neuromodulation, and lastly urinary diversion or augmentation.

REFERENCE

7. Chuang YC, Chancellor MB. Treatment of painful bladder syndrome and pelvic organ prolapse: Highlights of the 4th international consultation on incontinence, July 5–8, 2008, Paris, France. Rev Urol 2009;11(1):28–32.

PANETH CELL-LIKE CHANGE, PROSTATE

DESCRIPTION Describes the observation of prostatic glandular epithelium with distinct eosinophilic intracytoplasmic granules resembling Paneth cells, found in crypts of Lieberkühn in the small intestine. These cells are thought to represent a morphologic similarity to Paneth cells, rather than true 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 prostatic intracytoplasmic inclusions including secretory vacuoles, melanin, CMV viral inclusions, or virus-like particles.

REFERENCE

8. Weaver MG, et al. Paneth cell-like change of the prostate gland. Am J Surg Pathol 1992;16(1):62–68.

PAPILLARY ADENOMA PROSTATIC UTRICLE

DESCRIPTION The prostatic utricle is a 6-mm-thin orifice found in the verumontanum. Its origin is as a Müllerian remnant that projects back into the substance of the prostate. Papillary adenocarcinoma of the prostatic utricle is a rare malignancy with metastatic potential. Sometimes referred to as endometrial/endometrioid carcinoma of the prostate (because these tumors histologically resemble endometrial carcinoma). Histologically, these tumors are composed of tall columnar cells with clear to eosinophilic cytoplasm and large nucleoli. The cells form glands with scant intervening stroma.

TREATMENT

- Transurethral resection, radiotherapy, radical prostatectomy, or a combination of these has been utilized.
- Some advocate not using estrogen or castration, given the histologic resemblance to endometrial carcinoma.

REFERENCE

9. Merchant RF Jr. , Graham AR, Bucher WC, et al. Endometrial carcinoma of the prostatic utricle with osseous metastases. Urology 1976;8:169.

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, if any, cytologic 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].)

REFERENCE

Eble JN, et al. World Health Organization Classification of Tumours: Pathology and genetics of tumours of the urinary system and male genital organs. Lyon: IARC Press, 2004.

PAPILLOMA, BLADDER

DESCRIPTION A controversial diagnostic entity of the urinary bladder. The papillary lesion is small and unifocal, with a delicate fibrovascular stalk, and covered in cytologically and architecturally normal urothelium. Typically found in a younger age group than bladder cancer. Recurrences are common, and future development of invasive urothelial tumors of the urinary tract occurs in <10%. Many consider the lesion to be a very low-grade bladder cancer (grade I TCC) with limited potential to progress. Others propose that the terms low- and high-grade papillary urothelial carcinoma be replaced by low- and high-grade papillary intraurothelial neoplasia for all noninvasive urothelial cancers. (See also Section II: “WHO/ISUP Classification of Urothelial Neoplasms” [1998 and 2004].)

SYNONYMS

- WHO grade I papillary urothelial carcinoma
- Urothelial papilloma

TREATMENT

- Transurethral surgical resection is the main modality, with no defined role for intravesical therapy.
- These patients must be followed, due to the possible increased risk of having a urothelial malignancy.

REFERENCE

Van der Kwast TH, et al. Thirty-five years of noninvasive bladder carcinoma: A plea for the use of papillary intraurothelial neoplasia as new terminology. Anal Quant Cytol Histol 2008;30(6):309–315.

PAPILLOMA, RENAL PELVIS

DESCRIPTION An extraordinarily rare urothelial lesion in the upper urinary tract. A papilloma is a small, delicate proliferation with a fibrovascular core lined by normal urothelium. By WHO criteria, this is considered a benign lesion.

REFERENCE

Eble JN, et al. World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press, 2004.

PAPILLORENAL SYNDROME

DESCRIPTION Also called renal coloboma, this is an autosomal dominant disorder characterized by bilateral congenital optic disc anomalies and hypoplastic kidneys. It is associated with mutations in the PAX2 gene. Many patients suffer from renal failure due to renal hypoplasia or chronic pyelonephritis from vesicoureteral reflux.

REFERENCE

Nguyen D, Riordan-Eva P. Abnormal optic discs and renal failure: Papillorenal syndrome. Acta Ophthalmol Scand 2006;84:823–824.

PAQUIN URETERAL REIMPLANTATION

DESCRIPTION This repair is done using combined extravesical ureteral mobilization and intravesical implantation. A submucosal plane is developed toward the trigone with tenotomy succors, and the freshly spatulated ureter is reimplanted.

REFERENCE

Atala A, Keating MA. Vesicoureteral reflux and megaureter. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:1882–1896.

PARASTOMAL HERNIA

DESCRIPTION A parastomal hernia is an incisional hernia related to an abdominal wall stoma. In urologic surgery, parastomal hernias occur infrequently (<5% of cases) and are more likely to arise in loop-type stomas than in end-type stomas. 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

Israelsson LA. Parastomal hernias. Surg Clin N Am 2008;88:113–125.

PARTIN TABLES

DESCRIPTION Nomograms for patients with biopsy-proven prostate cancer, developed by Partin and associates at Johns Hopkins University, these charts incorporate PSA, TNM 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. Updated Partin tables can be found in Section VII.

REFERENCE

Partin AW, et al. Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. Urology 2001;58(6):843–848.

PATAU SYNDROME

DESCRIPTION This rare syndrome is associated with trisomy 13 and has a median survival of 3 mo. The incidence is 1 in 6000 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, hydronephrosis, and polycystic kidneys have been associated with Patau syndrome.

REFERENCE

Martlew RA, Sharples A. Anesthesia in a child with Patau's syndrome. Anesthesia 1995;50:980.

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 at all. (1 pt)
- My bladder condition causes me some very minor problems. (2 pt)
- My bladder condition causes me some minor problems. (3 pt)
- My bladder condition causes me (some) moderate problems. (4 pt)
- My bladder condition causes me severe problems. (5 pt)
- My bladder condition causes me many severe problems. (6 pt)

REFERENCE

Coyne KS, et al. The validation of the patient perception of bladder condition (PPBC): A single-item global measure for patients with overactive bladder. Eur Urol 2006;49:1079–1086.

PATIENT PERCEPTION OF INTENSITY OF URGENCY SCALE

DESCRIPTION A single-question tool to assess the patient's perception of the degree of his urgency. 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.

4. Urge incontinence: I leaked before arriving at the toilet.

REFERENCE

Staskin DR, et al. The urge to define urgency: Expert opinions on urgency study design and outcomes in OAB. 2007 AUA Annual Meeting Highlights. AUA News.

PCA3 DETECT (PROSTATE CANCER GENE 3 URINE ASSAY)

DESCRIPTION The PCA3 protein is over expressed in 95% of prostate cancers and is upregulated 66-fold in cancerous tissue as compared to normal tissue. No other human tissues have yet been shown to produce PCA3. Urine samples are collected after a careful digital rectal exam (recently, the test is modified to allow the determination without a prior rectal exam). PCA3 can be detected in the urine utilizing reverse transcriptase PCR techniques. It has shown excellent specificity and sensitivity in men undergoing confirmatory prostate biopsy, and its role in the diagnosis of prostate cancer is currently evolving.

REFERENCE

Parekh DJ, et al. Biomarkers for prostate cancer detection. J Urol 2007;178:2252–2259.

PEARLY PAPULES OF PENIS

DESCRIPTION These are normal anatomic structures located on the proximal glans penis or corona. They appear as minute, dome-shaped, flesh-colored papules. The incidence is 19–30%. These lesions are asymptomatic and can be confused with genital warts. Histologically, these papules are angiofibromas. No treatment is usually needed. Although these lesions represent a benign condition, psychological and cosmetic concerns often prompt patients to seek therapeutic removal. Multiple therapeutic modalities have been reported; however, use of CO_2 laser has proven to be the most effective to date.

REFERENCE

Lane JE, et al. Treatment of pearly penile papules with CO_2 laser. Dermatol Surg 2002;28(7):617–618.

PEDICULOSIS 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 shafts or the presence of “nits” (egg stage) on the hair shaft. (See also Section I: “Sexually Transmitted Disease [STD], General.”)

TREATMENT

- Lindane 1% shampoo applied for 4 min and washed off (avoid during pregnancy or lactation and in children <2 yr of age)
- Permethrin 1% cream rinse applied for 10 min and then washed off
- Piperonyl butoxide pyrethrin applied for 10 min and then washed off
- Nits need to be mechanically removed with a fin-toothed comb. Clothing and bedding need to be washed and dried.

REFERENCE

Buntin DM. The 1993 sexually transmitted disease treatment guidelines. Semin Dermatol 1994;13(4):269–274.

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 tissues or by primary or secondary neuropathy and myopathy. Many predisposing, inciting, and promoting factors can lead to pelvic floor dysfunction. Treatments range from conservative/behavioral therapies, to medications and surgical interventions.

REFERENCE

Bump RC, Norton PA. Epidemiology and natural history of pelvic floor dysfunction. Obstet Gynecol Clin 1998;25:723.

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 urologic 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 cystotomy, primary repair of the injury, or delayed repair after stabilization.

REFERENCE

Cass AS. The multiple injured patient with bladder trauma. J Trauma 1984;24:731.

PELVIC LIPOSARCOMA

DESCRIPTION Liposarcoma can present as a tumor of the spermatic cord or as a paratesticular tumor. Treatment includes inguinal orchiectomy with high ligation of the cord; adjuvant treatment is controversial but could include postoperative radiotherapy. Chemotherapy options are limited.

REFERENCE

Richie JP, Steele GS. Neoplasms of the testis. In: Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

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 not 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:

POP Q Grading System

Stage

Degree of Prolapse

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 farther than 2 cm less than the total vaginal length

IV

Complete vaginal eversion

This classification system exhibits excellent reliability, but it is more cumbersome to use than other systems and patient positioning can alter the results. (See also Section I: “Pelvic Prolapse, Cystocele and Enterocoele.”)

REFERENCE

Bump RC, Mattiasson A, Bo K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 1996;175:10–17.

PELVIC PAIN, MALE

See Section I: “Prostatitis, Chronic Nonbacterial, Noninflammatory (NIH CP/CPPS III A and B).”

PELVIS, BIFID

DESCRIPTION A normal variant seen in ~10% of patients in which the renal pelvis is divided into 2 major calyces just inside the kidney.

REFERENCE

Dähnert W. Radiology Review Manual. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2007.

PELVIS, EXTRARENAL

DESCRIPTION Most often a normal anatomic variant and can be mistaken for a pathologic condition (hydronephrosis, parapelvicor renal cyst, etc). Calyces are normal appearing on imaging with an unobstructed extrarenal pelvis but will be dilated with hydronephrosis. The extrarenal pelvis can also be associated with conditions such as renal malrotation or ectopic kidney and rarely may cause urinary stasis and difficulties with infection and stones.

REFERENCE

Kidneys. In: Dalrymple NC, et al., eds. Problem Solving in Abdominal Imaging. Elsevier: Philadelphia, 2009.

PEMPHIGUS FOLIACEUS AND VULGARIS

DESCRIPTION Pemphigus foliaceus and vulgaris refer to a group of rare autoimmune intraepidermal blistering diseases involving the skin and mucous membranes. The difference between pemphigus foliaceus and vulgaris involves the level of epidermis at which loss of cell–cell cohesion occurs. Almost all patients will have painful oral mucosal erosions and 50% may have cutaneous blisters involving the genitalia. The diagnosis is confirmed by light microscopy and immunofluorescence. Pemphigus carries a high mortality rate of 10% from sepsis as a result of skin breakdown and treatment-associated side effects.

TREATMENT

- Topical steroids (eg, clobetasol propionate 0.05% cream [mild cases])
- Glucocorticoids (prednisone) and immunosuppressants (cyclophosphamide, azathioprine, and IV immunoglobulin) for severe cases

REFERENCE

Habif TP. Vesicular and bullous diseases. In: Habif TP, ed. Clinical Dermatology, 4th ed. Philadelphia: Mosby, 2004.

PENILE AND CORPORAL BODY MASS

DESCRIPTION Penile masses are relatively rare lesions. Benign solid tumors of the penis include angioma, fibroma, lipoma, and myoma, as well as other dermatologic lesions. Abscesses and granulomas should be included in the differential. Malignant tumors of the penis are more often seen in adults and include squamous cell carcinoma, melanoma, and soft-tissue sarcoma. Cystic lesions are usually periurethral gland and retention cysts due to sebaceous glands in the skin. For malignant lesions, wide excision is recommended.

REFERENCE

Kocakoc E, et al. Postcircumcision granuloma: A rare cause of a penile mass in a boy. J US Med 2006; 25(12):1611–1613.

PENILE BRACHIAL PRESSURE INDEX (PBI)

DESCRIPTION The PBI can be defined as the penile systolic BP divided by the brachial systolic BP. A penile 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

Metz P, Bengtsson J. Penile blood pressure. Scand J Urol Nephrol 1981;15:161.

PENILE DOPPLER ULTRASOUND PARAMETERS

DESCRIPTION This type of minimally invasive vasculogenic imaging is used for men with ED who have a potentially surgically treatable cause (eg, younger men who may have suffered traumatic straddle injuries and do not respond to oral or intrac avernosal therapy). Penile Doppler US is used for evaluation of penile blood flow and requires intracavernous injection of vasodilators. 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 pudendal arteriography. Patients with severe ED will have a cavernous artery luminal diameter <0.7 mm and an increase of <75% in diameter postinjection. Patients with veno-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 = PSV – EDV/PSV) >0.9 (where EDV is end diastolic velocity) usually indicates no evidence of veno-occlusive dysfunction, whereas an RI of <0.75 was associated with venous leakage in 95% of cases.

REFERENCE

Wein AJ, Kavoussi LR, Novick AC, et al. Vascular surgery for erectile dysfunction. In: Wein AJ, et al., eds. Campbell-Walsh Urology 9th ed. Philadelphia: Saunders Elsevier, 2007.

PENILE 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 nodules, scrotalization of the penis, and erectile dysfunction.

REFERENCE

Van Driel MF, Schultz WC, Van de Wiel HB, et al. Surgical lengthening of the penis. BJU 1998;82(1):81–85.

PENILE PAIN SYNDROME

DESCRIPTION In contrast to other chronic pain syndromes of reproductive organs, chronic penile pain seems to be extremely rare. Penile pain can be understood by etiology, which includes local conditions such as dermatitis, infection, and ischemia; referred pain from bladder, prostate, lower back, and hips; neuropathic pain resulting from injury to dorsal nerve, pudendal nerve, or cauda equina; and psychiatric conditions that may lead to extreme hypersensitivity and allodynia. Persistent pain can be treated by treating the underlying disease (paraphimosis, priapism, Peyronie disease, herpes). One case in literature described a patient with episodic penile pain attacks and an inguinal hernia whose pain resolved after herniorrhaphy. His pain was likely due to the irritation of the ilioinguinal nerve in the inguinal canal, which also supplies the ventral base of the penis. In psychosomatic pain, analgesics may be helpful; however tricyclic antidepressants or anticonvulsants have also proven effective.

REFERENCE

Baranowski AP, Abrams P, Fall M. Urogenital Pain in Clinical Practice. Boca Raton, FL: CRC Press, 2007:248–252.

PENILE PROSTHESIS, MODELS AND DESCRIPTIONS

(See table below.)

Prosthesis Type

American Medical Systems

Mentor Corporation

Description

Advantages

Disadvantages

Semirigid

AMS Malleable 600

Acu-form

Malleable core rods that can be bent up and down

Low mechanical failure rate, easy to insert

Constant penile rigidity, increased risk of penile erosion

AMS Malleable 650

2-piece inflatable

Ambicor

2 cylinders connected to a small scrotal pump

Easy to insert

Increased risk of mechanical failure

3-piece inflatable

AMS 700 CX

Alpha I

2 cylinders, large abdominal fluid reservoir, and scrotal pump

Penile girth and rigidity most similar to normal erection

Highest risk of mechanical failure, technically more difficult, risk of autoinflation with physical activity

AMS 700 CXM

Titan

AMS 700 CXR
Titan Narrow Base

As above; increased penile length

AMS 700 Ultrex

References

Wein AJ, Kavoussi LR, Novick AC, et al. Prosthetic surgery for erectile dysfunction. In Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

PENILE REHABILITATION

DESCRIPTION A scheduled regimen of early pharmacologic (PDE5 inhibitors, prostaglandins) therapy, nonpharmacologic (vacuum erection devices) therapy, or a combination thereof immediately following radical prostatectomy is thought to increase potency rates and help maintain penile length and girth. Cavernosal hypoxia, resultant fibrosis, and venous leak is hypothesized as the predominant mechanisms for post-prostatectomy erectile dysfunction (ED). The aim of penile rehabilitation is to improve penile oxygenation and thus help prevent ED and penile shortening. More recent data examines the impact of chronic therapy on ED.

REFERENCE

Zippe CD, Pahlajani G. Penile rehabilitation following radical prostatectomy: Role of early intervention and chronic therapy. Urol Clin N Am 2007;34(4):601–618.

PENILE SHORTENING

DESCRIPTION Penile shortening may occur congenitally in patients with bladder exstrophy and more commonly after radical prostatectomy and penile revascularization. Patients with bladder exstrophy have penile shortening because of diastasis of the pubic symphysis and short corporal lengths (<50% the size of controls). More commonly, patients may have shortening of the penis following radical prostatectomy because of unopposed sympathetic stimulation of the penis, fibrosis resulting from hypoxia (as a consequence of denervation), or possibly as a result of retraction of the penile structures into the pelvis. Lastly, arterial revascularization surgery for vascular erectile dysfunction may result in penile shortening in 20% of patients as a result of scar formation.

REFERENCE

Gontero P, Galzerano M, Bartoletti R, et al. New insights into the pathogenesis of penile shortening after radical prostatectomy and the role of postoperative sexual function. J Urol 2007;178(2):602–607.

PENIS, AGENESIS (APHALLIA)

DESCRIPTION Penile agenesis is a rare anomaly with an estimated incidence of about 1 in 10 million live births. Most cases have a 46,XY karyotype. The usual appearance is that of a well-developed scrotum with descended testes and an absent penile shaft. Associated anomalies are common. Associated urethral absence is usually accompanied by fatal anomalies. Immediate investigations for associated anomalies and karyotype are essential. Caused by failure of development of the genital tubercle, surgical reconstruction/gender reassignment is recommended in the newborn.

REFERENCE

Oesch IL, Pinter A, Ransley PG. Penile agenesis: A report of six cases. J Pediatr Surg 1987;2:172–174.

PENIS, ANGIOSARCOMA

DESCRIPTION ~32 cases of penile angiosarcoma have been reported. No site of predilection is demonstrated, and the tumor may be well circumscribed or diffuse. Death may occur 1 wk to 5 yr after presentation (mean: 13 mo). The application of immunoperoxidase staining for factor VIII, present in normal endothelial cells, aids in diagnosis.

TREATMENT

- Local excision with lymph node dissection
- Local radiotherapy
- Systemic chemotherapy with more widespread tumor

REFERENCE

Kovacz J, Crouch RD. Sarcoma of the penis. J Urol 1958;80:43.

PENIS, ARTIFICIAL NODULES (TANCHO NODULES, BULLETUS, FANG MUK, CHAGAN BALLS)

DESCRIPTION Tancho 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.

REFERENCE

Wilcher G. Artificial penile nodules: A forensic pathosociology perspective: Four case reports. Med Sci Law 2006;46(4):349–356.

PENIS, BASAL CELL CARCINOMA

DESCRIPTION Basal cell carcinoma is a common cutaneous malignancy, but 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 metastasize. Lesions are successfully treated with simple local excision. (See also Section I: “Penis, Lesion, General.”)

REFERENCE

Bañón Pérez VJ, et al. Basal cell carcinoma of the penis. Arch Esp Urol 2000;53(9):841–843.

PENIS, BOWENOID PAPULOSIS

DESCRIPTION Bowenoid papulosis of the penis are benign lesions that appear as rounded, reddish, single or multiple papules on the glans or shaft of penis, although they can occur anywhere on the external genitalia or perianal regions of both male and females. These papules typically occur in sexually active patients who are 20–35 yr of age. They are caused by human papilloma virus and maybe confused with CIS of the penis. Histologically, these lesions show parakeratosis and acanthosis in squamous epithelium with disorganization of the epithelial cells. They can be distinguished from CIS by possessing less mitotic figures and cellular dysplasia. Treatment is local destruction, including superficial excision, laser surgery, and use of topical retinoic acid, podophyllum resin, and topical 5-fluorouracil. The recurrence rate is 20%.

REFERENCE

Bhojwani A, Biyani CS, Powell CS. Bowenoid papulosis of the penis. BJU 2003;80(3):508.

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 prepubic 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 iatrogenic hidden penis after circumcision is more properly called a trapped penis. Children who undergo neonatal circumcision with testicular swelling or with a hernia or a webbed penis are at risk for excess penile shaft skin loss and a trapped penis. Theoretically, obese adults who undergo circumcision are also at risk for removal of excess shaft skin. Symptoms can sometimes be associated (balanitis, UTI, painful voiding, ballooning of the foreskin, and urinary retention) with the condition.

SYNONYMS

- Inconspicuous penis (general term for buried, trapped, or webbed penis)

TREATMENT

- Surgical correction is optional and controversial.
- Liposuction has been used in cases of extreme obesity.

REFERENCE

Donatucci CF, et al. Management of the buried penis in adults. J Urol 1998;159(2):420–424.

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 corn is rare and is characterized by overgrowth of epithelium above a lesion that may be a wart, nevus, or tumor. It is important to note that the incidence of squamous cell carcinoma is 33% when penile horn is present. Treatment is surgical excision with a margin of tissue at base. Careful histologic evaluation of the base and close clinical follow-up of the excision site is highly recommended.

REFERENCE

Vera-Donoso CD, Lujan S, Gomez L, et al. Cutaneous horn in glans penis: A new clinical case. Scand J Urol Nephrol 2009;43(1):92–93.

PENIS, CYSTS

DESCRIPTION Epidermal cysts found on the ventral surfaces of the penis have been attributed to defective embryologic closure of the median raphe, anomalous developmental rests of the periurethral glands of Littré, development of apocrine cystadenomas ectopically, and anomalous budding and separation of urethral columnar epithelium from the urethra. Penile cysts are commonly found lying just beneath the median raphe and are most likely derived from urethral columnar epithelium. Patients are most often asymptomatic.

CAUSES

Congenital anomaly

TREATMENT

Surgical excision

REFERENCE

Paslin D. Urethroid cysts. Arch Dermatol 1983;119(1): 89–90.

PENIS, DUPLICATION (DIPHALLUS)

DESCRIPTION This is an extremely rare anomaly, with an incidence of 1 in 5–6 million births. According to Aleem's classification, the condition may be true diphallia (complete or partial), or bifid phallus (complete or partial bifid glans or bifid penis). Usually, the penises are unequal in size and lie side by side. Associated anomalies are frequent. US may help in differentiating true complete diphallia (2 corpora cavernous in each penis) from complete bifid phallus (only 1 corpus cavernous in each penis).

The condition is caused by a failure of fusion of paired mesodermal anlagen of the genital tubercle and treated by surgical reconstruction.

REFERENCE

Aleem AA. Diphallia: Report of a case. J Urol 1972;108:357.

PENIS, FIXED DRUG ERUPTIONS

DESCRIPTION A fixed drug eruption is an allergy that produces a plaque or blister at the same cutaneous site each time the drug is ingested. The most common drugs with side effects afflicting the penis are tetracycline, phenolphthalein, sulfonamides, barbiturates, salicylates, penicillins, foscarnet, and Coumadin. Foscarnet can cause periurethral ulcerations and Coumadin can cause a hemorrhagic necrosis of the penis.

REFERENCE

English JC 3rd, Laws RA, Keough GC, et al. Dermatoses of the glans penis and prepuce. J Am Acad Dermatol 1997;37(1):1–24.

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 US or angiography should be performed to delineate the anatomy. Treatment is surgical excision or laser ablation.

SYNONYMS

- Cavernous hemangiomas
- Subcutaneous hemangiomas
- Penile hemangiomas

TREATMENT

Surgical excision or laser ablation

REFERENCE

Alter GJ, Trengove-Jones G, Horton CE Jr. Hemangioma of penis and scrotum. Urology 1993;42(2):205–208.

PENIS, HIRSUTE PAPILLOMA (PEARLY PENILE PAPULES, CORONAL PAPILLAE)

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 STDs, and persists through life, gradually becoming less noticeable with increased age. Treatment is not required, but sometimes offered for cosmetic reasons. CO_2 laser is effective.

REFERENCE

Bylaite M, Ruzicka T. Images in clinical medicine. Pearly penile papules. N Engl J Med 2007;357(7):691.

PENIS, HYPOPLASIA

DESCRIPTION A small or hypoplastic penis may be the result of gonadotropin deficiency, hypospadias, or epispadias.

REFERENCE

Schneck FX, Bellinger MF. Anomalies of the testes and scrotum and their surgical management. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders Elsevier, 2007.

PENIS, KAPOSI SARCOMA

DESCRIPTION Kaposi sarcoma of the penis is rare, with only 37 cases reported in literature. Although most are associated with HIV, cases have been described in immunocompetent patients. It is clinically identified by painless, red-violaceous nodules, as well as papules, plaques, and wart-like pedunculated lesions. The lesions are most commonly found on the glans, although the foreskin, urethral meatus, and scrotum can also be affected. Treatments described include local surgery, radiotherapy, electrocoagulation, laser, and injection of interferon- into the lesion. (See also Section I: “Penis, Lesion, General.”)

REFERENCE

Hernández-Bel P, López J, Sánchez JL, et al. Primary Kaposi sarcoma of the penis in an HIV-negative patient. Actas Dermosifiliogr 2008;99(8).

PENIS, LEIOMYOMA

DESCRIPTION Penile leiomyoma is a rare benign tumor of smooth muscle that commonly involves the shaft, with glans penis involvement being next in frequency. These lesions tend to be small (1.0 cm in diameter), well-circumscribed, rubbery in consistency, with light yellow to white cut surfaces. 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

Leoni S, Prandi S, Mora A. Leiomyoma of the prepuce. Eur Urol 1980;6(3):188–189.

PENIS, LEIOMYOSARCOMA

DESCRIPTION Penile leiomyosarcoma is a very rare malignant smooth muscle tumor that usually occurs in the 5th–7th 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 urethra 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

Kathuria S, Jablokow VR, Molnar Z. Leiomyosarcoma of the penile prepuce with ultrastructural study. Urology 1986;27(6):556–557.

PENIS, LENGTH, NORMAL

DESCRIPTION Data on pediatric penile length considerations are discussed in Section II: “Microphallus (Micropenis).” At birth, dimensions of the normal-term infant phallus are 3.5 ± 0.7 cm in stretched length and 1.1 ± 0.2 cm in diameter. In adults, concern over phallus 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, Trapped, or Hidden)”). One recent study provided the following data for mean measurements in adults (length from penopubic skin to the meatus):

- Flaccid length: 8.85 cm; stretched length: 12.45 cm
- Erect length: 12.89 cm; flaccid girth: 9.71 cm; erect girth: 12.3 cm

REFERENCE

Wessels H, McAninich JW. Penis size: What is normal? Contemp Urol 1997;6671.

PENIS, LEUKOPLAKIA

DESCRIPTION These lesions present as solitary or multiple white plaques, usually involving the penile meatus. Histologically, parakeratosis, hyperkeratosis, and hypertrophy of the rete pegs are present, with dermal edema and lymphocytic infiltration. Leukoplakia is commonly associated with in situ squamous cell carcinoma and verrucous carcinoma of the penis. Thus, close follow-up of the excision site with periodic biopsy of incompletely excised lesions is necessary to detect early malignant change.

TREATMENT

- Elimination of chronic irritation and circumcision may be indicated.
- Surgical excision and radiation have been used in the treatment of leukoplakia.

REFERENCE

Bain L, Geronemus R. The association of lichen planus of the penis with squamous cell carcinoma in situ and with verrucous squamous carcinoma. J Dermatol Surg Oncol 1989;15(4):413–417.

PENIS, MALIGNANT FIBROUS HISTIOCYTOMA (MFH)

DESCRIPTION MFH is a rare sarcoma of the penis that may present as a subcutaneous penile mass in a patient with penile pain, priapism, or urinary retention.

TREATMENT

- Superficial tumors are treated with wide local excision vs. total amputation.
- Deep tumors arising from the corpora are treated with total penile amputation.
- Local recurrence is common, and complete amputation should be considered even for superficial tumors.
- Regional metastases are rare, and lymphadenectomy is unnecessary unless adenopathy is palpable.

REFERENCE

Katona TM, et al. Malignant fibrous histiocytoma of the glans penis: A case report. Anal Quant Cytol Histol. 2006;28(1):39–42.

PENIS, MELANOMA

DESCRIPTION Melanoma of the penis is extremely rare. It presents as a reddish-brown or blue black pigmented papule, plaque, or ulceration on the glans penis and less commonly on the prepuce. The depth of skin invasion (Clark classification) and thickness of the tumor (Breslow classification) are of prognostic importance.

TREATMENT

- Surgery is the mainstay of therapy via partial or total penile amputation.
- Foreskin lesions may be treated with circumcision.
- Glanular lesions may be treated with partial penectomy.
- Lesions on the shaft often require total penile amputation.

REFERENCE

Te CC, et al. Recurrent malignant of the penis. Urology. 2008;72(5):1185, e15–16.

PENIS, METASTASIS TO

DESCRIPTION Metastatic disease to the penis is rare, with roughly 200 cases reported during the past 100 yr. The bladder, prostate, rectum, and rectosigmoid are responsible for the greatest number of metastases. However, distal primaries (eg, lung) have been reported. Several mechanisms might lead to this condition: Direct extension, retrograde lymphatic spread, retrograde venous spread, direct arterial extension, secondary embolism, tertiary embolism, instrumental spread, and paradoxical spread. Patients may develop masses or malignant priapism. Most patients die within 6 mo of presentation. Penectomy may be indicated for pain or relief of urinary obstruction.

REFERENCE

Bachrach P, Dahlen CP. Metastatic tumors to the penis. Urology 1973;1(4):359–362.

PENIS, NEURILEMOMA (SCHWANNOMA)

DESCRIPTION Penile neurilemoma, also known as schwannoma, is a rare entity. It is an encapsulated tumor that arises from the sheaths of peripheral nerves. These are solitary, slow-growing, and often asymptomatic lesions. Most penile schwannoma are unifocal, benign, and tend to occur on the dorsal penile shaft, where the penile dorsal nerve is located, although cases on the glans penis have also been reported. A family history of neurofibromatosis is usually present. Malignant schwannomas are often associated with neurofibromatosis type I. Surgical excision is the treatment of choice, and regular follow-up is recommended because recurrence of benign schwannoma has been reported.

REFERENCE

Loeser A, Katzenberger T, Meuller JG, et al. Solitary schwannoma of the glans. Urology 2007;70(5):1007.e5–e6.

PENIS, NEUROFIBROSARCOMA (MALIGNANT SCHWANNOMA)

DESCRIPTION A malignant nerve sheath tumor arising from Schwann cells that very rarely occurs in the penis. These lesions most commonly occur on the dorsal aspect of the penis, near the dorsal nerve. Nodules from Peyronie disease are uncommon in this location. Patients may have a history of von Recklinghausen disease or neurofibromatosis, and an exam for café au lait spots and other nodules should be undertaken.

TREATMENT

- Complete excision
- Careful follow-up for recurrence
- Recurrent schwannomas may require total penectomy.

REFERENCE

Suzuki Y, et al. Schwannoma of the penis: Report of a case and review of the literature. Int Urol Nephrol 1998;30(2):197–202.

PENIS, SCLEROSING LIPOGRANULOMA (PARAFFINOMA)

DESCRIPTION This is a foreign-body reaction resulting 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, erectile dysfunction, and painful intercourse.

TREATMENT

- Complete excision of affected skin and subcutaneous tissue
- Skin graft coverage (full- or split-thickness skin graft)
- Flap coverage (usually scrotal) is required if skin graft does not take.

REFERENCE

Jeong JH, et al. A new repair for penile paraffinoma: Bilateral scrotal flaps. Ann Plast Surg 1996;37(4):386–393.

PENIS, SCLEROSING NONVENEREAL LYMPHANGITIS

DESCRIPTION Sometimes referred to as Mondor phlebitis of the penis, these are firm and often asymptomatic subcutaneous cordlike swellings along the dorsal shaft of the penis or around the coronal sulcus. They can be confused with lymphangioma 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

Kumar B, Narang T, Radotra BD, et al. Mondor's disease of penis: A forgotten disease. Sex Transm Infect 2005;81:480–482.

PENIS, STRANGULATION

DESCRIPTION Penile strangulation 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 constricting rings on the flaccid penis often result in the impossibility of their removal after erection, leading to vascular complications usually within a few hours. These injuries range from simple penile engorgement to ulceration, necrosis, urinary fistula, or even gangrene. The main objective in the treatment is acute decompression to avoid potential ischemic necrosis and autoamputation. Removing the constricting device is a challenge to the urologic surgeon, and each case requires an individual approach. Methods used include aspiration of the corpora, or the use of saws, grinders, and dental drills to remove object. The outcome is often good, but some can have serious complications such as penile amputation and urethrocutaneous fistula.

REFERENCE

Ivanovski O, Stankov O, Kuzmanoski M, et al. Penile strangulation: Two case reports and review of the literature. J Sex Med 2007;4(6):1775–1780.

PENIS, SYRINGOMA

DESCRIPTION Syringomas are benign appendageal tumors that normally occur in adolescents on the face, neck, axillae, or abdomen. They are extremely rare at the penis; only 6 cases have been reported in the literature to date. On exam, 2–5-mm flesh-colored papules are seen. A punch biopsy can be obtained to relieve patient fears of STD and cancer, and to rule out condyloma, lichen planus, and bowenoid papulosis, which may appear similarly. Because they are benign, treatment is usually considered cosmetic. CO2 laser has proved effective, as well as surgical excision and cryotherapy with liquid nitrogen.

REFERENCE

Olson JM, Robles DT, Argenyi ZB, et al. Multiple penile syringomas. J Am Acad Dermatol 2008;59(2 Suppl 1):S46–S47.

PENIS, THROMBOSIS OF DORSAL VEIN

DESCRIPTION Thrombosis of the superficial dorsal vein of the penis, also known as Mondor disease, is a rare, poorly understood clinical entity. Some predisposing factors include vigorous sexual activity, trauma, and surgery to the pelvis or external genitalia. It can also be a manifestation of metastatic pancreatic cancer, or can be associated with bladder and prostate cancers. Clinically, the patient complains of swelling and pain on the dorsal aspect of the penis. On exam, a cordlike structure is palpated. Doppler US can demonstrate a noncompressible portion of the superficial dorsal vein, as well as a lack of venous flow signals. Treatment is conservative, as the disease is self-limited and often spontaneously resolves. Abstinence from sex an danticoagulation with heparin is sometimes recommended. NSAIDs may relieve pain and diminish inflammation. Thrombus excision may be the last resort in cases without resolution. Spontaneous thrombosis of the deep dorsal penile vein has also been described following trauma, or in a patient with thrombophilia. This condition improves with anticoagulation treatment.

REFERENCE

Kartsaklis P, Konstantinidis C, Thomas C, et al. Penile Mondor’s disease: A case report. Cases J 2008;1(1):411.

PENIS, TORSION

DESCRIPTION Congenital rotation of the penile shaft such that the median raphe spirals obliquely around the penile shaft. The external genitalia are otherwise normal, but this condition may be associated with hypospadias or ventral hood penile deformity. The torsion tends to occur in a counterclockwise direction (ie, the twist is to the left). Mainly a cosmetic issue, repair is usually not necessary if the rotation is <60–90°.

TREATMENT

Mild cases require only simply freeing the penile shaft of its investing tissue.

REFERENCE

Pomerantz P, et al. Isolated torsion of penis. Report of six cases. Urology 1978;11(1):37–39.

PENIS, VERRUCOUS CARCINOMA

DESCRIPTION Squamous cell carcinoma (SCC) of the penis represents about 1% of cancers in men in the US and 11–12% of all cancers in men in countries where circumcision is not routinely practiced. Verrucous carcinoma is an uncommon variant that accounts for only 5–16% of all penile SCCs. Diagnosis of verrucous carcinoma may be difficult because biopsies are usually performed on the superficial portion of the lesion. Therefore, it is crucial to perform a deep biopsy. Verrucous carcinoma exhibits an exophytic warty lesion of SCC and endophytic growth where cellular atypia is noted. (See also Section II: “Penis Cancer, General.”)

SYNONYMS

- Giant condyloma
- Buschke-Lowenstein tumor

CAUSES

- Lack of circumcision
- Prior trauma
- Previous disease
- Poor hygiene
- Phimosis
- Tight prepuce

TREATMENT

Partial penectomy

REFERENCE

Kanik AB, Lee J, Wax F, et al. Penile verrucous carcinoma in a 37-yr-old circumcised man. J Am Acad Dermatol 1997;37(2):329–331.

PENIS, WEBBED

DESCRIPTION A congenital condition in which the scrotal skin extends onto the ventral aspect of the penile shaft. Although there are usually no associated abnormalities, there are a few reports of hypoplasia of the distal urethra. Occasionally, a webbed penis is the result of a circumcision in which there was excess removal of ventral penile shaft skin. Cosmetic repair is performed, as needed.

REFERENCE

Dilley AV, et al. Webbed penis. Pediatr Surg Int 1999;15(5–6):447–448.

PENN POUCH

DESCRIPTION A continent urinary reservoir is created based on the Mitrofanoff principle, which uses the appendix as the catheterizable continent apparatus. The pouch is made from joining a detubularized colon and ileum.

REFERENCE

Benson MC, Olsson CA. Continent urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:3190–3245.

PEREYRA URETHROPEXY

DESCRIPTION Pereyra, in 1959, was 1st to present a transvaginal approach to a urethropexy using a needle suture carrier, obviating the need for a transabdominal exposure. Through a T vaginal incision, the bladder neck and periurethral tissue are exposed. The suture carrier is passed through a suprapubic stab incision and, under digital guidance, delivered through the periurethral tissue. The bladder neck is then suspended with absorbable suture.

REFERENCE

Duggan ML. Another look at Pereyra's Stint urethropexy. South Med J. 1975;68(11):1381–1384.

PERINEAL PAIN, DIFFERENTIAL DIAGNOSIS

DESCRIPTION The differential diagnosis of perineal pain is long, with infectious, inflammatory, iatrogenic, anatomic, and other causes as listed below:

Infectious:

- Prostatitis
- Cystitis
- Epididymitis
- Orchitis
- Fournier gangrene
- Abscess
- Sexually transmitted infections (herpes, syphilis, chancroid)

Inflammatory:

- Painful bladder syndrome/interstitial cystitis
- Inflammatory dermatoses (lichen planus, lichen sclerosis, SLE, Behcet disease)

Iatrogenic:

- Sacral nerve stimulation
- Perineal sling
- Radiation therapy
- Cryotherapy
- Pelvic surgery

Prolapse:

- Bladder
- Urethra
- Vagina
- Uterus
- Rectum

Other:

- Ureteral stone
- Torsion (testicular, ovarian, appendix testis, appendix epididymis)
- Pudendal nerve entrapment
- Diabetic and HIV/AIDS neuropathy

REFERENCE

Warfield CA, Bajwa ZH. Perineal pain. In: Warfield CA, Bajwa ZH, eds. Principles and Practice of Pain Medicine, 2nd ed. New York: McGraw-Hill, 2005.

PERINEAL TRAUMA (STRADDLE INJURY)

DESCRIPTION This refers to fracture of all 4 pubic rami or simply to blunt force trauma to the perineum causing urethral injury or high-flow priapism. Patients with blood at the urethral meatus, perineal hematoma, or urinary retention after blunt force trauma should be suspected of having a urethral injury. A retrograde urethrogram should be performed in males and urethroscopy in females. Patients with urethral injuries may have an attempt at primary realignment with a catheter but suprapubic cystotomy remains the standard of care. Anastomotic urethroplasty should be considered the gold standard, with endoscopic treatments reserved for posterior urethral strictures <1 cm or strictures following anastomotic repair. Straddle injury may also cause nonischemic high-flow priapism from a cavernosal artery–corpora cavernosa fistula. This may require angiographic embolization if it fails to resolve on its own.

REFERENCE

Park S, Mc Aninch JW. Straddle injuries to the bulbar urethra: Management and outcomes in 78 patients. J Urol. 2004;171(2 pt 1):722–725.

PERINEURAL INVASION, UROLOGIC CONSIDERATIONS

DESCRIPTION Perineural invasion most commonly refers to a pathologic finding on needle biopsy of prostate or radical prostatectomy specimens. Perineural invasion on needle biopsy specimens correlates with an increased risk of extraprostatic extension, lymph node metastases, and postoperative progression. Surprisingly, perineural invasion in radical prostatectomy specimens does not have any prognostic significance, perhaps because it represents spread of tumor along a plane of decreased resistance, as opposed to invasion into vascular or lymphatic structures, which portends a worse prognosis.

TREATMENT

Patients should be counseled on treatment options, nerve-sparing vs. non–nerve sparing surgery, and prognosis based upon PSA, Gleason score, and TNM stage and possibly perineural invasion.

REFERENCE

Ng JC, Koch MO, Daggy JK, et al. Perineuralinvasion in radical prostatectomy specimens: Lack of prognostic significance. J Urol 2004;172:2249–2251.

Stone NN, Stock RG, Parikh D, et al. Perineural invasion and seminal vesicle involvement predict lymph node metastasis in men with localized carcinoma of the prostate. J Urol 1998;160:1722–1726.

PERIPHERAL NEUROPATHY, UROLOGIC CONSIDERATIONS

DESCRIPTION As it pertains to urology, peripheral neuropathy classically affects bladder and sexual function. The most common causes of peripheral neuropathy are diabetes, HIV/AIDS, alcoholism, side effects of chemotherapy, and B12 deficiency. The classic description of diabetic cystopathy is impaired bladder sensation, increased bladder capacity, decreased contractility, decreased flow rate, and increased residual volume. Patients may have involuntary bladder contractions and eventually develop areflexic bladders. Sexual function may be impaired, and patients may have erectile dysfunction or anorgasmia.

TREATMENT

- The underlying cause of neuropathy should be identified and treated, if possible.
- Careful evaluation for progression of disease should be sought, and patients may need to be on timed voiding or intermittent catheterization.
- Erectile dysfunction may require a vacuum erection device, medical therapy, or surgical intervention.

REFERENCE

Sasaki K, Yoshimura N, Chancellor MB. Implications of diabetes mellitus in urology. Urol Clin N Am 2003;30(1):1–12.

PERIURETHRAL ABSCESS

DESCRIPTION A life-threatening infection of the urethra and periurethral tissues that can spread rapidly to the adjacent soft tissues. It most commonly presents with scrotal edema (94%), fever (70%), urinary retention (19%), a draining abscess (11%), dysuria, and urethral discharge.

CAUSES

- Urethral catheterization
- Gonorrhea
- Urethral stricture

TREATMENT

- Broad-spectrum IV antibiotics
- Wide local debridement
- Suprapubic urinary drainage
- Biopsy of urethra to evaluate for urethral cancer

REFERENCE

Walther MM, Mann BB, Finnerty DP. Periurethral abscess. J Urol 1987;138(5):1167–1170.

PERLMAN SYNDROME

DESCRIPTION An overgrowth syndrome characterized by fetal gigantism, visceromegaly, distinct facial features, and nephroblastomatosis. Similar overgrowth syndromes include Beckwith-Weidemann, Sotos, and the Simpson-Golabi-Behemel syndromes. Neonatal mortality is extremely high. The kidneys are often dysplastic, with numerous cysts and nephrogenic rests. The cause is unknown, and the diagnosis is based entirely on the phenotypic description.

REFERENCE

Schilke K, Schaefer F, Waldherr R, et al. A case of Perlman syndrome: Fetal gigantism, renal dysplasia, and severe neurological deficits. Am J Med Genet 2000;91(1):29–33.

PET SCAN, UROLOGIC CONSIDERATIONS

DESCRIPTION The most common urologic applications for the PET scan are in seminoma, kidney cancer, and prostate cancer. Patients who are treated for seminoma and have a residual retroperitoneal mass >3 cm should have a PET scan performed. A positive scan implies viable tumor, whereas a negative scan implies freedom from disease. Emerging data from combination PET/CT scans show potential in identifying small renal masses with reported 94% sensitivity and 100% specificity rates for clear cell RCC, but is still considered experimental. PET scans may also be useful in prostate cancer for distinguishing local vs. distant failure, determining progression of disease, and assessing the degree of androgen receptor expression but are not yet standard of care studies.

REFERENCE

Larson SM, Schöder H. Advances in positron emission tomography applications for urologic cancers. Curr Opin Urol 2008;18(1):65–70.

PFANNENSTIEL INCISION

DESCRIPTION A transverse incision is centered ~2 fingerbreadths above the pubic symphysis. A transverse incision is made through the anterior rectus fascia, and entry into the retropubic space can be gained by separating the rectus muscle in the midline. Useful for bladder and other lower abdominal procedures.

REFERENCE

Montague DK. Surgical incisions. In: Novick AC, Streem SB, Pontes JE, eds. Stewarts Operative Urology. Baltimore: Williams & Wilkins, 1989:15–40.

PHIMOSIS, CLITORAL

DESCRIPTION Phimosis should be suspected in women with clitoral 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 creams to improve the elasticity of the prepuce and potentially antifungal agents such as nystatin or fluconazole. Rarely, lichen planus may result in a white scarring of the clitoris, prepuce, and perineum. Treatment with clobetasol cream may improve symptoms. Women with refractory symptoms may require a dorsal slit.

REFERENCE

Munarriz R, Talakoub L, Kuohung W, et al. The prevalence of phimosis of the clitoris in women presenting to the sexual dysfunction clinic: Lack of correlation to disorders of desire, arousal and orgasm. J Sex Marital Ther 2002;28(1):181–185.

PINWORMS, UROLOGIC CONSIDERATIONS

DESCRIPTION ~209 million people are infected with intestinal pinworm (Enterobius vermicularis) worldwide. They most commonly reside in the large intestine, and females lay ~15,000 eggs nightly on the perineum, causing intense perineal itching and sleep disturbances. Occasionally, worms may ascend the vagina and uterus and enter the peritoneal cavity 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 Enterobius in the bladder.

TREATMENT

- Mebendazole 100 mg PO once (1st-line) or pyrantel pamoate 11 mg/kg up to 1 g PO once (2nd-line)
- Treat household contacts.
- Clean bedrooms and bedding.

REFERENCE

Ben Musa NA. Intestinal parasites in school aged children and the 1st case report on amoebiasis in urinary bladder in Tripoli, Libya. J Egypt Soc Parasitol 2007;37(3):775–784.

Kucik CJ, Martin GL, Sortor BV. Common intestinal parasites. Am Fam Physician 2004;69(5): 1161–1168.

PIPE STEM URETHRA

DESCRIPTION A form of intrinsic sphincter deficiency 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
- Urethrolysis
- Artificial urinary sphincter

REFERENCE

Ghoniem GM, Shaaban A. Sub-urethral slings for treatment of stress urinary incontinence. Int Urogynecol J. 1994;5(4):228–239.

PLAP (PLACENTAL ALKALINE PHOSPHATASE)

DESCRIPTION PLAP is a fetal isoenzyme that has a different structure than the adult alkaline phosphatase. It is one of many tumor markers used for the diagnosis, staging, and monitoring of treatment response in patients with germ cell tumors, 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 of 1 or both in 80% of patients with active disease.

REFERENCE

Javadpour N. Multiple biochemical tumor markers in testicular cancer. Cancer 1983;52:887.

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. Five 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

Yang C, Motteram R, Sandeman TF. Extramedullary plasmacytoma of the bladder: A case report and review of literature. Cancer 1982;50:146.

PLASMACYTOMA, TESTICULAR

DESCRIPTION Neoplastic collections of plasma cells occurring in the testicles. These are very rare tumors, with an incidence of ~1 in 1000 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.

TREATMENT

Orchiectomy

REFERENCE

Oppenheim PI, et al. Testicular plasmacytoma. Arch Pathol Lab Med 1991;115(6):629–632.

PLOIDY ANALYSIS, BLADDER CANCER

DESCRIPTION Ploidy is the chromosomal content of cells, which can be measured using flow cytometry. Ploidy 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 ploidy 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

Bittard H, et al. Clinical evaluation of cell deoxyribonucleic acid content measured by flow cytometry in bladder cancer. J Urol 1996;(155):1887–1891.

PLOIDY ANALYSIS, PROSTATE CANCER

DESCRIPTION Ploidy is a variation in the number of chromosomes in a cell. Aneuploidy is a variation in the number of chromosomes in a cell that is other than a simple 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 state and ultimately the prognosis of any given lesion. The frequency of aneuploidy increases with advancing tumor stage. Inherent problems with ploidy analysis include heterogeneity of DNA cell sampling, as well as whether it will change clinical management.

REFERENCE

Dejter SW, et al. Prognostic significance of DNA ploidy in carcinoma of prostate. Urology 1989;33:361–366.

POLYARTERITIS NODOSA (PAN), UROLOGIC CONSIDERATIONS

DESCRIPTION PAN is not well understood, butis believed to be caused by the deposition of immune complexes on the walls of primarily medium-sized arteries, causing deformative changes in those walls. This may lead to thickening and aneurysmal changes, causing acute renal hemorrhage and often leading to chronic renal failure. Corticosteroids and azathioprine are used in the treatment of PAN. Treatment includes steroids and azathioprine.

REFERENCE

Litvak AS, et al. Urologic manifestation of polyarteritis nodosa. J Urol 1976;115(5):572–576.

POLYEMBRYOMA

DESCRIPTION A mixed germ cell tumor of the testis, containing embryonal carcinoma and yolk sac tumor. Histologic analysis reveals a distinctive, well-organized pattern of embryoid bodies in a myxoid stroma, which resembles extraembryonic mesenchyme.

REFERENCE

Ulbright TM. Germ cell neoplasms of the testis. Am J Surg Pathol 1993;17(11):1075–1091.

POLYOMA VIRUS (BK, JC), UROLOGIC CONSIDERATIONS

DESCRIPTION The polyoma viruses may cause transplant renal nephropathy, ureteral obstruction or stricture, and hemorrhagic cystitis. BK virus may cause transplant renal nephropathy in up to 6% of transplant recipients, and may cause ureteral obstruction secondary to fibrosis. It is also thought to be the causative agent in the majority of patients with hemorrhagic cystitis following immunosuppression for bone marrow or solid organ transplantation. BK and JK viruses can be diagnosed with PCR of the urine or blood. (See also Section II: “BK virus, Urologic Considerations.”)

TREATMENT

- Antiviral agents such as cidofovir

REFERENCE

Lin PL, Vats AN, Green M. BK virus infection in renal transplant recipients. Pediatr Transplant 2001;5(6):398–405.

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, and it may be accompanied by inguinal hernias, torsion, or cryptorchidism. It is most often discovered as an asymptomatic swelling in the scrotum; the supernumerary testis usually occurs 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

Surveillance, exploration, and biopsy, if indicated

REFERENCE

Thum G. Polyorchidism. J Urol 1991;145(2):370–372.

POLYPOID CYSTITIS

DESCRIPTION Also known as papillary cystitis, this condition results from inflammation and edema in the bladder lamina propria, leading to papillary and polypoid mucosal lesions. Technically, papillary cystitis refers to long finger-like papillae, and polypoid cystitis is for the more broad-based lesions. The lesions are caused by edema and hypervascularity of the mucosa. Clinically, indwelling catheters or enterovesical fistulas are common causes, and this condition should be differentiated from papillary bladder cancer.

SYNONYMS

Papillary cystitis

TREATMENT

Usually resolves within 3–6 mo after removal of the inflammatory stimulus; if necessary, the lesions can be resected. If the lesions persist, malignancy should be ruled out.

REFERENCE

Bostwick DG, Eble JN. Urologic Surgical Pathology. St. Louis: Mosby, 1997:179–181.

POLYPOID URETHRITIS

DESCRIPTION A urethral counterpart of polypoid cystitis, it occurs as single or multiple polypoid/papillary lesions. A non-neoplastic 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.

TREATMENT

Usually resolves after removal of the inflammatory stimulus; if necessary, resection of the lesions usually leads to a cure. If the lesions persist, malignancy should be ruled out.

REFERENCE

Bostwick DG, Eble JN. Urologic Surgical Pathology. St. Louis: Mosby, 1997:439.

POLYTHELIA, UROLOGIC CONSIDERATIONS

Polythelia (the presence of extra nipples) is linked with abnormalities of the urinary tract and is usually is found within the milk line extending from the axilla to pubic region. Urologic abnormalities include supernumerary kidneys, failure of renal formation, and carcinoma of the kidney. The association of polythelia and renal anomalies is not uniform but is supported by some studies. One group reported 40% of children with polythelia had obstructive renal anomalies or duplications of the excretory system. The presence of extra nipples in children should heighten the clinician's suspicion of possible renal anomalies.

REFERENCE

Grossl NA. Supernumerary breast tissue: Historical perspectives and clinical features. South Med J 2000;93(1):29–32.

POLYURIA

DESCRIPTION Generally defined as >3 L of urine output from a person without excessive fluid intake. Differentiate from nocturnal polyuria (the production of >1/3 of total 24-hr urine output between midnight and 8 AM). Normal is reduced urine output at night. It is useful to measure the urine osmolality to determine whether the polyuria is due to a water diuresis (urine osmolality <250 mOsmol/kg) or a solute diuresis (urine osmolality >300 mOsmol/kg). Polyuria has numerous causes. A solute diuresis may be caused by excessive hypertonic saline infusion, high-protein feedings, uncontrolled diabetes, or postobstructive diuresis. A water diuresis can be caused by multiple conditions, including polydipsia, loop diuretics, diabetes insipidus, and infusion of hypotonic solutions. (See also Section II: “Nocturnal Polyuria.”)

TREATMENT

Correct the underlying cause.

REFERENCE

Kujubu DA, Aboseif SR. An overview of nocturia and the syndrome of nocturnal polyuria in the elderly. Nat Clin Pract Nephrol 2008;4(8):426–435.

POST-ATROPHIC HYPERPLASIA OF THE PROSTATE

DESCRIPTION Post-atrophic hyperplasia is a histologic pattern showing atrophic and hyperplastic glands, sometimes with a small acinar configuration. Atrophy followed by hyperplasia results in acini with nuclear enlargement. Nucleoli are enlarged as well. The basal cell layer may be difficult to see, but its presence rules out prostate cancer. Immunohistochemistry with 34E12 stain, which stains for basal cell cytokeratin, may be helpful. This entity can be confused with prostate cancer on needle biopsy, but is a benign condition. (See also Section III: “Atypical Small Acinar Proliferation, Prostate [ASAP];” “Atypical Adenomatous Hyperplasia of the Prostate.”)

REFERENCE

Amin MB, et al. Postatrophic hyperplasia of the prostate gland: A detailed analysis of its morphology in needle biopsy specimens. Am J Surg Pathol 1999;23(8):925–931.

POSTCOITAL PROPHYLACTIC ANTIBIOTICS

DESCRIPTION Women who suffer recurrent UTIs may have an association of their UTIs with sexual activity. Gram-negative organisms colonizing the vagina are often the culprits. The problem is typically seen in premenopausal women.

TREATMENT

- Empty bladder immediately after intercourse.
- Suppressive antibiotic therapy immediately after intercourse

REFERENCE

Pfau A, Sacks T, Engelstein D. Recurrent urinary tract infections in premenopausal women: Prophylaxis based on an understanding of the pathogenesis. J Urol 1983;129(6):1153–1157.

POSTCOITAL TEST

DESCRIPTION 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, exocervix, 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/hpf considered adequate and excluding the cervical mucosa as cause of infertility. When these test results are poor, the specimens may be repeated on another occasion, 1–3 hr after coitus.

SYNONYMS

Sims-Huhner Test

REFERENCE

Moghissi KS. Postcoital test: Physiologic basis, technique, and interpretation. Fertil Steril 1976; 27(2):117–129.

POSTOPERATIVE SPINDLE CELL NODULE, BLADDER

DESCRIPTION These benign lesions appear 5 wk to 3 mo after surgical procedures in the lower urogenital tract. They grossly resemble a sarcoma and develop after damage to the bladder wall. Microscopically, they appear as intersecting spindle cells intermingled with inflammatory infiltrates. The main differential diagnosis is leiomyosarcoma. They have been reported most commonly in the bladder and prostate.

SYNONYMS

- Postoperative spindle cell nodule of Proppe
- Pseudosarcoma

TREATMENT

Transurethral resection

REFERENCE

Young RH, Eble JN. Non-neoplastic disorders of the urinary bladder. In: Bostwick DG, ed., Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER

DESCRIPTION An increased incidence of cancer is associated with the use of immunosuppression in transplant patients. Post-transplant lymphoproliferative disorders, including lymphoma and Kaposi sarcoma, have an incidence of 2.5% in cadaveric renal allografts. Epstein-Barr virus infection at the time of transplantation appears to be a significant risk factor. The lymphoproliferative disorder may be controlled by adjusting or stopping the immunosuppression.

REFERENCE

Cockfield SM, et al. Post-transplant lymphoproliferative disorder in renal allograft recipients. Transplantation 1993;56–60.

POST-VASECTOMY SYNDROME

DESCRIPTION Although pain for several weeks following vasectomy is common, this syndrome is characterized by chronic orchalgia beyond this time period. It occurs in ~1 in 1,000 men undergoing the procedure, and the 2 postulated mechanisms are obstructive epididymitis and sperm granuloma formation. Following vasectomy, the testicle continues to produce sperm at a normal rate, causing dilation of the epididymis and pain that is often exacerbated by ejaculation. If the testicular end of the vas is not ligated, sperm may spill into the scrotum, resulting in an immune response and granuloma formation.

TREATMENT

- Conservative therapy with NSAIDs
- Obstructive epididymitis is best treated with vaso-vasostomy and rarely with epididymectomy.
- Sperm granuloma is best treated with granuloma excision and vasal occlusion.

REFERENCE

Granitsiotis P, Kirk D. Chronic testicular pain: An overview. Eur Urol 2004;45(4):430–436.

POST-VOID DRIBBLING

DESCRIPTION This refers to urine that leaks out at the end of micturition and may be caused by bladder outlet obstruction, a urethral diverticulum, or vesicovaginal reflux of urine.

REFERENCE

Hassler E, Krakau I, Häggarth L, et al. Questioning questions about symptoms of benign prostatic hyperplasia. Fam Pract 2001;(3):328–332.

POTASSIUM SENSITIVITY TESTING

DESCRIPTION A diagnostic test proposed for PBS/IC. The pathogenic mechanism of painful bladder syndrome/interstitial cystitis (PBS/IC) may involve increased epithelial permeability or loss of tight junctions between epithelial cells. Patients with a normal urothelium and sensory nerves will have no pain associated with the instillation of 400 mM (0.4 M) of potassium chloride solution into the bladder, whereas those with PBS/IC may have pain. Patients may be asked to rank their degree of pain on a visual analogue scale. More recently, potassium chloride has been used to predict the responsiveness of patients to intravesical hyaluronic acid therapy.

REFERENCE

Parsons CL, Greenberger M, Gabal L, et al. The role of urinary potassium in the pathogenesis and diagnosis of interstitial cystitis. J Urol 1998;159(6):1862–1866.

POTTER SYNDROME/POTTER FACIES

DESCRIPTION A fetus with Potter syndrome may show signs of Potter facies (a flat nose, recessed chin, epicanthal folds, low-set ears) and limb abnormalities. These deformities are believed to be secondary to compression of the fetus due to severe oligohydramnios resulting from bilateral renal agenesis. Death usually results from respiratory insufficiency from lack of development of the alveolar sacs.

SYNONYMS

Oligohydramnios sequence.

TREATMENT

None; usually death immediately after birth.

REFERENCE

Potter EL. Bilateral renal agenesis. J Pediatr 1946;29:68.

POUCHITIS

DESCRIPTION Pain in the region of a catheterizable stoma, along with an increase in pouch contractility is referred to as pouchitis. The increased contractility can cause temporary loss of the continence mechanism. The patient may complain of sudden, explosive loss of urine through the catheterizable stoma. Most cases are caused by a bacterial infection that responds to a 10-day course of antibiotics based on sensitivity testing.

REFERENCE

Benson MC, Olsson CA. Continent urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3218.

PRADER-WILLI SYNDROME

DESCRIPTION This is secondary to a chromosomal abnormality consisting of partial deletion of the long arm of chromosome 15. Children often present as obese, hypotonic, and retarded, with hypogonadism, and cryptorchidism. Obesity and behavioral problems are the major cause of morbidity and mortality in affected individuals.

REFERENCE

Cassidy SB. Prader-Willi syndrome. J Med Genet 1997;34(11):917–923.

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 breast or pubic hair development in white girls <7 or in black girls <6 is precocious. Common causes include medications (exogenous estrogen or testosterone), idiopathic causes, pituitary and CNS tumors (hamartomas, others), CAH, adrenal tumor, ovarian cysts and tumors, McCune-Albright syndrome, Leydig cell tumors, hCG-secreting germ cell tumors, testotoxicosis, or pseudoprecocious puberty.

REFERENCE

Carel JC; Leger J Clinical practice. Precocious puberty. N Engl J Med 2008;358(22):2366–2377.

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.

REFERENCE

Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. Urol Clin N Am 2007;34(1):35–42.

PREGNANCY, HEMATURIA

DESCRIPTION Microscopic hematuria is a common finding during pregnancy, however it rarely impacts the outcome of the pregnancy. However, these patients should be assessed postpartum for continued microscopic hematuria to assess for further urologic or kidney disease.

REFERENCE

Brown MA, Holt JL, Mangos GJ, et al. Microscopic hematuria in pregnancy: Relevance to pregnancy outcome. Am J Kid Dis 2005;45:667–673.

PREGNANCY, RADIOLOGIC CONSIDERATIONS

DESCRIPTION Urologists are commonly confronted with pregnant patients with hydronephrosis, renal colic, and stone disease. Imaging is difficult to interpret due to anatomic and physiologic changes in the gravid patient, as well as because of the concern of exposing a fetus to ionizing radiation. The maximum safe dose of radiation allowable to the fetus in the 1st trimester is thought to be 20,000 mrads, and 50,000 mrads in the 2nd and 3rd trimesters. The initial imaging modality of choice should be abdominal ± transvaginal color Doppler US to evaluate renal resistive indices, ureteral dilation distal to the iliac vessels, and ureteral jets in the bladder. If further evaluation is needed, a diuretic MRU or low-dose CT (reported average exposure 705 mrads) can be performed. In the OR, stent placement can be done with intraoperative US and, if absolutely necessary, fluoroscopy with shielding of the fetus by placement of lead below the patient's lower abdomen and pelvis.

References

Goldstone K, Yates SJ. Radiation issues governing radiation protection and patient doses in diagnostic imaging. In: Grainger RG, Allison DJ, et al. Diagnostic Radiology, 5th ed. Philadelphia: Elsevier, 2008.

White WM, Zite NB, Gash J, et al. Low-dose computed tomography for the evaluation of flank pain in the pregnant population. J Endourol 2007;21(11):1255–1260.

PREGNANCY, RENAL TRANSPLANTATION

DESCRIPTION Successful renal transplantation restores normal ovulatory function and the potential for successful conception. Pregnancy does not appear to affect long-term graft survival. However, pregnancies after renal transplant are at significant risk for maternal and fetal complications including hypertension, preeclampsia, and infection, as well as preterm delivery and fetal growth restriction. Renal transplantation is not a contraindication to vaginal delivery and care should be taken during cesarean section not to injure the renal unit. General safe guidelines for pregnancy after renal transplantation are good health and functioning renal unit 2 yr after transplantation without any evidence of infection or obstruction and on low doses of immunosuppression.

REFERENCE

Fuchs KM, Wu D, Ebcioglu Z. Pregnancy in renal transplant recipients. Semin Perinatol 2007;31:339–347.

PREGNANCY, URINARY DIVERSION

DESCRIPTION Pregnancy after urinary diversion has not been well studied, and only 250 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 antepartum 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, stomal prolapse from increased intra-abdominal pressure, stomal stenosis from impaired blood flow, difficulty catheterizing continent pouches from stretching of the efferent limb, and an increased risk of UTI from the presence of bacteruria. 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.

REFERENCE

Hautmann RE, Volkmer BG. Pregnancy and urinary diversion. Urol Clin N Am 2007;(1):71–88.

PREGNANCY, URINARY TRACT OBSTRUCTION

DESCRIPTION Urinary tract obstruction during pregnancy most commonly occurs from a ureteral stone or extrinsic compression from the gravid uterus. Patients will commonly present with flank pain. US, 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 dilation and extrinsic compression.

TREATMENT

- Initially, conservative with IV hydration and analgesic therapy.
- Patients who fail may require stent or nephrostomy tube placement. Stents can rapidly encrust due to increased urinary calcium excretion and should be changed in a timely fashion.
- Ureteroscopy and laser lithotripsy

REFERENCE

McAleer SJ, Loughlin KR. Nephrolithiasis and pregnancy. Curr Opin Urol 2004;(2):123–127.

PREGNANCY, UROLOGIC MALIGNANCY

DESCRIPTION Urologic malignancies are rare in pregnancy but often misdiagnosed due to overlapping signs and symptoms with preeclampsia and eclampsia. The most common tumor is renal cell carcinoma (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 angiomyolipoma may present with flank pain, hematuria, and retroperitoneal hemorrhage, although it is sometimes incidentally diagnosed on imaging. Urothelial carcinoma of the upper or lower tracts is rare and presents with hematuria. If urine analysis reveals hematuria and the culture is negative, cytology, 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.
- AML with hemorrhage may be managed with embolization or partial or total nephrectomy.
- Urothelial 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 BCG.

REFERENCE

Martin FM, Rowland RG. Urologic malignancies in pregnancy. Urol Clin N Am 2007;34(1):53–59.

PREGNANCY, UROLOGIC MEDICATIONS

DESCRIPTION Medications in pregnancy have not been well studied or documented. Urologic issues include antibiotics for UTIs 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 C 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 fetal malformations 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.

REFERENCE

Shrim A, Garcia-Bournissen F, Koren G. Pharmaceutical agents and pregnancy in urology practice. Urol Clin N Am 2007;34(1):27–33.

PREHN SIGN

DESCRIPTION This test may aid in the differentiation of epididymitis vs. testicular torsion, although it is not always reliable. A positive test is indicated by relief of pain with elevation of the involved testicle, which suggests a diagnosis of epididymitis rather than testicular torsion. This is often not a reliable test.

REFERENCE

Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996:68–69.

PRENTISS MANEUVER

DESCRIPTION Additional cord length in an orchiopexy operation can be gained by incising the inguinal floor and ligating the inferior epigastric vessels. The internal ring and transversalis fascia are then closed lateral to the cord.

REFERENCE

Kelly CE. The relationship between pressure flow studies and ultrasound-estimated bladder wall mass. Rev Urol. 2005;(Suppl 6):S29–S34.

PREPUTIAL STONES

DESCRIPTION Preputial stones are rare occurrences, generally found in adults and associated with poor genital hygiene, low socioeconomic status, and phimosis. Factors in preputial stone formation include obstruction, stasis, foreign body, nidus formation, and infection.

SYNONYMS

Preputial calculi

TREATMENT

Removal of stone and elimination of the predisposing condition.

REFERENCE

Ellis DJ, et al. Preputial calculus: A case report. J Urol 1986;136(2):464–465.

PRESSURE-FLOW STUDIES

DESCRIPTION The simultaneous measurement of bladder pressure and uroflow throughout the entire voiding cycle. Performed as part of urodynamic study, these studies improve on some of the imitations of uroflowmetry alone. Measurements for this study can include the variables that affect the study: Intravesical pressure, rectal pressure, intraurethral pressure, sphincter electromyogram, and urine flow rate. 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.

REFERENCE

Elemen L, Sozubir S, Bulut M. An old technique for surgery of “high” undescended testis revisited 2008. J Pediatr Urol 2008;4(5):330–332.

PRIAPISM, ISCHEMIC (LOW FLOW, VENO-OCCLUSIVE PRIAPISM)

DESCRIPTION Priapism is an unwanted persistent penile erection. Patients present with a painful erection, corporal tenderness on exam, and cavernosal blood gases with a PO2 of <30 mm Hg, PCO2 of >60 mm Hg, and a pH <7.25. Ischemic or low-flow priapism is thought to result from deranged venous occlusive mechanisms and venous outflow obstruction that results in cessation of arterial inflow. This causes a compartment syndrome and is a surgical emergency. Long-term consequences of ischemic priapism include corporal fibrosis and erectile dysfunction. (See also Section I: “Priapism.”)

CAUSES

- Sickle cell disease
- Drug reaction (multiple medication classes)
- Illicit drug use (cocaine, recreational PDE-5 inhibitor)
- Total parenteral nutrition (particularly with high fat content)
- Hemodialysis
- Metastatic disease or primary malignancy of penis
- Hematologic dyscrasias

TREATMENT

- Evacuation of blood and irrigation with saline
- -Adrenergic intracorporeal injection of epineprine (0.03–0.05 mg or phenylephrine 0.1–1 mg) administration (with cardiovascular monitoring)
- Oral turbutaline 5 mg
- Shunt (distal, then proximal)

REFERENCE

Burnett AL, Bivalacqua TJ. Priapism: Current principles and practice. Urol Clin N Am 2007;34(4):61–62.

PRIAPISM, NONISCHEMIC (HIGH-FLOW, ARTERIAL PRIAPISM)

DESCRIPTION Nonischemic priapism is typically painless because arterial inflow and unobstructed outflow persists. It is most commonly the result of perineal trauma resulting in a cavernosal artery-to-corporal fistula. Blood gases will reveal a PO2 of >90 mm Hg, PCO2 of <40 mm Hg, and a pH of 7.4, similar to that of an arterial blood gas reading. Observation should be the initial treatment, as a majority will resolve spontaneously. (See also Section I: “Priapism.”)

TREATMENT

- Observation
- Arterial embolization (permanent vs. nonpermanent)
- Open surgical ligation

REFERENCE

Burnett AL, Bivalacqua TJ. Priapism: Current principles and practice. Urol Clin N Am 2007;34(4):61–62.

PRIAPISM, STUTTERING (INTERMITTENT PRIAPISM)

DESCRIPTION Priapism that is recurrent in nature should be treated initially as for ischemic priapism. Emphasis should be placed on long-term prevention using medical or self-injection therapy. (See also Section I: “Priapism.”)

SYNONYMS

- Recurrent priapism
- Intermittent priapism

TREATMENT

- Hormonal therapy (leuprolide, flutamide, bicalutamide)
- Self-injection therapy with phenylephrine

REFERENCE

Burnett AL, Bivalacqua TJ. Priapism: Current principles and practice. Urol Clin N Am 2007;34(4):61–62.

PROLACTIN, SERUM LEVEL

DESCRIPTION Elevated prolactin levels are associated with infertility and erectile dysfunction. Hyperprolactinemia may be caused by a pituitary tumor, stress, medications, hypothyroidism, or idiopathic causes. A pituitary tumor will result in low serum gonadotropin and testosterone levels and elevated prolactin levels. The mainstay of therapy for prolactinomas is medical management.

CAUSES

Elevated prolactin levels:

– Prolactinomas (serum prolactin value >50 ng/mL)

– Renal failure, stress, medications and hypothyroidism (serum prolactin value <50 ng/mL)

TREATMENT

- Cabergoline
- Bromocriptine
- Surgical

REFERENCE

Verhelst J, Abs R. Hyperprolactinemia: Pathophysiology and management. Treat Endocrinol 2003;2(1):23–32.

PROPANTHELINE STIMULATION TEST

DESCRIPTION This test is used when involuntary detrusor contractions are demonstrated during cystometry to predict the outcome of pharmacologic treatment with anticholinergics. Propantheline bromide is an anticholinergic with side effects that include dry mouth and blurred vision. Once involuntary detrusor contractions have been confirmed, 15 mg of propantheline bromide are administered parenterally. Once effects of the drug are noticed, cystometry is repeated. A positive response is defined as the complete abolition of involuntary detrusor contractions, or a 200% increase in the bladder volume at which they occur. If the parenteral dosage is effective, a favorable clinical response to the orally administered dose can be expected in most patients.

REFERENCE

Blaivis JG, et al. Urodynamic evaluation as a test of sacral cord function. Urology 1979;9:682.

PROPHYLACTIC ANTIBIOTICS, AUA GUIDELINES

DESCRIPTION New 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, anatomic anomalies of the urinary tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, externalized catheters, colonized endogenous/exogenous material, distant coexistent infection, and prolonged hospitalization.

Recommendations for specific procedures and agents are found in Section VII.

REFERENCE

Wolf JS Jr. , et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2008;179(4):1379–1390.

PROSTASCINT SCAN

DESCRIPTION A nuclear medicine imaging study designed to localize prostate cancer cells using a radiolabeled monoclonal antibody to prostate-specific membrane antigen. 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. 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.

REFERENCE

Taneja S. ProstaScint Scan: Contemporary use in clinical practice. Rev Urol 2004;S10:19–28.

PROSTATE CANCER, ACTIVE SURVEILLANCE AND WATCHFUL WAITING

DESCRIPTION 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 overtreatment of many men with prostate cancer. Deferred therapy for 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 curative therapy. This involves actively monitoring the course of prostate cancer with the intent of intervention with definitive local therapy (eg, radiation therapy, radical prostatectomy) 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.

Many different opinions exist concerning the optimum approach. This discussion is generally based on guidelines from the National Comprehensive Cancer Network. Characteristics of the patient and disease state in which the clinician may consider active surveillance are:

- Low-risk prostate cancer (T1–T2a and Gleason 2–6 and PSA <10 ng/mL) regardless of life expectancy
- Intermediate-risk prostate cancer (T2b–T2c or Gleason 7 or PSA 10–20 ng/mL with <10-yr life expectancy)

Surveillance protocol (if life expectancy) <10 yr, follow-up may be less frequent):

- Patients must have clinically localized disease and be candidates for definitive treatment, yet choose observation.
- DRE and PSA as often as every 6 mo but at least every 12 mo
- Repeat prostate needle biopsy within 6 mo of diagnosis if initial biopsy was <10 cores.
- Needle biopsy may be performed within 18 mo, with cores obtained initially, then periodically.

Cancer progression may have occurred if:

- Primary Gleason grade 4 or 5 cancer is found upon repeat prostate biopsy
- Prostate cancer is found in a greater number of prostate biopsies or occupies a greater extent of prostate biopsies
- PSA doubling time <3 yr or PSA velocity is >0.75
- A repeat prostate biopsy is indicated for signs of disease progression by exam or PSA.

Advantages of active surveillance include avoiding possible side effects and costs of definitive therapy that may be unnecessary, and maintaining quality of life. Disadvantages include chance of missed opportunity for cure, risk of progression and/or metastases, anxiety, increased physician visits and tests, and causing subsequent treatment to be more aggressive. (See also Section I: “Prostate Cancer, General”; Section II: “Life Expectancy, Urologic Considerations.”)

REFERENCE

Hardie C, et al. Early outcomes of active surveillance for localized prostate cancer. BJU Int 2005;95(7):956–960.

NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer V.2.2009. Available at www.nccn.org.

PROSTATE CANCER, BASAL CELL CARCINOMA

DESCRIPTION A very rare variant of prostate cancer comprising <0.01% of malignant tumors. Lesions exist in 2 distinct forms, adenoid cystic carcinoma (ACC), and basaloid carcinoma (BC), that may occur clinically separate or as mixed tumors with 1 dominant pattern. Immunohistochemical analysis reveals strongly positive results for both 34E12 and p63. Once thought to be a more indolent 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.

REFERENCE

Montironi R, et al. Basal cell hyperplasia and basal cell carcinoma of the prostate: A comprehensive review and discussion of a case with c-erbB-2 expression. J Clin Pathol 2005;58:290–296.

PROSTATE CANCER, CIRCULATING TUMOR CELLS (CTC)

DESCRIPTION Circulating tumor cells can be detected using molecular techniques such as RT-PCR. An identification assay for actual circulating cells (CellSearch assay) is commercially available for use in patients with hormone-refractory prostate cancer. In patients with advanced prostate cancer, men with 5CTCs per 7.5 mL blood prior to chemotherapy had a significantly shorter median survival (10 vs. 21 mo in those with <5 CTCs). 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, hormone-refractory disease and is not as useful for earlier stages of disease. (See also Section II: PSA, RT-PCR.)

REFERENCE

de Bono JS. Circulating tumor cells predict survival benefit from treatment in metastatic castration-resistant prostate cancer. Clin Cancer Res 2008;14(19):6302–6309.

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.

Relations

Risk of Prostate Cancer

Any relative

1.93

Any 1st degree

2.22

Any 2nd degree

1.88

Father

2.12

Brother

2.84

1st degree dx <60 yr

2.16

1st degree with breast cancer

1.24

REFERENCE

Bruner DW, et al. Relative risk of prostate cancer for men with affected relatives: Systematic review and meta-analysis. Int J Cancer 2003;107:797.

PROSTATE CANCER, LEIOMYOSARCOMA, AND OTHER UNCOMMON SARCOMAS

DESCRIPTION Leiomyosarcoma of the prostate extremely rare and 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. Rhabdomyosarcoma most common in pediatric patients and can be seen in adults. Other less common prostate sarcomas indude malignant fibrous histiocytoma and prostatic stromal sarcoma. Presentation can include urinary obstruction (frequency, urgency), hematuria, perineal and/or rectal, pain, constipation, burning on ejaculation, and constitutional symptoms. The diagnosis of prostate sarcoma was usually established with ultrasound-guided biopsy or transurethral resection, and PSA is usually normal. Multimodality therapy using surgery (radical prostatectomy, radical cystectomy, pelvic exenteration) with pre- or postoperative radiation and pre- or postoperative chemotherapy have been used with no standard of care. Doxorubicin-based combinations with agents such as cyclophosphamide, ifosfamide, vinblastine or vincristine have been reported with mixed results.

REFERENCE

Sexton WJ, et al. Adult prostate sarcoma: The M. D. Anderson cancer center experience. J Urol. 2001;166(2):521–525.

PROSTATE CANCER, MUCINOUS ADENOCARCINOMA

DESCRIPTION These very rare tumors are histopathologically defined as having lakes of extracellular mucin comprising at least 25% of the primary prostate tumor. They generally are considered to have a slightly worse prognosis than typical adenocarcinoma of the prostate. They appear to be hormonally refractory, and bone metastasis are common. Radiation and/or surgery can be considered.

REFERENCE

Ro JY, et al. Mucinous adenocarcinoma of the prostate: Histochemical and immunohistochemical studies. Hum Pathol 1990;21:593–600.

PROSTATE CANCER, PREVENTION (CHEMOPREVENTION)

DESCRIPTION Numerous medications, including selenium, statins, and teas, have been evaluated for the prevention of prostate cancer, but the most notable remain the 5-reductase inhibitors (5 ARIs) finasteride and dutasteride. The Prostate Cancer Prevention Trial (PCPT) demonstrated an almost 25% reduction in the incidence of prostate cancer but an increased incidence of higher Gleason score cancers. Some have hypothesized that this may be due to selective 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 radical prostatectomy specimens. The REduction DUtasteride of prostate Cancer (REDUCE) trial using dutasteride (a dual 5-reductase inhibitor) reported a 23% reduction in prostate cancer in high-risk men with no apparent 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. ASCO AUA 2008 Clinical Practice Guidelines are as follows:

- Asymptomatic men, PSA <3.0 ng/mL who are regularly screened or anticipate undergoing annual PSA screening may benefit from a discussion of risks and benefits of 5-ARIs for 7 yr for the prevention of prostate cancer.
- Men taking 5-ARIs for LUTS should also discuss risks and benefits.
- A reduction of PSA by 50% at 12 mo is expected in men on 5-ARIs; the panel did not recommend a specific cut-point to trigger a biopsy for men taking a 5-ARI.

REFERENCE

Andriole G. Headline results from the REduction by DUtasteride of prostate Cancer Events (REDUCE) study, AUA Annual Meeting Late Breaking Abstracts 2009 Chicago. www.medscape.com/viewarticle/702017. Accessed July 2009.

Kramer BS, et al. Use of 5-reductase inhibitors for prostate cancer chemoprevention: American Society of Clinical Oncology/American Urological Association 2008 Clinical Practice Guideline. J Urol 2009;181:1642–1657.

Lippman SM, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2009;301(1):39–51.

Lucia MS, et al. Finasteride and high-grade prostate cancer in the Prostate Cancer Prevention Trial. J Natl Cancer Inst 2007;99(18):1375–1383.

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 objectively assessing different aspects of prostate disease throughout its various stages of diagnosis and treatment. Most calculators are available online, with interactive modules that facilitate their incorporation into clinical practice (see below). Please see the nomograms/tables included in Section VII.

Clinical Stage

Calculator Origin

Interactive Location (Accessed)

Pre-biopsy

Sunnybrook Health Sciences Center, Toronto

http://www.sunnybrook.ca/media/item.asp?c=2&1=184&page=524

Pre-/post-biopsy

PCPT (Prostate cancer prevention trial)

http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp

Preoperative

Partin Tables

http://urology.jhu.edu/prostate/partintables.php

Pre-/postoperative

Kattan Nomograms MSKCC (Memorial Sloan Kettering Cancer Center)

http://www.mskcc.org/mskcc/html/10088.cfm

Postoperative

CPDR (Center for Prostate Disease Research and Treatment) Recurrence

http://reed.hjf.org:8080/Nomogram/index.jsp

REFERENCE

Kattan MW, et al. Prediction of progression: Nomograms of clinical utility. Clin Prostate Cancer. 2002;1(2):90–96.

Nam RK, et al. Assessing individual risk for prostate cancer. J Clin Oncol 2007;25(24):3582–3588.

Thompson IM, et al. Assessing prostate cancer risk: Results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst 2006;98:529–534.

PROSTATE CANCER, RISK STRATIFICATION

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 1992 AJCC T staging. One typical system is described here. Note that this is risk of PSA progression post-therapy 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 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 (>50% PSA progression at 5 yr posttherapy)

REFERENCE

D'Amico AV, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998;280(11):969–974.

PROSTATE CANCER, SMALL CELL (NEUROENDOCRINE)

DESCRIPTION A rare subtype of prostate malignancy that has a rapidly fatal course. Considered to be a variant of Gleason 5 adenocarcinoma of the prostate, it is identical to small-cell carcinomas 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. Neuroendocrine cells are identified by special staining (ie, neuron-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 acinar 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 patchy cells that stain as neuroendocrine cells. Large numbers of Gleason 5 cells in a prostate sample should prompt a neuroendocrine staining workup of the sample. Tumors can exhibit as pectrum 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. 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 cisplatinum have some activity.

REFERENCE

Moore SR, et al. Small cell carcinoma of prostate: Effectiveness of hormonal vs. chemotherapy. Urology 1992;39(5):411–416.

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 infarction, radiation, and hormonal therapy. Pure primary squamous cell carcinoma of the prostate does not respond to estrogen therapy, and it does not develop elevated serum PSA or PAP levels with metastatic disease. Bone metastases are osteolytic instead of osteoblastic. Median survival is about 14 mo.

REFERENCE

Bostwick DG. Neoplasms of the prostate. In: Bostwick DG, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

PROSTATE, BASAL CELL HYPERPLASIA

DESCRIPTION Basal cell hyperplasia is important in that it is commonly associated with benign prostatic hyperplasia and may sometimes be mistaken for prostate cancer. The prostatic 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 prostate glands and acini. Basal cell proliferation in the prostate gland exhibits a spectrum 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 (fetalization of prostate, embryonal hyperplasia, basal cell tumor, basal cell adenoma, basaloid carcinoma, adenoid cystic carcinoma). The differential diagnosis includes transitional cell hyperplasia, squamous metaplasia, transitional cell carcinoma of the prostate, adenocarcinoma of prostate, and adenoid cystic carcinoma of prostate.

REFERENCE

Bhat S, Thomas A, Nazar M, Joseph GC. Basal cell hyperplasia of prostate-an entity a urologist must know. Indian J Urol 2000;17:61–62.

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. 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 or total prostatectomy, if markedly symptomatic

REFERENCE

Klimas R, et al. Prostatic calculi: A review. Prostate 1985;7(1):91–96.

PROSTATE, FEMALE

DESCRIPTION A coined radiologic expression that refers to an impression at the base of the female bladder seen on excretory urography or cystogram. The impression resembles an enlarged prostate in the male and can be caused by urethral diverticulum, benign and malignant tumors of the anterior vaginal wall, urethral neoplasm, and repair of stress urinary incontinence.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:289.

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 American Urologic Association. Older patients with larger, more vascular prostates are more susceptible and can be managed with 5-reductase inhibitors or transurethral resection if bleeding is refractory to medical therapy.

Most often idiopathic, bleeding can also be iatrogenic (after prostate biopsy and endoscopic urologic procedures) or due to locally advanced prostate cancer (late manifestation).

TREATMENT

- 5-reductase inhibitors (1st-line therapy for benign prostatic hypertrophy bleeding)
- Intravesical alum, silver nitrate, and formalin (2nd-line therapy)
- Transurethral resection or vaporization of the prostate

REFERENCE

Rastinehad AR, Ost MC, VanderBrink BA, et al. Persistent prostatic hematuria. Nat Clin Pract Urol 2008;5(3):159–165.

PROSTATE HYPERPLASIA, SMALL ACINAR ATYPICAL

DESCRIPTION Histologic findings include nucleomegaly and prominent nucleoli. These lesions are found in ever-increasing numbers of prostate biopsies and are suspicious for but not diagnostic of malignancy. Subsequent biopsies have revealed adenocarcinoma in 45% of cases. Therefore, the histologic finding of atypical small acinar adenosis is highly predictive for malignancy.

TREATMENT

- Surveillance
- Repeat biopsy

REFERENCE

Iczkowski KA, et al. Atypical small acinar proliferation suspicious for malignancy in prostate needle biopsies. Am J Surg Pathol 1997;21(2):1489–1495.

PROSTATE, INFARCTION

DESCRIPTION The etiology of prostatic infarction is still unclear, although it has been linked to prostate hyperplasia. Histologic findings include infraction of prostatic epithelium, with hemorrhage and neutrophils in the intervening stroma. Recent infarcts generally do not have squamous metaplasia, whereas older ones do. Typically, the infarctions are multiple and located in the central and middle concentric zones of the middle third of the prostate. Prostatic infarction may elevate PSA levels.

REFERENCE

Brawn PN, et al. Characteristics of prostatic infarcts and their effect on serum prostate-specific antigen and prostatic acid phosphatase. Urology 1994;44(1): 71–74.

PROSTATE, MASSAGE

DESCRIPTION Repetitive prostatic massage is not a new tool in the urologists' armamentarium. It can be used to localize 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, it may be making a comeback to treat certain forms of prostatitis, such as chronic abacterial prostatitis or chronic pelvic pain syndrome (see Section III). 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 at the meatus to capture the expressed prostatic fluids (see also Section III: Stamey Test). The test is contraindicated in acute bacterial prostatitis.

REFERENCE

Nickel JC, Alexander R, Anderson R, et al. Prostatitis unplugged? Prostatic massage revisited. Techniques Urol 1999;5(1):1–7.

PROSTATE STENTS (UROLUMETM AND SPANNERTM)

DESCRIPTION The UroLumeTM stent is a woven tubular mesh designed to treat bladder outlet obstruction caused by the prostate. Numerous problems have plagued the stent, including short-term problems with irritative voiding symptoms, painful ejaculation, and stent migration. Long-term problems include stent encrustation and ingrowth of epithelial tissue causing restenosis. It may have a role in patients who present with urinary retention and are considered at high risk for surgical intervention, but it should otherwise not be used for patients who can tolerate a surgical procedure.

The SpannerTM stent is similar to a Foley catheter in that it has a proximal port to drain urine, a balloon that resides at the bladder neck to prevent migration, and a stent that spans the prostatic urethra.

REFERENCE

Vanderbrink BA, Rastinehad AR, Badlani GH. Prostatic stents for the treatment of benign prostatic hyperplasia. Curr Opin Urol 2007;17(1):1–6.

PROSTATIC ACID PHOSPHATASE (PAP)

DESCRIPTION Human PAP is a glycoprotein dimer of 102,000 MW. 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 a serum marker for the staging and detection of prostate cancer before the discovery of prostate-specific antigen. Although enzymatic elevation of PAP is associated with advanced prostate cancer, other causes of an elevated PAP are possible, including liver, skeletal, and renal disease.

REFERENCE

Remynse LC, Begun FP, Jacobs SC, et al. Juxtaglomerular cell tumor with elevation of serum erythropoietin. J Urol 1989;142(6):1560–1562.

Romas M, Kwan DJ. Prostatic acid phosphatase. Urol Clin N Am 1993;20:581–588.

PROSTATIC URETHRAL POLYPS

DESCRIPTION Urethral polyps are rare abnormalities in male children who present with hematuria or obstructive symptoms. Strangury (slow 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 polypoid masses of sarcoma botryoides.

TREATMENT

Transurethral excision of the polyps

REFERENCE

Leibovitch I, et al. Hematuria and voiding disorders in children caused by congenital urethral polyps. Principles of diagnosis and management. Eur Urol 1993;23:382.

PROSTATITIS, ASYMPTOMATIC INFLAMMATORY (NIH IV)

DESCRIPTION The 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.

REFERENCE

Habermacher GM, et al. Prostatitis/chronic pelvic pain syndrome. Annu Rev Med 2006;57:195–206.

PROSTATITIS, MYCOTIC

DESCRIPTION A type of granulomatous prostatitis caused by fungi and typically associated with systemic mycosis. Fungal infections can include blastomycosis, coccidiomycosis, cryptococcosis, histoplasmosis, and Candida. Diagnosis is based on prostatic histology and culture results. For systemic therapy, see the specific agent. (See Section I: Prostatitis, Granulomatous.)

REFERENCE

Schwartz J. Mycotic prostatitis. Urology 1982;19:1.

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.

- Category I: Acute bacterial prostatitis; acute infection of the prostate gland
- Category II: Chronic bacterial prostatitis; recurrent infection of the prostate
- Category III: Chronic abacterial prostatitis/chronic pelvic pain syndrome (CPPS); no demonstrable infection
  - Category IIIA: Inflammatory CPPS; WBCs in semen/EPS VB3
  - Category IIIB: Noninflammatory CPPS; no WBCs in semen/EPS VB3
- Category IV: Asymptomatic inflammatory prostatitis; no symptoms

REFERENCE

Krieger JN, et al. NIH consensus definition and classification of prostatitis. JAMA 1999;282(3): 236–237.

PROSTATITIS, STRESS

DESCRIPTION Classically defined as a subset of chronic abacterial noninflammatory 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

Miller HC. Stress prostatitis. Urology 1988;32:507.

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. Irritative voiding may be the only complaints; other complaints include perineal pain and infertility. On exam, the prostate may be hard, irregular, and nodular. On labs, urine analysis can demonstrate microscopic hematuria or sterile pyuria. Acid-fast bacilli staining of urine and semen has a sensitivity of only 52%; however, culture can take up to 8 wk. A transrectal ultrasound can demonstrate collections or abscess, and an IVU or CT scan should be done because 72% of patients with prostatic TB have renal TB.

TREATMENT

- Hospitalization is usually unnecessary.
- Transurethral resection of the prostate in patients with obstructive symptomatology is reasonable.
- Medication includes a 3-drug regimen of isoniazid, pyrazinamide, 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

Cek M, Lenk S, Naber KG, et al. EAU guidelines for the management of genitourinary TB. Eur Urol 2005;48(3):353–362.

PROSTATODYNIA

DESCRIPTION Classically described as a symptom complex of multiple complaints including pain in the perineum, lower back, or upon ejaculation; slow stream; and hesitancy. Patients exhibit no evidence of prostatic inflammation. Dysuria, frequency, and systemic signs are usually absent. This term is not currently considered to be appropriate and has been replaced by the designation chronic pelvic pain syndrome or CPPS (NIH Category III Chronic Abacterial Prostatitis).

REFERENCE

Orland SM, et al. Prostatitis, prostatosis, and prostatodynia. Urology 1985;25(5):439–459.

PROSTHESIS, INFECTED PENILE

DESCRIPTION A dreaded complication of penile prosthesis implantation. Rates of infection range from 1–8%; risk factors include spinal cord injury, diabetes mellitus (especially if poorly controlled with HgbA1C >11.5%), history of UTI, and multiple prosthesis operations. Infection usually occurs within 6 mo after implantation, but delayed infection is also reported. The most common symptom is persistent pain; patients also present with erythema, drainage, or fever. Causes of infection are Staphylococcus epidermidis (most common); gram-negative rods and yeast are also common.

TREATMENT

- Surgical removal
- Irrigation and antibiotic treatment
- Immediate salvage procedures with surgical removal
- Washout and immediate replacement have reported with good results: Vigorous intra-operative irrigation with 4 different solutions, including vancomycin; immediate reimplantation of a new inflatable penile prosthesis; and postoperative outpatient antibiotics, with oral ciprofloxacin or IV vancomycin or cefazolin.

REFERENCE

Kaufman JM, et al. Immediate salvage procedure for infected penile prosthesis. J Urol 1998;159(3):816–818.

PRURITUS, EXTERNAL GENITALIA, MALE

DESCRIPTION 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. The differential diagnosis of includes: eczema (atopic dermatitis), allergic dermatitis, seborrheic dermatitis, contact/irritant dermatitis, fixed drug reaction, balanitis, candidal infection, or herpes. Other STDs, such as scabies, can cause itching. Some patients manifest itching with or without a demonstrable local factor. The skin may appear normal or demonstrate excoriation. lichenification (skin thickening) from rubbing, or both. These patients tend to have chronic illness (eg, diabetes) or depression with no pathogen identified. Tricyclic antidepressants and topical steroids are used with varying results.

REFERENCE

Lynch PJ, Edwards L. In: Lynch PJ, ed. Genital Dermatology. New York: Churchill Livingstone, 1994:229–235.

PSA, AGE-ADJUSTED

DESCRIPTION An age-specific scale of normal PSA values has been proposed, based on the observation that PSA rises with age, in an effort to reduce unnecessary prostate biopsies.

Age (Yr)	Age-specific Reference Range
40–49	0.0–2.5 ng/mL
50–59	0.0–3.5 ng/mL
60–69	0.0–4.5 ng/mL
70–79	0.0–6.5 ng/mL

REFERENCE

Oesterling JE, et al. Serum prostate-specific antigen in a community based population of healthy men. JAMA 1993;270(7):860–864.

PSA BOUNCE

DESCRIPTION A transient rise in PSA (typically <1 ng/mL) in 10–12% of men following radiation therapy (external, brachytherapy, and high-dose brachytherapy) typically 18–24 mo after treatment for prostate cancer; usually returns to baseline, with a progressive rise suggesting recurrence.

REFERENCE

Satoh T, et al. Prostate-specific antigen “bounce” after permanent 125I-implant brachytherapy in Japanese men: A multi-institutional pooled analysis. BJU Int. 2009;103(8):1064–1068.

PSA DENSITY (PSAD)

DESCRIPTION PSAD is a ratio of prostate-specific antigen (PSA) level to prostate size, as measured by transrectal ultrasound. Proposed as a method to differentiate an elevated PSA of 4–10 ng/mL without evidence of prostate cancer on digital rectal exam or TRUS, as due to either benign prostatic hyperplasia or adenocarcinoma, to prevent unnecessary prostate biopsies. A PSAD of 0.15 would warrant prostate biopsy. Use of PSAD remains controversial.

REFERENCE

Seaman E, et al. Prostate specific antigen density (PSAD): Role in patient evaluation and management. Urol Clin N Am 1993;20:653–663.

PSA FAILURE, ASTRO AND PHOENIX DEFINITIONS

DESCRIPTION In order to standardize PSA testing for outcome after radiation therapy, the American Society for Radiation Oncology (ASTRO) convened 2 panels to define the criterion for progression

- ASTRO definition (1996): 3 consecutive PSA rises after nadir; the date failure is the midpoint between the PSA nadir and the first rise.
- Phoenix definition (2005): PSA nadir + 2 ng/mL with the date of failure is defined by the time the rise in PSA is noted; this definition is now preferred.

REFERENCE

Roach M 3rd, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: Recommendations of the RTOG-ASTRO Phoenix Consensus Conference. Int J Radiat Oncol Biol) Phys 2006;65(4):965–974.

PSA, FREE AND TOTAL

DESCRIPTION PSA is found either free in serum or bound to serum proteins. Patients with prostate cancer tend to have lower free PSA levels in proportion to total PSA. Measurement of the free PSA percentage can improve the specificity of PSA as a cancer screening test. Patients with mildly elevated PSA (4.0–10.0 ng/mL) should have prostate biopsy only if the free PSA percentage is low. The free PSA percentage threshold for biopsy is controversial, ranging from <15% to <25%, with a higher threshold having improved sensitivity and a lower threshold having improved specificity.

REFERENCE

Catalona WJ, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease. JAMA 1998;279(19):1542–1547.

PSA, RACE-ADJUSTED

DESCRIPTION PSA adjusted for race as well as age, has been proposed based on the observation that, in the absence of prostate cancer, African American males have higher average PSA values when adjusted for age. (some times called Water Reed/CPDR Reference Ranges) The adjusted scale was developed to improve the sensitivity of PSA as a screening test in the African American population, which has a significantly higher incidence and mortality from prostate cancer when compared with Caucasians. Use of these tables is controversial. (See also Section I: “PSA Elevation.”)

Race-specific Reference Range

Age (yr)

Whites

Blacks

40–49

0.0–2.5 ng/mL

0.0–2.0 ng/mL

50–59

0.0–3.5 ng/mL

0.0–4.0 ng/mL

60–69

0.0–3.5 ng/mL

0.0–4.5 ng/mL

70–79

0.0–3.5 ng/mL

0.0–5.5 ng/mL

REFERENCE

Morgan TO, et al. Age-specific reference ranges for serum prostate-specific antigen in black men. N Engl J Med 1996;335:304–310.

PSA RT-PCR

DESCRIPTION First clinically reported in 1992, RT-PCR is used to amplify mRNA transcripts of PSA. These PSA mRNA species should theoretically only be present in prostate tissues. Extraprostatic tissue of patients with biopsy-proven prostate cancer 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 circulating tumor cell assays (CTC).

REFERENCE

Gomella LG, et al. Reverse transcriptase polymerase chain reaction for prostate specific antigen in the management of prostate cancer. J Urol 1997; 158:326–337.

PSA VELOCITY (PSAV) AND PSA DOUBLING TIME (PSADT)

DESCRIPTION PSAV and PSADT are 2 parameters of the overall study of PSA change or PSA kinetics. PSAV is the change of PSA over the course of 1 yr measured by 3 separate values over a period of at least 18 mo. Initial studies suggested a diagnostic value of a PSAV of >0.75 ng/mL/yr; however, recent studies have lowered this threshold significantly, and some authorities believe it should no longer be considered as an indication for biopsy. However, a high pretreatment PSAV (>2.0 ng/mL/yr) has been shown to correlate with a worse prognosis after radiotherapy or radical surgery.

PSADT is defined as the time it takes for a patient's PSA value to double based on an exponential growth pattern. Pretreatment PSADT has little diagnostic value; it is, however, an important predictor of tumor progression, therapeutic outcome, and tumor-specific mortality. Following radical surgery or radiotherapy for prostate cancer, PSADT of <6 mo indicates distant disease progression whereas a more delayed PSADT indicates local recurrence. (See also Section I: "PSA Elevation.")

REFERENCE

Benecchi L, et al. Optimal measure of PSA kinetics to identify prostate cancer Urology 2008;71:390–394.

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 overcompensation of the continence mechanism. Diagnosis is based on urodynamic evidence of increased or vacillating 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, Occult Neuropathic Bladder].”)

SYNONYMS

- Nonneurogenic neurogenic bladder
- Hinman syndrome/Hinman-Allen syndrome (in children)
- Dysfunctional voiding syndrome

TREATMENT

- Children must be motivated to participate in the therapy.
- Teach how to void and defecate properly.
- Timed voiding, voiding diary, double voiding, psychotherapy, and biofeedback may all be appropriate in select children.
- Anticholinergics may control instability; -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 (eg, with upper tract changes, failure to respond to less invasive measures).
- Biofeedback

REFERENCE

Kaplan SA, et al. Pseudodyssynergia (contraction of the external sphincter during voiding) misdiagnosed as chronic nonbacterial prostatitis and the role of biofeedback as a therapeutic option. J Urol 1997; 157(6):2234–2237.

PSEUDOMYXOMA OVARII-LIKE POST-THERAPEUTIC ALTERATION IN PROSTATE ADENOCARCINOMA

DESCRIPTION Pseudomyxoma ovarii-like post-therapeutic alteration in prostate adenocarcinoma refers to histologic alterations observed in prostate cancer foci after exposure to total androgen blockade. Changes in nontumoral glands exposed to total androgen blockade characteristically display acinar atrophy, basal cell hyperplasia, squamous or transitional cell metaplasia, and stromal hypercellularity. Conversely, tumor glands may shrink in size and extravasate mucin. This extravasated mucin resembles pseudomyxoma ovarii. This is in an important distinction, as this appearance can be easily confused with mucinous carcinoma. It is important to recognize these post-treatment effects, as it may be the sole histologic evidence of therapeutic response and may guide definitive treatment after neoadjuvant hormone deprivation.

REFERENCE

Tran TA, et al. Pseudomyxoma ovarii-like posttherapeutic alteration in prostatic adenocarcinoma: A distinctive pattern in patients receiving neoadjuvant androgen ablation therapy. Am J Surg Pathol 1998;22:347–354.

PSMA (PROSTATE-SPECIFIC MEMBRANE ANTIGEN)

DESCRIPTION Membrane-bound protein found in 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, similar to PSA, is being investigated as a more accurate prognostic indicator.

REFERENCE

Murphy GP, et al. Evaluation and comparison of two new prostate carcinoma markers: Free-prostate specific antigen and prostate specific membrane antigen. Cancer 1996;78(4):809–818.

PSOAS ABSCESS, UROLOGIC CONSIDERATIONS

DESCRIPTION A psoas abscess is a discrete abscess or phlegmon in the retroperitoneum, adjacent to the psoas muscle. Usually the consequence of direct spread of infection from an adjacent structure; primary psoas abscesses are rare and are a result of hematogenous spread. A wide variety of etiologies are reported in the literature, including perinephric abscess; pyelonephritis; postoperative infection following renal, ureteral, or bladder surgery; complications from ESWL; and urothelial carcinoma metastasis. Clinical presentation includes fever, lower abdominal or back pain, referred lower extremity pain, limp, flexion deformity of the hip from a reflex spasm, flank mass, and a psoas sign. Rarely, a psoas abscess can directly obstruct the ipsilateral ureter 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.”)

REFERENCE

Hamano S, et al. Pyogenic psoas abscess: Difficulty in early diagnosis. Urol Int 2003;71:178–83.

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 deficit. The stretched bladder is then sutured to the fascia of the ilio-psoas muscle.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:370.

PSORIASIS, EXTERNAL GENITALIA

DESCRIPTION A chronic papulosquamous skin disease frequently affecting external genitalia, more commonly in males. Genital involvement is reported in 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 of genitalia. Treatment includes topical steroids, tar preparations and maintaining good hygiene.

REFERENCE

Farber EM, Nall L. Genital psoriasis. Cutis 1992; 50(4):263–266.

Loughlin KR. Psoriasis: Association with two rare cutaneous urological malignancies. J Urol 1997; 157(2):622–623.

PUDENDAL NERVE ENTRAPMENT/PUDENDAL NEUROPATHY

DESCRIPTION Compression of the pudendal nerve or its branches causing chronic perineal numbness or pain. The pudendal nerve carries sensations from the external genitalia, distal rectum, and the perineum. Symptoms can be seen if these nerve branches are compressed during pelvic surgery, a finding commonly seen in male and female pelvic sling operations (tension-free vaginal tape or transobturator tape) for incontinence, or it can occur spontaneously. A validated set of simple diagnostic criteria (Nantes criteria) include: (1) Pain occurs in the anatomic territory of the pudendal nerve, (2) is worsened by sitting, (3) the patient is not awakened at night by the pain, (4) no objective sensory loss is found on clinical exam, and (5) a positive response is seen to anesthetic pudendal nerve block. Exclusion criteria include purely coccygeal, gluteal, or hypogastric pain; exclusively paroxysmal pain; exclusive pruritus; or the presence of imaging abnormalities able to explain the symptoms. The diagnosis of pudendal neuralgia by pudendal nerve entrapment syndrome is essentially clinical. There are no specific clinical signs or complementary test results for this disease. However, a combination of criteria can be suggestive of the diagnosis. Initial symptoms should be managed conservatively with anti-inflammatory medications and analgesics. Physical therapy, infiltration with steroids, or surgical decompression are treatment options. If applicable, sling removal should be considered if symptoms persist >6 wk.

REFERENCE

Labat JJ, et al. Diagnostic criteria for pudendal neuralgia by pudendal nerve entrapment (Nantes criteria). Neurourol Urodyn 2008;27(4):306–310.

PULMONARY METASTASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION The lungs are the site of potential metastasis in all GU cancers. It is the most common site of metastasis in renal cell carcinoma and a common metastatic site in prostate, urothelial carcinoma, and testicular tumors. Chest CT is more sensitive at detecting pulmonary nodules as it can detect lesions <1 cm, the typical minimal size for plain film detection. Since a direct correlation exists between the likelihood of malignancy and size of pulmonary nodule, lesions <1 cm in size are usually nonclinical. Therefore, plain chest x-ray is the screening test of choice. Malignant nodules usually appear as noncalcified soft-tissue densities. Suspicious nodules on chest x-ray warrant a chest CT. Tissue diagnosis of suspicious lesions should be performed if doing so will alter the intervention. Although metastatic disease requires systemic therapy, resection of pulmonary renal cell carcinoma metastases has been shown to improve survival when compared to immunotherapy alone.

REFERENCE

Hofmann HS, et al. Prognostic factors and survival after pulmonary resection of metastatic renal cell carcinoma. Eur Urol 2005;48:77–81.

PYELITIS CYSTICA

DESCRIPTION Ingrowth of urothelial cells into lamina propria with subsequent liquefaction, giving cystlike appearance. Identical to cystitis cystica, 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. Presenting symptoms are related to chronic 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 urine cytology and biopsy are recommended to rule out other neoplastic conditions. (See also Section I: “Filling Defect, Upper Urinary Tract [Renal Pelvis and Ureter].”)

REFERENCE

Gronlund A, Glenthoj A, Kvist E. Pyelitis cystica. Scand J Urol Nephrol 1997;31(5):509–511.

PYELITIS GLANDULARIS

DESCRIPTION In this condition, combined urothelial hyperplastic and metaplastic 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 Vonbrunn nests and pyelitis cystica. It is not uncommon to see later hyperplastic changes and pyelitis glandularis in a single specimen. Intracellular 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 mucus-secreting columnar cells may be seen. Pyelitis 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, Upper Urinary Tract [Renal Pelvis and Ureter].”)

REFERENCE

Dabbs DJ. Cytology of pyelitis glandularis cystica. A case report. Acta Cytol 1992;36(6):943–945.

PYELOGENIC CYST

DESCRIPTION A pyelogenic cyst is a smooth intrarenal diverticulum that communicates directly with the renal pelvis. Conversely, a calyceal diverticulum communicates indirectly to the renal pelvis through a calyx or infundibulum. Pyelogenic cysts are lined with transitional cell epithelium. Diagnosis is best made by CT urogram or delayed-phase or retrograde pyelography showing contrast pooling in the cyst. Asymptomatic pyelogenic cysts do not require treatment. Pain, persistent or recurrent infections, stones, and milk of calcium warrant surgical intervention through ureteroscopic, percutaneous, laparoscopic, or open surgical techniques.

REFERENCE

Canales B, Monga M. Surgical management of the calyceal diverticulum. Curr Opin Urol 2003; 13(3):255–260.

PYOCYSTIS

DESCRIPTION Pyocystis is a severe UTI of the bladder associated with a nonfunctioning bladder or in patients with chronic oligo-/anuria. It is most common (incidence of 20–30%) in patients with a neurogenic bladder treated with urinary diversion. Pyocystis should be suspected in patients with a nonfunctioning bladder or in those who are oligo-/anuric presenting with systemic signs of infection. Bladder catheterization should be performed and 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 culture-specific antibiotics and bladder drainage. Some advocate periodic bladder irrigations and instillations with antibiotic solutions. Cystectomy is reserved for refractory pyocystis.

REFERENCE

Bibb JL, et al. Pyocystis in patients on chronic dialysis. A potentially misdiagnosed syndrome. Int Urol Nephrol 2002;34(3):415–418.

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 catheter drainage is essential.

REFERENCE

Baumgarten DA, Baumgartner BR. Imaging and radiologic management of upper urinary tract infections. Urol Clin N Am 1997;24(3):545–569.

PYOSPERMIA

DESCRIPTION The World Health Organization defines pyospermia as >1 × 106 WBCs/mL semen (either peroxidase or by immunohistological methods). Pyospermia (also referred to as leukocytospermia) has multifactorial causes, including infection, inflammation, and autoimmunity, and is considered to be one 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, epididymo-orchitis, cystitis, urethritis, urethral stricture, stone disease, foreign bodies, upper UTI, retrograde ejaculation, localized sepsis of the adjacent lower GI tract, and asymptomatic bacteriuria. The chronic infections that may result in pyospermia include fungal, mycobacterial, and congenital lesions causing infection of the urogenital tract. Autoimmune diseases that afflict the urogenital tract include Behçet syndrome and Reiter disease. There is no defined medical management of pyospermia since the specific cause cannot be reliably identified. Options include antibiotic treatment (doxycycline, trimethoprim-sulfamethoxazole, ofloxacin) and other medications such as calcium dobesilate, propofol, rebamipide, N-acetyl-L-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, vesicourethral reflux, prostatic obstruction and infection, retrograde ejaculation, and urethral valves. Although antibiotics are a commonly used empiric therapy, studies have not confirmed their benefit, and a high rate of spontaneous resolution occurs without specific therapy. (See also Section II: “Semen Analysis, Abnormal Findings and Terminology”; “Semen Leukocytes.”)

REFERENCE

Pentyala S, et al. Current perspectives on pyospermia: A review. Asian J Androl 2007;9(5):593–600.

Q-TIP TEST

DESCRIPTION The Q-tip test is useful to evaluate the urethral axis 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

1. Dupont MC, et al. Diagnosis of stress urinary incontinence. Urol Clin N Am 1996;23(3):407–415.

QUAKEL CORPORAL SHUNT

DESCRIPTION Used for the treatment of priapism. Through a scrotal perineal approach, a longitudinal incision is made in the outer bulbar urethra (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

2. Thomas AJ. Surgery for priapism. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989: 826–832.

SHORT TOPIC SECTION R

RADIATION, PELVIC, UROLOGIC CONSIDERATIONS

DESCRIPTION Pelvic radiation is commonly used as both a primary treatment for localized prostate cancer and also as treatment for local recurrence after surgery or nodal disease. Muscle-invasive bladder cancer is also treated with radiation. Urologists often encounter patients who have received previous pelvic radiation for gynecologic cancers such as cervical, ovarian, or rectal cancer. Radiation can cause several urologic complications, including cystitis, ureteral stricture, secondary bladder malignancy, fistula, and retroperitoneal fibrosis. Previous pelvic radiation is a contraindication for orthotopic neobladder reconstruction, and urinary diversion should be performed using bowel and with placement of the stoma outside the radiation field.

REFERENCE

1. Crew JP, et al. Radiation-induced haemorrhagic cystitis. Eur Urol 2003;43:111–123.

RADIATION, RENAL AND RETROPERITONEAL, UROLOGIC CONSIDERATIONS

DESCRIPTION Radiation therapy (RT) for renal cell carcinoma as primary therapy is ineffective, but it is useful for palliation of bone metastases. It can be utilized for renal sarcomas or lymphoma. Retroperitoneal radiation is used for seminoma but not for nonseminomatous testis tumors. Nonseminomatous germ cell tumors are generally less radiosensitive, and RT is typically not used. Side effects of renal and retroperitoneal RT include retroperitoneal fibrosis, ureteral stricture or obstruction, hematuria, enteritis, cardiovascular complications, and secondary malignancy.

REFERENCE

2. Garcia-Serra AM, et al. Long-term results of radiotherapy for early-stage testicular seminoma. Am J Clin Oncol 2005;119:119–124.

RADIOPHARMACEUTICALS (PHOSPORUS32, STRONTIUM89, SAMARIUM153 EDTMP)

DESCRIPTION Strontium89 and Samarium153 ethylene diamine tetramethylene phosphonate (EDTMP) are FDA-approved radioisotopes approved for the treatment of bony metastatic pain. Phosphorus32 has been used for bony metastases, although myelosuppression has limited its application. These radioisotopes are infused intravenously and taken up in bony areas of high metabolic activity. The radioactive decay has a toxic effect on tumor cells, and relief of symptoms generally begins 1–4 wk after initial infusion.

REFERENCE

3. Finlay IG, et al. Radioisotopes for the palliation of metastatic bone cancer: A systematic review. Lancet Oncol 2005;6:392–400.

RAPID PLASMA REAGIN (RPR) BLOOD TEST

DESCRIPTION The RPR test is a screening test for syphilis (Treponema 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 particle agglutination or florescent treponemal antibody test should be ordered. False-positives can be seen in some viral infections, and HIV can cause a false-negative reaction.

REFERENCE

4. Frenkl TL, Potts J. Sexually transmitted infections. Urol Clin N Am 2008;35:233–246.

RAZ BLADDER NECK SUSPENSION (URETHROPEXY)

DESCRIPTION This is one 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 urethrolysis, (2) fingertip guidance of a double-pronged suture carrier placed through a suprapubic opening, and (3) placement of helical nonabsorbable sutures through the urethropelvic 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

5. Stothers L, et al. Surgery for female stress urinary incontinence. Can J Urol 1995;2(Supp1):33–37.

RAZ VAGINAL WALL SLING

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 urethropexy, 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 serves as a backboard to the bladder neck and mid-urethra.

REFERENCE

6. Raz S, et al. Vaginal wall sling for anatomical incontinence and intrinsic sphincter dysfunction: Efficacy and outcome analysis. J Urol 1996;156(1):166–170.

RECTAL INJURY DURING RADICAL PROSTATECTOMY

DESCRIPTION Rectal injury is a rare but serious complication of prostatectomy using open, laparoscopic, robotic, or perineal approaches. The risk in open or laparoscopic/robotic prostatectomy is <1% but higher with the perineal approach. It most commonly occurs with dissection along the Denonvilliers fascia. When an injury is identified intraoperatively, it should be repaired primarily with a 2-layered closure after completion of the prostatectomy and bladder neck reconstruction, prior to the urethrovesical anastomosis. Omental interposition between the rectal repair and vesicourethral anastomosis may decrease the risk of rectovesical and rectourethral fistula. However, in postradiation salvage prostatectomy, a diverting colostomy should also be performed.

REFERENCE

7. Lepor H, et al. Intraoperative and postoperative complications of radical retropubic prostatectomy in a consecutive series of 1,000 cases. J Urol 2001;166:1729–1733.

RECTOCELE, UROLOGIC CONSIDERATIONS

DESCRIPTION Rectocele generally presents as a posterior vaginal wall defect with varying degrees of prolapse. It can present with urologic symptoms including sexual dysfunction and voiding symptoms, as well as constipation. If a patient presents with voiding dysfunction, a urodynamic study should be performed with the rectocele reduced to unmask the patient's underlying urodynamic parameters. Prior to repair, it is important to determine if there is evidence of enterocele or cystocele, to determine the appropriate reconstructive procedure. Treatment can be conservative using a vaginal pessary or surgical using one of several techniques, including open or laparoscopic, transvaginal, or endorectal. (See also Section I: "Pelvic Prolapse [Cystocele and Enterocele].")

REFERENCE

8. Cundiff GW, Fenner D. Evaluation and treatment of women with rectocele: Focus on associated defecatory and sexual dysfunction. Obstet Gynecol 2004;104:1403–1421.

REFLUX NEPHROPATHY

DESCRIPTION Renal scarring secondary to reflux of sterile or infected urine from the bladder to the kidney. Girls are at increased risk of developing reflux nephropathy because of the increased incidence of UTI. 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 cortical 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.”)

REFERENCE

9. Polito C, et al. Long-term evolution of renal damage associated with unilateral vesicoureteral reflux. J Urol 2007;178(3):1043–1047.

REIFENSTEIN SYNDROME

DESCRIPTION A form of incomplete male pseudohermaphroditism, usually presenting with perineoscrotal hypospadias and frequently cryptorchidism at birth, azoospermia and incomplete virilization at puberty, and infertility and gynecomastia at or after puberty. Caused by mutations in the DNA-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 leuteinizing hormone. Also known as Lubor Gilbert-Dreyfus Syndrome or type 1 incomplete male pseudohermaphroditism. Surgical repair of hypospadias and cryptorchidism as the treatment and supplemental testosterone is not beneficial.

REFERENCE

Klocker H, et al. Point mutation in the DNA binding domain of the androgen receptor in two families with Reifenstein syndrome. Am J Hum Genet 1992;50(6):1318–1327.

REINKE CRYSTALS

DESCRIPTION Cytoplasmic crystalloid 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.

REFERENCE

Kerr JB. Ultrastructure of the seminiferous epithelium and intertubular tissue of the human testis. J Electron Microsc Technique 1991;19(2):215–240.

REITER SYNDROME (REACTIVE ARTHRITIS)

DESCRIPTION The preferred term today is reactive arthritis, a classic triad of polyarthritis, conjunctivitis, and nongonococcal urethritis (in women, cervicitis). Anterior uveitis and skin or genital rash may be seen. Thought to be a systematic inflammatory response triggered by microbial infection in the GU or GI tracts, the condition is a member of the spondyloarthritis 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, and post-dysenteries. Causes include Chlamydia trachomatis, Salmonella sp., Shigella sp., Yersinia sp., and Ureaplasma urealyticum. The overall prognosis is good, with spontaneous remission or remission following NSAID therapy within 6 mo of onset. A small proportion have chronic persistent arthritis; a few will develop ankylosing spondylitis (more frequent if HLA-B27 positive). Usual treatment includes supportive care (NSAIDs, intraarticular or systemic steroids for polyarthritis). Antibiotic treatment is initiated for identified organisms, if possible, such as C. trachomatis (doxycycline 100 mg PO b.i.d. 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 unconvicted war criminal.)

REFERENCE

Hannu T, et al. Reactive arthritis or post-infectious arthritis? Best Pract Res Clin Rheumatol 2006;20(3):419–433.

RENAL ADENOMA (PAPILLARY ADENOMA)

DESCRIPTION The most common renal epithelial neoplasm and found in 4–37% of autopsy specimens. Controversial if these are small adenocarcinomas. Strict diagnostic criterion include papillary, tubular, or tubulopapillary architecture, <5 mm and no resemblance to any renal malignancy.

REFERENCE

Grignon DJ, Eble JN. Papillary and metanephric adenomas of the kidney. Semin Diagn Pathol. 1998;15(1):41–53.

RENAL AGENESIS (BILATERAL AND UNILATERAL)

DESCRIPTION This condition is defined by the congenital absence of one or both kidneys:

- 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 limbs, 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 undetected 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 Müllerian duct, Wolffian duct, and ureteric bud abnormalities and thus may involve the vas deferens, ureter, trigone, vagina, and seminal vesicles. 65% of patients have another urologic anomaly. Associated anomalies include reflux; contralateral UPJ obstruction, including single umbilical artery; absence of ipsilateral ureter and hemi-trigone; vaginal atresia/agenesis (Mayer-Rokitansky syndrome); unilateral vas deferens agenesis/atresia; and seminal vesicle cysts. Unilateral renal agenesis is also associated with anomalies of other systems such as cardiovascular in 30% (valvular or septal cardiac anomalies); GI in 25%; imperforate anus or atresia of anus or esophagus; and vertebral 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.

REFERENCE

Uetani N, Bouchard M. Plumbing in the embryo: Developmental defects of the urinary tracts. Clin Genet 2009;75(4):307–317.

RENAL ANATOMY, NORMAL RADIOGRAPHIC FINDINGS (SIZES, CALYCES)

DESCRIPTION The kidney can be imaged by plain film, US, CT, MRI, radionuclide scanning, or pyelography, either IV (excretory), antegrade, or retrograde. A normal adult kidney should measure 10–13 cm vertically, 5–7 cm transversely, and 3 cm anteroposteriorly. The right kidney tends to be shorter and wider than the left due to hepatic compression. The renal pedicle usually consists of a single renal artery and vein, although many normal anatomic variants exist. Many normal variants of calyceal anatomy also exist, but pathologic findings include debris and filling defects; dilation of calyces or a single calyx suggests ureteral and infundibular obstruction, respectively.

REFERENCE

Singer A, et al. Spectrum of congenital renal anomalies presenting in adulthood. Clin Imaging 2008;32:183–191.

RENAL ARTERY ANEURYSM

DESCRIPTION Incidence ranges from 0.3–1.0% on radiographic studies, accounting for 1% of all arterial aneurysms and 10% of visceral aneurysms. They are commonly bilateral or multiple (20% and 30%, respectively), and occur typically in the 5th–6th decades of life, slightly more frequently on the right. They are associated with hypertension (HTN), but a causal effect has not been shown. Spontaneous rupture is rare, but risk is increased during pregnancy. Presentation is usually secondary to HTN, flank pain, hematuria, or an incidental finding on radiographic study.

Causes include atherosclerosis, congenital, fibromuscular dysplasia, trauma, infectious disease (syphilis or TB), intrarenal aneurysms (collagen vascular diseases [polyarteritis nodosa, Wegener granulomatosis]).

TREATMENT

- Surgical repair is indicated for symptomatic lesions, lesions >4.0 cm, spontaneous rupture, or asymptomatic lesions in high-risk patients (women of childbearing age or patients with functional or anatomic solitary kidney).
- Repair includes primary repair with excision of aneurysmal segment, or aortorenal bypass with vein. Extra-anatomic bypass (hepatorenal, gastroduodenal-renal, or splenorenal) is useful for a severely calcified aorta or when aortic cross-clamping is undesirable.
- Autotransplantation is useful for complex repairs with long ischemic time.
- Percutaneous treatment with embolization or occlusion of aneurysmal segments is reserved for high-risk surgical candidates.
- Intraluminal vascular stent: Investigational

REFERENCE

Cinat M, et al. Management of renal artery aneurysms. Semin Vasc Surg 1996;9(3):236–244.

RENAL ARTERY FIBROMUSCULAR DYSPLASIA

DESCRIPTION Fibromuscular diseases of the renal artery account for 1/3 of cases of renovascular hypertension. 4 pathologic entities have been described. Intimal fibroplasia affects mainly children and young male adults. Angiographically, a smooth focal stenosis is typically seen at the mid renal artery or its branches. Prompt repair is advised because of the progressive nature of the disease. Fibromuscular hyperplasia of smooth muscle and fibrous tissue is rare, progressive, and affects mainly children and young adults. Medial fibroplasia is the most common (80%), affecting women in their 30s. On angiogram, it has the appearance of a string of beads. This lesion does not dissect, and complete occlusion has not been reported. Angioplasty is the treatment of choice. Perimedial fibroplasia is a tightly stenotic, progressive lesion, affecting women 15–30 yr of age. On angiography, extensive collateral vessels are commonly identified. Primary treatment is directed at BP control (ACE inhibitor or angiotensin II receptor blocker). Follow potassium and creatinine after initiation of therapy. Revascularization using percutaneous angioplasty is the definitive treatment of choice.

REFERENCE

Slovut DP, et al. Fibromuscular dysplasia. N Engl J Med 2004;350(18):1862–1871.

RENAL CARCINOID TUMOR

DESCRIPTION Rare tumor derived from enterochromaffin or amine precursor uptake and decarboxylation (APUD) cells, occurring most commonly in the GI tract and lung, but also in ovaries, testes, thymus, pancreas, 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 teratomatous epithelial cells within the kidney. Horseshoe kidneys are shown to have a markedly elevated risk of carcinoid tumor, although still very rare, and may have a more benign course.

REFERENCE

Krishnan B, et al. Horseshoe kidney is associated with an increased relative risk of primary renal carcinoid tumor. J Urol 1997;157(6):2059–2066.

RENAL CELL CARCINOMA, CHROMOPHOBE

DESCRIPTION Chromophobe renal cell carcinoma (RCC) is a subtype of RCC derived from the distal renal tubules, and it comprises about 3–5% of all RCCs. Tumor cells display a transparent cytoplasm with a plant cell appearance and a characteristic perinuclear halo. On electron microscopy, microvesicles are seen that stain positive for Hale's colloidal iron. There are 2 types. Type 1, or classic, is defined by loss of chromosomes 1, 2, 6, 10, 13, 17, or 21 and has a better prognosis than type 2, or eosinophilic variant. The eosinophilic variant is part of Birt-Hogg-Dube syndrome. In general, chromophobe RCC has a better prognosis than other RCC histologies. Chromophobe RCC is difficult to distinguish from oncocytoma on biopsy, making definitive diagnosis difficult without a complete pathologic exam. (See also Section I: "Renal Cell Carcinoma, General.")

REFERENCE

Klatte T, et al. Pathobiology and prognosis of chromophobe renal cell carcinoma. Urol Oncol 2008;26(6):604–609.

RENAL CELL CARCINOMA, PAPILLARY TYPES 1 AND 2

DESCRIPTION An uncommon variant of renal cell carcinomas (RCCs), representing ~10% of cases. The lesions exhibit a tubulo-papillary growth pattern. A hereditary pattern is demonstrated in a small number of families, tending to be multifocal, bilateral, and associated with loss of short arm of chromosome 3. Subtypes are cytologically classified as type 1 with small single-layer cells, and type 2 with large pseudostratified cells. Type 1 papillary RCC typically exhibits genetic alterations including gains of chromosome 7 and 17 and loss of Y, with has a better prognosis; type 2 has more heterogeneous genetic alterations and a poorer prognosis. (See also Section I: “Renal Cell Carcinoma, General.”)

REFERENCE

Kuroda N, et al. Review of papillary renal cell carcinoma with focus on clinical and pathobiological aspects. Histol Histopathol 2003;18(2):487–494.

RENAL CELL CARCINOMA, SARCOMATOID

DESCRIPTION An uncommon histologic variant of renal cell carcinoma, with an approximate incidence of 5–10% of all cases. Histologically, the lesion is composed of clear cells and pleomorphic spindle cells resembling sarcoma. It tends to have a more malignant behavior and worse prognosis, with higher local recurrence, more frequent metastasis, and shorter survival. (See also Section I: “Renal Cell Carcinoma, General.”)

REFERENCE

Oda H, et al. Sarcomatoid renal cell carcinoma. A study of its proliferative activity. Cancer 1993;71(7):2292–2298.

RENAL CHOLESTEROL EMBOLISM SYNDROME

DESCRIPTION Cholesterol microembolism (also called cholesterol emboli and cholesterol crystal emboli) of the kidney is an uncommon cause of hypertensive urgency, affecting mainly 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 emboli, and eosinophilia. Dialysis for renal insufficiency might be necessary. Diagnosis is made from clinical history, physical exam, lab findings, and selective renal angiogram, and is confirmed by renal biopsy. In the kidneys, intralobular and arcuate arteries are most frequently affected. Treatment is supportive and preventative with management of hypertension and renal insufficiency through control of the underlying pathology.

CAUSES

- Angiographic manipulation
- Anticoagulant medications
- Cardiovascular surgery
- Iatrogenic
- Spontaneous

REFERENCE

Hitti WA, et al. Cholesterol emboli-induced renal failure and gastric ulcer after thrombolytic therapy. South Med J 2005;98(2):235–237.

RENAL HEMANGIOMA

DESCRIPTION These benign vascular neoplasms are usually diagnosed in the 3rd–5th decade, with no sex predilection. The most common presenting symptom is intermittent hematuria. Angiographic appearance varies markedly, with hypervascular, hypovascular, and normal lesions being reported. In the past, a clinical finding of unilateral hematuria and a suggestive angiographic pattern were the basis of preoperative diagnosis. Currently, hemangioma can be identified ureteroscopically, without the need for a biopsy, where they may appear as small, red or bluish spots on the tip or base of a papilla, or they may be large, bulbous, erythematous lesions on the papillary tips. Pathologically, hemangiomas have the gross appearance of a well-demarcated lesion that shows a cluster of blood-filled vascular channels. Microscopically, the majority of cases conform to the typical features of cavernous hemangioma, with variable, large, blood-filled vascular tributaries in a disorganized tangle. Variation in vascular wall thickness and structure indicates arterial and venous components. The benign cytologic feature of flat lining endothelial cells allows for differentiation of this lesion from angiosarcoma.

TREATMENT

- Ureteroscopic electrocauterization or laser ablation using holmium, ND:YAG, or a combination of both
- Surgical resection

REFERENCE

Waller JI, Throckmorton MA, Barbosa E. Renal hemangioma. J Urol 1995;74:186.

RENAL HEMANGIOPERICYTOMA

DESCRIPTION A rare primary sarcoma of the kidney, accounting for 1–3% of renal malignancies. Solid hypervascular mass with calcifications, originating from pericytes, located external to endothelial cells of capillaries, and enveloped by basement membrane. It can be metabolically active, secreting renin. Common presenting signs include flank pain, flank mass, hypertension, hypoglycemia, and hematuria. It can be treated by radical nephrectomy, with reports of nephron-sparing surgery.

REFERENCE

Brescia A, et al. Renal hemangiopericytoma: Case report and review of the literature. Urology 2008;71(4):755.e9–e12.

RENAL LEIOMYOMA

DESCRIPTION A rare benign renal tumor, with an incidence of 5% on autopsy series, it originates from smooth muscle, usually from renal capsule or vessels, and less commonly from renal pelvis. Radiographically, it can appear as solid or cystic mass, difficult to differentiate from renal cell carcinoma, thus usually prompting radical nephrectomy. Imaging findings that can help to suggest the diagnosis of renal leiomyomas are tumors that are hyperdense before contrast, with density similar to that of muscles, and with lower enhancement than the adjacent renal parenchyma. Most are peripheral, without involvement of the renal cortex and with well-defined margins.

REFERENCE

Derchi LE, et al. Imaging of renal leiomyomas. Acta Radiol 2008;49(7):833–838.

RENAL LEIOMYOSARCOMA

See Section I: Renal Sarcomas, Adult and Pediatric.

RENAL LYMPHANGIECTASIA

DESCRIPTION A very uncommon benign disorder of renal lymphatics with unknown pathophysiology, the condition can present with perinephric collections, ascites, abdominal pain, and reversible hypertension. Imaging demonstrates enlarged kidneys with fluid collections seen to be abutting the surrounding structures. Perinephric fluid analysis usually demonstrates elevated protein levels with leucocytes (mostly lymphocytes). Management alternatives range from percutaneous drainage in symptomatic cases to medical therapy (antihypertensives and diuretics).

REFERENCE

Ashraf K, et al. Renal lymphangiectasia. Br J Radiol 2007;80(954):e117–118.

RENAL MALROTATION

DESCRIPTION The abnormal orientation of the kidney, so that there is no medial position of the renal pelvis, and the calyces are pointing laterally. This condition may occur in cases of ectopia, fusion, and complete renal ascent; it has an incidence of 1 in 390. 3 types:

- Nonrotation: The renal pelvis is anterior.
- Reverse rotation: The renal pelvis is lateral.
- Hyperrotation: The renal pelvis is posterior.

Symptoms are usually absent; occasionally, vague abdominal pain and/or vomiting due to renal obstruction may occur. Patients may develop ureteral obstruction, infections, or calculi. Diagnosis is made typically on excretory urography with altered orientation of the calyces and pelves. Retrograde pyelography is often useful in defining the anatomy. No treatment is necessary unless symptoms, stones, or obstruction become problematic. Follow-up US to evaluate for stones or hydronephrosis is recommended.

REFERENCE

Kelalis P, King L, Belman B, eds. Clinical Pediatric Urology, 3rd ed. Vol. 1. Informa Healthcare, 1992:505–507.

RENAL OSTEODYSTROPHY

DESCRIPTION Renal osteodystrophy is defined by the National Kidney Foundation as bone morphology alterations 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 a patient is on dialysis. Treatment may include treating hyperphosphatemia, Calcitrol, vitamin D analogs, calcimimetics, or parathyroidectomy.

REFERENCE

Moe S, et al. Definition, evaluation, and classification of renal osteodystrophy: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2006;69:1945–1953.

RENAL PSEUDOTUMOR

DESCRIPTION Benign condition of the kidney, mimicking renal neoplasm on radiographic studies. Most commonly is hypertrophied column of Bertin (sometimes referred to as an anomalous calyx), a prominent medullary column usually located between upper and middle pole calyceal infundibula 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 fetal lobulation, lobar dysmorphism, dromedary hump, lobar nephronia, and renal sinus lipomatosis. (See also Section I: “Renal Mass.”)

REFERENCE

Bosniak MA. Problems in the radiologic diagnosis of renal parenchymal tumors. Urol Clin N Am 1993; 20(2):217–230.

RENAL SINUS ABNORMALITIES

DESCRIPTION The renal sinus is a central spacious cavity in which major branches of the renal artery and vein, along with the major and minor calices of the collecting system, are located. 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 parapelvic simple cysts, lipomatosis, cysts, urinomas, and vascular lesions such as renal artery aneurysm or AV fistula. Malignant tumors originating in renal pelvis or parenchyma, such as transitional cell carcinoma and renal cell carcinoma, may also protrude or even invade and obliterate renal sinus fat. Primary tumors, such as hemangioma, fibroma, leiomyoma, and malignant fibrous histiocytoma are rare but may develop in the space.

REFERENCE

Rha SE, et al. The renal sinus: Pathologic spectrum and multimodality imaging approach. Radiographics 2004;24(Suppl 1):S117–131.

RENAL TRANSPLANTATION AND NEOPLASIA

DESCRIPTION Transplant recipients have an elevated risk of cancer. There is a very small risk of primary malignancy harbored in the graft being transferred to the recipient, but the most common malignancies that form after transplantation are Kaposi sarcoma, non-Hodgkin lymphoma, nonmelanoma skin cancers, and renal cell carcinoma. Immunosuppression is thought to have a causative role. Recipients who have been on hemodialysis are also at a higher risk of acquired cystic disease and subsequent primary renal malignancy.

REFERENCE

Wong G, Chapman JR. Cancers after renal transplantation. Transplant Rev (Orlando) 2008;22(2):141–149.

RENAL VEIN, LEIOMYOSARCOMA

DESCRIPTION A rare tumor arising from the smooth muscle element of renal vein, most commonly on the left side. Striking female predominance (85% of the 27 reported cases) is noted, usually in 6th decade of life. Presenting symptoms include flank or abdominal pain, weight loss, and a palpable abdominal mass. Visualized with CT, which 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.

TREATMENT

- Aggressive surgical resection with nephrectomy and en bloc resection
- Nonsurgical treatment with XRT and chemotherapy is ineffective.

REFERENCE

Brandes SB, et al. Leiomyosarcoma of the renal vein. J Surg Oncol 1996;63(3):195–200.

RENAL–RETINAL SYNDROME

DESCRIPTION Also called juvenile nephronophthisis with retinal disease, this condition is actually a subtype of juvenile nephronophthisis. (See Section II: “Juvenile Nephronophthisis.”) It occurs in about 1 of 7 cases of juvenile nephronophthisis and is an autosomal recessive disease mapped to chromosome 2. 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. Midperipheral ring scotoma gradually widens, and the retina becomes darkly pigmented, with a bony-spiculed appearance. The disc may look yellow and waxy. Treatment is supportive, with renal replacement therapy as needed.

REFERENCE

Lippert M. Renal cystic disease. In: Gillenwater JY, Grayhack JT, Howards SS, et al., eds. Adult and Pediatric Urology, 3rd ed. St. Louis: Mosby, 1996.

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.

REFERENCE

Rossi GP, et al. Renal vein renin measurements accurately identify renovascular hypertension caused by total occlusion of the renal artery. J Hypertens 2002;2:975–984.

RENINOMA (RENIN-SECRETING JUXTAGLOMERULAR CELL TUMOR)

DESCRIPTION A rare tumor of the juxtaglomerular apparatus, its usual presentation is in a young female with severe, refractory, frequently paroxysmal hypertension with hypokalemia, hyperaldosteronism, and elevated plasma renin levels. Tumors are typically small and not always visualized on CT. Selective renal vein sampling for renin may help localize the lesion. It is generally a benign tumor, although untreated hypertension can be fatal. Treatment is usually by radical nephrectomy.

REFERENCE

Wong L, et al. Reninoma: Case report and literature review. J Hypertens 2008;26(2):368–373.

RENO-ALIMENTARY FISTULA

DESCRIPTION A broad group of nonanatomic communications between the upper urinary collecting system and the alimentary canal, with nephrocolic and right renal pelvis and duodenal 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/chronic)
- Malignancy of either intestinal or renal origin
- Iatrogenic (eg, percutaneous surgery)
- Trauma
- Ulcer disease

TREATMENT

- Conservative: Stenting or nephrostomy tube
- Nephrectomy with removal of fistula tract and bowel resection

REFERENCE

Bissada NK, Cole AT, Fried FA. Reno-alimentary fistula: An unusual urological problem. J Urol 1973;110:273.

RENO-BRONCHIAL FISTULA

DESCRIPTION Fistulous communication between pleural cavity and kidney, associated with pyelonephritis and perinephric abscess. Usually presents with flank or abdominal pain with ipsilateral pneumonia, and patients commonly have a history of pyelonephritis or abdominal abscess. It can involve pleural space alone or erode into lung parenchyma and bronchial tree. Diagnosis is made with CT.

SYNONYMS

- Nephrobronchial fistula
- Renal, bronchopleural fistula

CAUSES

- Pyelonephritis with perinephric abscess
- Xanthogranulomatous pyelonephritis
- Most common pathogens: E. coli and Proteus sp.
- Tubercular infections also reported

TREATMENT

- Percutaneous or open drainage and antibiotic therapy acutely
- Often requires nephrectomy

REFERENCE

O'Brien JD, Ettinger NA. Nephrobronchial fistula and lung abscess resulting from nephrolithiasis and pyelonephritis. Chest 1995;108(4):1166–1168.

RENOMEDULLARY INTERSTITIAL CELL TUMOR

DESCRIPTION Also referred to as medullary fibromas, this is a benign tumor of interstitial cells found within the juxtaglomerular apparatus, which are involved in prostaglandin metabolism and counterbalance the renin-angiotensin system. Small tumor nodules composed of interstitial cells are common at autopsy, occurring in 44% of older individuals. Often incidentally discovered at nephrectomy for other causes, they do not appear to have any undue effect on arterial BP.

REFERENCE

Bircan S. Renomedullary interstitial cell tumor. Urol Int 2000;65(3):163–166.

RESIDUAL URINE (POST-VOID RESIDUAL [PVR])

DESCRIPTION PVR is the amount of urine remaining immediately after a void. It can be measured by US (bladder scan) or directly by catheterization. Significant variability occurs between PVR measurements in any 1 individual, and several separate measurements should be performed. The absolute value of PVR has little significance but can indicate voiding dysfunction in symptomatic individuals. Therefore, PVR should be part of any assessment of patients with incontinence, lower urinary tract symptoms, recurrent UTI, suspected bladder outlet obstruction, or neurogenic bladder.

REFERENCE

Kaplan SA, et al. Urinary retention and post-void residual urine in men: Separating truth from tradition. J Urol 2008;180:47–54.

RESISTIVE INDICES (RI)

DESCRIPTION The RI is a measurement of renal blood flow using Doppler US. It is defined as the peak systolic velocity (PSV) minus the end-diastolic velocity divided by PSV. It used to evaluate upper-tract urinary obstruction as well as graft function in transplanted kidneys. Although there are no accepted parameters of normal RI, values >0.7 suggest obstruction or graft hypoperfusion.

REFERENCE

Nezami N, et al. Doppler ultrasonographic indices after renal transplantation as renal function predictors. Transplant Proc 2008;40:94–99.

RETE TESTIS, ADENOCARCINOMA

DESCRIPTION A rare, highly malignant tumor arising from rete testis that usually occurs in older men, but has been reported in men as young as 17. It commonly presents with painless scrotal mass or symptoms related to metastasis. Pathology reveals papillary adenocarcinoma in the rete testis, commonly with local invasion. May be associated with maldescended testis or adenomatous hyperplasia of the rete testis. Prognosis is poor, with <50% survival at 1 yr. Metastatic sites include retroperitoneal lymph nodes, lungs, bone, and liver. The diagnostic criteria include:

- Tumor in mediastinum separate from body of testis
- Transition in rete testis from normal epithelium to neoplastic cells
- No evidence of teratoma
- No primary tumor elsewhere
- Intact parietal tunica

TREATMENT

- Radical orchiectomy 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

Sogni F. Primary adenocarcinoma of the rete testis: Diagnostic problems and therapeutic dilemmas. Scand J Urol Nephrol 2008;42(1):83–85.

RETROCAVAL/CIRCUMCAVAL URETER

DESCRIPTION A rare congenital anomaly in which the infrarenal vena cava (IVC) is derived from the right subcardinal or postcardinal vein, anterior to the ureter. The term circumcaval ureter refers to the ureter emerging medial to IVC after running behind it, whereas the term retrocaval applies to those ureters that only knuckle behind the IVC but reemerge laterally. Not all retrocaval/circumcaval ureters are obstructed. Males are affected 3 times more often than are females. Pain in the 2nd, 3rd, or 4th decade is the most common presentation. However, despite its congenital origin, symptoms are usually absent in childhood. Less commonly, patients present with hematuria or UTI.

REFERENCE

Bateson EM, Atkinson D. Circumcaval ureter: A new classification. Clin Radiol 1969;20:173.

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 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 catheter under low pressures while obtaining a series of plain films. An oblique view allows best visualization of the entire urethra.

REFERENCE

Berná JD, et al. Urethrography in the male: The clamp method. Acta Radiol 2009;50(2):233–237.

RETROPERITONEAL HEMATOMA

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 angiomyolipoma or renal cell carcinoma), or abdominal vessel hemorrhage. Ecchymosis may be observed around the umbilicus (Cullen sign) or flank (Grey-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, has an expanding pulsatile hematoma, or renal hemorrhage 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 Abscess”; “Retroperitoneal Masses and Cysts.”)

REFERENCE

Heyns CF. Renal trauma: Indications for imaging and surgical exploration. BJU Int 2004;93:1165–1170.

RETROPERITONEAL LIPOSARCOMA

DESCRIPTION Retroperitoneal liposarcoma is a common retroperitoneal sarcoma arising from adipose tissue. 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 obstruction, but other symptoms can include early satiety, obstruction, or retroperitoneal bleeding. A germ cell tumor must be ruled out by tumor markers, and a biopsy is necessary if there is diagnostic uncertainty. Complete resection is the only potentially curative treatment. Radiotherapy combined with surgical resection may offer a survival benefit in certain patients. (See also Section I: “Retroperitoneal Masses and Cysts.”)

REFERENCE

Chouairy CJ, et al. Retroperitoneal liposarcoma. J Urol 2007;177:1145.

RETROPERITONEAL LYMPHOMA

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 a ureteral obstruction is visualized with US or IVP. (See also Section I: “Retroperitoneal Masses and Cysts.”)

TREATMENT

- CHOP chemotherapy (cyclophosphamide, Adriamycin, vincristine, prednisolone) and radiation therapy
- Obstructive uropathy may require ureteral stenting or percutaneous decompression prior to chemotherapy.

REFERENCE

Klein EA, et al. Intraoperative consultation for the retroperitoneum and adrenal glands. Urol Clin N Am 1985;12(3):411–421.

Terao T, et al. Retroperitoneal malignant lymphoma showing follicular type: Report of a case. Hinyokika Kiyo 1992;38(10):1151–1155.

RETROPERITONEAL RHEUMATOID NODULES

DESCRIPTION Rheumatoid nodules (necrobiotic granulomas) are a common extraarticular manifestation of rheumatoid arthritis, usually found in subcutaneous tissue. They have been reported in numerous other locations, including blood vessels, larynx, pharynx, sclera, and extradural space. GU involvement is rare and includes renal cortex and bladder. Retroperitoneal occurrence has been reported and can cause ureteral compression and obstruction requiring ureterolysis and repair. (See also Section I: “Retroperitoneal Masses and Cysts.”)

REFERENCE

Adelson GL, Saypol DC, Walker AN. Ureteral stenosis secondary to retroperitoneal rheumatoid nodules. J Urol 1982;127(1):124–125.

RETROPERITONEAL SARCOMA

DESCRIPTION Retroperitoneal sarcomas are soft-tissue tumors that typically present at an advanced stage. Approximately half of retroperitoneal sarcomas are high-grade tumors, with the most common type being liposarcoma (41%), followed by leiomyosarcoma (28%). (See also Section I: “Retroperitoneal Masses and Cysts.”) These tumors rarely cause symptoms until they reach significant size. Median age at presentation is 50, although they can occur at any age. At the time of presentation, more than 1/2 are >20 cm in size. Symptoms are nonspecific and include nausea and vomiting, abdominal pain, and weight loss. Signs include increased abdominal girth. Compression by the mass can cause paresthesia, weakness, and swelling of lower extremities. Differential diagnosis of a retroperitoneal mass includes benign masses such as lipoma, leiomyoma, or malignancies such as lymphoma, pancreatic cancer, testicular neoplasm, or renal or adrenal masses. Retroperitoneal sarcomas carry a worse prognosis than extremity sarcomas due to the difficulty of complete resection, involvement of critical structures, and delay of diagnosis. CT with both IV and oral contrast is the imaging modality of choice, and the role of guided biopsy is controversial if clinical suspicion is high. Complete surgical resection is considered the only curative modality. Radiotherapy combined with surgery may provide a survival advantage in the neoadjuvant, intraoperative, or adjuvant setting depending on resection margin status and recurrence. (See also Section I: “Retroperitoneal Masses and Cysts.”)

REFERENCE

Hueman MT, Herman JM, Ahuja N. Management of retroperitoneal sarcomas. Surg Clin N Am 2008;88:583–597.

RHABDOID TUMOR, MALIGNANT

DESCRIPTION The most lethal renal neoplasm, formerly believed to be a form of Wilms tumor. It comprises 2% of all renal tumors and affects children, with a median age of 1 yr. It has a tendency to early metastatic spread. The most common presentation is an abdominal mass detected in these young patients. Histologically, the cells are large, with large nuclei and very prominent nucleoli. In most cases, cytoplasmic eosinophilic inclusions (fibrils) can be demonstrated on electron microscopy. Although these large cells may suggest rhabdomyoblasts, the actual presence of muscle could not be confirmed by light or electron microscopy. If striated muscle can be identified, as in conventional Wilms tumor, the diagnosis of rhabdoid tumor can be excluded, and the outlook is better. Rhabdoid tumors tend to metastasize to the brain and have a high association with independent primary CNS tumors. Extrarenal rhabdoid tumors also have been reported. The term pseudomalignant rhabdoid tumor refers to neoplasms lacking prominent nucleoli, exhibiting a serpentine growth pattern, or containing malignant rhabdoid tumor-like cells in the background of a typical Wilms tumor.

REFERENCE

Alavi S. Rhabdoid tumor of the kidney presenting with hemiplegia: Report of a case. Pediatr Hematol Oncol. 2007;24(2):123–128.

Beckwith JB, Palmer NF. Histopathology and prognosis of Wilms' tumor: Results from the 1st National Wilms' Tumor Study. Cancer 1978;41:1937.

RHABDOMYOLYSIS

DESCRIPTION Clinical syndrome of acute renal failure and myoglobinuria caused by damage or destruction of skeletal muscle. The mechanism of renal failure is thought to be multifactorial, including hypovolemia from fluid sequestration in damaged muscle, direct tubular toxicity of the myoglobin metabolite hematin, or tubular obstruction due to myoglobin precipitation in an acidic environment. (See also Section II: “Myoglobinuria and Myoglobin Nephrotoxicity.”)

CAUSES

- Burn injury
- Crush injury
- Compartment syndrome or ischemic injury to large muscle groups
- Seizures or malignant hyperthermia
- Prolonged coma
- Exaggerated lithotomy position during laparoscopic, urologic, gynecologic, or orthopedic procedures

TREATMENT

- Aggressive fluid resuscitation with forced diuresis and urinary alkalinization
- Supportive care with intensive monitoring

REFERENCE

Glassman DT, et al. Rhabdomyolysis after laparoscopic nephrectomy. JSLS 2007;11(4):432–437.

RIEGER SYNDROME

DESCRIPTION In the majority of cases, this is an autosomal dominant syndrome. It is manifested by ocular anomalies; maxillary hypoplasia; broad, flat nasal root; microdontia or anodontia; deafness; mental retardation; heart defects; and GU anomalies in the form of hypospadias. An association with Down syndrome and Marfan syndrome has also been reported.

REFERENCE

Henkind P, et al. Mesodermal dysgenesis of the anterior segment: Rieger's anomaly. Arch Ophthalmol 1965;73:810.

RIFLE CRITERION FOR ACUTE RENAL INJURY

DESCRIPTION RIFLE criteria grades 3 levels of 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/hr for 6 hr
- Injury: 2× increase in creatinine or 50% GFR decrease or urine output <0.5 mL/kg/hr for 12 hr
- Failure: 3× increase in creatinine or 75% GFR decrease or urine output of <0.5 mL/kg/hr for 24 hr, or anuria for 12 hr
- Loss: Complete loss of kidney function (eg, renal replacement therapy necessary) for >4 wk
- ESRD: Complete loss of kidney function (eg, renal replacement therapy necessary) for >3 mo.

The RIFLE criteria is correlated with prognosis, with a stepwise increase in the risk of death in patients who met the RIFLE criteria for various stages of acute kidney injury. Compared to patients without acute kidney injury, patients in the RIFLE stages of risk, injury, and failure had increased mortality risks of 2.4, 4.15, and 6.37 respectively. (See also Section II: “Acute Kidney Injury [AKI].”)

REFERENCE

Bellomo R, et al. Acute renal failure–definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8(4):R204.

RIM SIGN (RIM NEPHROGRAM)

DESCRIPTION A radiographic appearance in which only a thin peripheral rind of renal tissue is visible. This condition occurs as a result of marked thinning of the parenchyma due to end-stage obstructive atrophy, and it usually denotes irretrievable renal function.

REFERENCE

Bedon WE, et al. Hydronephrosis in infants and children: Value of high dosage excretory urography in predicting renal salvageability. AJR 1970;109:380.

ROBINOW SYNDROME

DESCRIPTION An autosomal dominant disease characterized by small genitalia (genital hypoplasia), cryptorchidism, flat face, and short forearms. The gene for the autosomal recessive form is the ROR2 gene on chromosome 9q22.

REFERENCE

Patton MA, Afzal AR. Robinow syndrome. J Med Genet 2002;39(5):305–310. Review.

ROBSON STAGING SYSTEM

DESCRIPTION Robson's modification of Flocks and Kadesky's staging system for renal cell carcinoma was the most commonly used in the US. The fact that long-term evaluation of patients with stage IIIA lesions, without disease extension into perinephric fat and lymph nodes, has shown survivals comparable to those of stages I and II, has currently led many investigators to prefer the TNM system prosed by IUAC. (See Section I: "Renal Cell Carcinoma, General"; Section VII: "TNM Kidney.")

- 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 area (including adrenal).
- Stage IIIA: Tumor involves the renal vein or inferior vena cava.
- Stage IIIB: Tumor involves regional lymph nodes.
- Stage IIIC: Tumor involves both local vessels and regional lymph nodes.
- Stage IVA: Tumor involves adjacent organs other than the adrenals (colon, pancreas, etc.).
- Stage IVB: Distant metastasis.

REFERENCE

Robson CJ, Churchill BM, Andreson W. The results of radical nephrectomy for renal cell carcinoma. Trans Am Assoc Genitourin Surg 1968;60:122.

ROKITANSKY-KUSTER-HOUSER SYNDROME

DESCRIPTION Absence of the vagina, with abnormal or absent uterus; the condition is usually discovered during evaluation of a normal-appearing girl who presents with failure of menstruation at the time of expected puberty. Renal agenesis and skeletal anomalies are common. Müllerian agenesis is the cause. In some patients, cyclic abdominal pain suggestive of some functional endometrium is noted. Vaginal reconstruction with bowel or skin grafting is performed.

REFERENCE

Griffin JE, et al. Congenital absence of the vagina. The Mayer-Rokitansky-Kuster-Houser syndrome. Ann Intern Med 1976;85:224.

ROSEWATER SYNDROME

DESCRIPTION An infertility disorder associated with germ cell aplasia. On testicular 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.

REFERENCE

Craig JM. The pathology of infertility. Pathol Ann 1975;10:299.

ROVSING POLYCYSTIC KIDNEY OPERATION

DESCRIPTION A procedure that entails multiple unroofing of kidney cysts. This procedure does not prevent deterioration of renal function but may improve flank pain if the cysts cause obstruction of the collecting system.

REFERENCE

Novick AC, Streem AB. Surgery of the kidney. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:3055–3056.

ROVSING SYNDROME

DESCRIPTION This is a symptom complex associated with horseshoe kidney, in which the patient experiences pain, nausea, and vomiting on hyperextension of the spine, due to compression of the isthmus of the fused kidney on the vena cava and aorta, accentuated by hypertension and accompanied by a sensation of fullness.

REFERENCE

Glenn JF. Analysis of 51 patients with horseshoe kidney. N Engl J Med 1959;261:684.

SHORT TOPIC SECTION S

SACRAL NEUROMODULATION

DESCRIPTION Sacral neuromodulation (SNM) is a 2nd-line treatment for refractory lower urinary tract dysfunction, such as nonobstructive chronic urinary retention, urgency-frequency syndrome (overactive bladder), and urgency incontinence. A continuous or cycling mode of electrical pulses to activate or inhibit neural reflexes associated with lower urinary tract function via stimulation of the sacral nerves, which innervate the lower urinary tract and pelvic floor. The mechanism of action is unclear. One theory is that indirect stimulation of the pudendal nerve and direct inhibition of the preganglionic neurons, which suppress detrusor over activity and therefore improve symptoms. An alternate theory is that stimulation may inhibit involuntary reflex voiding by altering the transmission of sensory input from the bladder to the pontine micturition center, inhibiting ascending afferent pathways but not the descending pathways. In the patient with nonobstructive urinary retention, SNM most likely causes an inhibition of the guarding reflex, with a reduction in sphincteric over activity that may reduce bladder outlet and urethral resistance.

Patients should have failed conservative management with medications and or behavioral therapies and should undergo extensive evaluation including urodynamics. The procedure involves implantable, programmable device that delivers a pulse low amplitude stimulation to the sacral nerves (interStim). The procedure is typically performed in 2 stages. Percutaneous placement of the electrode is performed under fluoroscopic guidance near the S3 foramina. Position is tested by either verbal response from the patient or motor responses, such as tightening of the levators or a bellows response in the anal area as well as plantar flexion of the great toe. During a 1–3-wk trial, the electrode is connected to an external generator and the patient maintains a log of their voiding pattern. If improvement is noted (usually >50%), a permanent generator can be implanted.

REFERENCE

1. Leng W, Morrisore S. Sacral nerve stimulation for the overactive bladder. Urol Clin N Am 2006;33(4):491–501.

SCABIES, UROLOGIC CONSIDERATIONS

DESCRIPTION An intensely pruritic parasitic infection that affects simultaneous areas of the body, including the genitalia, anus, legs, hands, umbilicus, and axillae. Diagnosis can be made by identifying the mite (Sarcoptes scabiei), expressed from the papular or linear burrow-like lesion. Transmission occurs from fomites or by direct contact with infected individuals, including sexual contact.

TREATMENT

- Lindane 1% cream, washed off after 8 hr. Do not use in pregnant or lactating women or in children <2 yr.
- Permethrin 5% cream, washed off after 8–14 hr
- Crotamiton 10% cream for 2 consecutive nights; wash off 24 hr after the 2nd application.
- Treat sex partners and close contacts.

REFERENCE

2. Peterson CM, Eichenfeld LF. Scabies. Pediatr Ann 1996;25(2):97–100.

SCARDINO-PRINCE PYELOPLASTY

DESCRIPTION An inverted J-configured incision is started on the anterior surface of the pelvis and brought down across the UPJ obstruction to a 1–2-cm point beyond the obstruction. The upper apex of the flap is then flipped down to the apex of the ureterotomy, where a 5-0 chromic stay suture is placed. The medial aspect of the flap is sutured to the lateral edge of the ureterotomy. The lateral edge of the flap is sutured to the lateral aspect of the ureterotomy, and the pelvis is closed. Used to treat UPJ obstruction.

REFERENCE

3. Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:220–233.

SCHILLER-DUVAL BODIES

DESCRIPTION Perivascular papillary structures seen in histologic specimens of yolk sac tumors, similar to the endodermal sinuses of Duval in the placenta of the rat.

REFERENCE

4. Moran CA, Suster S. Hepatoid yolk sac tumors of the mediastinum: A clinicopathologic and immunohistochemical study of four cases. Am J Surg Pathol 1997;21(10):1210–1214.

SCHISTOSOMIASIS, UROLOGIC CONSIDERATIONS

DESCRIPTION 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, hematogenous migration to perivesical venous plexus, transmural migration into bladder, and shedding into urine. Typically, patients will exhibit polypoid urothelial mucosal lesions (active infection) or "sandy patch" flat, tan lesions (inactive infection). 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 old); this is most commonly squamous cell carcinoma (60–90%) and adenocarcinoma (5–15%). The presence of fluke eggs in urinary sediment is diagnostic of schistosomiasis.

TREATMENT

- Medical management: Metrifonate and praziquantel
- Surgical management: Infection refractory to medical management; ureteral or bladder outlet obstruction; persistent or refractory hematuria; or malignancy

REFERENCE

5. Michaud DS. Chronic inflammation and bladder cancer. Urol Oncol 2007;25(3):260–268. Review.

SCHWANNOMA, RENAL

DESCRIPTION Also called neurinoma or neurilemmoma, a tumor arising from Schwann cell neural elements of the kidney. Treatment is surgical removal of the tumor; radiotherapy or chemotherapy is of unknown efficacy.

REFERENCE

6. Romics I, Bach D, Beutler W. Malignant schwannoma of the renal capsule. Urology 1992;40(5):453–455.

SCLERODERMA, UROLOGIC CONSIDERATIONS

DESCRIPTION Scleroderma (systemic sclerosis) is a systemic, acquired disorder of connective tissue, including cutaneous sclerosis, visceral organ fibrosis, and vascular lesions. The condition commonly affects kidneys, with renal disease affecting 10–50% of patients. Lower urinary tract manifestations are also reported, including bladder fibrosis, microscopic hematuria, urodynamic abnormalities, and poor compliance and obstructive uropathy. Lower urinary tract symptoms include urinary urgency, frequency, and incontinence.

REFERENCE

7. Lally EV, et al. Pathologic involvement of the urinary bladder in progressive systemic sclerosis. J Rheum 1985;12:778–781.

SCLEROSING ADENOSIS OF THE PROSTATE

DESCRIPTION Also called pseudoadenomatoid tumor, part of histologic differential diagnosis of prostate cancer. Small glands with a proliferative stroma may be seen in needle biopsy or TUR specimens, and these have been misdiagnosed as cancer. The specimen will be immunoreactive with S-100 and smooth muscle actin, indicating a myoepithelial differentiation. Other features differentiating this condition from cancer are that cells have bland nuclei and are sometimes surrounded by a hyaline-like sheath. (See also Section II: “Atypical Adenomatous Hyperplasia of the Prostate and Post-atrophic Hyperplasia of the Prostate.”)

REFERENCE

8. Epstein JI. Non-neoplastic diseases of the prostate. In: Bostwick D, et al. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

SCROTAL PEARLS (SCROTOLITHS)

DESCRIPTION Benign calcifications within the scrotum, usually free floating. Usually diagnosed by US, these are described as a hyperechoic density in the scrotal wall that demonstrates acoustic shadowing. Scrotal pearls can occur from infection or trauma. They may also be noticed as artifacts after torsion of the appendix testis or epididymis.

REFERENCE

9. Chen P, John S. Ultrasound of the acute scrotum. Appl Radiol 2006;35(3):8–17.

SCROTUM, ACCESSORY AND ECTOPIC

DESCRIPTION Accessory scrotum is a rare condition in which a small empty pouch of scrotal tissue is attached to the scrotum or the perineum. Ectopic scrotum is an anomalously positioned hemiscrotum usually found near the external inguinal ring. The testis generally accompanies the hemiscrotum to its abnormal position and may be normal or dysplastic. These lesions are often accompanied by other GU anomalies (upper tract). Surgical repair involves an attempt to bring down the scrotum and the testis. If the gonad is dysplastic and the ectopic scrotum is rudimentary, removal of 1 or both structures is reasonable.

REFERENCE

Kumar V, et al. Unilateral inguinal ectopic scrotum with covered exstrophy. Pediatr Surg Int 2002;18(5–6):511–513.

SCROTUM, BIFID

DESCRIPTION A disorder characterized by separation of the labioscrotal folds, seen with mid scrotal or perineal hypospadias and intersex disorders. Embryologically, a failure of the genital swellings to fuse at the midline. The condition represents a spectrum of penoscrotal transposition abnormalities (see Section II: “Scrotum, Engulfment [Penoscrotal Transposition].”) Surgical realignment at the midline and hypospadias repair is recommended management.

REFERENCE

Sule JD, et al. Perineal lipoma and the accessory labioscrotal fold: An etiological relationship. J Urol 1994;151(2):475–477.

SCROTUM, ENGULFMENT (PENOSCROTAL TRANSPOSITION)

DESCRIPTION The most extreme form of penoscrotal transposition, in which the scrotum is located in a cephalad position with respect to the penis. A milder form is bifid scrotum. Major renal anomalies include complete agenesis of the urinary system, unilateral or bilateral renal agenesis, polycystic or dysplastic kidneys, horseshoe kidney, ectopic pelvic kidney, and obstructive uropathy. Abnormalities of the external genitalia include a disproportionately long flaccid penis, complete urethral atresia, and hypospadias. Treated by hypospadias repair with scrotoplasty using an inverted omega skin incision around the scrotal skin and the base of the penis. This allows placement of the scrotal flaps beneath the penis.

REFERENCE

Parida SK, et al. Penoscrotal transposition and associated anomalies: Report of five new cases and review of the literature. Am J Med Genet 1995;59(1):68–75.

SCROTUM, EPIDERMAL INCLUSION CYST

DESCRIPTION Epidermal (epidermoid) 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 cheesy material that is a combination of keratin and cholesterol, often in a laminated configuration arising from a stratified squamous epithelial wall. They can be asymptomatic or more commonly rupture or become infected. Local excision is the treatment, since epidermoid inclusion cysts can mimic rare malignant tumors such as liposarcoma, fibrosarcoma, and even metastatic disease.

REFERENCE

Yang WT, et al. Extratesticular epidermal cyst of the scrotum. AJR Am J Roentgenol 2004;183:1084.

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 testis. If the diagnosis is made with US and shows the classic presentation, conservative management can be employed.

REFERENCE

Donohue A, Utley WLF. Idiopathic fat necrosis in the scrotum. Br J Urology 2008;47(3):331–333.

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

Fernandez MJ, Martino A, Khan H, et al. Giant neurilemmoma: Unusual scrotal mass. Urology 1987;30(1):74–76.

SCROTUM, HEMANGIOMA

DESCRIPTION These lesions should be differentiated from angiokeratoma of Fordyce that appear in older men (see also Section II: “Angiokeratoma of Fordyce [Penile and Scrotal Angiokeratomas]”). Scrotal hemangiomas are rare benign vascular lesions of the scrotum that can be seen in ~1% of newborns. Cutaneous hemangiomas (also called strawberry angiomas) may grow for up to 6 mo and then undergo involution such that most do not need therapy. Subcutaneous hemangiomas are even more infrequent but tend to expand gradually and may clinically resemble a varicocele.

TREATMENT

- Large cutaneous lesions can be excised surgically or ablated with a laser.
- Most smaller lesions can be expected to involute over time.
- Subcutaneous lesions usually require surgical excision.

REFERENCE

Alter GJ, Trengove-Jones G, Horton CE Jr. Hemangioma of the penis and scrotum. Urology 1993;42(2):205–208.

SCROTUM, HYPOPLASIA

DESCRIPTION The unilateral or bilateral underdevelopment of the scrotum, which simulates labia majora, this condition is most commonly associated with cryptorchid testes and ambiguous genitalia.

TREATMENT

- A testicular prosthesis can improve the cosmetic appearance of the scrotum.
- Testosterone cream can also be applied for an improved cosmetic result on the affected side.

REFERENCE

Maat-Kievit A, Brunner HG, Maaswinkel-Mooij P. Two additional cases of the Ohdo blepharophimosis syndrome. Am J Med Genet 1993;47(6):901–906.

SCROTUM, IDIOPATHIC CALCINOSIS

DESCRIPTION Patients with this condition are typically young men who present with multiple hard nodules throughout the scrotal wall. Although the skin is usually intact, lesions may ulcerate. Thought to be caused by calcification of the scrotal dermal connective tissue (eccrine sweat glands) for unknown reasons. No therapy is necessary unless recurrent episodes of infection occur; then surgical excision may help.

REFERENCE

Yahya H, Rafindadi AH. Idiopathic scrotal calcinosis: A report of four cases and review of the literature. Int J Dermatol 2005;44(3):206–209. Review.

SEAPI INCONTINENCE CLASSIFICATION SYSTEM

DESCRIPTION SEAPI is an acronym for stress incontinence, emptying ability, anatomy, protection, and instability. Is useful as a reliable and uniform method of following the short- and long-term outcome of SUI surgery. This system is similar to the TNM tumor staging classification system in that each component is graded with a score from 0 (no symptoms) to 3 (severe symptoms). After completion of the evaluation of the incontinent patient, a preoperative subjective and objective SEAPI score is determined. These scores are then compared with postoperative SEAPI scores to access treatment outcome.

REFERENCE

Raz SR, Erickson DR. SEAPI QMM incontinence classification system. Neurourol Urodyn 1992;11:187.

SEBORRHEIC DERMATITIS

DESCRIPTION Commonly referred to as dandruff, this condition can be seen on the penis, anus, or pubic hair. Itching is the rule, with the lesions in hair-bearing areas having a red base and waxy yellow crust. While the organism Pityrosporon orbiculare is suspected, the exact agent is unknown.

TREATMENT

Standard antidandruff 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.

REFERENCE

Margolis DJ. Cutaneous diseases of the male external genitalia. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998.

SEMEN ANALYSIS, ABNORMAL FINDINGS AND TERMINOLOGY

DESCRIPTION A significant overlap exists between fertile, subfertile, and infertile populations, therefore, absolute parameters for infertility (except for aspermia or azoospermia) are difficult to measure precisely. In general, fertile populations demonstrate mean sperm densities of 70–80 million/mL. Assisted reproductive technologies are now able to overcome many of these abnormalities. (See also Section I: “Infertility”; Section II: “Semen Analysis, Technique, and Normal Values.”)

SYNONYMS

- Aspermia: No semen ejaculated
- Asthenospermia: <50% of spermatozoa with forward progression of 3–4
- Asthenozoospermia: Poor motility and/or poor forward progression
- Azoospermia: No spermatozoa found in semen
- Globozoospermia: Round-headed sperm devoid of acrosome
- Hematospermia: Blood present in an ejaculate/semen
- Hyperspermia: Volume of ejaculate >6.5 mL
- Hypospermia: Volume of ejaculate <1.5 mL
- Leukocytospermia/pyospermia: Excess white cells (>1 WBC × 106/mL) in semen
- Necrozoospermia: No live sperm in ejaculated semen
- Oligoasthenoteratospermia: Very generalized abnormalities in sperm concentration, motility, and morphology; often associated with varicocele
- Oligoasthenoteratozoospermia: Signifies disturbance of all 3 variables (combinations of 2 prefixes may also be used)
- Oligozoospermia: Low concentration of sperm <20 × 106/mL
- Polyspermia: Abnormally high sperm density (>250 × 106/mL)
- Polyzoospermia: Excessive number of sperm in ejaculate sample
- Pyospermia/leukocytospermia: Excess white cells (>1 WBC × 106/mL) in semen
- Teratozoospermia: Reduced percentage of morphologically normal sperm, usually <50% spermatozoa with normal morphology

REFERENCE

Gilbert BR, Cooper GW, Goldstein M. Semen analysis in the evaluation of male factor subfertility. AUA Update Series, Vol. XI, Lesson 32, 1992.

Grimes DA. Oligozoospermia, azoospermia, and other semen-analysis terminology: The need for better science. Fertil Steril 2007;88(6):1491–149.

Rowe PJ, et al., eds. WHO manual for the standardized investigation, diagnosis and management of the infertile male. New York: Cambridge University Press, 2000.

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 as close to body temperature as possible and delivered to the lab within 1.5 hr. Analysis includes (may vary slightly by laboratory) total seminal volume, sperm concentration, sperm motility, 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 displacements. 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 I: “Infertility”; and Section II: “Semen Analysis, Abnormal”; also see Section II for topics on specific semen abnormalities.)

Typical Reference Laboratory Values for Routine Semen Analysis

Volume

1.5–5.0 mL

Appearance

White, viscid, opaque

pH

7.2–7.8

Sperm density

>20 × 105/mL

Total sperm count

>40 × 106/mL

Motility

>60%

Forward progression

>50% or >2 + on a scale of 0–4 (0 no movement, 4 excellent forward progression)

Morphology

>60% normal

Viability

>50% (by dye exclusion)

Fructose, quantitative

>13 mol per ejaculate

Liquefaction

10–20 min (measured on a scale of 0–4)

Agglutination

Minimal clumping (increased clumping suggests inflammatory/immunologic process)

Normal Semen Analysis Parameters Published by the WHO

Parameter

Minimum Value

Volume

2.0 mL

Sperm concentration

20 million/mL

Motility

50%

Forward progression

3 (0–4)

Normal morphology (WHO)

30%

Normal morphology (Strict)

14%

Total sperm count

40 million

Total motile sperm

20 million

Total functional sperm

6 million

Based on data from Rowe PJ, et al., eds. WHO manual for the standardized investigation, diagnosis and management of the infertile male. New York: Cambridge University Press, 2000.

REFERENCE

McLachlan RI, et al. Semen analysis: Its place in modern reproductive medical practice. Pathology 2003;35(1):25–33.

SEMEN LEUKOCYTES

DESCRIPTION The leukocyte is the most common non–sperm cell seen in 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 sample (>1 WBC × 106/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 I: “Infertility”; Section II: “Semen Analysis, Abnormal Findings and Terminology”; “Semen Analysis, Technique, Normal Values and Pyospermia.”)

REFERENCE

Agarwal A, Bragais FM, Sabanegh E. Assessing sperm function. Urol Clin N Am 2008;35:157–171.

SEMINAL VESICLE AGENESIS

DESCRIPTION Can be unilateral or bilateral (very rare). Unilateral agenesis results from an embryologic insult before separation of the ureteral bud from the mesonephric ducts. Unilateral agenesis is associated with ipsilateral agenesis of the ductus deferens and with renal agenesis in 79%, ipsilateral renal abnormalities in 12%, and only 9% had normal kidneys bilaterally. The contralateral seminal vesicle is often hypoplastic.

REFERENCE

Trigaux JP, et al. Male genital tract malformations associated with ipsilateral renal agenesis: sonographic findings. J Clin Ultrasound 1991;19:3–10.

SEMINAL VESICLE, AMYLOIDOSIS

DESCRIPTION A benign localized condition characterized by subepithelial deposition of amyloid in the seminal vesicles. Amyloid are low-molecular-weight fibrils found in extracellular tissues; they consist of a variety of proteins. Its incidence increases with increased age and can often be misinterpreted as regional spread of bladder or prostate cancer. No treatment is necessary if asymptomatic.

REFERENCE

Erbersdobler A. Seminal vesicle amyloidosis does not provide any protection from invasion by prostate cancer. BJU Int 2009;103(3):324–326.

SEMINAL VESICLE, CARCINOMA

DESCRIPTION Primary tumors of the seminal vesicles are rare and the seminal vesicles are commonly 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; these patients typically have a normal PSA but elevate CEA levels. Sarcomas (leiomyosarcoma, angiosarcoma, and Müllerian adenosarcoma-like tumor) are aggressive and have distinct features seen only on biopsy. Carcinoid tumor is another rare malignancy. Radical prostatectomy and/or cystoprostatectomy including pelvic lymph node dissection, offers curative treatment. Adjuvant or neoadjuvant chemotherapy is of unproven worth, but a combination of hormonal deprivation and radiotherapy seems to be more effective than any chemotherapy.

REFERENCE

Möhring C, et al. A primary adenocarcinoma of the seminal vesicles. Case report of a rare malignancy. Urologe A 2008;47(5):616–619.

SEMINAL VESICLE, CYSTS

DESCRIPTION Cysts, of either congenital or acquired origin, located in the seminal vesicles. Many studies in the past have linked such cysts to other GU issues, including renal agenesis, infertility, hematospermia, GU infection, and adult polycystic kidney disease. Causes are congenital, ejaculatory duct obstruction, or a basement membrane defect, especially in cysts associated with adult polycystic kidney disease.

TREATMENT

- No treatment is necessary if asymptomatic.
- Aspiration, marsupialization, or excision, if symptomatic

REFERENCE

Labanaris AP, et al. A case of a large seminal vesicle cyst associated with ipsilateral renal agenesis. Sci World J 2008;8:400–404.

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 penile, scrotal, or perineal pain; painful ejaculation; hematospermia; lower abdominal or back pain; and lower urinary tract symptoms. Diagnosis is often one of exclusion of other more common causes made with positive cultures from the ejaculate as well as imaging via transrectal US, CT, or MRI. Pyospermia/leukocytospermia 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. (See also Section II: “Pyospermia.”)

REFERENCE

Zeitlin SI, et al. Seminal vesiculitis. In: Nickel JC, ed. Textbook of Prostatitis, 1st ed. Informa HealthCare, 1999.

SEMINOMA, ANAPLASTIC

DESCRIPTION Histological subtype of seminoma, seen in up to 10% of all seminomas. Anaplastic seminoma is typically more aggressive and invasive compared to classic and spermatocytic seminoma, demonstrating increased mitotic activity and more -hCG production than its counterparts. It is associated with increased local invasion and rate of metastatic growth as well. Patients usually present at a higher stage. Despite these findings, no survival difference after treatment has been reported when compared to classic seminoma, stage for stage. Treatment depends on tumor stage. Radical orchiectomy followed by either surveillance, radiation therapy, and/or chemotherapy are performed, depending on the extent of disease. (See also Section I: “Testis, Seminoma.”)

REFERENCE

Neill M, et al. Management of low-stage testicular seminoma. Urol Clin N Am 2007;34(2):127–136.

SEMINOMA, CLASSIC

DESCRIPTION The most common histologic subtype of seminomatous germ cell tumors, accounting for ~85% of cases. Typically presents in males in the 3rd–5th decades of life. Syncytiotrophoblastic elements are seen in 10% of lesions. These elements produce -hCG, which can be used as a tumor marker to help assess resolution or recurrence of disease after treatment. Like all testicular tumors, treatment depends on tumor stage. Radical orchiectomy followed by either surveillance, radiation therapy, and/or chemotherapy are performed, depending on the extent of disease. (See also Section I: “Testis, Seminoma.”)

REFERENCE

Neill M, et al. Management of low-stage testicular seminoma. Urol Clin N Am 2007;34(2):127–136.

SEMINOMA, SPERMATOCYTIC

DESCRIPTION Accounts for ~2% of all seminomatous germ cell tumors. 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 line, which likely contributes to its more favorable presentation. Due to its low metastatic potential, no further treatment is often recommended after radical orchiectomy. (See also Section I: “Testis, Seminoma.”)

REFERENCE

Neill M, et al. Management of low-stage testicular seminoma. Urol Clin N Am 2007;34(2):127–136.

SEX REVERSAL SYNDROME (XX MALE)

DESCRIPTION These patients demonstrate small, firm testes; frequent gynecomastia; a small to normal penis; and azoospermia. Testicular biopsy may demonstrate seminiferous tubule sclerosis, causing elevated gonadotropins and decreased testosterone levels. Individuals are shorter than average height. There is no increase in the incidence of mental retardation, but there is an increase in hypospadias. Although karyotyping demonstrates 46XX, molecular biologic mapping suggests that portions of the Y chromosome are present. It has been hypothesized that the portion of the Y chromosome containing the testes-determining factor has been translocated. Diagnosis is based on karyotype, molecular biologic mapping, and PCR using Y-specific probes. If necessary, phenotypic gender assignment is done very early, and appropriate surgical correction is performed. After puberty, management is more difficult because of androlologic problems such as hypogonadism, micropenis, undescended testes, lack of secondary sex characteristics, and impotence. Treatment plans must address these issues.

REFERENCE

Yamamoto M, et al. A case of sex reversal syndrome with sex-determining region. Nagoya J Med Sci 1995;58(3–4):111–115.

SEXUAL ANHEDONIA/EJACULATORY ANHEDONIA

DESCRIPTION Lack of appropriate pleasure from sexual activity. Patients typically elicit a failure of genital response. Men have difficulty initiating or sustaining an erection; 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 selective serotonin reuptake inhibitors have been reported to cause this phenomenon as well.

REFERENCE

Hatzimouratidis K, Hatzichristou D. Sexual definitions: Classifications and definitions. J Sex Med 2007;4(1):241–250.

Ralph DJ, Wylie KR. Ejaculatory disorders and sexual function. BJU Int 2005;95(9):1181–1186.

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 (see Section VII). It addresses the relevant domains of male sexual function: Erectile function (EF), orgasmic function (OF), sexual desire (SD), intercourse satisfaction (IS), and overall satisfaction. EF is represented in items 1, 2, 3, 4, 5, and 15 of the questionnaire, with a score range of 0 (or 1) to 5, a minimum score of 1, and a maximum score of 30. OF is represented in items 9 and 10, with a score range of 0–5, a minimum score of 0, and a maximum score of 10. SD is represented in items 11 and 12, with a score range of 1–5, a minimum score of 2, and a maximum score of 10. IS is covered in items 6, 7, and 8, with a score range of 0–5, a minimum score of 0, and a maximum score of 15. OS is covered in items 13 and 14, with a score range of 1–5, a minimum score of 2, and a maximum score of 10. In general, the lower the score, the worse the erectile function. (See Section VII: “Survey Instrument.”)

REFERENCE

Rosen RC, et al. I: The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822–830.

SEXUAL HEALTH INVENTORY FOR MEN (SHIM) SCORE

DESCRIPTION The SHIM, sometimes called International Index of Erectile Function (IIEF-5), is a validated questionnaire that assesses male sexual function and can be used as an adjunct for the assessment and treatment of ED. This is an abridged version of the original 15-question IIEF questionnaire. The SHIM questionnaire consists of 5 questions pertaining to the quality of the patient's erections and sexual satisfaction over the last 6 mo. Each question is graded on a scale from 1–5. ED is then assessed based on the cumulative value of the SHIM score: 22–25, no ED; 17–21, mild ED; 12–16, mild to moderate ED; 8–11, moderate ED; 5–7, severe ED. (See Section VII for the SHIM Instrument.)

REFERENCE

Rosen RC, et al. 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(6): 319–326.

SIGNET RING CARCINOMA, PROSTATE

DESCRIPTION A rare. high-grade neoplasm that carries a poor prognosis. A GI primary tumor should be considered with this pathology. Immunohistochemical exam demonstrates cytoplasmic immunoreactivity to prostate-specific antigent in signet-ring cancer cells, with intracytoplasmic vacuoles in the signet-ring cells staining positively for mucous with periodic acid-Schiff. This malignancy is more aggressive than other cell types; >50% of these patients die within a year of diagnosis.

REFERENCE

Matsuoka Y, et al. Primary signet-ring cell carcinoma of the prostate. Can J Urol 2007;14(6):3764–3766.

SILBER VASOEPIDIDYMOSTOMY

DESCRIPTION In 1978, Silber was the first to report the use of the microscope to perform a vasoepididymostomy. The distal epididymis is cut and, with aid of the microscope, the tubule exuding semen is identified. The freshly cut mucosal lumen of the vas deferens is anastomosed to this tubule, and the adventitia of the vas is then anchored to the epididymal tunic. The procedure is used in selected cases of obstructive infertility.

REFERENCE

Thomas AJ. Vasovasostomy. In: Novick AC, Streem SB, Pontes JE., eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:767–773.

SKENE (PARAURETHRAL) GLAND ADENOCARCINOMA

DESCRIPTION Extremely rare; primary urethral carcinoma is present in <0.1% of all urogenital cancers in females. Adenocarcinomas account for 10% of these urothelial cancers. Presence of PSA in tissue and/or serum confirms a Skene gland origin, due to its homology to the male prostate. Only 6 cases have been reported in literature. PSA levels normalize after treatment. Complete excision, using a technique similar to repair of urethral diverticulum, is curative.

REFERENCE

Pongtippan A, et al. Skene's gland adenocarcinoma resembling prostatic adenocarcinoma. Int J Gyn Pathol 2004;23(1):71–74.

SKENE (PARAURETHRAL) GLAND, INFLAMMATION/ADENITIS

DESCRIPTION Skene glands are homologous to the male prostate gland and are located along the anterior vaginal wall, adjacent to the urethral meatus. These glands may become infected and present as a tender, fluctuant periurethral nodule. Infection or inflammation of the Skene glands can cause exquisite tenderness and may be associated with dyspareunia and vulvar vestibulitis. The most common pathogen is Neisseria gonorrhea. Treatment includes culture 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.

REFERENCE

Metts JF. Vulvodynia and vulvar vestibulitis: Challenges in diagnosis and management. Am Fam Physician 1999;59(6):1547–1556.

SKIN TAGS, EXTERNAL GENITALIA (ACROCHORDON, PEDUNCULATED PAPILLOMA)

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 hyperpigmented and are more common on obese individuals. Usually asymptomatic, these lesions are often found in skin folds (neck, axillae, groin) and rarely involve the external genitalia. They may accompany hamartomatous skin lesions (fibrofolliculomas and trichodiscomas) associated with 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 cosmesis or irritation, then the tags may be treated by electrocautery, simple scissor excision, suture ligation of the base, or cryotherapy.

REFERENCE

Emir L, Ak H, Karabulut A, et al. A huge unusual mass on the penile skin: Acrochordon. Int Urol Nephrol 2004;36(4):563–565.

SLEEP APNEA, UROLOGIC CONSIDERATIONS

DESCRIPTION Patients with obstructive sleep apnea may have their condition exacerbated by testosterone replacement therapy; 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. Obstructive sleep apnea may also be involved with nocturia and daytime overactive bladder in women.

REFERENCE

Hanafy HM. Testosterone therapy and obstructive sleep apnea: Is there a real connection? J Sex Med 2007;4(5):1241–1246.

Lowenstein L, et al. The relationship between obstructive sleep apnea, nocturia, and daytime overactive bladder syndrome in women. Am J Obstet Gynecol 2008;198(5):598.e1–5.

SLING MATERIALS

DESCRIPTION Slings, usually mid-urethral, are a common option for the treatment of intrinsic sphincteric deficiency. Sling materials are either autologous, allografts, xenografts, or synthetic. (See also Section I: “Incontinence, Female”; “Incontinence, Male”; Section II: “Urethral Sling.”)

- Autologous grafts (harvested at the time of surgery):
  - Rectus fascia
  - Fascia lata
  - Vaginal wall
  - Round ligament
  - Dermis
- Allografts (processed by freeze-drying or solvent dehydration):
  - Cadaveric fascia
  - Cadaveric dermis
- Xenografts:
  - Porcine dermis
  - Porcine small intestinal submucosa
- Synthetic slings:
  - MarlexTM
  - Gore-TexTM
  - Silicone
  - Transvaginal tape (polypropropylene mesh)

REFERENCE

Wilson TS, Lemack GE, Zimmern PE. Management of intrinsic sphincteric deficiency. J Urol 2003;169(5): 1662–1669.

SMEGMA

DESCRIPTION A substance composed of desquamated cells that originate from the epithelium of the glans penis and on the inner surface of the foreskin. Smegma is composed of 26% fat and 13% protein. It remains unclear whether smegma is only desquamated epithelial cells or whether secretions from preputial glands at the coronal sulcus contribute to smegma. The issue of smegma carcinogenicity is still controversial. Some believe that phimosis allows for retention of smegma, which is an irritant that produces malignant transformation of the epithelium by direct contact. 50% of men harbor Mycobacterium smegmatis in the preputial sac; this organism has been implicated in the conversion of sterols in smegma into carcinogenic compounds. Good puerperal hygiene is recommended if uncircumcised.

REFERENCE

Maden C, Sherman KJ, Beckmann AM, et al. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. J Natl Cancer Inst 1993; 85(1):19–24.

SMITH-LEMLI-OPITZ SYNDROME

DESCRIPTION An autosomal recessive multisystemic disease found in newborns that present with hypospadias and cryptorchidism. Anomalies in other systems include pernicious anemia, mental retardation, syndactyly, renal abnormalities, and microcephaly. These patients have an inborn error of cholesterol biosynthesis (defect of 5,7-sterol, 7-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

Jira P, Wevers R, de-Jong, et al. Treatment of Smith-Lemli-Opitz syndrome. Am J Med Genet 1997; 68(3):311–314.

SOAP-BUBBLE NEPHROGRAM

DESCRIPTION Caused by end-stage obstruction atrophy, this is a radiographic appearance of the dilated pyelocalyceal system in which overlapping curved, white densities several millimeters in thickness appear after IV or intraarterial injection of contrast material. Dilated calyces are represented by bubbles, and remnants of Bertin columns appear as thin opacities between adjacent calyces.

REFERENCE

Ransley PG. Opacification of the renal parenchyma in obstruction and reflux. Pediatr Radiol 1976;4:226.

SPERM GRANULOMA

DESCRIPTION Sperm granulomas form from the testicular end of the vas 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 post vasectomy, is diagnostic.

TREATMENT

- When chronic postvasectomy pain is localized to the sperm granuloma, the lesion should be excised and occluded with electrocautery.
- Postvasectomy congestive epididymitis may be relieved with open-ended vasectomy, which will produce a pressure-relieving sperm granuloma.

REFERENCE

Awsare NS, et al. Complications of vasectomy. Ann R Coll Surg Engl 2005;87(6):406–410.

SPERM PENETRATION ASSAY (SPA; HAMSTER TEST)

DESCRIPTION Also called hamster oocyte penetration test (and in some publications Humster 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. This assay requires the sperm to be able to undergo capacitation, the acrosome reaction, fusion with the oolemma, and incorporation into the ooplasm. If sperm penetration is 10–30%, the sample is considered normal, but this bioassay 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 laboratory performing this test. Although there are controversies surrounding SPA, it is a test that should be performed for unexplained infertility.

REFERENCE

Aitken RJ. Sperm function tests and fertility. Int J Androl 2006;29(1):69–75.

SPERM VITALITY

DESCRIPTION Also referred to as sperm viability or sperm motility, this is one 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 I: “Infertility”; Section II: “Semen Analysis, Technique, and Normal Values.”)

REFERENCE

Cooper TG, Hellenkemper B. Method-related estimates of sperm viability. J Androl 2009;16. Epub ahead of print.

SPERMATIC CORD, LIPOSARCOMA

DESCRIPTION Rare paratesticular tumor that is often mistaken for hydrocele, cord lipoma, or incarcerated hernia. Patients usually present with painless paratesticular swelling. Tumors as large as 50 cm have been reported. The majority of tumors are well differentiated. Late recurrences and metastases may be seen, particularly with high-grade lesions. Radical orchiectomy with high ligation of spermatic cord, similar to surgical management of testicular tumors, is the treatment. Wide local excision may be required to ensure complete tumor removal. Radiation therapy may be required in cases of incomplete resection leaving residual tumor or extensive local disease. (See also Section I: “Spermatic Cord Mass and Tumors.”)

REFERENCE

Bouropoulos C, et al. Liposarcoma of the spermatic cord. Int Urol Nephrol 2001;33(2):397–398.

SPINA BIFIDA/SPINA BIFIDA OCCULTA, UROLOGIC CONSIDERATIONS

DESCRIPTION Spina bifida is a birth defect that results in the incomplete closure of the embryologic neural tube, leading to incomplete development of the spinal cord and vertebrae. This usually involves the lumbar and sacral areas. As a result, many patients develop a neurogenic bladder dysfunction requiring long-term urologic care. Although 90% of patients born with spina bifida have normal upper urinary tracts, over 1/2 of these patients will show signs of renal deterioration if no urologic intervention is performed. Spina bifida occulta is the mildest 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 aggressive 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 urodynamic study (UDS) is also performed during this period to evaluate bladder compliance, detrusor pressures, capacity, leak pressures, contractions, and sphincter dyssynergia. Some institutions recommend prophylactic antibiotics and clean intermittent catheterization (CIC) until the neonate’s first UDS. Patients with poorly compliant bladders with elevated filling pressures (typically above 40 cm H_2O) are in danger of upper tract deterioration and are typically started on CIC and anticholinergic therapy. If a patient fails conservative medical therapy, surgical procedures such as intravesical botulinum toxin 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 I: “Myelodysplasia (Spinal Dysraphism), Urologic Considerations.”)

REFERENCE

Joseph DB. Current approaches to the urologic care of children with spina bifida. Curr Urol Rep 2008;9(2):151–157.

SPINAL CORD COMPRESSION, UROLOGIC CONSIDERATIONS

DESCRIPTION Epidural spinal cord compression, if 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. Vertebral 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 paralysis. 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. 46% of patients survive <6 mo, and 20% <2 mo. (See also Section I: “Spinal Cord Injury, Urologic Considerations.”) Diagnosis is based on findings of CT and MRI.

TREATMENT

- Glucocorticoids, high-dose steroids 100 mg IV then 24 mg IV every 6 hr for 3 days, then taper
- Orchiectomy, high-dose ketoconazole (200–400 mg PO t.i.d.) or LHRH antagonist (degarelix) to rapidly reduce serum testosterone if hormone naïve
- External radiation therapy with or without vertebrectomy (note decompressive laminectomy has not been as successful as vertebrectomy with spinal stabilization, as most disease is located anterior to the spinal cord)

REFERENCE

Kuban DA, et al. Characteristics of spinal cord compression in adenocarcinoma of prostate. Urology 1986;28(5):364–369.

Patchell RA, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: A randomised trial. Lancet. 2005;366(9486):643–648.

SPINAL SHOCK

DESCRIPTION After acute spinal cord injury, 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 resolves. Treatment is supportive during this period of detrusor areflexia. Clean internittent catheterization (CIC) is the recommended means of emptying the bladder, although an indwelling Foley catheter may be another alternative. (See also Section I: “Spinal Cord Injury, Urologic Considerations.”)

REFERENCE

Watanabe T, Rivas DA, Chancellor MB. Urodynamics of spinal cord injury. Urol Clin N Am 1996;23(3):459–473.

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 (splenocolic, splenorenal, splenophrenic) with the kidney and other nearby organs and structures. The splenic artery can be found crossing the upper pole of the left kidney, dividing into segmental 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; pancreatitis or pancreatic fistula formation; and pleural effusion.

REFERENCE

Merchant A, et al. Management of intraoperative splenic injury. Operative Techniques Gen Surg 2008;10(1):4–10.

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 gonad 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. One-third of all reported cases are associated with other congenital abnormalities, especially peromelia. The majority of cases present with scrotal mass or scrotal tenderness. Some are found incidentally during herniorrhaphy or orchidopexy. Although evaluation is usually done in the operating room, a technetium99 colloid liver spleen scan can easily identify splenic tissue in the scrotum if splenogonadal fusion is suspected preoperatively. Scrotal US does not help to diagnosis 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 the continuous variety, exploratory laparotomy is necessary to identify the anatomy involved and deal with the continuous cord.

REFERENCE

Gouw AS, et al. The spectrum of splenogonadal fusion. Case report and review of 84 reported cases. Eur J Pediatr 1985;144(4):316–323.

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 splenic pulp in the abdominal or thoracic cavities. Hematogenous spread has also been reported. Patients are asymptomatic, and the discovery of splenosis is usually incidental on imaging studies. Splenosis in the abdominal cavity has been mistaken for primary malignancies, such as primary renal cell carcinoma. Similarly, thoracic splenosis can mimic metastatic urologic 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

Fremont RD, Rice TW. Splenosis, a review. South Med J 2007;100(6):589–593.

SQUAMOUS METAPLASIA, GENITOURINARY

DESCRIPTION The replacement of normal urothelium by mature squamous epithelium. Nonkeratinizing squamous metaplasia is thought to be a normal variant in premenopausal women, occurring under hormonal influence. This form is commonly found in the trigone; cystoscopically, 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 catheters, a bladder stone, vesical schistosomiasis; long-term observation is warranted for the development of squamous carcinoma of the bladder.

SYNONYMS

- Pseudomembranous trigonitis
- Vesical leukoplakia

TREATMENT

Transurethral resection ablation and biopsy in cases of keratinizing squamous metaplasia

REFERENCE

Ahmad I, et al. Keratinizing squamous metaplasia of the bladder: A review. Urol Int 2008;81(3):247–251.

STAMEY PROCEDURE (URETHROPEXY)

DESCRIPTION Stamey was the first to report the use of the cystoscope to aid in the performance of a transvaginal urethropexy. In addition, the nonabsorbable sutures that are placed with a needle carrier incorporate a Dacron pledget to buttress the suture at the level of the bladder neck. Used to treat stress incontinence in women; of the patients who have undergone this procedure, 82% of 192 were improved, and 65% of the 192 would be willing to undergo the procedure again. Another study showed that although the Stamey procedure has a high early success rate, the long-term results were poor. After 5 yr, only 18% of 28 women remained dry. Concomitant abdominal hysterectomy, respiratory disease, and obesity were likely to point to a lower long-term cure rate. Possible complications include long-term erosion of sutures into the urinary tract and long-term urinary retention if sutures are tied too tightly.

REFERENCE

O'Sullivan DC, et al. Should Stamey colposuspension be our primary surgery for stress incontinence? Br J Urol 1995;75(4):457–460.

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 origin of RBCs or bacteria. Although this method is effective in localizing the cause 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 (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, urethral and prostatic infection can be differentiated by comparing the bacterial colony counts of VB1 and prostatic (EPS and VB3) counts. In urethral 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× dilution of prostatic fluid. When the bladder urine is infected, the infection cannot be localized, 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-/post-prostatic massage urine sample. The pre-massage and post-massage 2-glass test has strong concordance with the 4-glass test and is a reasonable alternative when expressed prostatic secretions are not obtained. The technique and diagnosis algorithm is discussed in Section I: “Prostatitis, General.”

REFERENCE

Meares EM, Stamey TA. The diagnosis and management of bacterial prostatitis. Br J Urol 1972;44(2):175–179.

Nickel JC, et al. How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4–glass test in men with chronic prostatitis/chronic pelvic pain syndrome? J Urol 2006;176(1):119–124.

STAUFFER SYNDROME

DESCRIPTION A syndrome associated with nonmetastatic hepatic dysfunction commonly seen in cases of renal cell carcinoma. Symptoms include fever, fatigue, and weight loss. The patient has unusual liver function tests, WBC loss, and areas of hepatic necrosis without hepatic metastasis. The presence of hepatic dysfunction should not be a contraindication to surgery. Hepatic function usually returns to normal after nephrectomy. If the syndrome persists, it is a sign of recurrent tumor. Diagnostic indicators are elevation of alkaline phosphatase and bilirubin, hypoalbuminemia, prolonged PTT, and hypergammaglobulinemia.

REFERENCE

Jacobi GH, Philipp T. Stauffer's syndrome: Diagnostic help in hypernephroma. Clin Nephrol 1975;4(3): 113–115.

STEINSTRASSE

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 ureteroscopic lithotripsy.

REFERENCE

Weinerth JL, et al. Lessons learned in patients with large Steinstrasse. J Urol 1989;142:1425.

STING PROCEDURE

DESCRIPTION Subureteric Teflon injection (called STING) is performed to correct vesicoureteral reflux. Pyrolyzed Teflon particles suspended in glycerin are injected deep into the ureter. Because migration of these Teflon particles to the pelvic lymph nodes, liver, lung, and brain has been demonstrated in laboratory models, other substances, such as collagen, may be used. The success rate is inferior to that of open surgery. About 70% have reflux resolution after 1 procedure. With repeat Sting procedures, the success rate increases to 90–95%.

REFERENCE

Aubert D, et al. Sting procedure in the treatment of secondary reflux in children. Eur Urol 1990;17(4):307–309.

STRANGURIA

DESCRIPTION Slow, painful, spasmodic expulsion of urine in a drop-wise fashion, usually occurring at the end of micturition (also called strangury or terminal dysuria) due to spasm of the bladder and urethra. Associated with an irritative process in the GU system, it often refers pain to the urethral meatus. Cause include cystitis, granulomatous disease, prostatitis, urethritis, cowperitis, and lower urinary tract malignancy. The term is not commonly used in human medicine, but is firmly entrenched in veterinary medicine.

REFERENCE

Brendler CB, Gerber GS. Evaluation of the urologic patient. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007.

STREAK GONAD

DESCRIPTION Patients with streak gonad usually present with female phenotype, primary amenorrhea, infantile breast status, sparse pubic and axillary hair, infantile external genitalia and vagina, atrophic vaginal smear, immature uterus, 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 II: “Gonadal Dysgenesis, Mixed and Pure.”)

TREATMENT

- Management includes laparotomy with excision of any intraabdominal testis or streak gonads. These masses progress to malignancies, which may develop before puberty.
- Female sex assignment and reconstructive surgery are advised in cases with severely deficient virilization of the genitalia.

REFERENCE

Calabrese F, Valente M. Mixed gonadal dysgenesis: Histological and ultrastructural findings in two cases. Int J Gynecol Pathol 1996:15(3):270–275.

STRICKLER URETERAL ANASTOMOSIS

DESCRIPTION Through an extracolonic approach, a small linear incision is made in the taenia, and a small clamp is used to create a submucosal 3–4-cm tunnel exiting out of the colon laterally. The ureter is delivered through the tunnel, the spatulated end is anastomosed to the mucosa, and the taenia is closed while incorporating ureter adventitia.

REFERENCE

McDougal WS. Use of intestinal segments and urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3137–3144.

STRUVITE

DESCRIPTION The mineral name for magnesium ammonium phosphate hexahydrate stones. (See also Section I: “Urolithiasis, Staghorn.”)

REFERENCE

Healy KA, Ogan K. Pathophysiology and management of infectious staghorn calculi. Urol Clin N Am 2007;34(3):363–374.

STUDER POUCH

DESCRIPTION An orthotopic neobladder is made, based on 60 cm of marsupialized ileum, which is configured and sutured into a W to create a broad intestinal plate. In addition, a non-tubularized segment of ileum extends from a limb of the W, simulating a chimney. The ureters are implanted into the chimney. The intestinal plate is anastomosed to the urethra and then closed into a sphere.

REFERENCE

Colombel M, et al. A procedure for bladder replacement using a low-pressure ileal reservoir. Ann Urol (Paris) 1993;27(1):36–41.

SUPERFICIAL INGUINAL POUCH OF DENIS-BROWNE

DESCRIPTION A superficial inguinal pouch is defined as the space distal to the internal inguinal ring, but above the inguinal canal, between the external oblique fascia and Scarpa fascia. Studies suggest that a testis in the superficial inguinal pouch is, in reality, a cryptorchid testis.

REFERENCE

Herzog B, et al. Is a testis located at the superficial inguinal pouch (Denis-Browne pouch) comparable to a true cryptorchid testis? J Urol 1992;148(2 Pt 2):622–623.

SUPERNUMERARY KIDNEY

DESCRIPTION Supernumerary kidney is a rare condition in which a free accessory renal organ exists as a distinct entity, with its own blood supply, and the presence of 2 normal kidneys. It is distinguished by its small size and/or abnormal position. The kidney is either a component of a bifid 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.

REFERENCE

N'Guessan G, Stephans FO. Supernumerary kidney. J Urol 1983;130:649.

SUPINE STRESS TEST

DESCRIPTION Nonurodynamic method to test for intrinsic sphincteric deficiency, it is performed by placing the patient in lithotomy position and filling the empty bladder with 200 cc saline under gravity. The patient is then asked to cough and perform a Valsalva 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 a relatively quick and inexpensive test that has a sensitivity of 93.5% and specificity of 90.0%.

REFERENCE

Hsu TH, et al. The supine stress test: A simple method to detect intrinsic urethral sphincter dysfunction. J Urol 1999;162(2):460–463.

SWYER SYNDROME (XY SEX REVERSAL)

DESCRIPTION A type of pure gonadal dysgenesis; girls with Swyer syndrome have usual XY male chromosomes. Patients have bilateral streak gonads and often present as adolescent phenotypic females with delayed puberty. A 46XY genotype may develop rapid breast or clitoral enlargement due to hormonally active gonadoblastomas within the streak gonads. (See also Section II: “Gonadal Dysgenesis [Mixed and Pure].”)

REFERENCE

Moreira-Filho CA, et al. H-Y antigen in Swyer syndrome and the genetics of XY gonadal dysgenesis. Hum Genet 1979;53(1):51–56.

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE (SIADH)

DESCRIPTION SIADH is the most frequent cause of hyponatremia. The condition usually results when plasma levels of antidiuretic hormone or arginine vasopressin are elevated when normal physiologic secretion of vasopressin from the posterior pituitary should be suppressed, causing a euvolemic hypo-osmolar hyponatremia. There are many causes of this syndrome of inappropriate diuresis, which include malignancies (such as small-cell lung cancer, cancers of the GI tract, lymphoma), pulmonary diseases (pneumonia, TB, cystic fibrosis, asthma), disorders of the CNS (neurologic diseases as well as infection, bleeding, or trauma-related), and drugs. Intranasal desmopressin (DDAVP) to treat nocturnal enuresis can be associated with this condition. Acute management requires evaluation of the clinical status of the patient, assessment of the type of hyponatremia, and treatment based on the degree of hyponatremia. After the patient is stabilized, treatment can then be focused on determining the underlying cause of SIADH. If possible, removal or treatment of the underlying cause can result in full resolution. Long-term treatment consists of fluid restriction and possible use of pharmacologic agents such as demeclocycline (causes a nephrogenic diabetes insipidus) or vasopressin receptor antagonists.

REFERENCE

Ellison DH, Berl T. The syndrome of inappropriate antidiuresis. N Engl J Med 2007;356(20):2064–2072.

SYSTEMIC LUPUS, UROLOGIC 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 biopsy 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. Urine sediment typically shows >5 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. Rarely, certain medications (eg, anti-TNF therapy (infliximab and etanercept), chlorpromazine, diltiazem, hydralazine, interferon-, isoniazid (INH), minocycline, penicillamine, quinidine, methyldopa, procainamide) can cause drug-induced SLE. Mild forms are not treated, but more severe forms are treated with cytotoxic agents (cyclophosphamide therapy) and prednisone. Renal replacement may be needed in the most severe forms.

REFERENCE

Waldman M, Appel GB. Update on the treatment of lupus nephritis. Kidney Int 2006;70(8):1403–1412.

SHORT TOPIC SECTION T

TABES DORSALIS

DESCRIPTION Tertiary syphilis involving the dorsal spinal roots and posterior spinal column. This condition can present with voiding dysfunction, presumably due to loss of bladder sensation, with high residual volumes and urinary retention. Urodynamic evaluation reveals detrusor atony and detrusor areflexia. (See Section I: “Syphilis.”)

SYNONYMS

- Neurosyphilis
- Tabetic bladder
- Tertiary syphilis

TREATMENT

- Penicillin for syphilis
- Clean intermittent catheterization for bladder atony

REFERENCE

1. Erturk E, et al. Voiding dysfunction in tertiary syphilis. Urology 1987;30(3):284–286.

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, 69% of penile fractures are due to this mechanism and were encountered at an average of 1 per wk. Treated as described in Section I: “Penis, Trauma.”

REFERENCE

2. Zargooshi J. Penile fracture in Kermanshah, Iran: Report of 172 cases. J Urol 2000;164(2):364–366.

TAKAYASU ARTERITIS, UROLOGIC CONSIDERATIONS

DESCRIPTION An inflammatory disease of unknown etiology affecting the aorta and its main branches, causing stenosis or aneurysmal dilation of the affected vessels. Involvement of renal arteries might lead to renovascular hypertension. The disease is progressive and difficult to manage; it is often treated by angioplasty.

REFERENCE

3. Kumar S, et al. Percutaneous transluminal angioplasty in non-specific aortoarteritis (Takayasu's disease): Experience in 16 cases. Cardiovasc Intervent Radiol 1990;12:321.

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 abdominal wall)

Stage 2: Sparse 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

Stage 4: Hair is adult in type, but covering smaller area than in adult; no spread to medial surface of thighs

Stage 5: Adult in type and quantity, with horizontal distribution (feminine type)

External genitalia (boys)

Stage 1: Prepubertal

Stage 2: Enlargement of scrotum and testes; scrotum skin reddens and changes in texture

Stage 3: Enlargement of penis (length at first); further growth of testes

Stage 4: Increased size of penis, with growth in breadth and development of glans; testes and scrotum larger, scrotum 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

REFERENCE

4. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969; 44(235):291–303.

5. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child 1970; 45(239):13–23.

TERATOMA, SACROCOCCYGEAL, UROLOGIC CONSIDERATIONS

DESCRIPTION Sacrococcygeal tumors are usually diagnosed in the neonate (1 in 40,000 births) and less frequently in infants or adults. Females are more affected than males. Clinical presentation is usually in the form of palpable mass, skin discoloration, or hairy nevus. Related diseases include bilateral hydronephrosis, neurologic deficit, bladder or bowel dysfunction (obstruction or incontinence), high-output cardiac failure, or fetal hydrops. Sacrococcygeal tumors of the newborn and young adults are generally benign, whereas those discovered during infancy have a 50% chance of being malignant. Wide, local excision of the tumor is primary management.

REFERENCE

6. Okada T, et al. Management and outcome in prenatally diagnosed sacrococcygeal teratomas. Pediatr Int 2008;50(4):576–580.

TESTICULAR FEMINIZATION SYNDROME

DESCRIPTION Now commonly described as complete androgen insensitivity syndrome, this syndrome involves phenotypic women with a 46XY karyotype and normal development of testes in utero, but with a genetic defect in the androgen receptor that leads to insensitivity to androgens. (See also Section II: “Androgen Insensitivity Syndrome.”)

REFERENCE

7. Conn J, et al. Revealing the diagnosis of androgen insensitivity syndrome in adulthood. BMJ 2005;331(7517):628–630.

TESTICULAR PROSTHESIS

DESCRIPTION Prosthetic device implanted in the scrotum to help cope with the psychological distress of losing a testicle from torsion, malignancy, trauma, or agenesis. Studies have shown that the improved cosmetic result increases patient self-esteem, body image, and sexual function. Implants were typically made of silicone rubber filled with silicone gel until 1995, when they were taken off the US market due to concerns about the association of silicone and connective tissue disease. Currently, in the US, the testicular prosthetic of choice is comprised of a silicone rubber shell filled with saline to achieve desired size and consistency. Implantation is fairly simple and well tolerated. The most common major complication reported was extrusion of the implant, occurring in 2%; the most common minor complication was postoperative discomfort or pain, occurring in 9% of patients.

REFERENCE

8. Turek PJ, Master VA, and the Testicular Prosthesis Study Group. Safety and effectiveness of a new saline filled testicular prosthesis. J Urol 2004;172(4):1427–1430.

TESTIS, CARCINOID

DESCRIPTION Carcinoid tumors of the testis 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-hydroxyindoleacetic acid (5-HIAA), a metabolite of serotonin. Carcinoid 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. Carcinoid tumors of the testis can be divided into 3 groups: Primary, metastasis from a primary site, or carcinoid tumor originating from a testicular teratoma. Most patients present with a painless scrotal mass; unlike germ cell tumors, there is no predilection for a particular age group. ~16% of patients have carcinoid syndrome. Tumors localized to the testis have an excellent prognosis; however long-term follow-up is needed, due to risk of late metastases.

As with all testicular neoplasms, treatment begins with radical orchiectomy, with high-ligation of the spermatic cord. Chemotherapy or radiation therapy has been reported, but these treatment modalities have poor efficacy. Octreotide analogues have been reported to stabilize disease progression, as well as help relieve symptoms of carcinoid syndrome. Once discovered, other extratesticular sources of carcinoid tumor should be determined. 5-HIAA can be measured in the urine and can be a useful adjunct. GI endoscopy, CT scan, MIBG scintigraphy, or somatostatin receptor scintigraphy can be used to search for GI sources of carcinoid tumor.

REFERENCE

9. Stroosma OB, Delaere KP. Carcinoid tumours of the testis. BJU Int 2008;101(9):1101–1105.

TESTIS, CARCINOMA IN SITU (CIS)/INTRATUBULAR GERM CELL NEOPLASIA (ITGCN)

DESCRIPTION Testicular CIS is considered to be the precursor to all germ cell tumors, 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 cancer. Risk factors for testicular CIS are cryptorchidism, contralateral testis cancer, extragonadal germ cell tumor, infertility, and intersex patients with a Y chromosome. There is controversy concerning the screening, management, and treatment of testicular CIS. Diagnosis is made through testis biopsy. Treatment options involve surveillance, radiation, and orchiectomy. Cisplatin-based chemotherapy has been associated with incomplete irradiation or recurrence. High-risk patients may be offered testicular biopsy and subsequent treatment, 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 fact that effective treatment of germ cell tumors exist. Radiation (14–20 Gy) may be performed in the patient with a testicular tumor 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 cryopreserve sperm should be offered as well. (See also Section II: “Testis, Microlithiasis.”)

REFERENCE

Hoei-Hansen CE, et al. Carcinoma in situ testis, the progenitor of testicular germ cell tumours: A clinical review. Ann Oncol 2005;16(6):863–868.

TESTIS, CYSTS

DESCRIPTION Non-neoplastic testicular cysts include hydatid, epidermoid, simple, and cystic dysplasia. These are very rare lesions and are generally clinically interpreted as neoplastic, until proven otherwise at the time of post-orchiectomy pathology. Hydatid cysts are rarely seen, except in the Middle East.

REFERENCE

Kumar PVN, Johanshahi SL. Hydatid cyst of testis: A case report. J Urol 1987:137:511.

TESTIS, DERMOID CYST

DESCRIPTION A primary non–germ cell tumor representing 1% of testis tumors, with half of the patients presenting in their 20s. Grossly, the lesions present as encapsuled intratesticular nodules, which are round and sharply circumscribed, with firm consistency. The cut surface reveals a grayish white, cheesy, amorphous mass. The microscopic picture is that of dense fibrous tissue lined by stratified squamous keratinized epithelium with degeneration and macrocalcification. The benign behavior of these tumors is the rule. These are categorized separately from mature testicular teratoma because of the malignant nature of the latter in postpubertal patients. Testicular US may aid in this tumor's differentiation from germ cell tumor. Most cases have been managed by radical orchiectomy, although local excision has been equally successful in a small number of patients.

REFERENCE

Ulbright TM, et al. Dermoid cyst of the testis: A study of five postpubertal cases, including a pilomatrixoma-like variant, with evidence supporting its separate classification from mature testicular teratoma. Am J Surg Pathol 2001;25(6):788–793.

TESTIS, LEUKEMIA

DESCRIPTION Of children with acute lymphoblastic leukemia (ALL), 5% will develop testicular disease at initial presentation or at first relapse. The testis is a common site of primary relapse (8%) after treatment of ALL. Children with T-cell lymphoblastic leukemia and/or a high initial leukemia cell burden are at higher risk of initial testicular involvement, as well as of testicular relapse. The condition commonly presents as either unilateral or bilateral testicular painless mass or swelling. Diagnosis is made with testicular biopsy.

Irradiation of both testes with 18–24 Gy plus systemic chemotherapy is the standard recommended treatment. Orchiectomy may be considered, depending on the extent of infiltration.

REFERENCE

Gutjahr P, Humpl T. Testicular lymphoblastic leukemia/lymphoma. World J Urol 1995;13(4): 230–232.

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 orchiectomy. Bilateral involvement occurs in ~50% of cases (10% are synchronous). Treatment is multimodal; orchiectomy is performed, followed by systemic chemotherapy (doxorubicin), CNS prophylaxis, and local radiation.

REFERENCE

Vitolo U, et al. Primary testicular lymphoma. Crit Rev Oncol Hematol 2008;65(2):183–189.

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 common primary malignancies are prostate, lung, GI tract, melanoma, and kidney cancers.

REFERENCE

Rosevear HM, et al. Unusual Scrotal pathology: An overview. Nat Rev Urol 2009; epub ahead of print.

TESTIS, MICROLITHIASIS

DESCRIPTION Numerous and diffuse calcifications throughout the entire testicle seen on US. It is reported in undescended testicles (0.3% incidence), prepubertal Klinefelter syndrome, and male pseudohermaphroditism, and is slightly more common in prepubertal males. Infertility and malignancy have been reported to be associated with the condition, and some consider it possibly premalignant. Both seminomas and nonseminomatous germ cell tumors have been described in association with microlithiasis. Others suggest an association with carcinoma in situ of the testicle, but this is not settled. Many advocate close surveillance of patients with testicular microlithiasis, such as yearly testicular US, physical exam, and judicious tumor marker determinations.

REFERENCE

Furness PD III, et al. Multi-institutional study of testicular microlithiasis in childhood: A benign or premalignant condition? J Urol 1998:160(3 Pt 2): 1151–1154.

TESTIS, NORMAL SIZE

DESCRIPTION Testis size measurements can be made by US (most accurate) or Prader orchidometer. 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 4.5–5.5 cm with a volume ranging from 15–30 cm3.

REFERENCE

Krone KD, Carroll BA. Scrotal ultrasound. Radiol Clin N Am 1985;23:121–139.

Keefer JR. Endocrinology. In: Siberry GK, Iannone R, eds. Harriet Lane Handbook, 15th ed. St. Louis: Mosby, 2000.

TESTIS, RETRACTILE

DESCRIPTION A testicle that can ride high in the scrotum or near the external inguinal ring; caused by a brisk cremasteric reflex. The testicle is able to be gently manipulated into the scrotum. Usually considered a variant of normally descended testes, 32% of retractile testes may ultimately become undescended (ascending or acquired undescended), and this is seen more frequently in boys <7 yr old. Boys with retractile testes should be followed annually until the outcome of descent or nondescent is clear, which in many cases won’t be until puberty.

REFERENCE

Agarwal PK, et al. Retractile testis: Is it really a normal variant? J Urol 2006;175(4):1496.

TESTIS, SEX CORD STROMAL TUMORS

DESCRIPTION These tumors arise from the supporting structures of the testis and not the germ cells. They usually present as a mass, are rarely hormonally active, and do not produce tumor markers such as hCG. Leydig cell tumors comprise about 3% of testicular neoplasms. They occur in both adults (80% of cases) and children. Sertoli cell tumors (<1% of testicular tumors) can be found in children and middle-aged adults, and ~10% can be malignant. Granulosa cell tumor is usually found in older men and can present with gynecomastia. The testicular juvenile granulosa cell tumor is the most common neoplasm of the testis in the 1st 6 mo of life (yolk sac tumors peak after 6 mo). Other tumors sometimes placed in this category include malignant mesothelioma of the tunica vaginalis, paratesticular rhabdomyosarcoma, and adenocarcinoma of the rete testis.

REFERENCE

Young RH. Sex cord-stromal tumors of the ovary and testis: Their similarities and differences with consideration of selected problems. Mod Pathol 2005;18:S81–S98.

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. Theories include a displacement of primitive germ cells that takes place during early embryonic migration from the yolk sac endoderm, and pluripotential cells that persist in sequestered primitive rests during early somatic development. Histologically, all types of germ cell tumors are represented, with pure seminoma accounting for half of mediastinal and retroperitoneal tumors. Clinically, males are affected more often than females, with the exception of sacrococcygeal tumors, where females predominate. 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 vascular obstruction. Tumors of the pineal gland usually present in children and young adults, with symptoms of increased intracranial pressure, oculomotor dysfunction, hearing loss, hypopituitarism, or hypothalamic disturbances.

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 (a CSF shunt may be required).

REFERENCE

Garnick MB, et al. Treatment and surgical staging of testicular and primary extragonadal germ cell cancer. JAMA 1983:250:1733.

TESTOSTERONE (FREE AND TOTAL) LABORATORY TESTING

DESCRIPTION Measurement of serum testosterone is most commonly used as the initial test for hypogonadism in males; it is less commonly used in the evaluation of virilism and hirsutism in females. Testosterone assays are recommended to be drawn from 8 AM to 10 AM, due to higher morning plasma levels from the typical male circadian rhythm. In males, increased testosterone levels can be found in complete androgen resistance (testicular feminization syndromes). Decreased levels occur in hypogonadism, surgical orchiectomy, estrogen or LHRH analogue or antagonist therapy, Klinefelter syndrome, hypopituitarism, and hepatic cirrhosis:

- Normal ranges (may vary by lab):
  - Prepubertal children: 5–20 ng/dL (0.17–0.7 nmol/L)
  - Men (17 yr): 300–1000 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) of <200 ng/dL (or 6.9 nmol/L) (American Association of Clinical Endocrinologists) or <300 ng/dL (or 10 nmol/L) (FDA) 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 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.

REFERENCE

Miner MM, Sadovsky R. Evolving issues in male hypogonadism: Evaluation, management, and related comorbidities. Cleve Clin J Med 2007;74:(Suppl 3)S38–S46.

TESTOSTERONE REPLACEMENT FOLLOWING RADICAL PROSTATECTOMY

DESCRIPTION Both prostate cancer and hypogonadism become more prevalent as men age; up to 20% of men who undergo radical prostatectomy are found to be hypogonadal. Patients with hypogonadism may have decreased muscle mass, erectile dysfunction, osteopenia, decreased libido, depression, and impaired cognitive function. Studies have shown that testosterone replacement therapy does not increase the risk of prostate cancer development in men with both normal and increased risk. In addition, post-prostatectomy testosterone replacement does not correlate with biochemical recurrence or increases in PSA. Testosterone replacement may help to preserve erectile function and improve quality of life, but the supplementation of testosterone in hypogonadal men after treatment for prostate cancer remains controversial.

REFERENCE

Khera M, Lipshultz LI. The role of testosterone replacement therapy following radical prostatectomy. Urol Clin N Am 2007;34(4):549–553.

TETHERED CORD

DESCRIPTION Tethered cord is an acquired or congenital occurrence that results from tissue attachments causing restriction of the normal movement of the spinal cord. It is most often seen in patients with spina bifida or meningomyelocele who have undergone surgical closure of the spine. This may result in scar tissue formation that adheres to the spinal cord. Patients may also present with a congenital tethered cord, mostly seen in patients with spina bifida occulta. As the child moves or grows, the tethered spinal cord is stretched, causing direct trauma to the cord, as well as compromising blood flow by stretching blood vessels. Tethering may also occur after spinal cord injury when scar tissue prevents fluid flow around the cord. This causes pressure to build up, as well as cyst formation. The degree of tethering and strain placed on the spinal cord is correlated to severity and time of presentation of symptoms. The constellation of symptoms caused by a tethered cord is called tethered cord syndrome. (See also Section II: “Spina Bifida/Spina Bifida Occulta, Urologic Considerations”; “Tethered Cord Syndrome.”)

REFERENCE

Agawalla PK, et al. Tethered cord syndrome. Neurosurg Clin N Am 2007;18(3):531–547.

TETHERED CORD SYNDROME

DESCRIPTION Late sequelae of spinal dysraphism, in which fixation or scarring of the spinal cord and conus medullaris, due to prior spinal surgery, prevents normal cephalad migration of spinal cord with childhood growth and causes spinal cord ischemia. Usually manifests with changes in voiding pattern, or with neurologic or musculoskeletal deficits. Urodynamic evaluation typically reveals detrusor hyperreflexia or detrusor areflexia. Detrusor-external sphincter dyssynergia or poor detrusor compliance with elevated bladder pressure can also be seen and warrant aggressive intervention. MRI is usually diagnostic. (See also Section I: “Myelodysplasia [Spinal Dysraphism].”)

TREATMENT

- Surgery to untether spinal cord
- Urologic intervention, based on urodynamic findings

REFERENCE

Palmer LS, Richards I, Kaplan WE. Subclinical changes in bladder function in children presenting with nonurologic symptoms of the tethered cord syndrome. J Urol 1998;159(1):231–234.

THIERSCH-DUPLAY HYPOSPADIAS REPAIR

DESCRIPTION The distal urethral plate is tubularized to advance the meatus. The glans is reapproximated over the repair. Thiersch urethroplasty is the most commonly performed technique after surgical correction of penoscrotal transposition.

REFERENCE

Sunay M, et al. Our 21-year experience with the Thiersch-Duplay technique following surgical correction of penoscrotal transposition. Urol Int 2009;82(1):28–31.

THOMPSON PYELOPLASTY

DESCRIPTION A surgical procedure used when insufficient renal pelvis is available to close lesions due to trauma or scarring. A triangular flap of renal capsule is sharply developed, then flipped over onto the renal pelvic opening and closed with 5-0 chromic sutures.

REFERENCE

Kay R. Procedures for ureteropelvic junction obstruction. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:220–233.

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. Aside from the ectopic location, the renal anatomy is essentially normal; the kidney is usually not malrotated. The ureter may be longer due to its higher position, however it inserts into the bladder orthotopically. Similarly, the renal vessels usually arise from their normal origins, although in some cases they may insert in a position more cranially. The vast majority of patients are asymptomatic. (See also Section I: “Renal Ectopia.”)

REFERENCE

Donat SM, Donat PE. Intrathoracic kidney: A case report with a review of the world literature. J Urol 1988;140(1):131–133.

TINEA CRURIS (JOCK ITCH)

DESCRIPTION Dermatophytic infection of the crural areas of the genitalia. Caused by dermatophytes Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum. Clinically, reddish brown lesions with an elevated red border can be identified in the crural area, inner thigh, and scrotum. 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. Scraping should be performed on the active border of the lesion and reveals branching septate hyphae. Differential diagnosis includes erythrasma, psoriasis, and seborrheic dermatitis. Recurrent disease is not unusual, and treatment should be aimed toward active disease rather than postinflammatory hyperpigmentation. (See also Section II: “Pruritus, External Genitalia, Male.”)

TREATMENT

- Prevent skin maceration by keeping skin dry.
- Apply antifungal agents on overt lesions. Agents include Lotrimin, Mycelex, Loprox, Spectazole, Lamisil, and others for up to 14 days.
- Rarely, oral agents may be needed if topical agents fail: Ketoconazole (Nizoral) for 14 days (requires baseline laboratory monitoring CBC, LFTs)

REFERENCE

Geer DL. An overview of common dermatophytes. J Am Acad Dermatol 1994;31:S112.

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 (for example, every 1 hr); the time between voids is then slowly increased, usually until he or she establishes an acceptable period (usually 2–4 hr) of continence.

REFERENCE

Wallace SA, et al. Bladder training for urinary incontinence in adults. Cochrane Database Syst Rev 2004;(1):CD001308.

TRANSESOPHAGEAL ECHOCARDIOGRAM (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

Zini L. Renal cell carcinoma associated with tumor thrombus in the inferior vena cava: Surgical strategies. Ann Vasc Surg 2005;19(4):522–528.

TRANSSEXUALISM, UROLOGIC CONSIDERATIONS

DESCRIPTION Transsexualism, also known as gender identity disorder, is the strong desire to be and also identify with the opposite sex, which includes the desire to change the body hormonally and/or surgically to be similar to the aspired sex. This disorder causes severe impairment and distress. Treatment is multidisciplinary, and starts with an evaluation with an experienced mental health professional to discuss initiating hormonal and/or surgical procedures that are long-term and irreversible. Consultation with plastic surgeons, urologists, and gynecologists in high-volume centers is essential. Genital sex reassignment surgeries are available for male-to-female patients, and involve clitoroplasty, vulvuloplasty, and vaginoplasty. However, no consensus operative standard has been agreed upon regarding female-to-male reassignments, particularly regarding neophallus creation.

REFERENCE

Sohn M, Bosinski HA. Gender identity disorders: Diagnosis and surgical aspects. J Sex Med 2007;4(5):1193–1207.

TRI-MIX

DESCRIPTION A custom-compounded formulation for intracorporal injection therapy of erectile dysfunction. Typically consists of prostaglandin E1 (5.88 g/mL), papaverine (18 mg/mL), and phentolamine (0.6 mg/mL).

TRICHOMONIASIS

DESCRIPTION Sexually transmitted infection caused by the protozoan Trichomonas vaginalis. It is a rare cause of nongonococcal urethritis in men, common cause of vaginitis in women (from 4–35%). It is associated with a high prevalence of coinfection with other STDs. Signs and symptoms include urethral discharge, dysuria, and the presence of neutrophils in urethral secretions. T. vaginalis has, if any, only minor influence on male fertility. In women, it can cause premature rupture of the membranes and preterm delivery, as well as tubal infertility and cervical neoplasia. Females may have an elevated vaginal pH of >4.5. A positive diagnosis is made by identification of the protozoan on wet mount (must be examined in <10–20 min). Culture on Diamond's medium may take up to 7 days; a more rapid commercial culture method is available (In Pouch T vaginalis culture system, with results in 3 days). Treatment is metronidazole 2 g PO in a single dose for patient and sexual partners. It is not considered mandatory to identify the organism in partners before treating (CDC Expedited partner therapy). (See also Section I: "Sexually Transmitted Diseases"; Section II: "Vaginal Discharge, Urologic Considerations and Vaginosis.")

References

Centers for Disease Control and Prevention. Expedited partner therapy in the management of sexually transmitted diseases. Atlanta, GA: US Department of Health and Human Services, 2006.

Sena AC, et al. Trichomonas vaginalis infection in male sexual partners: Implications for diagnosis, treatment, and prevention. Clin Infect Dis 2007; 44(1):13–22.

TRIGONITIS

DESCRIPTION Sometimes referred to as Pseudomembranous trigonitis, this is a common cause of microscopic hematuria in women. Nonkeratinized squamous epithelium is commonly seen on the trigone and bladder neck in up to 86% of women of reproductive age and in up to 75% after menopause. Considered a normal finding and distinct from squamous metaplasia, which is considered a premalignant lesion. Cystoscopically, these are pale white-grey areas with irregular borders. This condition is not seen in men, except for some reports in men receiving estrogens for prostate cancer. Treatment is not necessary. (See also Section II: “Squamous Metaplasia, Genitourinary.”)

REFERENCE

Stephenson TJ, et al. Pseudomembranous trigonitis of the bladder: Hormonal aetiology. J Clin Pathol 1989;42(9):922–926.

TRISOMY 4 P

DESCRIPTION This trisomy features hypertelorism and GU anomalies in the form of hydronephrosis, hypospadias, and undescended testes.

REFERENCE

Barakat AY, Seikaly MG, Derkaloustian VM. Urogenital abnormalities in genetic disease. J Urol 1986;136:778.

TRISOMY 8

DESCRIPTION A trisomy associated with a large, square head; a prominent forehead; widely spaced eyes; a slender body; and GU anomalies in the form of hydronephrosis, horseshoe kidney, reflux, hypospadias, and undescended testis.

REFERENCE

Mininberg D. The genetic basis of urologic disease. AUA Update Series 1992;9:218.

TRISOMY 9

DESCRIPTION This trisomy is characterized by a small cranium and GU anomalies in the form of renal hypoplasia and hypospadias.

REFERENCE

Barakat AY, Seikaly MG, Derkaloustian VM. Urogenital abnormalities in genetic disease. J Urol 1986;136:778.

TRISOMY 9 P

DESCRIPTION This trisomy produces strabismus and GU anomalies in the form of a pancake kidney and undescended testis.

REFERENCE

Barakat AY, Seikaly MG, Derkaloustian VM. Urogenital abnormalities in genetic disease. J Urol 1986;136:778.

TRISOMY 10 Q

DESCRIPTION A trisomy characterized by oval, flat face and GU anomalies in the form of hydronephrosis and small penis.

REFERENCE

Mininberg D. The genetic basis of urologic disease. AUA Update Series 1992;9:218.

TRISOMY 11 Q

DESCRIPTION A trisomy producing flat nose, wide glabella, cleft lip/palate, and micropenis.

REFERENCE

Mininberg D. The genetic basis of urologic disease. AUA Update Series 1992;9:218.

TRISOMY 13

DESCRIPTION This trisomy is associated with polydactyly, congenital heart disease, and cystic kidney.

REFERENCE

Barakat AY, Seikaly MG, Derkaloustian VM. Urogenital abnormalities in genetic disease. J Urol 1986;136:778.

TRISOMY 18 (EDWARDS SYNDROME)

DESCRIPTION A trisomy producing hypertonia and GU anomalies in the form of hydronephrosis and small penis. Hypoplasia of the labia majora may cause a false impression of a large clitoris.

REFERENCE

Barakat AY, Seikaly MG, Derkaloustian VM. Urogenital abnormalities in genetic disease. J Urol 1986;136:778.

TRISOMY 20 P

DESCRIPTION A trisomy characterized by short nose, dental abnormalities, vertebral abnormalities, and polycystic kidney.

REFERENCE

Mininberg D. The genetic basis of urologic disease. AUA Update Series 1992;9:218.

TRISOMY 21

DESCRIPTION See Section II: “Down Syndrome, Urologic Considerations.”

TRISOMY 22

DESCRIPTION A trisomy producing microcephaly, low-set ears, cleft palate, beaked nose, and microphallus.

REFERENCE

Mininberg D. The genetic basis of urologic disease. AUA Update Series 1992;9:218.

TRISOMY SYNDROME

DESCRIPTION A congenital condition characterized by the presence of 3 instead of the normal pair of homologous or sex chromosomes; these disorders often result in a wide range of phenotypical expressions, including GU anomalies. Examples include trisomy 13 and 18, which produce cryptorchidism; trisomy 4p and 9p, which produce micropenis; and trisomy 7, which is associated with sporadic papillary renal cell carcinoma.

REFERENCE

Kliegman RM. Nelson Textbook of Pediatrics, 18th ed. Philadelphia: Saunders, 2007.

TRUE HERMAPHRODITISM

DESCRIPTION One of 4 entities that comprise the spectrum of intersex abnormalities. Often presenting with ambiguous genitalia, true hermaphroditism requires expression of both ovarian and testicular tissue. This may be the result of sex chromosome mosaicism, chimerism, or Y-chromosome translocation. The most common karyotype in the US is 46,XX (with translocation); however 46,XY or 46,XX/46,XY may occur with the remaining etiologies. The common genital phenotype is ambiguous with hypospadias, cryptorchidism, and incomplete fusion of labioscrotal folds. In these individuals, gonads may be a testis on one side and an ovary on the other, an ovotestis on one side with either a testis or ovary contralaterally, or some combination thereof. (See also Section I: “Disorders of Sexual Development [DSD].”)

REFERENCE

Kolon TF, et al. A practical approach to intersex in the newborn period. Urol Clin N Am 2004;31:435–443.

TUBERCULOSIS, BLADDER AND URETHRA

DESCRIPTION The hematogenous dissemination of TB can affect entire urinary system. Bladder TB is caused by descending infection from renal TB. Urethral TB is rare and can present as periurethral fistulas and abscess. Symptoms include urinary frequency, urgency, and dysuria, with mucosal ulcerations and thickening, and diminished bladder capacity. (See also Section I: “Tuberculosis, Genitourinary.”)

DIAGNOSIS

- Urine culture of acid-fast bacilli: Typically first 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

Raghavaiah NV. Tuberculosis of the male urethra. J Urol 1979 Sep;122(3):417–418.

TUBERCULOSIS, MALE EXTERNAL GENITALIA

DESCRIPTION Rare manifestation of TB that may present as a papulonecrotic ulcer, tubercular cavernositis, or a solid nodule, which may be clinically indistinguishable from malignant disease. Diagnosis is confirmed on biopsy. Treatment is systemic antituberculous medication. (See also Section I: “Tuberculosis, Genitourinary.”)

REFERENCE

Wu WC, et al. Penile tuberculosis associated with monoclonal gammopathy of undetermined significance. J Formos Med Assoc 2006;105(9): 753–755.

TUBEROUS SCLEROSIS

DESCRIPTION An autosomal dominant disease mapped to chromosome 16 or 9 that clinically presents with a classic triad of epilepsy, mental retardation, and adenoma sebaceum. Named for the tubers or periventricular calcifications seen on CT scan. Adenoma sebaceum describes the facial angiofibromas around nasolabial regions and cheeks. The renal system may be free of anomalies or may display cysts (10%), angiomyolipomas (AML) in (40–80%), or both. AML can bleed, with increasing risk at 3.5 cm. Renal failure is a result of parenchymal compression by expanding cysts. Hypertension may also occur. Renal cell carcinoma is present in 2% of patients. (See also Section I: “Renal Angiomyolipoma.”)

SYNONYMS

- Tuberous sclerosis complex
- Bourneville disease

TREATMENT

- Absolute indications for intervention include suspicion of malignancy, hemorrhage with significant hypotension or symptoms, persistent hematuria
- Symptomatic AML or lesion >4 cm: Selective arterial embolization or nephron-sparing surgery
- Surveillance best for lesions <4 cm
- Embolization is 1st-line treatment for acute hemorrhage from AML.
- mTOR inhibitors are under study.

REFERENCE

Wong IY, Shortliffe LD. The management of renal angiomyolipomas in a patient with tuberous sclerosis. Nat Clin Pract Urol 2009;6(3):168–172.

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. Lab investigations would reveal hyperkalemia, hypocalcemia, hyperphosphatemia, and concurrent metabolic acidosis, as well as severe hyperuricemia with eventual renal failure. If these patients are being treated with allopurinol, they are at risk of acute renal failure and xanthine stone formation (See also Section II: “Nephropathy, Urate and Xanthine”; “Urolithiasis [Xanthinuria].”)

TREATMENT

- Prevention with adequate hydration (urine output of >80–100 mL/m2/hr)
- Cautious use of rasburicase; some recommend allopurinol
- Urinary alkalinization should not be done, as it may cause further precipitation of calcium phosphate in the kidney and other tissues.

REFERENCE

Coiffier B, et al. Guidelines for the management of pediatric and adult tumor lysis syndrome: An evidence-based review. J Clin Oncol 2008; 26(16):2767–2778.

TUNICA VAGINALIS TUMORS

DESCRIPTION Malignant mesothelioma of the tunica vaginalis is rare. 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, fibrous, or a combination of both. The malignant nature of the disease is indicated by its frequent mitosis, nuclear atypia with prominent nucleoli, and invasion of adjacent structures or lymphatics. Positive staining with keratin and failure to stain with carcinoembryonic antigen 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. Adjunct chemotherapy may be tried. However, its value has not been established. (See also Section I: “Scrotum and Testicle, Mass.”)

REFERENCE

Chen KTK, Arhelger RB, Flam RS, et al. Malignant mesothelioma of tunica vaginalis testis. Urology 1982;20:316.

TURNER SYNDROME (XO 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. Neonates may have lymphedema. Clinically, patients present with short stature, primary amenorrhea, webbed neck, shield-like chest, streak gonads, hypertension, and coarctation of the aorta. GU anomalies include horseshoe kidney, anomalous blood supply to the kidney, and infantile genitalia. 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-chromosome mosaicism, as these individuals are at increased risk of gonadoblastoma (germ cell tumor).

TREATMENT

- ECG at diagnosis to detect cardiovascular anomalies (coarctation 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, induction of secondary sexual characteristics, and menarche

REFERENCE

Stochholm K, et al. Prevalence, incidence, diagnostic delay, and mortality in Turner syndrome. J Clin Endocrinol Metab 2006;91(10):3897–902.

TURNER-WARWICK INLAY URETHROPLASTY

DESCRIPTION Through a midline scrotal incision, the urethral stricture is opened and scarred tissue is removed, leaving a strip of urethra in place. The edges of the scrotal incision are sutured to the urethral strip. In a second stage, the mature marsupialized urethra is tubularized with the surrounding scrotal skin and closed.

REFERENCE

Devine CJ, Devine PC. Operations for urethral stricture. In: Novick AC, Streem SB, Pontes JE, eds. Stewart's Operative Urology. Baltimore: Williams & Wilkins, 1989:550–680.

SHORT TOPIC SECTION U

UISS-UCLA INTERNATIONAL KIDNEY CANCER STAGING SYSTEM

DESCRIPTION A prognostic system for renal cell carcinoma 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

1. Patard JJ, et al. Use of the University of California Los Angeles integrated staging system to predict survival in renal cell carcinoma: An international multicenter study. J Clin Oncol 2004;22(16):3316–3322.

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 46XY karyotype and present with a spectrum of phenotypes from complete external feminization, to ambiguous genitalia, to phenotypically infertile 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. Spermatogenesis may or may not be impaired. Patients may have elevated luteinizing 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 ART.

REFERENCE

2. Gottlieb B, et al. Molecular pathology of the androgen receptor in male (in)fertility. Reprod Biomed Online 2005:42–48.

UNINHIBITED DETRUSOR CONTRACTION

DESCRIPTION Uninhibited detrusor contraction leads to an overactive bladder. Bladder overactivity can result from damage to central inhibitory pathways, sensitization of peripheral afferent 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 Section I: “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

3. Anonymous. The overactive bladder: From basic science to clinical management consensus conference. Urology 1997;50[Suppl 6A]:1–114.

URACHAL ABNORMALITIES

DESCRIPTION The urachus is a tubular connection between the allantoic stalk and the dome of the bladder. Faulty embryologic resolution of this connection results in urachal abnormalities. Microscopic 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 bladder. 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 suppuration (Latin “calor, rubor, dolor”) in the lower abdominal wall. Occasionally, a urachal cyst will present as an asymptomatic midline lower abdominal mass or tenderness.
- Patent urachus: Persistence of the urachal channel between the bladder and umbilicus; an uncommon type of urachal abnormality.
- Urachal diverticulum of the bladder: May result from drainage of a urachal cyst to the bladder; presents with UTI

Urachal carcinoma is a malignant adenocarcinoma that presents later in life. (See also Section I: “Urachal Carcinoma and Umbilical Abnormality, Urologic Considerations.”)

REFERENCE

4. Mesrobian H, et al. Ten years of experience with isolated urachal anomalies in children. J Urol 1997;158:1316.

UREAPLASMA UREALYTICUM

DESCRIPTION Common bacterial inhabitant of the lower GU tract in adult men and women who are sexually active, it can also be transmitted venereally 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. 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/d for 2 wk or a single dose of azithromycin 1 g PO. (See also Section I: “Sexually Transmitted Diseases.”)

REFERENCE

5. Frenkl TL. Sexually transmitted infections. Urol Clin N Am 2008;35(1):33–46.

URETER, AGENESIS/ATRESIA

DESCRIPTION Bilateral 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 atresia or agenesis is unilateral, it is usually asymptomatic and of no clinical significance. However, it can be associated with infection (UTI) on occasion.

REFERENCE

6. Morozumi M, et al. Distal ureteral atresia associated with crossed renal ectopia with fusion: Recovery of renal function after release of a 10 yr ureteral obstruction. Int J Urol 1997;4(5):512–515.

URETER, DIVERTICULUM

DESCRIPTION Diverticula can be congenital or acquired, although most have been discovered in adults. Most diverticula are solitary outpouchings involving the distal ureters and upper portions of the pelvis. They are true diverticula composed of a muscular wall, which is lined by transitional cell epithelium. Renal pelvic diverticula tend to be larger than those found in the ureter. Diverticula may be associated with other pathology, such as Ask-Upmark kidney. The most common complications are infection and/or stone formation. Unlike diverticula found in the bladder and urethra, major complications and development of transitional cell carcinoma are rare.

REFERENCE

7. Murphy W. Urological Pathology, 2nd ed. Philadelphia: Saunders, 1997:127.

URETER, 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 ureterocele, all of which are more commonly found in females than in males. Incomplete duplication is most often associated with ureteropelvic junction obstruction of the lower pole of the kidney. Common clinical presentations include UTIs and urinary incontinence. Diagnosis is made usually in childhood by US, excretory urography, and voiding cystourethrography.

Also known as bifid ureter (if partial duplication) or double ureters (if complete duplication). Treatment is ureteroneocystostomy in the presence of persistent reflux or ureteropyelostomy if obstructed without reflux.

REFERENCE

8. Fernbach SK, et al. Ureteral duplication and its complications. Radiographics 1997;17(1):109–127.

URETER, ECTOPIC (URETERAL ECTOPIA)

DESCRIPTION Ectopic ureters open in a position other than on the trigone and can be associated with both reflux and obstruction and with ureteroceles. The predispose to UTI and may cause hematuria or abdominal/flank pain. Up to 80% are associated with a duplicated collecting system in females and ~20% are nonduplicated ureters usually in males with an absent hemi-trigone. In females, the ureter typically inserts in the urethra or vagina (distal to the sphincter) 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

9. Hanson GR, Gatti JM, Gittes KG. Diagnosis of ectopic ureter as a cause of urinary incontinence. J Ped Urol 2007;3(1):53–57.

URETER, FIBROEPITHELIAL POLYPS

DESCRIPTION Fibroepithelial polyps are rare benign neoplasms. The majority of these polyps are found at the ureteropelvic junction. Signs and symptoms usually associated with ureteral obstruction include flank pain and hematuria. In addition, varying degrees of hydroureteronephrosis 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. Ureteroscopy is often necessary to confirm the diagnosis.

SYNONYMS

- Fibromyxoma
- Myxoma
- Fibroma
- Vascular fibrous polyps

TREATMENT

- Ureteroscopic resection
- Open ureterotomy with polypectomy or partial ureterectomy is a viable conservative treatment option if the diagnosis can be confirmed preoperatively.
- Many patients undergo nephroureterectomy for suspected malignancy.

REFERENCE

Bahnson RR, et al. Fibroepithelial polyps of the ureter. J Urol 1984;132:343.

URETER, FISH HOOK (REVERSE J)

DESCRIPTION A radiographic appearance of the type I (low-loop) circumcaval ureter, in which the dilated proximal part of the ureter takes a characteristic fish hook or reverse J course. Ureteral dilation usually ends 1–2 cm lateral to the inferior vena cava, where the ureter turns upward at the border of the psoas muscle.

REFERENCE

Kenawi MM, Williams DI. Circumcaval ureter: A report of four cases in children with a review of the literature and a new classification. Br J Urol 1976;48:183.

URETER, HEMANGIOMA

DESCRIPTION Hemangiomas are benign ureteral tumors. They may be the most common cause of chronic unilateral hematuria. Symptomatology may include hematuria, pain, hydronephrosis, bladder irritations, and palpable tumor. Varicoceles have also been found, but less frequently. Like other ureteral tumors, hemangiomas usually cause incomplete obstruction and may eventually cause complete obstruction with dilation of the urinary tract. They present as red, slightly elevated structures, fairly diffusely, and demarcated from their surroundings. Urothelial malignancies must be excluded, especially in the elderly. Flexible ureteropyeloscopy is considered a good diagnostic and therapeutic option in selected patients with unilateral hematuria of uncertain etiology.

REFERENCE

Biyani CS, et al. An unusual filling defect in the ureter. Urol Int 1998;61(2):124–125.

URETER, J HOOKING

DESCRIPTION With progressive benign prostatic hypertrophy, elevation of the trigone occurs, resulting in a characteristic J hooking of the distal ureters. This is a reliable sign on IVP of significant prostatic hypertrophy.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:320.

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 predominantly in the 4th–5th decades of life. The left ureter is more frequently affected. Immunohistochemical studies confirm the diagnosis. Conservative management (urethroscopic or partial ureterectomy) is treatment of choice.

REFERENCE

Naruse K, et al. A case of primary leiomyoma of the ureter. Int J Urol 2007;14(3):248–250.

URETER, LEIOMYOSARCOMA

DESCRIPTION Leiomyosarcoma originating from the ureters 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-yr disease-specific survival. Patients present with flank pain, hematuria, and/or UTI. Radiographic exam includes IVP, retrograde pyelogram, 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
- Adjuvant radiation therapy may be helpful.

REFERENCE

Griffin JH, Waters WB. Primary leiomyosarcoma of the ureter. J Surg Oncol 1996;62(2):148–152.

URETER, METASTASIS TO

DESCRIPTION Carcinoma metastatic to the ureter is rare. The sites of primary tumors that later involve the ureter, in order of frequency, are breast, colon/rectum, cervix, prostate, bladder, retroperitoneal lymphoma, and miscellaneous. A predilection exists for the lower 1/3 of the ureter. Furthermore, the longest time interval from primary tumor to diagnosis of ureteral obstruction ranged from 8 mo to 9 yr. Therapy of ureteral obstruction secondary to metastatic tumor must be considered carefully against the patient’s prognosis.

REFERENCE

Richie JP, et al. Ureteral obstruction secondary to metastatic tumors. Surg Gynecol Obstet 1979:355–357.

URETER, NEPHROGENIC ADENOMA

DESCRIPTION Nephrogenic adenoma is rarely found in the ureter, but is more common in the bladder. It is a benign papillary and tubular proliferation in response to trauma, infection, or ionizing radiation.

Biopsy and figuration are appropriate, as it is treated as a low-grade urothelial malignancy.

REFERENCE

Bostwick OG, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

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. Neurofibromas frequently recur and can cause death by urinary obstruction and renal failure. Endoscopic or open excision is the treatment of choice.

REFERENCE

Bostwick DG, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

URETER, PIPE-STEM

DESCRIPTION A radiographic appearance seen in late stages of tuberculous involvement of the ureter. On IVP, the ureter appears straight with a narrow lumen, due to diffuse fibrotic changes of the wall.

REFERENCE

Murphy DM, et al. Tuberculous stricture of ureter. Urology 1982;20:382.

URETER, RADIATION INJURY TO

DESCRIPTION Clinically, radiation injury to the ureter will present as obstruction. Upper urinary tract obstruction secondary to the effects of radiation is generally reported to occur in ~5% of patients with ureteral encroachment, and in <1% of all treated patients. The ureters are relatively resistant to the effects of radiation, although some factors are postulated to increase the chance of injury after radiation exposure, such as infection of the ureter, necrosis of the tumor invading the ureteral wall, and direct radiation injury to the ureteral wall. Radiation therapy of 8,000 Gy results in a 40% urologic complication rate. A dose of 6,000 Gy results in a <2% complication rate. (See also Section I: “Ureter, Obstruction.”)

REFERENCE

Resnick MI, Kursh ED. Extrinsic obstruction of the ureter. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:409–410.

URETER, RETROCAVAL (CIRCUMCAVAL, POSTCAVAL)

DESCRIPTION A retrocaval ureter is a congenital anomaly in which the problem arises from the inferior vena cava rather than the ureter. Normally, the vena cava derives from the supracardinal vein, which lies posterior to the ureter. If the derives from either the persistent right subcardinal or postcardinal vein, both of which lie anterior to the ureter, a portion of the lumbar ureter becomes trapped behind the vena cava. Clinically, a retrocaval ureter may present as ureteral obstruction. Males are affected more than females. (See “Ureter-Shepherd’s Crook.”)

Treatment is surgery with transection of the ureter and reanastomosis in front of the inferior vena cava.

REFERENCE

Chung BI, Gill IS. Laparoscopic dismembered pyeloplasty of a retrocaval ureter: Case report and review of the literature. Eur Urol 2008;54(6):1433–1436.

URETER, SHEPHERD'S CROOK

DESCRIPTION An S-shaped appearance of the circumcaval ureter on retrograde ureterography, in which a normal-caliber ureter emerging at the medial aspect of the inferior vena cava runs inferiorly between it and the aorta. On frontal projection, the ureter is medial to the lower lumbar pedicles, where it crosses anterior to the right iliac vessels to enter the pelvis. (See also Section II: "Ureter, Retrocaval [Circumcaval, Postcaval].")

REFERENCE

Kenawi MM, Williams DI. Circumcaval ureter: A report of four cases in children, with a review of the literature and a new classification. Br J Urol 1976:48:183.

URETER, STRICTURE

DESCRIPTION Strictures are one of the main causes for ureteral obstruction that might lead to hydronephrosis and renal function impairment. Ureteral strictures may present with an insidious onset of irreversibly damaged renal parenchymal due to slow development of silent hydronephrosis. Common signs of symptomatic stricture are flank pain, elevated creatinine level, or decreased urine output. Imaging studies with contrast are an essential part of the diagnostic workup. The location and length of obstruction are important parameters for treatment planning. (See also Section I: “Ureter, Obstruction.”)

CAUSES

- Congenital
- Extrinsic trauma
- Iatrogenic (gynecologic or other pelvic surgeries)
- Inflammatory and infectious factors (Crohn disease)
- Instrumentation (ureteroscopy)
- Malignant (intrinsic or extrinsic)
- Post chemotherapy and radiation therapy
- Sclerosing retroperitoneal fibrosis

TREATMENT

- Relieve the obstruction with concomitant antibiotic coverage, if needed.
- Surgical correction with endoscopic, laparoscopic, robotic, or open surgery
- Reimplantation with excision for distal strictures

REFERENCE

Ogan K, et al. Laparoscopic ureteral reimplant for distal ureteral strictures. JSLS 2008;12(1):13–17.

URETER, VALVES

DESCRIPTION Ureteral valves obstruct the forward flow of fluid, causing a proximal hydronephrosis. About 35% of ureteral valves occur at the UPJ; 60% occur near the ureterovesical junction, and 5% in the upper ureter. Valves are 3 times more common in males. They are usually unilateral, although they may be bilateral, and, if so, usually lead to renal failure. 75% of valves occur on the left side. Treatment depends on the location of the valve and may include ureteral reimplantation (distal ureter), endoscopic ablation (midproximal ureter), or ureteropelvic junction repair.

REFERENCE

Amis ES, Newhouse JH, eds. Essentials of Uroradiology, 1st ed. Boston: Little, Brown, 1991:63.

URETERITIS CYSTICA

DESCRIPTION A benign and rare condition, ureteritis cystica is characterized by multiple cysts and space-filling defects in urothelium. Usually asymptomatic, it may present with hematuria, and if obstruction occurs, may lead to stone formation, UTIs, and renal compromise. The etiology is unknown, but associated with chronic UTI. Space-filling defects seen on retrograde pyelography or excretory urography may appears as smooth, round or oval filling defects of varying sizes that protrude into the lumen. Treatment is ureteroscopy and the mechanical disruption of cysts or instillation of chemicals such as silver nitrate to relieve obstruction.

REFERENCE

Parker B, et al. Ureteritis cystica presenting as a retractile ureteral polyp. J Urol 2002;168(1):195–196.

URETHRA, ADENOCARCINOMA OF ACCESSORY GLANDS

DESCRIPTION In males, the urethral accessory glands can develop rare, aggressive neoplasms that are difficult to diagnose because of the local destructive nature of the lesions (Cowper and Littré glands). Cowper gland cancers are found in the bulbous urethra, while Littr gland lesions can arise along the entire urethra, but tend to arise distally. In females, the Skene glands can develop adenocarcinoma as well. Patients typically present with hematuria, dysuria, and progressive urinary obstruction. Management is similar to that for urethral adenocarcinoma. (See also Section II: “Cowper Gland Carcinoma”, and other sites.)

SYNONYMS

- Adenocarcinoma of Cowper gland
- Adenocarcinoma of Littré glands
- Adenocarcinoma of Skene (periurethral) glands

REFERENCE

Reuter V. Urethra. In: Bostwick DG, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

URETHRA, ADENOMATOUS 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. Cores 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. Hematuria, enuresis, and obstruction are common. Cystourethroscopy is usually diagnostic.

SYNONYMS

- Villous polyp of the urethra
- Ectopic prostatic tissue in the urethra

TREATMENT

Transurethral or suprapubic resection is curative.

REFERENCE

Chan JKC, et al. Prostatic-type polyps of the lower urinary tract: Three histogenetic types? Histopathology 2007;11(8):789–801.

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 of crush injury to the pelvis. 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 undershorts in preadolescents. Urethrorrhagia is a benign lesion and self-limited in most cases. (See also Section I: “Urethra, Trauma (Anterior and Posterior);” Section II: “Urethrorrhagia, Idiopathic.”)

CAUSES

- Posterior urethral injury (prostatic and membranous urethra, proximal to urogenital diaphragm) associated with pelvic fracture and deceleration/shear injury
- Anterior urethral injury (bulbous and pendulous urethra, distal to urogenital diaphragm) associated with straddle injury and iatrogenic laceration
- Traumatic urethral catheterization; more common in men
- Nontraumatic causes: Idiopathic urethrorrhagia, malignancy (urethral, prostate, bladder), urolithiasis, urethral condyloma, urethral diverticulum, urethral stricture, benign prostatic bleeding, urethral hemangioma

TREATMENT

- In cases of urethral trauma, standard trauma management; shock and hemorrhage control
- Avoid urethral catheterization
- Retrograde urethrogram (12 Fr catheter in fossa navicularis with 3 cc in balloon; 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 cystostomy tube; delayed urethral repair (3 mo after injury) with silicone urethral catheter placement concomitant with primary anastomosis
  - Negative extravasation: Careful urethral catheter placement; cystography

REFERENCE

Smith DR, et al. Smith’s General Urology. New York: McGraw-Hill, 2004:291–304.

URETHRA, CALCULI

DESCRIPTION Urethral calculi comprise <2% of all urinary stone disease in the Western world, with a greater incidence in men than women, given increased urethral length. They are classified as migrant, from the proximal GU system, or native, developing in the urethra itself. Stones <10 mm should pass spontaneously. Although native stones tend to be asymptomatic, urethral calculi may present with irritative voiding symptoms, hematuria, a palpable mass, and/or urethral discharge.

CAUSES

- Migrant calculi: See Section I: “Urolithiasis, Adult, General and Bladder Calculi”
- Native calculi: Urinary stasis (urethral strictures, diverticula, foreign-body entrapment, hair-bearing graft following urethroplasty), chronic infections (UTIs, schistosomiasis)

TREATMENT

- Depends on location and size of stone
- Acute retention: Suprapubic tube placement (allows for definitive planning)
- Trial of spontaneous expulsion with 2% intraurethral lidocaine
- Forceps extraction with or without meatotomy
- Antegrade massage/milking of calculus
- Retrograde manipulation with intravesical lithotripsy
- Intraurethral/endoscopic lithotripsy and fragment extraction
- Open urethrotomy (2-layer closure)

REFERENCE

Koga S, et al. Urethral calculi. Br J Urol 1990;65(3):288–289.

URETHRA, CONDYLOMA (WARTS)

DESCRIPTION Condyloma (condylomata acuminatum, venereal warts) are a common finding in the lower genital tract, but a rare finding in the urinary tract. Condyloma of the urethra or bladder is often associated with immunosuppression. It is estimated that 0.5–5.0% of patients with condylomata of the genitalia may also have urethral involvement. Clinically, urethral involvement is suspected when pyuria or urethral discharge appears in a patient with genital verrucae. The cause is human papilloma virus, and primary treatment is ablative with cryotherapy, laser, or surgical excision. (See also Section I: “Condylomata Acuminata [Venereal Warts].”)

REFERENCE

Huguet Perez J, et al. Urethral condyloma in the male: Experience with 48 cases. Arch Esp Urol 1996;49(7):675–680.

URETHRA, DISCHARGE

DESCRIPTION Most commonly presented by STDs. A purulent discharge that is thick, profuse, and yellow to gray is typical of gonococcal urethritis; discharge in patients with nonspecific urethritis is usually scant and watery. A bloody discharge is suggestive of carcinoma of the urethra in the absence of trauma. Urethral discharge studies include Gram stain and culture, as well as voided urine PCR evaluation for Chlamydia and gonorrhea. (See Section I: “Urethritis, Gonococcal and Nongonococcal”; Section II: “Urethritis, Acute; Urethra, Bleeding [Blood at Meatus].”)

REFERENCE

Frenkl TL. Sexually transmitted infections. Urol Clin N Am 2008;35(1):33–46.

URETHRA, DIVERTICULAR CARCINOMA

DESCRIPTION Carcinoma of the urethral diverticulum is a rare pathologic entity commonly found in females, with an average age at presentation of 52. Reported symptoms include urethral bleeding (most common), dysuria, vaginal mass, and urethral obstruction. Adenocarcinoma occurs more frequently than transitional and squamous cell cancers combined and carries a more favorable diagnosis. (See Section I: “Urethra Diverticula, Female”; “Urethra, Carcinoma, General.”)

TREATMENT

- 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.

REFERENCE

Clayton M, et al. Urethral diverticular carcinoma. Cancer 1992;70:665.

URETHRA, DIVERTICULUM, MALE

DESCRIPTION Urethral diverticulum are usually found in the ventral anterior urethra but have been reported from the bulbous to the mid pendulous. These can be acquired (often iatrogenic from the treatment of urethral pathology) and very rarely, congenital. Congenital urethral diverticula may be either saccular or tubular. The saccular type has a true neck and may cause urinary obstruction when the cavity fills at the beginning of micturition. The tubular or diffuse type is located proximal to the urethral bulb, where urinary stasis can cause infection and/or calculous formation. Most are asymptomatic unless infection or obstruction develops. A mass can be palpated in the ventral aspect of the anterior urethra, which empties with compression. The diagnosis made by cystoscopy, urethrography, and voiding urethrography. Management can be endoscopic unroofing for small diverticulum with open repair reserved for larger lesions.

REFERENCE

Ballesteros Sampol JJ, et al. Acquired male urethra diverticula. Report of seven cases. Bibliographic review. Arch Esp Urol 2008;61(1):1–6.

URETHRA, DUPLICATION

DESCRIPTION Duplication of the urethra is rare and afflicts mainly boys. Duplication of the urethra may be complete, extending from the bladder to the dorsum of the penis, or partial, extending from the dorsal surface or, less commonly, the ventral surface of the penis and ending blindly. In only 15% of cases of duplicated urethra, whether complete or partial, is there a connection with the functional urethra. Urethral duplication is often associated with GU and GI abnormalities that maybe be severe. Most cases are asymptomatic, but the most common complication is infection. Patients may have urinary obstruction caused by compression of the functional urethra by a mass of material in the blind, accessory urethra. In other cases, patients may complain of incontinence or double urinary streams. Complete resection of the nonfunctioning urethra, if symptomatic, is curative.

REFERENCE

Arena S, et al. Urethral duplication in males: Our experience in ten cases. Pediatr Surg Int 2007;23(8):789–794.

URETHRA, FOREIGN BODY

DESCRIPTION Cases of self-inflicted foreign bodies in male urethra have been reported, including objects such as fishhooks, bones, screws, safety pins, and light bulbs. Cause for inserting foreign bodies varies, including psychiatric 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 stricture disease, therefore close urologic follow-up is recommended.

REFERENCE

Rahman NU, et al. Self-inflicted male urethral foreign body insertion: Endoscopic management and complications. BJU Int 2004;94(7):1051–1053.

URETHRA, HEMANGIOMA

DESCRIPTION Urethral hemangiomas are extremely rare tumors. The lesion is believed to be congenital, arising from the embryonic rest 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 II: “Urethra, Bleeding [Blood at Meatus].”)

REFERENCE

Parshad S, Yadav SP, Arora B. Urethral hemangioma. An unusual cause of hematuria. Urol Int 2001;66(1):43–45.

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. 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. (See also Section I: “Urethral Mass.”)

REFERENCE

Saad AG, Kaouk JH, Kaspar HG, et al. Leiomyoma of the urethra: Report of three cases of a rare entity. Int J Surg Pathol 2003;11(2):123–126.

URETHRA, LEIOMYOSARCOMA

DESCRIPTION Leiomyosarcoma is a smooth muscle tumor that often exhibits necrosis, hemorrhage, and cystic degeneration. 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: “Urethral Mass.”)

REFERENCE

Bostwick DG, ed. Urologic Surgical Pathology, 1st ed. St. Louis: Mosby, 1997.

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. It is treated by biopsy and ablation.

REFERENCE

Benson RC, et al. Relationship of urethral leukoplakia to urothelial malignancy. J Urol 1984;13:507–511.

URETHRA, LYMPHOMA

DESCRIPTION Primary malignant lymphoma rarely affects the lower urinary tract. When it does, it generally affects the bladder. Initial presentation within the urethra is extremely rare. Concurrent or subsequent regional or systemic lymphoma is generally the rule. Only 11 cases of lymphoma presenting in the urethra have been documented, and 10 were in women. (See Section II: “Lymphoma, Urologic Considerations.”)

TREATMENT

- The high probability of regional or systemic extension is an argument against radiotherapy as a primary treatment.
- Chemotherapy is an excellent treatment, and the prognosis is good.

REFERENCE

Hatcher PA, et al. Primary lymphoma of the male urethra. Urology 1997;49(1):142–144.

URETHRA, MALACOPLAKIA

DESCRIPTION This designation refers to a peculiar pattern of inflammatory reaction, characterized macroscopically by soft, yellow, slightly raised mucosal plaques (classic intracytoplasmatic Michaelis-Gutmann bodies and von Hansemann cells). The disease shows a predilection for involving the bladder, ureter, renal pelvis, ureteropelvic junction, and urethra. The disease predominates in females by a 4:1 ratio, and the peak age is in the 6th decade. Apart from symptoms associated with UTIs, the clinical manifestations are usually unremarkable. Most often, the bladder is involved, and symptoms of bladder irritability or hematuria may be present. Malacoplakia occurs with increased frequency in immunosuppressed transplant recipients. Pathogenesis is unknown, but an altered host response is suspected. There is an association with diabetes mellitus, alcoholic liver disease, sarcoidosis, and mycobacterial infection. When the lower urinary tract is involved, long-term antibiotics are successful.

REFERENCE

Karaiossifidi H, et al. Malacoplakia of the urethra: A case of unique localization with follow-up. J Urol 1992;148(6):1903–1904. Review.

URETHRA, MALIGNANT MELANOMA

DESCRIPTION Primary urethral 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 inguinal and pelvic lymph nodes. Hematogenous spread to liver, lung, and brain is also common. Staging for urethral melanoma has not yet been standardized. Prognosis depends on the thickness of the lesion.

TREATMENT

- Surgical: Urethrectomy or penectomy with regional lymph node dissection
- The role of radiotherapy, immunotherapy, or chemotherapy is yet to be defined.

REFERENCE

Kokatas NS, Kallis EG, Fokitis PJ. Primary malignant melanoma of male urethra. Urology 1982;18:392.

URETHRA, MEATUS, NORMAL CALIBER

DESCRIPTION Normal limits of male urethral calibration are as follows:

- 6 wk–3 yr: 15% <8 Fr; 85% 10 Fr
- 4–10 yr: 8% tight at 8 Fr; 76% 12 Fr
- 11–12 yr: 5% <10 Fr; 75% 14 Fr

Normal limits for female urethra are as follows:

- 2–4 yr: 14 Fr
- 6–10 yr: 16 Fr
- 12 yr: 20 Fr
- >14 yr: 24 Fr

REFERENCE

Elder JS. Congenital abnormalities of the genitalia. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell’s Urology, 7th ed. Philadelphia: Saunders, 1998:2128, 2137.

URETHRA, METASTASIS TO

DESCRIPTION Metastatic lesions to the urethra usually originate from the prostate, bladder, and rectum, although origin from distant sites has been reported. In a patient with a known malignancy, pain, hematuria, and/or urethral obstruction may suggest the diagnosis.

REFERENCE

Roberts TW, Melicow MM. Pathology and natural history of urethral tumors in females. Urology 1977;10:583.

URETHRA, NEPHROGENIC METAPLASIA (ADENOMA)

DESCRIPTION Nephrogenic metaplasia is a rare metaplastic lesion of urethral epithelium, with a classic triad of tubular, cystic, and papillary–polypoid patterns microscopically. Occurs at all ages, with a 3:1 male predominance. 15% of nephrogenic metaplasia is found in the urethra. Etiology is unknown, but resembles distal renal tubules and is associated with surgical trauma, calculi, indwelling catheter, chronic infections, and immunosuppression. This condition must be differentiated from prostatic carcinoma. Presenting symptoms include irritative voiding symptoms and hematuria, or the patient may be asymptomatic. Diagnosed by cystoscopy and biopsy, the clinical course is usually benign, although the problem may persist or recur. Rarely, a metaplastic lesion can cause carcinoma.

SYNONYMS

- Adenomatoid metaplasia
- Adenomatoid tumor
- Adenomatous metaplasia
- Hamartoma
- Tubular metaplasia
- Nephrogenic adenoma

TREATMENT

- Regular cystoscopic exam
- Removal of underlying cause
- Transurethral excision

REFERENCE

Xiao GQ, et al. Nephrogenic adenoma: Immunohistochemical evaluation for its etiology and differentiation from prostatic adenocarcinoma. Arch Pathol Lab Med 2006;130(6):805–810.

URETHRA, OBSTRUCTION

DESCRIPTION Urethral obstruction can occur anywhere from the meatus to bladder neck, and can be congenital or acquired. Posterior urethral valves are the most common cause of obstructive uropathy in boys. The incidence of posterior urethral valves is 0.25–0.5:10,000 births and anterior urethral valves occur 10 times less frequently than posterior valves. Other causes of urethral obstruction in both sexes include meatal stenosis, stricture, foreign body, phimosis (males), urethral calculus, urethral abscess, urethral diverticulum (acquired or congenital), or urethral neoplasm. (See also Section I: “Urethra, Mass.”)

REFERENCE

Narasimhan KL, Choudhary SK, et al. Anterior urethral valves. Indian Pediatr 2005;42:708–710.

URETHRA, POLYPS (FIBROEPITHELIAL, ADENOMATOUS, INFLAMMATORY)

DESCRIPTION Uncommon 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. Fibroepithelial polyps consist of stromal elements. 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 inflammation (eg, catheter or stone removal) if present. (See Section II: “Cystitis, Polypoid and Papillary;” “Urethritis, Polypoid.”)

REFERENCE

Walsh IP, et al. Benign urethral polyps. Br J Urol 1993;72:937–938.

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. Primarily a disease of African American girls, vaginal bleeding is often the presenting symptom, followed by urinary complications such as dysuria. Associated factors involve 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 urethroplasty.

REFERENCE

Fernandes ET, et al. Urethral prolapse in children. Urology 1993;41(3):240–242.

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 embryologic origin similar to that of rectosigmoid. Urinary obstruction and/or hematuria can be presenting symptoms. Best treated by complete removal, due to the premalignant changes seen in some lesions and malignant potential seen in adenomas of the colon.

REFERENCE

Ulgaba F, et al. Villous adenoma of the prostatic urethra. Eur Urol 1988;14:255–257.

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-lubricated sterile cotton-tipped applicator is placed into the bladder, then withdrawn to the point of resistance. The patient is then asked to strain. Hypermobility is defined as a resting or straining angle 30% from horizontal. Treatment is periurethral collagen injection or pubovaginal sling procedure.

REFERENCE

Bakas P, et al. Q-tip test and tension free vaginal tape in management of female patients with genuine stress incontinence. Gynecol Obstet Invest 2002;53(3):170–173.

URETHRAL PRESSURE PROFILE (UPP)

DESCRIPTION The UPP is a graphic representation of the intraluminal pressure along the length of the urethra. This static study provides no assessment of physiologic urethral function during voiding. The micturitional 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.

REFERENCE

Sullivan MP, et al. Micturitional urethral pressure profilometry. Urol Clin N Am 1996;23(2):263–278.

URETHRAL SLING

DESCRIPTION Urethral slings are surgically placed to support pelvic structures or lift the urethra to enhance urine retention for patients with stress urinary incontinence. Slings can be made from autologous, allograft, xenograft, or synthetic tissues that provide strength. Slings can be placed at the proximal urethra (pubovaginal slings) or mid urethra (tension-free transvaginal tape [TVT] and transobturator [TOT] and other mid urethral slings). The urethral sling is a very effective treatment for SUI, with cure rates of 80–90% vs. other options such as the periurethral injection of bulking agents. Complications include erosion into associated structures such as vagina, urethra, and bladder, as well as causing obstructive voiding dysfunction. (See also Section I: “Incontinence, Urinary, Adult Female;” Section II: “Sling Materials.”)

REFERENCE

Schulz JA. Midurethral minimally invasive sling procedures for stress urinary incontinence. J Obstet Gynaecol Can 2008;30(8):728–740.

URETHRA, STENOSIS/STRICTURE, FEMALE

DESCRIPTION A decrease in the caliber of the urethra, uncommon 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 stricture 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. Intermittent catheterization has been used successfully, with internal urethrotomy or urethroplasty also as options.

REFERENCE

Smith AL, et al. Female urethral strictures: Successful management with long-term clean intermittent catheterization after urethral dilatation. BJU Int 2006;98(1):96–99.

Tsivian A. Dorsal graft urethroplasty for female urethral stricture. J Urol 2008;176(2):8-611–613.

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 (eg, frequent voiding), then pursue the differential diagnosis and treatment options for each symptom. The concept of chronic or acute urethral syndrome is now essentially historical, and is no longer used in modern medical literature.

REFERENCE

Hanno PM. Painful bladder syndrome/interstitial cystitis and related disorders. In: Wein AJ, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia, Saunders, 2007.

URETHRITIS, ACUTE

DESCRIPTION Syndrome of urethral inflammation marked by painful urination, urethral pruritus, and discharge. Usually caused by a STD, but other causes are not uncommon. Untreated cases may gradually resolve, but complications, such as urethral stricture in males or pelvic inflammatory disease in women, may ensue. Cause is predominantly Neisseria gonorrhoeae and Chlamydia trachomatis infection; often together. Less common infectious agents include Ureaplasma urealyticum, Trichomonas vaginalis, herpesvirus, and Mycoplasma genitalium. Rare noninfectious causes include foreign bodies, soaps, shampoos, douches, spermicides, and urethral instrumentation. Gram stain of discharge with >5 WBC/HPF strongly suggests urethritis. Intracellular gram-negative diplococci are strongly indicative of gonorrhea. Cultures may be difficult to obtain, but are important for antimicrobial sensitivity testing and should be performed in all symptomatic patients. Routine urine analysis may be normal in simple urethritis. First-void urine is often positive for leukocyte esterase and should show 10 WBC/HPF in acute urethritis. NAAT 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. Syphilis, HIV, and hepatitis B serology is performed as indicated to rule out concomitant STDs.

TREATMENT

- The United States Preventative Services Task Force recommends screening all sexually active women 25 yr old and all other women at increased risk of infection.
- All sexual partners who came in contact with the patient within 60 days should be evaluated, tested, and treated for gonorrhea and chlamydia.
- Gonorrhea: Ceftriaxone: 125 mg IM single dose or cefixime: 400 mg PO single dose
- Chlamydia: Azithromycin: 1 g PO single dose or doxycycline: 100 mg PO b.i.d. for 7 days
- Trichomoniasis: Metronidazole 2 g PO single dose or 250 mg t.i.d. for 7 days

REFERENCE

Urtehritis Zola JC, Gomella LG. In: Domino FJ, ed. The 5-Minute Clinical Consult, 17th ed. Philadelphia: Lippincott, 2009.

URETHRITIS, CHRONIC, FEMALE

DESCRIPTION Chronic urethritis is a common urologic problems of females, as the distal urethra normally harbors pathogens. Infection may be increased by wearing contaminated diapers, by insertion of an indwelling catheter, by spread from cervical or vaginal infections, or by intercourse with an infected partner. Urethral inflammation may also occur from the trauma of intercourse or childbirth, particularly if urethral stenosis, either congenital or following childbirth, is present. The urethral mucosa is reddened, sensitive, and often stenotic. Granular areas are often seen, and polypoid 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 dilations may help if stenosis is found (dilate to 36 Fr). Empiric doxycycline or azithromycin can be tried.

REFERENCE

Tanagho EA, et al. Disorders of the female urethra. In: Tanagho EA, McAninch JW, eds., Smith's General Urology, 17 ed. New York: McGraw-Hill, 2008.

URETHRITIS, POLYPOID

DESCRIPTION An inflammatory reaction in the urethra, secondary to mechanical irritation, pressure, and/or cytotoxic effects, caused by indwelling catheters. The lesion is similar to that seen in polypoid cystitis, and is caused by similar macroscopic and microscopic mucosal changes. Microscopically, the mucosa is usually polypoid in appearance, often with evidence of microabscesses and an inflammatory infiltrate. Its similarity to polypoid cystitis suggests that polypoid urethritis is reversible with removal of the indwelling catheter or treating the inflammatory source. (See Section II: “Cystitis, Polypoid and Papillary;” “Urethra, Polyps [Fibroepithelial, Adenomatous, Inflammatory].”)

REFERENCE

Norlen U, et al. Effects of indwelling catheters on the urethral mucosa (polypoid urethritis). Scand J Urol Nephrol 1988:22:81–86.

URETHRITIS, SENILE

DESCRIPTION After physiologic (or surgical) menopause, hypoestrogenism occurs and retrogressive (senile) changes take place in the vaginal (vaginal atrophy) and the urethral walls. Some eversion of the mucosa about the urethral orifice, from atrophy of the vaginal wall, is usually seen and can be misdiagnosed as a caruncle. Many postmenopausal women have symptoms of vesical irritability (burning, frequency, urgency) and stress incontinence. Dysuria may occur due to urine contact with the inflamed atrophic tissues themselves or because of the increased incidence of UTIs in these women. Best treated symptomatically or with DES vaginal suppositories 0.1 mg nightly for 3 wk.

REFERENCE

Tanagho EA, et al. Disorders of the female urethra. In: Tanagho EA, McAninch JW, eds., Smith's General Urology, 17 ed. New York: McGraw-Hill, 2008.

URETHROCELE

DESCRIPTION Urethrocele 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 urethrocele can cause voiding difficulty, some degree of incontinence, UTI, and dyspareunia. The condition can also develop in children after urethroplasty, with distal obstruction causing proximal dilation of the neourethra; it is very rarely congenital. (See also Section I: “Pelvic Prolapse [Cystocele and Enterocoele].”)

URETHRORRHAGIA, IDIOPATHIC

DESCRIPTION Bleeding from the urethra or blood spotting on the undershorts in preadolescents (average age around 10 yr); this is a benign condition, self-limited in most cases. The etiology is unknown. Routine radiographic, laboratory, and endoscopic evaluation is unnecessary for evaluating urethrorrhagia. Watchful waiting is indicated, as the condition resolves in 71% and 91.7% of patients at 1 and 2 yr, respectively. Evaluation should be considered in patients with prolonged urethrorrhagia because urethral stricture may be identified. (See also Section II: “Urethral, Bleeding [Blood at Meatus].”)

REFERENCE

Walker BR, et al. The natural history of idiopathic urethrorrhagia in boys. J Urol 2001;166(1):231–232.

URGE INCONTINENCE

DESCRIPTION Urge urinary incontinence 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, as from stroke or multiple sclerosis; or non-neurogenic, including infection, bladder stones, and cancer. Initial workup includes a good history and physical, evaluation for other associated urinary symptoms, check of post-void residual, urine analysis, cystoscopy, and urodynamics evaluation. After ruling out malignancy, infection, and obstruction, treatment focuses on symptomatic control. Dietary and behavioral modifications, such as limiting chocolate or other caffeinated substances, and timed voiding should be the initial treatment. Kegel exercises may help. Anticholinergics are 1st-line medical therapy. Further treatment options for patients who are refractory to these conservative treatments include Botox injections into the bladder, sacral nerve modulation, and augmentation cystoplasty. (See also Section I: “Incontinence, Female;” “Incontinence, Male.”)

REFERENCE

Holroyd-Leduc JM. What type of urinary incontinence does this woman have? JAMA 2008;299(12):1446–1456.

URGENCY PERCEPTION SCORE (UPS)

DESCRIPTION The UPS is a system based on the grade of sensation of bladder fullness at each micturition. This system proposes that urgency is always abnormal, that it lies on a continuum, and that it can be graded on a scale of 0–4 where 0 is no urge; 1, mild urge; 2, moderate (can hold >10–60 min); 3 severe (can hold <10 min); and 4, desperate urge (must go immediately). The UPS can be a useful tool in a bladder diary, and it becomes a treatment outcome tool because improvements can be shown as decreases in grade, and in number or urgency of voids.

REFERENCE

Blaivas JG, et al. The Urgency Perception Score. J Urol 2007;177(1):199–202.

URINARY ASCITES (UROPERITONEUM)

DESCRIPTION Urinary ascites is usually seen in infants, because of the relative lack of dilation of the newborn collecting system, when compared to that in adults. The condition most often occurs in neonates due to intraperitoneal bladder or upper-tract perforation as a result of distal urinary obstruction. It is rare in adults. The most common cause is posterior urethral valves, accounting for 70% of cases. Persistent cloaca may allow the reflux of urine into the peritoneal cavity without perforation. Mortality rate is as high as 70%. Signs and symptoms may include abdominal distention, acidosis, electrolyte abnormalities, and respiratory compromise from increased abdominal pressure. In older patients, hyponatremia and increased serum creatinine can be observed. Diagnosis includes imaging (CT or US), voiding cystourethrography, and paracentesis to check creatinine levels in ascitic fluid. Treatment is directed at relieving obstruction (ie, ablation of posterior urethral valves) and correction of fluid balance and electrolyte abnormalities. Catheter bladder drainage in posterior urethral valves and upper tract drainage may be necessary. Direct repair at the perforation site is usually not indicated.

REFERENCE

Adams MC, et al. Prenatal urinary ascites and persistent cloaca: Risk factors for poor drainage of urine or meconium. J Urol 1998;160(6 Pt 1):2179–2181.

URINARY DIVERSION, ELECTROLYTE, AND OTHER ABNORMALITIES

DESCRIPTION Fluid and electrolyte complications can arise from solute transfer from urine across a bowel segment used for urinary diversion. The specific segment of bowel used, the amount and time of contact of urine with bowel mucosa, the duration of the conduit, and renal function are all factors that can affect fluid and electrolyte balances:

- Ileal and colonic conduits can produce hyperchloremic metabolic acidosis. The mechanism is the absorption of ammonium chloride (a weak acid) in exchange for carbonic acid (CO_2 and water). Treatment, if necessary, consists of urinary alkalinization (sodium bicarbonate, Bicitra, Polycitra) or blockade of chloride transport (chlorpromazine 25–50 mg t.i.d. or nicotinic acid 400 mg t.i.d.)
- Jejunum is least attractive for use in urinary diversions, due to its high absorptive capacity, and it is associated with hyponatremic, hyperkalemic metabolic acidosis with azotemia.
- Stomach segments cause a hypochloremic, hypokalemic metabolic alkalosis. Normally not a significant problem unless renal failure develops and the segment needs to be taken down.
- Distal ileum resection may result in macrocytic anemia due to B12 deficiency over long periods and may require supplementation.
- Abnormal drug metabolism: Methotrexate toxicity in patients with ileal conduits is well recognized, and patients with continent diversion who receive chemotherapy should be monitored closely and stay well hydrated; the reservoir is drained during treatment.

Other drugs reported to be absorbed from intestinal segments in the urinary tract include phenytoin, theophylline, and antibiotics. Diabetics have enhanced ability to absorb glucose from intestinal reservoirs so screening with urine tests may be inaccurate. Glucose blood testing is recommended.

REFERENCE

Hautmann RE, et al. Urinary diversion. Urology 2007;69(Suppl 1A):17–49.

URINARY DIVERSION, RISK OF MALIGNANCY

DESCRIPTION Segments of bowel used for urinary diversion have an increased risk of malignant transformation. Some studies have shown an increase from 5% up to as high as 40% 10–20 yr after a urinary diversion. The etiology is unknown; adenocarcinomas, adenomatous polyps, sarcomas, transitional cell carcinomas, signet ring carcinomas, and squamous cell carcinomas 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.

REFERENCE

North AC, Lakshmanan Y. Malignancy associated with the use of intestinal segments in the urinary tract. Urol Oncol 2007;25(2):165–167.

URINARY FLOW RATE (UROFLOWMETRY)

DESCRIPTION Uroflowmetry is the study of urinary flow rate. Urinary flow rate is defined as the product of detrusor contractility against bladder outlet resistance. Deviations from normal urinary flow rate may represent abnormalities of either process. It should not be used alone, but in rather combination with a determination of bladder residual volume and symptoms to determine the presence of bladder outlet obstruction. To interpret a uroflow, a voided volume of at least 125–150 mL is required for an adequate study. Some normal values are listed here, although clinical scenarios vary widely, with no given cutoff value to document the appropriateness of therapy:

- Males: <40 yr: >22 mL/s; 40–60 yr: >18 mL/s; >60 yr: >13 mL/s
- Female: <50 yr: >25 mL/s; >50 yr: >18 mL/s

A Qmax of <15 mL/s does not differentiate between obstruction and bladder decompensation. Men with >15 mL/s Qmax seem to have a poorer outcome with bladder outlet procedures such as prostatectomy. The study consists of a graphical flow rate pattern, along with values for maximum flow rate, also called peak flow rate (Qmax), average flow rate (Qave), maximum flow time, and total flow time. Various nomograms have been published to aid in the interpretation of uroflow data (Siroky, Abrhams, and Griffiths). A normal graphical flow rate pattern represents a bell-shaped curve. (See also Section II: “Pressure Flow Studies.”)

REFERENCE

Smith JC. The measurement and significance of the urinary flow rate. BJUI. 2008;38(6):701–706.

URINARY RESIDUAL VOLUME (POST-VOID RESIDUAL)

DESCRIPTION Urinary residual volume is the amount of urine present in the urinary bladder immediately after a complete voiding. Also known as post-void residual, it can assist in differentiating between disorders of emptying and disorders of storage in urinary incontinence. It provides clinical quantitative information on the degree of obstruction in certain conditions, such as BPH, or efficiency of bladder emptying in neurogenic bladder. Chronic high urinary residual volumes can predispose to infection, bladder hypertrophy, ureterovesical reflux, increased intravesical pressure, incontinence, or loss of detrusor muscle tone. Residual volume is measured by US or catheterization and is usually interpreted in the context of uroflowmetry. Treatment of high urinary residual volumes is to treat the underlying cause.

REFERENCE

Simforoosh N, et al. Accuracy of residual urine measurement in men: Comparison between real-time US and catheterization. J Urol 1997;158:59–61.

URINARY RETENTION FOLLOWING BRACHYTHERAPY

DESCRIPTION Urinary retention occurs in up to 22% of patients who undergo brachytherapy. Risk factors for post-brachytherapy retention include large prostate (>36 g) and elevated International Prostate Symptom Score scores prior to treatment. Medical therapy that may aid with retention include corticosteroids, celecoxib, and -blockers. Clean intermittent catheterization is done to allow drainage of urine. Patients who fail medical therapy can safely undergo transurethral resection of the prostate.

REFERENCE

Mabjeesh NJ, et al. Preimplant predictive factors of urinary retention after iodine 125 prostate brachytherapy. Urology. 2007;70(3):548–553.

URINARY RETENTION, POSTOPERATIVE

DESCRIPTION Postoperative urinary retention occurs in 4% of surgical patients, although abnormal voiding is seen up to 80% of postop patients. Subclinical obstructive uropathy, overdistention of bladder during operation, sympathomimetic and anticholinergic medication use, and inability to stand after surgery are common causes. Treatment with decompression of the bladder using an indwelling Foley catheter or with clean intermittent catherization should also include early ambulation and a bowel regimen to prevent constipation, as well as limited use of narcotic pain meds.

REFERENCE

Changchien CR, et al. Postoperative urinary retention after primary colorectal cancer resection via laparotomy: A prospective study of 2,355 consecutive patients. Dis Colon Rectum 2007;50(10):1688–1696.

URINARY TRACT INFECTION (UTI), CATHETER-RELATED

DESCRIPTION UTI is the most common hospital-acquired infection in the US and a major focus to improve patient outcomes. Any passage of a urethral 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, 10–25% develop symptomatic UTI, and 4% may develop bacteremia. Avoiding unnecessary catheterization, removing 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 catheterization should be managed with intermittent catheterization, if possible. This approach is associated with a lower rate of bacteriuria and symptomatic UTI than management with long-term indwelling catheterization. Prophylactic antibiotics are of no consistently proven benefit.

REFERENCE

Saint S, et al. Preventing hospital-acquired urinary tract infection in the US: A national study. Clin Infect Dis 2008;46(2):243–250.

URINE, ABNORMAL COLOR

DESCRIPTION Normal urine is clear and pale to dark yellow due to the presence of urochrome. Foods, medications, metabolic products, and infection can cause abnormal urine colors. (See also Section IV: “Urine Studies.”):

- Cloudy: Phosphaturia (precipitated phosphate crystals in alkaline urine), pyuria (UTI), fungal infection, chyluria, lipiduria, hyperoxaluria, diet high in purine-rich foods (hyperuricosuria)
- Colorless: Diabetes insipidus, diuretics, excess fluid intake
- Brown: Nitrofurantoin, metronidazole (Flagyl), aloe, porphyria, bile pigments, myoglobin
- Brown-black: Bile pigments, melanin, acute intermittent porphyria, methemoglobin, cascara, levodopa, methyldopa, senna
- Deep yellow: Very concentrated urine, carrots, cascara
- Green-blue: Indigo carmine, methylene blue, amitriptyline, indomethacin, doxorubicin, pseudomonal UTI
- Muddy: Pyuria, phosphaturia, chyluria
- Orange-yellow: Phenothiazines, phenazopyridine, laxatives, vitamin B, Pyridium, rifampin, warfarin, bile pigments.
- Pink or red: Hematuria, hemoglobinuria, myoglobinuria, porphyria, anthocyanin in beets, blackberries, rhubarb, phenolphthalein, rifampin
- Tea-colored: Old blood

References

Hanno PM, et al. Clinical Manual of Urology, 3d ed. New York: McGraw-Hill, 2001:75.

Simerville JA, et al. Urinalysis: A comprehensive review. Am Fam Physician 2006;74(7):1096.

URINE, CYTOLOGY

DESCRIPTION Urine cytology is the microscopic evaluation of shed urothelial cells in the urine. A positive reading suggests the existence of urothelial malignancy. It is highly specific (94% for high-grade tumors), but has low sensitivity (40–60%) especially for low-grade tumors (11%). It is combined with cystoscopy and upper-tract imaging for workup for urothelial malignancy.

REFERENCE

Jones, JS. DNA-based molecular cytology for bladder cancer surveillance. Urology 2006;67(3 Suppl 1):35–45.

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. Additionally, the ellipsoid shape of protein molecules at the air–water interface produces increased surface activity. These factors establish an environment in which molecules are unable to reorient in a monolayer due to electrostatic repulsion; this produces foam. Occasionally, foaming is transient and caused by a forceful urination into water in a toilet. (See also Section IV: “Urine Studies.”)

TREATMENT

- Treat the underlying cause of proteinuria
- Qualitative dipstick analysis, 24-hr urine collection, renal workup

REFERENCE

Diskin CJ, Stokes TJ, Dansby LM, et al. Surface tension, proteinuria, and the urine bubbles of Hippocrates. Lancet 2000;355:901–902.

URINE, ODOR

DESCRIPTION Urine odor is related to the volume, concentration, and composition of a variety of excreted chemicals and physiologic contributions from the urinary system. Normally, dilute urine ranges from odorless to mildly aromatic, often described as nutty 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 decomposition, cystinuria	Sulfured	Dehydration
Strong	Diabetic ketoacidosis	
Sweet, fruity odor	Enterovesicular fistula	
Feculent	Retained urine	
Ammonia-like	Stagnant urine, room temperature urine	
Ammonia like	UTI	
Pungent	Food and medications	
Asparagus	Pungent, rotten cabbage	
Fish oils	Fishy	
Vitamin B6	Pungent, vitamin-like	
Inborn errors of metabolism	Glutaric and isovaleric acidemia	

Sweaty feet, acrid

Hawkinsinuria

Swimming pool

Hypermethioninemia

Boiled cabbage

Maple syrup urine disease

Maple syrup

Multiple carboxylase deficiency

Tomcat urine

Oasthouse urine disease

Hops-like

Phenylketonuria

Musty, mousey

Trimethylaminuria

Rotting fish

Tyrosinemia

Boiled cabbage, rancid butter

References

Rezvani I. Metabolic diseases. In: Kliegman R, et al., eds. Nelson Textbook of Pediatrics, 18th ed. Philadelphia: Saunders, 2007.

Robertson J, Shikofski N. Inborn errors of metabolism. In: Gunn VL, et al., eds. The Harriet Lane Handbook, 17th ed. Elsevier Mosby. Philadelphia: Elsevier Mosby, 2005.

URINE, PARTICLES IN

DESCRIPTION In the gross observation of particulate matter in the urine, differential diagnoses include infection (bacterial, fungal), enterovesical fistula (mucous, feces, or undigested food particles), blood clots from hematuria of any cause, papillary necrosis, ATN, chyluria, urolithiasis, crystalluria, bilharzia (schistosomiasis), urothelial or other carcinoma with sloughing tissue, clumping of excessive urinary cast or protein, postoperative (eg, suture 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 [in <2 hr] should be refrigerated. Clearing of the specimen after addition of a small amount of acid indicates that precipitation of salts is the probable cause.

URINOMA (PERINEPHRIC PSEUDOCYST)

DESCRIPTION A collection of urine outside the urinary tract (extravasation), commonly seen from rupture of the collecting system (usually calyceal rupture) due to high pressures from obstruction (stones, posterior urethral valves, strictures, others), postoperative surgical leak (ureteral anastomosis, collecting system closure, urethral anastomosis, etc.), or traumatic disruption of the urinary tract (iatrogenic, penetrating, or blunt). Leakage of urine into the perirenal or periureteral 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 a 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 lymphocele. Classically, the urinoma is thin-walled and smooth, and the walls tend to enhance secondary to inflammatory neovascularity. In contrast, the walls of abscesses and hematomas tend to be thick and more irregular with even more prominent vascularity. Typically, urinomas demonstrate homogenous Hounsfield units between –10 to +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 reabsorb spontaneously, and drainage is not necessary. If the urinoma is large, CT- or US-guided drainage or aspiration can be performed. In perirenal urinomas due to trauma to the kidney, viability of the parenchyma must be assessed by contrast-enhanced CT. If nonviable 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, Adult.")

REFERENCE

Heikkilä J, et al. Urinomas associated with posterior urethral valves. Urology 2008;180(4):1476–1478.

URINOTHORAX

DESCRIPTION Urinothorax 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 retroperitoneal urinoma and then its passage into the pleural space directly or via lymphatics. Cases have been reported in the setting of interventions including percutaneous nephrolithotomy, 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 persistent urine leak and thoracentesis or chest tube placement is therapeutic.

REFERENCE

Agarwal HA. Urinothorax: An unusual cause of pleural effusion. Singapore Med J 2007;48(11):E289.

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. Precise results provided by urodynamic studies are necessary to correctly treat the incontinent patient.

Urodynamic Indications

Normal Urodynamic Values

- Failure of empiric treatments
- Volume Voided (mL): 338 ± 234
- Symptomatic voiding dysfunction prior to beginning incontinence therapy
- Voiding Time (sec): 28 ± 22
- Inability to demonstrate incontinence clinically despite subjective patient complaints
- Max Flow (mL/sec): M 24 ± 10, W 30 ± 10
- Significant morbidity of proposed incontinence treatment course
- Average Flow (mL/sec): M 14 ± 5, W 22 ± 14
- Following prior surgical therapy for incontinence
- Maximum Capacity (mL): M 552 ± 132, W 453 ± 146
- Following pelvic radiation
- Compliance (mL/cm water): M 56 ± 37, W 71 ± 40
- Following radical pelvic surgery
- Postvoid Residual (mL): 20 ± 50
- Known or suspected neurologic disorder that may influence bladder function (ie Spinal Cord Injury)

- Simpler diagnostic tests have been inconclusive

M, Men; W, Women.

REFERENCE

Wyndaele JJ. Normality in urodynamics studied in healthy adults. J Urol 1999;161:899–902.

UROGENITAL DISTRESS INVENTORY (UDI-6)

DESCRIPTION The UDI-6 is a 6-item questionnaire that assesses lower urinary tract symptoms, including incontinence, in women. All questions are relatively easily understood by patients, and individual responses have been shown to correlate with different types of urinary incontinence (#3 >2 = stress urinary incontinence; #1, #2 >2 = detrusor overactivity; #5 > all other scores = bladder outlet obstruction). (See table at top of page.)

Urogenital Distress Inventory–Short Form

Do you experience and, if so, how much are you bothered by:

Not at All

A Little Bit

Moderately

Greatly

UDI#1

Frequent urination

0

1

2

3

UDI#2

Urine leakage related to urgency

0

1

2

3

UDI#3

Urine leakage related to physical activity

0

1

2

3

UDI#4

Small amounts of urine leakage (drops)

0

1
2
3
UDI#5
Difficulty emptying your bladder
0
1
2
3
UDI#6
Pain or discomfort in the lower abdomen/genitalia
0
1
2
3
REFERENCE
Lemack GE, Zimmern PE. Predictability of urodynamic findings based on the Urogenital Distress Inventory-6 Questionnaire. Urology 1999;53(3):461–466.

UROLITHIASIS, CYSTINE AND CYSTINURIA (HYPERCYSTINURIA)

DESCRIPTION Accounting for about 1–2% of adult and 6–8% of pediatric nephrolithiasis, cystine lithiasis is the clinical expression of an autosomal recessive metabolic disorder (mutations in 2 genes, SLC3A1 and SLC7A9) resulting in excessive urinary excretion (secondary to reduced tubular absorption) of cystine disulfate. Clinical consequences present only when crystals precipitate (low cystine solubility at normal urinary pH values). There is a transport defect of dibasic amino acids including cystine, ornithine, lysine, and arginine (COLA).(See also Section I: “Urolithiasis, Pediatric.”)

Phenotypic Classification of Cystinuria (Hypercystinuria)

Type I

Heterozygotes do not form stones; urinary excretion <100 mg/d

Type II

Autosomal recessive incomplete; urinary excretion 250–1,400 mg/d; similar to type I homozygotes

Type III

Autosomal recessive incomplete; urinary excretion 100–300 mg/d

Cystine urolithiasis should also be suspected in patients with a first stone in childhood or adolescence (rarely, may be delayed to adulthood), the presentation of a large branched calculi, or based on family history. With cysteine stones, a KUB may show stones with a fuzzy gray appearance, as these stones are less radiopaque than calcium stones. Pathognomonic hexagonal cystine crystals can be seen on urine analysis. The urine is screened for cystine using the cyanide-nitroprusside test (positive with cystine >75 mg/L). If positive, a 24-hr urine quantitative test is performed. Normal cystine excretion is 30 mg/d (0.13 mmol/d), with cystinurics >400 mg/d (1.7 mmol/d). Heterozygotes for cystinuria and with the Fanconi syndrome, excrete <250 mg/d (1 mmol) and usually do not form stones.

TREATMENT

- Create high urine volume (>1.5 L/m2/d).
- Alkalize urine to pH of >7.5 (3–4 mEq/kg/d potassium citrate/bicarbonate, in 3–4 divided doses. Alkaline urine increases solubility of cysteine).
- Restrict sodium and protein.
- Use chelating agents (bind cystine) only if the above conservative methods do not work: Thiola, D-penicillamine, tiopronin

REFERENCE

Vella M, et al. Pathophysiology and clinical aspects of urinary lithiasis. Urol Int 2007;79(Suppl I):26–31.

UROLITHIASIS, INDINAVIR

DESCRIPTION A spectrum of asymptomatic crystalluria and renal colic secondary to urolithiasis, with or without dysuria or urgency, seen in patients who are HIV infected and being treated with indinavir. (See Section II: “HIV Infection, Urologic Considerations.”)

REFERENCE

Hermieu J, et al. Urolithiasis and the protease inhibitor indinavir. Eur Urol 1999;35:239–241.

UROLITHIASIS, INFECTIOUS (STRUVITE)

DESCRIPTION Composed of magnesium, ammonium, and phophate mixed with carbonate; struvite stones directly correlate with the presence of urease-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 stone. (See also Section I: “Urolithiasis, Staghorn.”)

CAUSES

- Foreign body in the urinary tract
- Neurogenic bladder
- Urinary diversion
- LUTS
- Indwelling catheter

REFERENCE

Vella M, et al. Pathophysiology and clinical aspects of urinary lithiasis. Urol Int 2007;79(Suppl I):26–31.

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 calculi can be confused with uric acid calculi because they are radiolucent. Matrix calculi, however, are usually associated with alkaline urine from a UTI, whereas uric acid calculi usually form in acidic sterile urine. Standard treatment techniques such as ureteroscopic lithotripsy are used. (See also Section I: “Urolithiasis, Adult, General.”)

REFERENCE

Kim SH, et al. CT and ultrasound features of renal matrix stones with calcified center. J Comput Assist Tomogr 1996;20(3):404–406.

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 (cyanuric acid, ammelide, ammeline) has industrial use as a resin or adhesive, and has been deliberately added to raw 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 cyanuric acid (a by-product 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 renal failure if indicated; use blood or peritoneal dialysis.
- Consider surgical pyelolithotomy in refractory cases.

REFERENCE

World Health Organization. Melamine and cyanuric acid: Toxicity, preliminary risk assessment and guidance on levels in food (25 Sept 2008). Available online at: www.who.int/foodsafety/fs_management/melamine.pdf.

UROLITHIASIS, TRIAMTERENE

DESCRIPTION Renal calculus consisting either completely or partially of triamterene, a potassium-sparing diuretic often used with hydrochlorothiazide in the treatment of hypertension. Promotion of nucleation and growth of renal calculi, especially calcium oxalate monohydrate, has been shown to occur from triamterene and its metabolites. They are usually radiopaque. Although rare, they usually occur in a patient with a history of urolithiasis. (See also Section II: “Urolithiasis, Adult, General.”)

TREATMENT

- Avoid use of triamterene in patients with a history of urolithiasis.
- Discontinue use of triamterene in patients with triamterene urolithiasis.

REFERENCE

Carr MC, et al. Triamterene nephrolithiasis: Renewed attention is warranted. J Urol 1990;144(6):1339–1440.

UROLITHIASIS, XANTHINE

DESCRIPTION Renal calculus composed of xanthine are usually associated with hereditary xanthinuria, an autosomal recessively inherited inborn error of metabolism characterized by a deficiency of xanthine oxidase. Other causes include allopurinol use in patients with Lesch-Nyhan syndrome, APRT deficiency, or endogenous uric acid overproduction. Xanthine calculi can be confused with uric acid calculi because they are both radiolucent. Xanthine calculi, however, are associated with low serum uric acid levels. Treat with high fluid intake and standard lithotripsy or stone removal techniques. (See also Section II: “Urolithiasis, Adult, General.”)

REFERENCE

Cameron JS, et al. Gout, uric acid, and purine metabolism in paediatric nephrology. Pediatr Nephrol 1993;7:105–118.

SHORT TOPIC SECTION V

VACTERL ASSOCIATION

DESCRIPTION Also called VATER syndrome, a congenital abnormality involving defects in 3 of the following: Vertebral defects, anal atresia, cardiac defects, esophageal atresia and/or tracheo-esophageal fistula, renal dysplasia, and limb defects, especially radial limb defects.

REFERENCE

1. Botto LD, et al. The spectrum of congenital anomalies of the VATER association: An international study. Am J Med Genet 1997;71:8–15.

VAGINAL AGENESIS

DESCRIPTION Absence or failure of formation of the vagina. Occurs in 1 in 4,000 to 1 in 5,000 female births. 50% of the time, vaginal agenesis is associated with renal abnormalities, such agenesis or ectopia. Uterine abnormalities are commonly associated as well. Etiology has been theorized to be a defect in the embryologic development of a single mesonephric duct. The patient usually comes to attention due to primary amenorrhea. Surgical reconstruction with the use of grafts or flaps is the treatment of choice.

REFERENCE

2. Marshall FF. Vaginal abnormalities. Urol Clin N Am 1978;5(1):155–159.

VAGINAL ATROPHY, UROLOGIC CONSIDERATIONS

DESCRIPTION Thinning and inflammation of the vaginal walls secondary to lack of estrogen. Most common following menopause, the condition affects 50% of that population, but may also occur with breast-feeding and other low estrogen states. The condition presents as vaginal burning and itching with or without discharge; often linked with dyspareunia. It is often associated with increased urinary frequency, urgency, and/or dysuria. Increased number of UTIs and urinary incontinence have also been reported.

SYNONYMS

- Atrophic vaginitis
- Genitourinary atrophy

TREATMENT

- Local estrogen therapy: Topical cream, vaginal suppositories, pessaries/rings
- Systemic estrogen therapy: Pill, patch, gel (must use with progestin to avoid uterine lining dysplasia)

REFERENCE

3. Harms RW, et al. Vaginal Atrophy. MFMER 2006;9(5):1–10.

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 VII: “Vaginal Discharge Algorithm.”)

CAUSES

- Noninfective: Physiologic vaginal sloughing, cervical ectopy, retained foreign bodies, vulval dermatitis, sexual abuse
- Nonsexually transmitted infective: Bacterial vaginosis, candidal infections
- Sexually transmitted infective: Chlamydia trachomatis, Neisseria gonorrhea, Trichomonas vaginalis

REFERENCE

4. Elder JS. This month in pediatric urology. J Urol 2006;176(6):2333–2334.

5. Spence D. Vaginal discharge. BMJ 2007;335:1147–1151.

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 uterovaginal canal to regress or by abnormalities in the fusion of paramesonephric ducts during weeks 8–9 of embryologic development of the upper vagina. The lower vagina develops from the urogenital sinus when the sinovaginal 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.

REFERENCE

6. Burbige KA, Hensle TW. Uterus didelphys and vaginal duplication with unilateral obstruction presenting as a newborn abdominal mass. J Urol 1984;132(6):1195–1198.

VAGINAL FUSION

DESCRIPTION Sometimes referred to as vulvar fusion, vulvar atresia, or labial agglutination, this is a complete or partial adherence of the labia minora. Usually presents between 3 months and 4 years of age with an incidence of 3.3%. The condition predisposes patients to asymptomatic bacteruria and recurrent UTIs. Rarely, near-complete fusion can cause urinary outlet obstruction with resultant bladder distention and/or hydronephrosis. Causes include diaper rash, infections, vulvovaginitis, irritants, mechanical trauma, and sexual abuse.

Treatment is initially observation, as spontaneous resolution can be seen. Medical treatment is topical estrogen cream for 4–8 weeks, followed by 1–3 months of topical petroleum jelly application to minimize recurrence.

REFERENCE

7. Leung AKC, et al. Treatment of labial fusion with topical estrogen therapy. Clin Pediatr 2005;44:245.

VAGINAL MASS, NEWBORN

DESCRIPTION Rare interlabial or periurethral 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 cystourethrogram is usually warranted.

CAUSES

- Hydrocolpos (imperforate hymen)
- Paraurethral cyst
- Prolapsed ectopic ureterocele
- Rhabdomyosarcoma of the vagina
- Urethral polyp
- Urethral prolapse

REFERENCE

8. Nussbaum AR, Lebowitz RL. Interlabial masses in little girls. Am J Roentgenol 1983;141(1):65–71.

VAGINAL PESSARIES, UROLOGIC CONSIDERATIONS

DESCRIPTION A passive device 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. Despite a wide range in published results, when combined with pelvic floor muscle rehabilitation (ie, Kegel exercise, biofeedback), patients using a pessary should expect complete resolution in <20% of cases, but vast improvement of symptoms 50–75% of the time. This may be used as a final treatment mechanism in patients at high operative risk, or as a bridge to surgical correction of laxity in the pelvic anatomy.

REFERENCE

9. Junemann KP. The management of female stress urinary incontinence: II. The use of devices. BJU Int 2001;87:449–455.

VAGINAL PROLAPSE

DESCRIPTION Disruption of the neuromuscular, ligamentous, or fascial components involved in normal vaginal support, resulting in the externalization of a portion of the vaginal canal. Despite a complex anatomic framework, implicated causative etiologies include the uterosacral and cardinal ligaments, as well as the endopelvic fascia. Urologically notable is the association with intraoperative ureteral injury during surgical correction (11%) and postoperative association with SUI once the pelvic anatomy is restored. (See also Section I: “Pelvic Prolapse [Cystocele and Enterocoele].”)

SYNONYMS

- 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 vagina)

TREATMENT

- Abdominal sacrocolpopexy: Anterior and posterior grafts bridging vaginal wall to the sacral promontory via an abdominal incision
- Vaginal vault suspension: Apogee system (artificial recreation of the cardinal ligaments)
- Intravaginal slingplasty: Polypropylene sling recreation of the suspensory ligament
- Sacrospinous fixation: Elevation and fixation of vaginal apex to sacrospinous ligaments
- Iliococcygeal or uterosacral suspension: Via vaginal incision and fixation to surrounding structures

REFERENCE

Biller DH, Davila GW. Vaginal vault prolapse. Clev Clin J Med 2005;72(4):S12–S19.

VAGINOSIS

DESCRIPTION The most common type of vaginal infection, resulting from an imbalance between the standard vaginal flora (Lactobacillus sp.) and potentially harmful organisms (typically Gardnerella vaginalis, Mobiluncus, Bacteroides, 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 (typically pH >4.5), a positive “whiff test” (malodorous/fishy odor when secretions are combined with 10% KOH), or by the presence of “clue cells” (epithelial cells coated with bacteria) on microscopic normal saline wet mount. (See also Section II: “Trichomonas.”)

TREATMENT

- Oral metronidazole 500 mg PO b.i.d. for 7 days
- Vaginal metronidazole (MetroGel) 1 applicatorful b.i.d. for 7 days
- Tinidazole (Tindamax) 2 g PO once a day for 2 days OR 1 g PO once a day for 5 days
- Avoid douches, feminine hygiene sprays.

REFERENCE

Austin NM, et al. Susceptibility of vaginal bacteria and tinidazole. Anaerobe 2006;12:227.

VALSALVA MANEUVER

DESCRIPTION A maneuver effected by a forced expiratory effort against a voluntarily closed airway, which causes increased intrathoracic and intra-abdominal pressure and impedes venous return to the right atrium. The maneuver may increase the degree of varicocele dilatation, thus aiding in diagnosis. It can also be used to measure the pressure required to cause leakage in the absence of a bladder contraction, which correlates with the degree of urinary incontinence (called the “leak point pressure”). The Valsalva maneuver can also be used to aid in micturition in those with hypotonic bladders by increasing intravesical pressure. (See also Section III: “Leak Point Pressure.”)

REFERENCE

Desautel MG, et al. Sphincteric incontinence: The primary cause of post-prostatectomy incontinence in patients with prostate cancer. Neurourol Urodyn 1997;16(3):153–160.

VANISHING TESTIS SYNDROME

DESCRIPTION A condition in which a normal genotypic 46XY male has absent or rudimentary testes with otherwise normal differentiation of internal and external structures. Etiology is vascular compromise in utero, infection in utero, or testicular torsion in utero. Infertility is inevitable, despite aggressive testosterone replacement therapy to induce virilization.

SYNONYMS

- Bilateral anorchia
- Gonadal agenesis
- Testicular regression syndrome
- XY agonadism

TREATMENT

Testosterone replacement therapy to induce virilization

REFERENCE

Gong M, Geary ES, Shortliffe LM. Testicular torsion with contralateral vanishing testis. Urology 1996;48(2):306–307.

VAS DEFERENS, CALCIFICATION (CVD)

DESCRIPTION CVD is a rare finding primarily detected through radiologic examinations. It usually presents asymptomatically. A majority of the patients with calcification of the vas deferens are diabetics in their 5th–6th decades. For these diabetic patients, CVD has a bilateral and symmetrical presentation. In addition, a minority of patients will present with postinflammatory CVD, which usually has a unilateral and segmental presentation.

REFERENCE

Grunebaum M. The calcified vas deferens. Isr J Med Sci 1971;7:311.

VAS DEFERENS, OBSTRUCTION

DESCRIPTION Genital duct obstruction is a potentially curable cause of male infertility that may be bilateral or unilateral and may occur at multiple locations (epididymal, vasal, or ejaculatory duct). The prevalence is 7–12% of infertile men. Unilateral obstruction should not adversely affect fertility, although it has been identified as a risk factor for developing antisperm antibodies. Complete obstruction yields the pathognomonic clinical findings of acidic, fructose-negative, low-volume ejaculate azoospermia. Diagnostic modalities include static (TRUS, MRI, seminal vesicle aspiration) and dynamic (vasography, seminal vesiculography) testing. (See also Section I: “Infertility, Vas Deferens, Congenital Absence.”)

CAUSES

- Congenital: Malformations, congenital bilateral absence of the vas deferens (CBAVD), Wolffian duct anomalies/agenesis
- Acquired: Infection, iatrogenic injury, vasectomy

TREATMENT

- Varies with etiology and location of obstruction
- Ejaculatory duct: Transurethral resection, balloon dilation, antegrade seminal vesicle lavage, laser incision, vasoepididymostomy
- Vasectomy reversal (vasovasostomy)
- Sperm retrieval (aspiration vs. open biopsy) with IVF/ICSI

REFERENCE

Jarow JP. Male infertility. In: Wein AJ et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: Saunders, 2007.

VASCULITIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Vasculitis is a common reaction to injury caused by a multitude of different processes, including autoimmunity, infection, and hypersensitivity. Various types include Henoch-Schönlein purpura, polyarteritis nodosa (PAN), hypersensitivity angitis, Wegener granulomatosis, and lymphomatoid granulomatosis. A very strong correlation exists between the presence of antineutrophil cytoplasmic antibodies (ANCA) and the various types of systemic vasculitis that cause crescentic glomerulonephritis and/or focal necrotizing glomerulonephritis. Depending on the type of vasculitis, patients present with different signs and symptoms. Furthermore, some types can progress to chronic renal failure. However, upon renal biopsy, similar pathologic presentations are demonstrated. (See also Section II: “Henoch-Schönlein Purpura.”)

TREATMENT

- ANCA titers 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.
- Cytotoxic agents and corticosteroids are effective, depending on the type of vasculitis.

REFERENCE

Rees AJ. Vasculitis and the kidney. Curr Opin Hephrol Hypertens 1996;5(3):273–281.

VASECTOMY, GENERAL CONSIDERATION AND COMPLICATIONS

DESCRIPTION Surgical disruption of the vasa is the safest, least expensive, and most reliable form of sterilization, with success rates of 99.9%. Postoperative semen analysis should be performed; however a second sample with rare, immotile sperm obtained 12 weeks postoperatively is most predictive of successful sterility. Factors most likely to predict a future request for reversal include patient age <30 at the time of procedure and a change in marital status. Older data on the increased risk of prostate cancer after vasectomy are not longer considered valid. The vasectomy techniques include the following steps:

- Accessing the vasa (single incision, double incision, no-scalpel technique)
- Disrupting the vasa (suture ligation, electrocautery, fascial interposition); excision of a segment of vas with pathologic confirmation is recommended by some.
- Scrotal closure (clips, clamps, sutures, tissue adhesive)

COMPLICATIONS

- Bleeding with hematoma. Traditional techniques up to 10%; about 2% with no-scalpel techniques.
- Infections are less common with no-scalpel techniques compared to open (~1% vs. up to 4%).
- Sperm granuloma (see Section II: “Sperm Granuloma”)
- Postvasectomy pain syndrome: A chronic dull testicular ache, often made worse by ejaculation and distinct from the normal postoperative pain. Thought to be due to epididymal obstruction and congestion. Reported in 10–15% of men, and severe in a few percent. Management is NSAIDs and local therapy (warm baths, local heat); local nerve blocks and excision of a tender sperm granuloma may help. Vasectomy reversal and epididymectomy is reserved for the most severe cases.

REFERENCE

Dassow P, Bennett JM. Vasectomy: An update. Am Fam Physician 2006;74(12):2069–2074.

Awsare NS, et al. Complications of vasectomy. Ann R Coll Surg Engl 2005;87(6):406–410.

VASECTOMY REVERSAL, GENERAL CONSIDERATIONS

DESCRIPTION Usually accomplished with a 2-layer microsurgical vasovasotomy (8 10-0 nylon mucosal sutures, 10 9-0 nylon muscular sutures). Although surgical reversal of vasectomy can be technically performed on most patients, operative decision-making requires workup. Gynecologic 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 (sperm appear in semen), with postprocedural conception rates at 50–70%.

TREATMENT

- Vasovasostomy (when some component of sperm are present, grade I–IV vas fluid)
- Vasoepididymostomy (when no sperm are present in vas fluid)
- Postoperative scrotal support with abstinence for 2 weeks

REFERENCE

ASRM Practice Committee. Vasectomy Reversal. Fertil Steril 2006;86(4):S268–S271.

VASOGRAPHY, 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. Recently seminal vesicle aspiration and vesiculography mainly replaced vasography for the diagnosis of ejaculatory duct obstruction. Therefore, the primary indication for vasography is the assessment of vasal obstruction within the inguinal vas deferens. Inguinal obstruction of the vas deferens should be suspected in patients with azoospermia and previous surgeries, including orchiopexies, hernias repair, ureteral surgery, and even appendectomy (iatrogenic injuries to the vas deferens). 4 techniques for vasography have been described: Vasopuncture, vasotomy, retrograde catheterization via cystoscopy and transrectal puncture. Isolated vasography (by vas puncture) is rarely performed because of the risk of subsequent vasal 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 scrotal 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 incised vertically and vasal vessels preserved. A short segment of the vas is cleaned and hemitransected using a 15.0 ultrasharp knife until the lumen is revealed. The sheath of 25-gauge angiocatheter is inserted into the abdominal portion of the vas deferens. The vas is then flushed with normal saline (the term vasogram at this point is a misnomer, since no contrast is injected and no X-rays are taken). If injection is easily achieved with minimal pressure, the vas deferens is patent. In case of resistance to the injection, the formal vasogram is performed with 1:2 diluted nonionic contrast, while gentle pressure is applied to the Foley catheter to prevent reflux of the contrast into the bladder and the table is put in the slightly reversed Trendelenburg position. If obstruction is confirmed at the level of ejaculatory duct, methylene blue may be added to the contrast since it enables the control of the depth and efficacy of transurethral resection of the ejaculatory duct.

The application of a 32-gauge soft radiopaque epidural catheter has been described for the vasography. The catheter is advanced down the vas deferens, and the vasogram is performed. Because the catheter is radiopaque, its position in the vas can be confirmed prior to injection. If needed, the catheter could be advanced further to obtain better details. If no further microsurgical reconstruction is performed, the vasotomy site is closed with a microsurgical technique using 10-0 monofilament Prolene or nylon for mucosa, 9-0 nylon for muscularis, and 6-0 Prolene for the adventitial layer.

The puncture technique employs a 30-gauge lymphangiogram needle placed through the wall of the vas deferens in the direction of the prostate. This technique, also less invasive, may be associated with a higher risk of creating submucosal false passages, with subsequent scarring and obstruction. Complications include stricture of the vas deferens, hematoma, injury to the vasal blood supply, and sperm granuloma.

REFERENCE

Kolettis PN, et al. Prediction of vasography outcomes based on clinical and laboratory data. Fertil Steril 2005;84(1):S219–S220.

Turek PJ. Vasography, seminal vesicle aspiration and testicular biopsy. Diagn Surg 2008;1–16.

VENOUS LEAK SYNDROME

DESCRIPTION Venous leakage is a common cause of vascular impotence due to venoocclusive dysfunction. Possible leak sites are the superficial and deep dorsal veins, cavernosal venous system, and glans or corpus spongiosum. The majority of patients have >1 leak site. Diagnosis can be demonstrated by pharmacocavernosography (caversonography performed after the intracorporal injection of paravarine or phentolamine).

CAUSES

- Congenital
- Iatrogenic
- Neovascularity associated with inflammatory reactions secondary to stricture disease or Peyronie disease.

TREATMENT

- Surgical correction
- Combination of pharmacologic injection therapy with a venous constriction system or a vacuum device

REFERENCE

Shabsigh R, et al. Venous leaks: Anatomical and physiological observations. J Urol 1991;146:1260.

VESICOBULLOUS LESIONS, EXTERNAL GENITALIA

DESCRIPTION Dermatologic lesions on the external genitalia mandate screening for STDs. They may be painful or painless, single or multiple, exophytic or ulcerated, confined to the genitalia or occurring elsewhere on the body. Treatments vary widely based on etiology, and may require partner treatment in the case of STDs. (See also Section I: “Penis, Lesion, General”; “Sexually Transmitted Disease.”)

VE Sicobullous Lesions, External Genitalia

Etiology

Examples

Infective, Non–sexually transmitted

Balanitis/posthitis: Ulcerated lesion preceded by 2–3 days of irritation, usually associated with foul discharge and edema.

Folliculitis/furunculosis: Hair follicle infection marked by pointed lesions with central pustules; usually enlarge and rupture leaving edema/erythema for days to weeks.

Pediculosis pubis: Parasitic infestation (lice) with red, itchy papules and white/gray eggs visible attached to hair.

Scabies: Mite infestation. Organisms burrow under skin causing crusted papules 1–10 cm at the genitalia with satellite lesions on the extremities.

Tinea cruris: Superficial fungal infection (jock itch) with raised, scaling patches on the inner thigh or groin with severe pruritus.

Infective, Sexually transmitted

Chancroid: H. ducreyi infection with 1 (or more) painful, deep, ulcerated lesions on the genitalia; bleeds easily with marked lymphadenopathy.

Genital herpes: HSV (usually 1 or 2) produces fluid-filled vesicles on genitals and/or mouth or anus, which may rupture leaving shallow painful ulcers. Associated with prodrome of numbness and tingling.

Genital warts: HPV causes painless pink/red pedunculated lesions varying in size; may have cauliflower appearance and become malodorous.

Syphilis: 2–4 weeks following T. pallidum infection, 1 small, red, fluid-filled papules erupt to form a painless deep ulcer with a clear base; may become systemic and is associated with unilateral lymphadenopathy.

Noninfective

Bowen disease: Brownish red, raised, scaly plaque with well-defined borders; possible ulceration; premalignant.

Leukoplakia: White, scaly patches on glans/prepuce with skin thickening and fissures; premalignant.

Penile cancer: Painless, enlarging wartlike lesion on glans or foreskin; occasionally associated with pain and malodorous discharge.

Urticaria: Systemic allergic reactions may present with genital hives; erythematous, intensely pruritic with systemic eruption.

Drug eruption: Similar in appearance to urticaria; associated with phenolphthalein, barbiturates, tetracyclines, and sulfonamides.

REFERENCE

Springhouse. Handbook of Signs and Symptoms, 3rd ed. Philadelphia: Lippincott, 2005.

VIDEOURODYNAMICS

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 seconds. Adding simultaneous video enhances the evaluation of all patients, especially for more complex urodynamic 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 neurogenic patients with dyssynergia 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 cystocele present. In neurogenic bladders, simultaneous video screening aids in diagnosing proximal and distal sphincter dyssynergia 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: Urodynamics.)

REFERENCE

McGuire EJ, et al. Video-urodynamic studies. Urol Clin N Am 1996;23(2):309–321.

VILLOUS ADENOMA, BLADDER/URETHRA

DESCRIPTION Villous adenomas of the bladder and urethra are rare and histologically identical to those found in the colon. These tumors are more frequently found in the urachus at the dome of the bladder. On cystoscopy, these villous adenomas appear as exophytic papillary masses. Histologically, villous adenomas are complex branching 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 urinary retention, hematuria, 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, 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, cystogram, cystoscopy, or biopsy. Treatment is transurethral resection with selective cystectomy.

REFERENCE

Channer JL, Williams JL, Henry L. Villous adenoma of the bladder. J Clin Pathol 1993;46(5):450–452.

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, renal cell carcinoma) may coexpress keratin and vimentin. (See also Section II: “Immunohistochemical Staining, Urologic Considerations.”)

REFERENCE

Cotran R, Kumar V, Robbins S. Pathologic Basis of Disease, 5th ed. Philadelphia: Saunders, 1995:299.

VINCENT CURTSY

DESCRIPTION Holding maneuver used by children to postpone voiding or suppress urinary urgency. Vincent curtsy is performed by squatting with a hand or heel pressed firmly into the perineum. Other common holding maneuvers including standing on tiptoe or forceful crossing of the legs.

REFERENCE

Vincent SA. Postural control of urinary incontinence. The curtsy sign. Lancet 1966;2:631.

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 external genitalia only in 0.3% of the adult male population. Treatment is optional and can include steroids, UV light, skin grafting, and cosmetic covering.

REFERENCE

Margolis DJ. Cutaneous diseases of the male external genitalia. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998.

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-hour period, typically documents the following:

- Time of urge to void
- Strength of urge or pain
- Time of actual void
- Voided volume
- Incontinence (stress, urge, unaware)
- Amount of leakage (small, medium, large)

(See Section VII: “Voiding Diary.”)

REFERENCE

Stav K, et al. Women overestimate daytime urinary frequency: The importance of the bladder diary. Urology 2009;181(5):2176–2180.

VOIDING SYMPTOMS, DEFINITIONS (INTERNATIONAL CONTINENCE SOCIETY DEFINITIONS)

DESCRIPTION The International Continence Society in 2002 published updated guidelines to define and categorize lower urinary tract symptoms into 3 main groups including storage, voiding, and post-micturition, as defined and subdivided here:

- Storage symptoms are experienced during storage phase of bladder:
  - Increased day-time frequency
  - Nocturia: Complaint that individual wakes up more than once to void
  - Urgency: Complaint of sudden compelling desire to void that is difficult to defer
  - Urinary incontinence: Complaint of any involuntary loss of urine
- Voiding symptoms are experienced during voiding phase:
  - Slow stream
  - Splitting 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
  - Terminal dribble: Term used when an individual describes prolonged final part of micturition
- Post-micturition symptoms are experienced immediately after micturition:
  - Feeling of incomplete emptying
  - Post-micturition dribble describes the involuntary loss of urine after the patient finishes passing urine.

REFERENCE

Abrams P, et al. The standardization of terminology in lower urinary tract function. Neurourol Urodyn 2002;21:167–178.

VULVAR MALIGNANCY, UROLOGIC CONSIDERATIONS

DESCRIPTION Vulvar carcinoma encompasses any malignancy that arises in the skin, glands, or underlying stroma of the perineum, including the mons, labia minora, labia majora, Bartholin glands, or clitoris. Early detection (lesions <2 cm) allow for local resection without node dissection. Cases 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, parametrium, 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

Gershenson DM, et al. Pelvic exenteration for primary and recurrent vulvar cancer. Gynecol Oncol 1995;58:202–205.

VULVODYNIA

DESCRIPTION Vulvar discomfort, most often described as burning pain, occurring in the absence of relevant or visible findings or specific, clinically identifiable, neurologic disorder. Lifetime prevalence reported at 16%. The condition is often reported with dyspareunia, but not associated with urinary complaints. However, 11% of women with vulvodynia will concomitantly be diagnosed with interstitial cystitis.

REFERENCE

Clemens JQ, Bogart JM. Symptoms of interstitial cystitis, painful bladder syndrome and similar diseases in women: A systematic review. J Urol 2007;177:450–456.

VURD SYNDROME

DESCRIPTION VURD stands for vesicoureteral reflux associated with renal dysplasia. This term applies to children with posterior urethral valves in which there is massive reflux into a dysplastic nonfunctioning kidney; ~15% of the patients with posterior urethral valves have this syndrome. Some believe that severe unilateral vesicoureteral reflux is protective of the contralateral nonrefluxing kidney. Diagnosis is made using kidney US, voiding cystourethrogram, nuclear imaging of kidneys, and serum creatinine levels. The patient should be observed first to see if kidney function returns. If function does not return, then nephrectomy is considered.

REFERENCE

Donnelly LF, et al. Unilateral vesicoureteral reflux: Association with protected renal function in patients with posterior urethral valves. AJR 1997;168(3):823–826.

SHORT TOPIC SECTION W

WAGR SYNDROME (WILMS TUMOR, ANIRIDIA, GENITAL ANOMALY, RETARDATION SYNDROME)

DESCRIPTION This is one of the Wilms tumor–associated syndromes, presenting in children <3 years. It causes mental retardation and GU manifestations in the form of renal hypoplasia, ectopia, fusions, duplications, cystic disease, hypospadias, cryptorchidism, and pseudohermaphroditism. Physical exam may also reveal ear deformities, umbilical/inguinal hernias, and aniridia.

REFERENCE

1. Kirsch AJ, Snyder HM III. What's new and important in pediatric urologic oncology. AUA Update Series 1998;17:83.

WALLACE URETERAL ANASTOMOSIS

DESCRIPTION A surgical procedure in which the spatulated ureters are laid adjacent and the apex of each is sutured. The medial and lateral walls are then sutured together in either an interrupted or running fashion. The Y configured ureters are then anastomosed to the end of the small bowel segment.

REFERENCE

2. McDougal WS. Use of intestinal segments and urinary diversion. In: Walsh PC, Retik AB, Vaughan ED, et al., eds. Campbell's Urology, 7th ed. Philadelphia: Saunders, 1998:3137–3144.

WALTER REED STAGING SYSTEM, TESTIS CANCER

DESCRIPTION Lymphangiographic criteria used to evaluate the presence 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

3. Maier JG, Schamter DT. The role of lymphangiography in the diagnosis and treatment of malignant testicular tumors. AJR 1972;114:482.

WATERHOUSE URETHRAL STRICTURE REPAIR

DESCRIPTION Through a combined abdominal and perineal approach, a wedge of pubis is resected with a Gigli saw. The membranous stricture is identified and excised. The distal urethra is mobilized off the corporal bodies, and the spatulated urethral edges are reanastomosed.

REFERENCE

4. Devine CJ, Devine PC. Operations for urethral stricture. In: Novick AC, Streem SB, Pontes JE, eds. Stewarts Operative Urology. Baltimore: Williams & Wilkins, 1989:650–680.

WATERHOUSE-FRIDERICHSEN SYNDROME

DESCRIPTION Acute adrenocortical insufficiency in children suffering from septicemia with Pseudomonas or meningococcemia, leading to acute hemorrhagic destruction of both adrenal glands.

REFERENCE

5. Rao RH, et al. Bilateral massive adrenal hemorrhage: Early recognition and treatment. Ann Intern Med 1989;116:227.

WEDDELLITE

DESCRIPTION Mineralogic name for renal calculi composed of calcium oxalate dihydrate. (See Section I: “Urolithiasis, Calcium Oxylate/Phosphate.”)

WEGENER GRANULOMATOSIS, UROLOGIC CONSIDERATIONS

DESCRIPTION Systemic granulomatous vasculitis, most commonly affecting the upper and lower respiratory tracts and the kidneys, involving small arteries and venules. Respiratory infiltrates or sinusitis are commonly the presenting symptoms, as well as constitutional symptoms (weight loss, fever, etc.). Renal involvement is usually vasculitis-induced chronic renal failure, but acute fulminant glomerulonephritis and occasional interstitial nephritis can be present. Red cells, red cell and other casts, and proteinuria are noted. Other urologic manifestations include granulomatous necrotizing prostatitis, urethritis, or epididymoorchitis. Hemorrhagic cystitis is common, but usually iatrogenic secondary to cyclophosphamide treatment. Progressive renal insufficiency with end-stage reanl disease occurs in up to 25% of patients.

DIAGNOSIS

- Granulomatous necrotizing vasculitis: Lung biopsy
- Focal necrotizing glomerulonephritis: Renal biopsy
- Red cell casts in voided urine: Glomerulonephritis
- Antineutrophil cytoplasmic antibodies: Useful for follow-up

TREATMENT

- Cyclophosphamide
- Corticosteroids
- Other cytotoxic and immunosuppressive agents: Methotrexate, cyclosporine, FK-506
- Surveillance cystoscopy when cyclophosphamide used

REFERENCE

6. Aasarod K, et al. Wegener’s granulomatosis: Clinical course in 108 patients with renal involvement. Nephrol Dial Transplant 2000;15(5):611–618.

WEISS CRITERION

DESCRIPTION Most commonly used histopathologic system to provide diagnostic criteria for malignant adrenocortical tumors. Originally proposed in 1984, it has since undergone one revision. Original Weiss Criteria (requires 3 of the following):

- Fuhrman nuclear grade III or IV
- 5+ mitotic figures/HPF on 10+ fields
- Atypical mitotic figures (spindles)
- Clear or vacuolated cells <25% or tumor
- Diffuse architecture (>1/3 of tumor patternless organization)
- Microscopic necrosis
- Venous invasion
- Sinusoidal invasion
- Capsular invasion

Modified Weiss Criteria (using 1 if factor is present in tumor, 0 otherwise):

- 2× mitotic rate + 2× clear cytoplasm + abnormal mitoses + necrosis + capsular invasion
- Score total of 3 suggests malignancy

REFERENCE

7. Aubert S, et al. Weiss system revisited: A clinicopathologic and immunohistochemical study of 49 adrenocortical tumors. Am J Surg Pathol 2002;26(12):1612.

WHEWELLITE

DESCRIPTION Mineralogic name for renal calculi composed of calcium oxalate monohydrate. (See also Section I: “Urolithiasis, Calcium Oxylate/Phosphate.”)

WHITAKER TEST

DESCRIPTION Antegrade pressure-flow study to assess for renal obstruction. Used to determine if pelvocaliectasis or hydronephroureterosis seen radiographically 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. Elevation of renal pelvic pressure over bladder pressure indicates some degree of renal obstruction. A Foley catheter must be in the bladder.

Renal Pelvis, Bladder Pressure Differential

Degree of Obstruction

<13 cm H_2O

Normal

14–20 cm H_2O

Mild obstruction

21–34 cm H_2O

Moderate obstruction

>35 cm H_2O

Severe obstruction

SYNONYMS

- Urodynamic antegrade pyelogram
- Ureteral perfusion test
- Pressure-flow Whitaker exam

REFERENCE

8. Whitaker RH. The Whitaker Test. Urol Clin N Am 1979;6(3):529–539.

WHITLOCKITE

DESCRIPTION Mineralogic name for renal calculi composed of tricalcium phosphate. (See Section II: “Urolithiasis, Calcium Oxylate/Phosphate.”)

WHO/ISUP CONSENSUS CLASSIFICATION OF UROTHELIAL NEOPLASMS (1998 AND 2004)

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, grade 1–3) into low- and high-grade carcinoma. Additionally, a new entity was recommended for low-grade papillary lesions, entitled papillary urothelial neoplasm of low malignant potential (PUNLMP). The WHO/ISUP classification:

- Normal
- Hyperplasia
- Flat hyperplasia
- Papillary hyperplasia
- Flat lesions with atypia
- Reactive (inflammatory) atypia
- Atypia of unknown significance
- Dysplasia (low-grade intraurothelial neoplasia)
- Carcinoma in situ (high-grade intraurothelial neoplasia)
- Papillary neoplasms
- Papilloma
- Inverted papilloma
- PUNLMP
- Papillary carcinoma, low-grade
- Papillary carcinoma, high-grade
- Invasive neoplasms
- Lamina propria invasion
- Muscularis propria (detrusor muscle) invasion

REFERENCE

9. Epstein JI, et al. The World Health Organization/International Society of Urological Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. Bladder Consensus Conference Committee. Am J Surg Pathol 1998;22(12):1435–1448.

WILMS TUMOR STAGING SYSTEM, INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY (SIOP)

DESCRIPTION Developed by the International Society of Pediatric Oncology, this staging system is based on post-chemotherapy surgical evaluation. It is used extensively in Europe. The National Wilms Tumor Staging System is based upon surgical evaluation before chemotherapy. It is used throughout the US and Canada. (See table below). (See also Section I: “Wilms Tumor”; Section II: “Wilms Tumor Staging System, National (NWTS)”

Wilms Tumor Staging System, International Society of Pediatric Oncology (SIOP)

Stage

Following Chemotherapy

I

Tumor is limited to kidney or surrounded with fibrous pseudocapsule if outside of the normal contours of the kidney, the renal capsule or pseudocapsule may be infiltrated with the tumor, but it does not reach the outer surface, and is completely resected (resection margins clear)

The tumor may be protruding into the pelvic system and dipping into the ureter (but it is not infiltrating their walls)

The vessels of the renal sinus are not involved

Intrarenal vessel involvement may be present

II

The tumor extends beyond kidney or penetrates through the renal capsule and/or fibrous pseudocapsule into perirenal fat but is completely resected (resection margins clear)

The tumor infiltrates the renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma but is completely resected

The tumor infiltrates adjacent organs or vena cava but is completely resected

III Residual tumor confined to the abdomen

Incomplete excision of the tumor, which extends beyond resection margins (gross or microscopical tumor remains postoperatively)

Any abdominal lymph nodes are involved

Tumor ruptures before or intraoperatively (irrespective of other criteria for staging)

The tumor has penetrated through the peritoneal surface

Tumor thrombi are present at resected margins of vessels or ureter, transected or removed piecemeal by surgeon

The tumor has been surgically biopsied (wedge biopsy) prior to preoperative chemotherapy or surgery

Regional lymph node involvement was considered stage II in the previous SIOP staging system.

IV

Hematogenous metastases (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdomino-pelvic region

V

Bilateral renal tumors at diagnosis

REFERENCE

Ahmed HU. An update on the management of Wilms' tumour. J Surg Oncol 2007;33(7):824–831.

Metzger ML, Dome JS. Current therapy for Wilms' tumor. Oncologist 2005;10(10):815–826.

WILMS TUMOR STAGING SYSTEM, NATIONAL (NWTS)

DESCRIPTION A unified system developed to aid in the conduct of clinical trials now widely used for clinical staging treatment decisions (see table above). The NWTS system is based upon surgical evaluation prior to the administration of chemotherapy. It is used throughout the US and Canada. The SIOP system is based upon post-chemotherapy 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].”)

Stage

Before Chemotherapy

I

Tumor limited to the kidney, completely excised

Tumor was not ruptured before/during removal

The vessels of the renal sinus are not involved beyond 2 mm

There is no residual tumor beyond the margins

II

Tumor extends beyond the kidney but is completely excised

No residual tumor at or beyond the margins of excision

Tumor thrombus in vessels outside the kidney is stage II if the thrombus is removed en bloc with the tumor

Although tumor biopsy or local spillage confined to the flank were considered stage II by NWTSG in the past, such events will be considered stage III in upcoming Children’s Oncology Group (COG) studies.

III Residual tumor confined to the abdomen

Lymph nodes in the renal hilum, the periaortic chains, or beyond are found to contain tumor

Diffuse peritoneal contamination by the tumor

Implants are found on the peritoneal surfaces

Tumor extends beyond the surgical margins (microscopically or grossly)

Tumor is not completely resectable because of local infiltration into vital structures

IV

Hematogenous metastases or metastases to distant lymph nodes

V

Bilateral renal involvement at initial diagnosis

REFERENCE

D’Angio GJ, et al. Treatment of Wilms’ tumor: Results of the Third National Wilms’ Tumor Study. Cancer 1989;64:349–360.

Metzger ML, Dome JS. Current therapy for Wilms’ tumor. Oncologist 2005;10(10):815–826.

WINTER CORPORAL SHUNT

DESCRIPTION A shunt between the corpora and glans penis. 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. Used in the treatment of priapism, it is also referred to as a percutaneous glanducavernous shunt.

REFERENCE

Thomas AJ. Surgery for priapism. In: Novick AC, Streem SB, Pontes JE, eds. Stewarts Operative Urology. Baltimore: Williams & Wilkins, 1989:826–832.

WOLFFIAN DUCT REMNANTS

DESCRIPTION Normally, an embryo develops 2 sets of paired Müllerian and Wolffian (mesonephric) ducts. In females, virilization of the Wolffian system fails to occur, and Wolffian vestiges may persist as the epoophoron, Gartner duct, or the appendix vesiculosa, commonly forming paraovarian cysts. In males, virilization of the Wolffian duct gives rise to epididymis, vas deferens, ejaculatory duct. and seminal vesicles. The rostral end of the Wolffian duct occasionally persists as a vestigial remnant, the appendix epididymis. Remnants of the mesonephric tubules may persist as a cystic structure, the paradidymis. (See also Section I: “Torsion, Testis; Testicular Appendages.”)

SYNONYMS

- Paradidymis
- Appendix epididymis

REFERENCE

Wilson JD, et al. The role of gonadal steroids in sexual differentiation. Recent Prog Horm Res 1981;37:1.

WOUND DEHISCENCE, UROLOGIC CONSIDERATIONS

DESCRIPTION Development of a gap or defect in the peritoneal suture line with or without evisceration. Prevalence is in 1–3% of patients and carries a risk of mortality as high as 44%. Risk factors include anemia, hypoalbuminemia, 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 56% success rate with sutures and/or retentions, whereas the use of an interposition mesh confers an initial 100% success rate.

REFERENCE

Abbott DE, et al. Management of laparotomy wound dehiscence. Am Surg 2007;73(12):1224–1227.

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, external/indwelling catheters, distant infection, and prolonged hospitalization. The need for periprocedural antimicrobial prophylaxis has been well documented. Antibiotics should be given within 60 minutes of procedure start time, and selected based on patient history, as well as anticipated procedure. (See Section II: “Prophylactic Antibiotics, AUA Guidelines”; Section VII: “Antibiotic Prophylaxis: AUA Guidelines.”)

TREATMENT

- Cellulitis: Antimicrobial therapy and local wound care
- Superficial abscesses: Opening of the surgical wound, drainage and local wound care

REFERENCE

Wolf JS, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2008;179:1379–1390.

WUNDERLICH SYNDROME

DESCRIPTION Clinical condition classically described as spontaneous renal bleeding of non-traumatic origin, confined to the subcapsular and perirenal space. Presentation may be insidious, but the Lenk triad (flank pain, palpable mass, and deterioration with hypovolemic shock) has been described in the event of an acute onset.

CAUSES

- Angiomyolipoma
- Cysts (pancreatic, etc.)
- Idiopathic
- Tumor (urothelial carcinoma, renal cell carcinoma)
- Vasculitis and/or inflammation

REFERENCE

Albi G, et al. Wunderlich syndrome: Causes, diagnosis and radiologic management. Clin Radiol 2002;57:840–845.

SHORT TOPIC SECTION X

XANTHOMA, BLADDER

DESCRIPTION Collection of foamy histocytes found in the lamina propria in patients with disorders of lipid metabolism.

REFERENCE

1. Nishimura K, et al. Xanthoma of the bladder. J Urol 1995;153:1912.

X-LINKED SPINAL AND BULBAR ATROPHY SYNDROME (KENNEDY SYNDROME)

DESCRIPTION Kennedy syndrome is a late-onset, bulbar–spinal type of muscular atrophy, with X-linked recessive inheritance (genetic marker is CAG repeat sequences in the androgen receptor gene on chromosome X). The majority evidence of altered androgen sensitivity is restricted 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 wasting and weakness; 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

2. Jordan CL, et al. Spinal and bulbar muscular atrophy: A motoneuron or muscle disease? Curr Opin Pharmacol 2008;8(6):752–758.

XX GONADAL DYSGENESIS (46,XX)

DESCRIPTION Clinically, patients present with primary amenorrhea and lack of secondary sexual characteristics. This presentation is consistent with ovarian failure and may be associated with a host of X-chromosome aberrations. Specifically, 46,XX gonadal dysgenesis is marked by normal female chromosome constitution and hypergonadotropic hypergonadism with concurrent ovarian failure. Etiologies may be sporadic or inherited, but the condition is rarely linked to other somatic abnormalities. Other clinical manifestations include short stature, episodic metabolic acidosis, and normal intelligence.

SYNONYMS

- Ovarian failure
- Ovarian dysgenesis
- Streak ovaries

REFERENCE

3. Pober BR, et al. 46,XX gonadal dysgenesis, short stature and recurrent metabolic acidosis in two sisters. Am J Med Genetics 2001;98:121–124.

XX MALE REVERSAL SYNDROME (XX MALE)

DESCRIPTION A rare disorder of phenotypic males who have a 46XX karyotype. Physical exam may reveal short stature; small, firm testes; a small- to normal-sized penis; hypospadias; and gynecomastia. Azoospermia is typical. Seminiferous tubule sclerosis can be shown on testicular biopsy. Lab investigations reveals high gonadotropin levels and decreased testosterone levels. In most cases, DNA fragments from the short arm of the Y chromosome can be detected in the distal end of the short arm of the X chromosome.

REFERENCE

4. Petit C, et al. An abnormal terminal X-Y interchange accounts for most but not all cases of human XX maleness. Cell 1987;49:595.

XXX SYNDROME

DESCRIPTION Triple X chromosome abnormality occurs in ~1.2 in 1000 liveborn females. There are no specific diagnostic features. Menstrual irregularities and mental retardation have been reported. Fertility is usually preserved, and many XXX females have normal offspring.

REFERENCE

5. Sills JA, et al. XXX syndrome associated with immunoglobulin deficiency and epilepsy. J Pediatr 1978;93:469.

XXXY SYNDROME

DESCRIPTION Rare variant of Klinefelter syndrome (47XXY), with an additional X chromosome (48XXXY). Phenotype is similar to 47XXY, with more pronounced features; these patients frequently exhibit microphallus, hypoplastic testicles, cryptorchidism, hypospadias, and gynecomastia. They are infertile (azoospermia), usually are mentally retarded, and have characteristic facies.

TREATMENT

Supplemental testosterone may be beneficial for virilization at puberty.

REFERENCE

6. Linden MG, et al. Sex chromosome tetrasomy and pentasomy. Pediatrics 1995;96(4 Pt 1);672–682.

XXY SYNDROME (KLINEFELTER SYNDROME)

DESCRIPTION A syndrome characterized by the presence of an extra X chromosome, resulting in a hypogonadal male. It is the most common chromosomal aberration among men, with an estimated frequency of 1:500 among newborns. Caused by a nondisjunction of the meiotic 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 tubular sclerosis is a common finding on testicular biopsy. The diagnosis may be made with a chromatin-positive buccal smear, indicating the presence of an extra X chromosome. Karyotypes usually demonstrate 47XXY or the milder mosaic pattern, 46XY, 47XXY.

TREATMENT

- No therapy improves spermatogenesis in Klinefelter syndrome.
- In mosaic Klinefelter syndrome with severe oligospermia, intracytoplasmic injection with IVF is technically possible.

REFERENCE

7. Klinefelter HG Jr., et al. Syndrome characterized by gynecomastia, aspermatogenesis without aleydigism and increased secretion of follicle stimulating hormone. J Clin Endocrinol 1942;2:615.

8. Paduch DA, et al. New concepts in Klinefelter syndrome. Curr Opin Urol 2008;18(6):621–627. Review

YOLK SAC TUMOR, BLADDER

DESCRIPTION Yolk sac tumor of the bladder is very rare and appears to have a predilection for the urachal remnant. It has the same pathologic characteristics as its counterparts in any other part of the body, and it is managed in the same way. (See Section II: “Yolk Sac Tumor, Prostate.”)

REFERENCE

9. Huang HY, et al. Primary yolk sac tumor of the urachus. Arch Pathol Lab Med 2002;126(9):1106–1109.

YOLK SAC TUMOR, PROSTATE

DESCRIPTION Extragonadal germ cell 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 germ cell tumor is reported with Klinefelter syndrome. Fetoprotein levels are commonly elevated, and are used as a tumor marker; human chorionic gonadotropin is not elevated. Schiller-Duval bodies are evident on histology. Treatment is multimodal, using cisplatinum-based combination chemotherapy and radical surgery.

REFERENCE

Tay HP, et al. Primary yolk sac tumor of the prostate in a patient with Klinefelter's syndrome. J Urol 1995;153(3):1066–1069.

YOUNG CLASSIFICATION OF POSTERIOR URETHRAL VALVES

DESCRIPTION Young described 3 general types of posterior urethral valves:

- Type I: The valves are continuous with the verumontanum and take an anterior course, dividing into 2 forklike processes in the region of the bulbomembranous junction. Usually, anterior fusion of the valves is not complete; however, some cases exhibit complete anterior fusion and cleft between the folds posteriorly. A subdivision of type I consists of a single, 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, tend to pass from the upper aspect of the verumontanum toward the internal sphincter, where it divides into 2 forklike 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 entire circumference of the urethra at any level, with a small opening in the center; they have been called iris valves due to their resemblance to the iris of the eye. Incomplete varieties of this type (crescentic or semilunar) have been described. Type III valves are a more distal diaphragmatic obstruction, similar to a urethral membrane.

REFERENCE

Young HH, et al. Congenital obstruction of the posterior urethra. J Urol 1919;3:289.

YOUNG-DEES-LEADBETTER BLADDER RECONSTRUCTION

DESCRIPTION This procedure is used to achieve a functional bladder neck closure (ie, establish continence) in children with exstrophy; and also for urinary incontinence in nonexstrophy conditions, although the technique is generally no longer widely used. Through an anterior cystotomy, a rectangular area between the distal urethra and trigone is demarcated. Flaps lateral to this are developed and used to tubularize a neourethra over a 10 Fr catheter.

REFERENCE

Ouckett JW, Caldamone AA. Bladder and urachus. In: Kelalis P, King L, Belman B, eds. Clinical Pediatric Urology, 2nd ed. Philadelphia: Saunders, 1985:735.

YOUNG SYNDROME

DESCRIPTION Obstructive azoospermia in patients with frequent respiratory infections or bronchiectasis. Motile sperm, with normal cilia and vas deferens are present. The condition is caused by inspissated secretions, causing epididymal obstruction, and treated by vasoepididymostomy; fertility rates remain poor.

REFERENCE

Hughes TM III, et al. Young's syndrome: An often unrecognized correctable cause of obstructive azoospermia. J Urol 1987;137(6):1238–1240.

SHORT TOPIC SECTION Z

ZELLWEGER SYNDROME (CEREBROHEPATORENAL SYNDROME)

DESCRIPTION A family of diseases of inborn errors of metabolism caused by agenesis or disruption of peroxisomes (subcellular organelles). It follows an autosomal recessive inheritance pattern, with an incidence of 1 in 25 000 to 1 in 50,000 live births. Characteristics include severe developmental delay, sensorineural deafness, renal cortical cysts, retinal dysfunction, hepatomegaly, and characteristic facies (thus, cerebrohepatorenal syndrome). Usually lethal in childhood, rare patients survive into adolescence and adulthood. Positive diagnosis is made by serum assay of very long chain fatty acids and dihydroxyacetone phosphate acyl transferase. Hyperoxaluria and nephrocalcinosis may also be present. No known treatment exists.

REFERENCE

1. van Woerden CS, et al. High incidence of hyperoxaluria in generalized peroxisomal disorders. Mol Genet Metab 2006;88(4):346–350.

ZINNER SYNDROME

DESCRIPTION Ejaculatory duct obstruction (EDO) resulting from a unilateral seminal vesicle cyst with associated ipsilateral kidney, the condition is caused by a congenital Müllerian/Wolffian/utricular abnormality. Although EDO accounts for <1% of infertility, it is a treatable entity, using transurethral resection of ejaculatory duct.

REFERENCE

2. Pace G, et al. Ejaculatory duct obstruction caused by a right giant seminal vesicle with an ipsilateral upper urinary tract agenesia: An embryologic malformation. Fertil Steril 2008;89(2):390–394.

ZIPPER ENTRAPMENT

DESCRIPTION Usually an emergency department presentation, this penile problem usually results from the entrapment of the foreskin between the fastener device and zipper teeth as a result of the caudal motion of the zipper. Often occurs in children 3–6 years of age. Treatment should not include extraction of the foreskin or urgent circumcision, but instead should involve the release of the median bar using orthopedic bone pliers. An alternate method of release involves cutting the closed portion of the actuator (zipper teeth) with trauma shears to release the closed portion of the zipper from around the tissue.

REFERENCE

3. Yamamoto LG, et al. Comparing two methods of emergency zipper release. Am J Emer Med 2005;23:480–482.

ZONA PELLUCIDA BINDING ASSAY

DESCRIPTION An assay used to counsel patients about their chances of success with IVF. Being species-specific, the human sperm-ZP binding requires human oocytes. Different sources of oocytes can be used, such as postmortem, IVF surplus, or surgical specimens. Oocytes are bisected, and half 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

4. Oehninger S, et al. Hemizona assay and its impact on the identification and treatment of human sperm dysfunctions. Andrologia 1992;24:307.

SECTION III ALGORITHMS

SECTION IV Urine Studies

URINE STUDIES

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 alkalinized with precipitation of salts.)

Pour 5–10 mL of well-mixed urine into a centrifuge tube.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, a spun sample is more desirable.Spin a capped sample at 3,000 rpm for 3–5 min.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, ketone, urobilinogen, bilirubin, and blood). Other strips may provide less. Agents that color the urine (eg, phenazopyridine [Pyridium]) may interfere with the reading. Dipstick specific gravity is also available on some assay strips.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 microscope slide. Cover with a coverslip.Examine 10 low-power fields (LPFs; 10× objective) for epithelial cells, casts, crystals, and mucus. Casts are usually reported as number per low-power field and tend to collect around the periphery of the coverslip.Examine several high-power fields (HPFs; 40× objective) for epithelial cells, crystals, RBCs, WBCs, bacteria, and parasites (trichomonads). RBCs, WBCs, and bacteria are usually reported as number per high-power field.

NORMAL URINE ANALYSIS VALUES

- Appearance: Yellow, clear, or straw-colored
- Specific gravity:
  - Neonate: 1.012
  - Infant: 1.002–1.006
  - Child and adult: 1.001–1.035 (with normal fluid intake 1.016–1.022)
- pH:
  - Newborn/neonate: 5–7
  - Child and adult: 4.6–8.0
- Negative for bilirubin, blood, acetone, glucose, protein, nitrite, leukocyte esterase, reducing substances

- Trace: Urobilinogen
- RBC: The exact definition of microscopic hematuria is debated, but is generally defined as >3 RBC/HPF (40×).
- WBC: 0–4/HPF
- Epithelial cells: Occasional
- Hyaline casts: Occasional
- Bacteria: None
- Crystals: Some limited crystals, based on urine pH (see below)

DIFFERENTIAL DIAGNOSIS FOR ROUTINE URINE ANALYSIS

- Appearance (see Section II: “Urine, Abnormal Color”; Section II: “Urine, Foaming; Urine, Odor; and Urine, Particles”)
- pH:
    - Acidic: High-protein (meat) diet, ammonium chloride, mandelic acid and other medications, acidosis (due to ketoacidosis [starvation, diabetes], chronic obstructive pulmonary disease [COPD])
    - Basic: Urinary tract infections (UTIs), renal tubular acidosis, diet (high-vegetable, milk, immediately after meals), sodium bicarbonate therapy, vomiting, metabolic alkalosis, diuretic therapy
- Specific gravity:
    - Usually corresponds to osmolarity, except with osmotic diuresis. A value >1.023 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, pyelonephritis, glomerulonephritis, water load with normal renal function
- Bilirubin:
    - Positive: Obstructive jaundice (intrahepatic and extrahepatic), hepatitis (Note: False positive with stool contamination)
- Blood:
    - Positive: See Section I: “Hematuria”
    - 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 lyse if the pH is <5 or >8), or there may be myoglobin present because of a crush injury, burn, or tissue ischemia.

- Glucose:
    - Positive: Diabetes mellitus, pancreatitis, pancreatic carcinoma, pheochromocytoma, Cushing syndrome, shock, burns, pain, steroids, hyperthyroidism, renal tubular disease, iatrogenic causes

(Note: The glucose oxidase technique in many kits is specific for glucose and will not react with lactose, fructose, or galactose.)

- Ketones:
    - Detects primarily acetone and acetoacetic acid and not -hydroxybutyric acid:
    - Positive: Starvation, high-fat/low-carbohydrate diet, diabetic ketoacidosis, vomiting, diarrhea, hyperthyroidism, pregnancy, febrile states (especially in children)
- Nitrite:
    - Many bacteria will convert nitrates to nitrite. (See also the section on “Leukocyte Esterase,” below.)
        - Positive: Infection (A negative test does not rule out infection, because some organisms, such as Streptococcus faecalis and other gram-positive cocci, will not produce nitrite, and the urine must also be retained in the bladder for several hours to allow the reaction to take place.)
- Protein:
    - Indication by dipstick of persistent proteinuria should be quantified by 24-hr urine studies:
        - Positive: Pyelonephritis, glomerulonephritis, Kimmelstiel-Wilson syndrome (diabetes), nephrotic syndrome, myeloma, postural causes, preeclampsia, inflammation, and malignancies of the lower tract, functional causes (fever, stress, heavy exercise), malignant hypertension, congestive heart failure
- Leukocyte esterase (see Section I: “Pyuria”.):
    - This test detects 5 WBCs/HPF or lysed 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)
- Reducing substance:
    - Positive: Glucose, fructose, galactose, false-positives (vitamin C, salicylates, antibiotics, etc.)
- Urobilinogen:
    - Positive: Cirrhosis, CHF with hepatic congestion, hepatitis, hyperthyroidism, suppression of gut flora with antibiotics (Note: With obstructive jaundice, urobilinogen is usually normal, but bilirubin is elevated.)

URINE SEDIMENT

Many labs no longer do microscopic examinations unless specifically requested or if the dipstick test shows evidence of an abnormal finding (such as positive leukocyte esterase):

- RBCs: Trauma, pyelonephritis, genitourinary tuberculosis (TB), cystitis, prostatitis, stones, tumors (malignant and benign), coagulopathy, and any cause of blood on dipstick test (see above on hemoglobin)
- WBCs: Infection anywhere in the urinary tract, TB, renal tumors, acute glomerulonephritis, radiation, interstitial nephritis (analgesic abuse)
- Epithelial cells: Acute tubular necrosis (ATN), necrotizing papillitis (most epithelial cells are from an otherwise unremarkable urethra)
- Parasites: Trichomonas vaginalis, Schistosoma haematobium infections
- Yeast: Candida albicans infection (especially in diabetics, immunosuppressed patients, or if a vaginal yeast infection is present)
- Spermatozoa: Normal in males immediately after intercourse or nocturnal emission
- Crystals: Note that urine should be examined fresh and warm because clouding due to phosphate precipitation may be observed when urine cools:
    - Abnormal: Cystine, sulfonamide, leucine, tyrosine, cholesterol
    - Normal in acidic urine: Oxalate (small square crystals with a central cross), uric acid
    - Normal in alkaline urine: Calcium carbonate, triple phosphate (resemble coffin lids)
- Contaminants: Cotton threads, hair, wood fibers, amorphous substances (all usually unimportant)
- Mucus: Large amounts suggest urethral disease (normal from ileal conduit or other forms of urinary diversion).
- Glitter cells: WBCs are lysed in hypotonic solution.
- Casts: The presence of casts in a urine sample localizes some or all of the disease process to the kidney itself:
    - Hyaline casts (occasionally acceptable, unless they are numerous), benign hypertension, nephrotic syndrome, after exercise:
    - RBC casts: Acute glomerulonephritis, lupus nephritis, subacute bacterial endocarditis (SBE), Goodpasture disease, after a streptococcal infection, vasculitis, malignant hypertension
    - WBC casts: Pyelonephritis
    - Epithelial (tubular) casts: Tubular damage, nephrotoxin, virus
    - Granular casts: Breakdown of cellular casts leads to waxy casts; dirty brown granular casts typical for ATN

- Waxy casts (end stage of granular casts): Severe, chronic renal disease; amyloidosis
- Fatty casts: Nephrotic syndrome, diabetes mellitus, damaged renal tubular epithelial cells
- Broad casts: Chronic renal disease

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 2 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 usefulness of this assay is limited because of large variations in daily fluid and salt intake, and the results are usually indeterminate if a diuretic has been given. (See also Section I: “Anuria and Oliguria”.)
    - Sodium <10 mEq/L (mmol/L): Volume depletion, hyponatremic states, prerenal azotemia (CHF, shock, etc.), hepatorenal syndrome, glucocorticoid excess
    - Sodium >20 mEq/L (mmol/L): Syndrome of inappropriate antidiuretic hormone (SIADH), ATN (usually >40 mEq/L), postobstructive diuresis, high salt intake, Addison disease, hypothyroidism, interstitial nephritis
    - Chloride <10 mEq/L (mmol/L): Chloride-sensitive metabolic alkalosis (vomiting, excessive diuretic use), volume depletion
    - Potassium <10 mEq/L (mmol/L): Hypokalemia, potassium depletion, extrarenal loss
- Spot urine for protein (normal: <10 mg/dL [0.1 g/L] or <20 mg/dL [0.2 g/L] for a sample taken in the early morning)
  - See Section I: “Proteinuria” for the differential diagnosis of protein in the urine.
- Spot urine for eosinophils (present with Hansel/Wright light microscopy):
  - Associated with acute interstitial nephritis (especially nephritis associated with drug hypersensitivity) or acute cystitis
  - Present with interstitial nephritis; absent with tubular disorders (ATN).
- Spot urine for erythrocyte morphology:
  - The morphology of RBCs in a sample of urine that tests positive for blood may give some indication of the nature of the hematuria. Eumorphic red cells are typically seen in cases of postrenal, nonglomerular bleeding. Dysmorphic red cells are more likely associated with glomerular causes of bleeding. Each reference lab has standards, but as a general rule, the presence of >90% dysmorphic erythrocytes in patients with asymptomatic hematuria indicates a renal glomerular source of bleeding, especially if associated with proteinuria and/or casts (ie, IgA nephropathy, poststreptococcal GN, sickle cell disease or trait, etc.). If <90% eumorphic erythrocytes or even mixed results (10–90% eumorphic erythrocytes), this indic-

ates a post-renal cause of hematuria, requiring a complete urologic evaluation (ie, hypercalcuria, urolithiasis, cystitis, trauma, tumors, hemangioma, exercise-induced, benign prostatic hypertrophy [BPH], etc.).

- Spot urine for osmolality (ranges from 40–1,400 mOsm/kg water [mmol/kg]; varies with water intake):
    - Patients with normal renal function should concentrate >400–800 mOsmol/kg (mmol/kg) after a 14-hr fluid restriction; <200–400 mOsmol/kg (mmol/kg) is a sign of renal impairment:
        - Increased: Dehydration, CHF, hypercalcemia, SIADH, adrenal insufficiency, glycosuria, high-protein diet
        - Decreased: Excessive fluid intake, diabetes insipidus, acute renal failure, medications (acetohexamide, glyburide, lithium)
- Spot urine for myoglobin (qualitative negative):
    - Positive: Skeletal muscle conditions (crush injury, electrical burns, carbon monoxide poisoning, delirium tremens, surgical procedures, malignant hyperthermia), polymyositis

CREATININE CLEARANCE AND GLOMERULAR FILTRATION RATE

CREATININE CLEARANCE

- Normal:
  - Adult male: Total creatinine 1–2 g/24 hr (8.8–17.7 mmol/d); clearance 85–125 mL/min/1.73 m2
  - Adult female: Total creatinine 0.8–1.8 g/24 hr (7.1–15.9 mmol/d); clearance 75–115 mL/min 1.73 m2 (1.25–1.92 mL/s/1.73 m2)
  - Child: Total creatinine (>3 yr) 12–30 mg/kg/24 hr; clearance 70–140 mL/min/1.73 m2 (1.17–2.33 mL/s/1.73 m2)
  - Decreased: A decreased creatinine clearance results in an increase in serum creatinine, usually secondary to renal insufficiency. See Section I: “Renal Failure, Acute”, and “Renal Failure, Chronic” for the differential diagnosis of increased serum creatinine.
  - Increased: Early diabetes mellitus, pregnancy

DETERMINATION OF CREATININE CLEARANCE

Creatinine clearance (CrCl) is a sensitive indicator of early renal insufficiency and is a measure of glomerular filtration rate (GFR); however, the GFR does not provide no informaton on the etiology 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 (eg, 12 hr), but the formula must be corrected for this change; a 24-hr sample is less prone to collection error.

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 if 24-hr collection is used.

To determine if there is a valid, full 24-hr collection, the sample should contain 18–25 mg/kg/24 hr of creatinine for adult males or 12–20 mg/kg/24 hr for adult females. If the patient is an adult (150 lb = body surface area of 1.73 m2), adjustment of the clearance for body size is not routinely done. Adjustment for pediatric patients is a necessity.

If the values in the previous example were for a 10-yr-old boy who weighed 70 lb (1.1 m2), the clearance would be:

75 mL/min (1.73 m2 ÷ 1.1 m2) = 118 mL/min

2. Estimated Creatinine Clearance (eGFR)

Estimated glomerular filtration rate (eGFR) is based on SCr combined with other factors such as age, sex, and race and has generally replaced 24-hr urinary CrCl determinations. Online calculators for adults and children are found at: www.nkdep.nih.gov/professionals/gfr_calculators/idms_con.htm (accessed May 17, 2009)

Adult:

A. Modification of Diet in Renal Disease (MDRD) equation (Ann Intern Med 1999;130, 137–147): Although more cumbersome than Cockcroft-Gault, the MDRD equation is believed to be more accurate. The equation does not require weight; results are normalized to 1.732 body surface area (BSA), an accepted adult average BSA:

GFR (mL/min/1.73 m2) = 175 for (Scr)1.154 × (age)0.203 × (0.742 if female) × (1.210 if African American)

B. Cockcroft-Gault equation:

Children:

Use the Schwartz equation:

GFR (mL/min/1.73 m2) = k (height)/SCr

Where:

- k = Constant (0.33, premature infant; 0.45, term infants to 1 yr; 0.55, children to 13 yr; 0.65, adolescent males; 0.55, adolescent females)
    - Height in cm, and SCr in mg/dL

24-HR URINE STUDIES

- Calcium, urine:
    - Normally ordered as part of a urolithiasis metabolic evaluation:
        - Normal: Calcium-free diet <150 mg/24 hr (3.7 mmol/d); average calcium diet (600–800 mg/24 hr) 100–250 mg/24 hr (2.5–6.2 mmol/d)
        - Increased: Hyperparathyroidism, hyperthyroidism, hypervitaminosis D, distal renal tubular acidosis (type I), sarcoidosis, immobilization, osteolytic lesions (bony metastasis, multiple myeloma), Paget disease, glucocorticoid excess
        - Decreased: Medications (thiazide diuretics, estrogens, oral contraceptives), hypothyroidism, renal failure, steatorrhea, rickets, osteomalacia, vitamin D deficiency
    - Catecholamines, fractionated (norepinephrine, epinephrine, and dopamine):
        - Used to evaluate pheochromocytoma and paraganglioma. Avoid drugs that can interfere with the test, leading to falsely high catecholamines: Tricyclic antidepressants, labetalol, levodopa, methyldopa (Aldomet), sotalol, benzodiazepines, amphetamines, decongestants, and most psychoactive agents. All these drugs should be discontinued 2 weeks prior to testing:
        - Normal: Values are variable and depend on the assay method used. Norepinephrine 15–80 mg/24 hr (89–473 nmol/24 hr), epinephrine 0–20 mg/24 hr (SI: 0–118 nmol/24 hr), dopamine 65–400 mg/24 hr (SI: 384–2,364 nmol/24 hr)
        - Increased: Pheochromocytoma (levels are > twice the upper normal value), paraganglioma, epinephrine administration, presence of drugs (see above)
    - Cortisol, free:
        - Used to evaluate adrenal cortical hyperfunction; screening test of choice for Cushing syndrome:
        - Normal: 10–55 g/24 hr (SI: 27–150 nmol)
        - Increased: Cushing syndrome (adrenal hyperfunction from a pituitary tumor secreting ACTH or ectopic secretion of ACTH by other tumors such as bronchial carcinoid or adrenal tumor secreting cortisol), stress during collection, pregnancy
    - Cystine:
        - Used to detect cystinuria, homocystinuria:
        - Normal: <30–40 mg/d (0.13 mmol/d):
        - Increased: Homozygotic cystinuria: 400 mg/d (1.7 mmol/d); heterozygotes cystinuria and Fanconi syndrome: Up to 250 mg/d (1 mmol)
    - Electrophoresis, protein (24-hr urine protein, 24-hr urine globulins):
        - Used to evaluate overall renal function; screen for myeloma, macroglobulinemia, lymphoma, amyloidosis; can differentiate types of proteinuria (see table above)

Electrophoretic Zones
Pattern Description (Type of Proteinuria)
Protein, total (mg/d)
Albumin
1
2

Normal
<150
±

±
±
Glomerular, mild
<1,500
++

+
+

Glomerular, severe
>1,500
+++

++
++

Glomerular, nonselective
>3,000
+++
++
++

++
++
Tubular
<1,500
Tr/+
Tr
++
++
Tr
Mixed, glomerular & tubular

+++
+
++
+
+
Albuminuria
>150
++

Overflow, acute phase response

Tr/+
++
++
Tr
Tr
Overflow, monoclonal spike

Sp/++

Sp/++

KEY: Tr = trace; Sp = spike; ± = may or may not be present; + = mildly elevated; ++ = moderately elevated; +++ = markedly elevated.

- 5-Hydroxyindoleacetic acid (5-HIAA):
  - 5-HIAA is a serotonin metabolite and is useful in diagnosing carcinoid syndrome:
    - Normal: 2–8 mg (SI: 10.4–41.6 mmol)/24-hr urine collection
    - Increased: Carcinoid tumors (except rectal), certain foods (banana, pineapple, tomato, walnuts, avocado), phenothiazine derivatives
- Heavy metals:
  - Measures exposure to arsenic (total), arsenic (inorganic), cadmium, lead, and mercury, usually following occupational or environmental exposure:
    - Normal: Arsenic (total): 0–50 g/24 hr (<50 g/L); arsenic (inorganic): <20 g/L; cadmium: <3.0 g/24 hr (<2 g/g creatinine); lead: <80 g/24 hr (< 50 g/L); mercury: <20 g/L
    - Increased: Indicative of exposure
- Metanephrines:
  - These metabolic products of epinephrine and norepinephrine are a primary screening test for pheochromocytoma and paraganglioma (in conjunction with urinary catecholamines). Avoid drugs that can interfere with the test, leading to falsely high catecholamines: Tricyclics antidepressants, labetalol, levodopa, methyldopa (Aldomet), sotalol, benzodiazepines, amphetamines, decongestants, and most psychoactive agents. All these drugs should be discontinued 2 weeks prior to testing:
    - Normal: <1.3 mg/24 hr (7.1 mmol/L) for adults, but variable in children
    - Increased: Pheochromocytoma, paraganglioma, false positive with drugs (see above)
- Protein (see Section I, Proteinuria):
  - Normal: <150 mg/24 hr (<0.15 g/d)
  - Increased: Nephrotic syndrome is usually associated with >4 g/24 hr.
- 17-Ketogenic steroids (17-KGS, corticosteroids):
  - Overall adrenal function test, largely replaced by serum or urine cortisol levels:
    - Normal: Males: 5–24 mg/24 hr (17–83 mmol/24 hr); females: 4–15 mg/24 hr (14–52 mmol/24 hr)
    - Increased: Adrenal hyperplasia (Cushing syndrome), adrenogenital syndrome
    - Decreased: Panhypopituitarism, Addison disease, acute steroid withdrawal
- 17-Ketosteroids, total (17-KS):

- Measures dehydroepiandrosterone (DHEA), androstenedione (adrenal androgens); largely replaced by assay of individual elements in the blood (serum DHEA-S and serum androstenedione):
    - Normal: Adult males: 8–20 mg/24 hr (28–69 mmol/L); adult females: 6–15 mg/dL (21–52 mmol/L). Note: Low values in prepubertal children
    - Increased: Adrenal cortex abnormalities (congenital adrenal hyperplasia, adrenal carcinoma, Cushing syndrome)
    - Decreased: Panhypopituitarism, Addison disease
- Urea nitrogen, urine (urine nitrogen, nitrogen balance, blood urea nitrogen (BUN):
    - Measures urine nitrogen concentration:
        - Normal: 12,000–20,000 mg/24 hr
        - Increased: Nitrogen wasting with hyperalimentation, bladder tap with amniocentesis
        - Decreased: Poor nitrogen balance with hyperalimentation
- Vanillylmandelic acid (VMA):
    - VMA is the urinary product of both epinephrine and norepinephrine; the 24-hr urinary VMA excretion has poor diagnostic sensitivity and specificity compared to fractionated 24-hr urinary fractionated metanephrines. Can be affected by many foods. No longer recommended by most endocrinologists:
        - Normal: <7–9 mg/24 hr (35–45 mmol/L)
        - Increased: Pheochromocytoma, paraganglioma, factitious (chocolate, coffee, tea, methyldopa)

REFERENCES

Simerville JA. Urinalysis: A comprehensive review. Am Fam Physician 2005;71(6):1153–1162.

Gomella LG. Urine Studies. In: Gomella LG, Haist SA, eds. Clinician's Pocket Reference, 11th ed. New York: McGraw- Hill, 2007.

SECTION V

Alternative Urologic Therapies (Phytotherapy)

AFRICAN PLUM (Pygeum Africanum)

These common agents are not US Food and Drug Administration (FDA) approved but are available through health food stores and other commercial outlets. Phytotherapies and other supplements are under study, but few have undergone trials in the United States. Most have not demonstrated any significant efficacy. Many of these products are sold as part of combination therapies, and they are sold under many trade names. There have been growing concerns about the potential toxicities of these products and their interactions with standard pharmaceuticals. According to the FDA, manufacturers of dietary supplements can make claims about how their products affect the structure or function of the body, but they may not claim to prevent, treat, cure, mitigate, or diagnose a disease without prior FDA approval.

REFERENCE

Lowe FC. Complementary and alternative medicine in urology: What we need to know in 2008. BJU Int 2008;102.

AFRICAN PLUM (Pygeum africanum)

The extract, tadenan, is derived from the bark of the African plum tree and is taken for the treatment of benign prostatic hypertrophy (BPH) and lower urinary tract symptoms (LUTS). Pygeum is usually found in most combination prostate health formulations. Its mode of action is thought to be via inhibition of fibroblast growth and anti-inflammatory effects. Some inconclusive data show a decrease in symptoms and an increase in flow rate. However, the T-IPSS study, a randomized double-blind placebo-controlled trial using tadenan was completed but never released or published. Only some minor gastrointestinal side effects have been noted with this product.

REFERENCE

Ishani A, et al. Pygeum africanum for the treatment of patients with benign prostatic hyperplasia: A systematic review and quantitative meta-analysis. Am J Med 2000;109:654–664.

BAZOTON (Radix urticae)

This plant extract has been used in the treatment of BPH. The active ingredients are thought to include its steroid-glycoside composition. It is an inhibitor of sex-steroid binding globulin. There is a paucity of clinical data that show it decreases symptom scores, and it has little effect on flow rates. Side effects are minor and usually related to its smell and taste.

REFERENCE

Schneider T, Rubben H. Stinging nettle root extract (Bazoton-uno) in long-term treatment of benign prostatic syndrome (BPS). Results of a randomized, double-blind, placebo-controlled multicenter study after 12 months. Urologe A 2004;43:302–306.

CAPSAICIN (Capsicum)

Capsaicin is the main pungent ingredient of hot peppers. It has been used as an intravesical therapy for overactive bladder. The mode of action is by the selective activation of sensory nerve fibers and by a neurotoxic effect on C afferent fibers. Multiple studies have documented its efficacy in terms of symptom improvement and urodynamic changes. Adverse effects include suprapubic pain, hematuria, and incontinence, which are all self-limiting.

REFERENCE

Chancellor MB. Intravesical capsaicin and resiniferatoxin therapy: Spicing up the ways to treat the overactive bladder. J Urol 1999;162:3–11.

CRANBERRIES (Vaccinum macrocarpon) Juice and Supplements

Cranberry is widely used to prevent UTIs; it was originally believed that this fruit acidified the urine. However, cranberry appears to work by inhibiting the adhesion of type I and P-fimbriated uropathogens (eg, uropathogenic E. coli) to the uroepithelium, thus impairing colonization and subsequent infection. It contains a unique blend of organic acids—quinic, malic, and citric—as well as nondialyzable polymeric compounds that provide this antibacterial adherence effect.

Studies using cranberry juice, cranberry-lingonberry juice, and cranberry tablets compared with placebo for preventing UTIs, bacteruria, or pyuria concluded that cranberry juice and cranberry products significantly reduced UTIs among women with recurrent infections. Recommended doses range from 90–480 mL of cranberry cocktail twice daily or 15–30 mL of unsweetened 100% cranberry juice daily. The frozen concentrate has almost 30 times the strength of the juice, and 30–45 mL b.i.d. has been used. Capsule doses range between 1 and 6 capsules of 300–400 mg concentrated extract b.i.d. High pediatric doses of >300 mL daily have been associated with adverse effects such as hypersensitivity or gastrointestinal distress such as diarrhea.

The findings of several reviews support the potential use of cranberry products in the prophylaxis of recurrent UTIs in young and middle-aged women, but it should not be used as a substitute for antibiotics, as it is an ineffective treatment for established infections. Patients with a history of nephrolithiasis should avoid the use of cranberry products (possible increases in urinary calcium and oxalate concentration). Due to the heterogeneity of clinical study designs and the lack of consensus regarding the dosage regimen and formulation to use, cranberry products cannot be broadly recommended for the prophylaxis of recurrent UTIs at this time. May potentiate anticoagulant effects of warfarin.

REFERENCE

Guay DR. Cranberry and urinary tract infections. Drugs 2009;69(7):775–807.

Santillo VM, Lowe FC. Cranberry juice for the prevention and treatment of urinary tract infections. Drugs Today 2007;43:47–54.

GINKGO BILOBA

Primarily used for memory deficits, dementia, and neurologic dysfunction, ginkgo biloba is also promoted as a treatment for impotence and selective serotonin reuptake inhibitor (SSRI)-induced sexual dysfunction, with a recommended dose range of 60–80 mg standardized dry extract orally b.i.d.–t.i.d. Studies have shown small cognition benefits with dementia, but no other demonstrated benefit in healthy adults. Use cautiously with aspirin (ASA), salicylates, warfarin.

REFERENCE

Cohen AJ. Ginkgo biloba for antidepressant-induced sexual dysfunction. J Sex Marital Ther 1998;24(2):139–143.

HEATHER (Calluna vulgaris)

The medicinal portion of common heather consists of the entire herb (leaves, flower, roots) ground and boiled to create a product that is taken for its diuretic properties in the treatment of kidney ailments and BPH/LUTS. Active compounds are thought to include flavonoids and sitosterols. The claimed efficacy has never been documented. No clinical trials are available.

HORNY GOAT WEED (Epimedium)

Epimedium is a Chinese herbal remedy promoted as a safe and natural alternative to sildenafil citrate (Viagra). However, extracts of epimedium are strongly estrogenic due to the presence of novel potent phytoestrogens of the prenyl-flavone family. It has been reported to cause tachyarrhythmias.

REFERENCE

Yong EL, et al. Standardization and evaluation of botanical mixtures: Lessons from a traditional Chinese herb, epimedium, with estrogenic properties. Novartis Found Symp 2007;282:173–88; discussion 188–191, 212–218.

PC-SPES

This product is no longer commercially available because of issues associated with quality control. It was found to be tainted with diethylstilbestrol, warfarin, and alprazolam. It was used for treatment of prostate cancer, particularly in hormone-refractory patients. It consisted of 7 Chinese herbs (Chrysanthemum, Isatis, licorice, Ganoderma lucidium, Panax pseudoginseng, Rabdosia rubescens, Scutellaria [skullcap], and saw palmetto berry). It had potent antiestrogenic effects. Its use was associated with deep venous thrombosis, breast tenderness, loss of libido, and decreased prostate-specific antigen (PSA) and testosterone levels. Other companies have made similar combinations but have not achieved as widespread us-

age.

REFERENCE

DiPaola RS, et al. Clinical and biologic activity of an estrogenic herbal combination (PC-SPES) in prostate cancer. N Engl J Med 1998;339:785–791.

Marks LS, et al. PC-SPES: Herbal formulation for prostate cancer. Urology 2002;60:369–375.

PANAX GINSENG

This product has been used for numerous indications in traditional Chinese medicine. It is frequently used for decreased libido and erectile dysfunction in the urologic arena. It reportedly has androgenic effects and stimulation, although improvements in penile endothelial L-arginine–nitric oxide activity have been suggested.

Clinical trials are not conclusive of its effectiveness.

REFERENCE

Tamler R, Mechanick JI. Dietary supplements and nutraceuticals in the management of andrologic disorders. Endocrinol Metab Clin North Am 2007;36:533–552.

Xiang YZ, et al. A comparison of the ancient use of ginseng in traditional Chinese medicine with modern pharmacological experiments and clinical trials. Phytother Res 2008;22:851–858.

PERMIXON (Serenoa repens)

This is the branded saw palmetto extract produced in France. It is the lipido-sterolic extract of the dried fruit (berry) of the dwarf palm. It is the most widely studied of all phytotherapies for the treatment of BPH/LUTS. From in vitro studies, it has been postulated to have many mechanisms of action including antiprostaglandin, antiandrogenic, and antiestrogenic effects. It has almost no effect upon prostate size and no effect upon PSA levels. There are no known significant health risks or adverse effects.

REFERENCE

Boyle P, et al. Updated meta-analysis of clinical trials of Serenoa repens extract in the treatment of symptomatic benign prostatic hyperplasia. BJU Int 2004;93:751–756.

PUMPKIN SEED (Cucurbita pepo)

Fresh and dried seeds are taken whole or ground for the treatment of BPH or overactive bladder. Active compounds are thought to be phytosterols. There are no recent clinical trials and therefore no evidence establishing its efficacy. There are no known side effects.

REFERENCE

Carbin BE, et al. Treatment of benign prostatic hyperplasia with phytosterols. Br J Urol 1990;66:639–641.

RYE POLLEN (Secale cereale)

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 -sitosterols. It is used for the treatment of BPH and prostatitis and chronic pelvic pain syndrome (CPPS). In vitro inhibition of epithelial and stromal cell growth has been demonstrated. No long-term conclusive clinical studies exist. Side effects are reportedly minimal.

REFERENCE

Habib FK, et al. The identification of a prostate inhibitory substance in a pollen extract. Prostate 1995;26:133–139.

MacDonald R, et al. A systematic review of Cernilton for treatment of benign prostatic hyperplasia. BJU Int 2000;85:836–841.

SAW PALMETTO BERRY (Serenoa repens, Sabal serrulata)

There are many different extraction processes and therefore many different brands of saw palmetto. The composition of these brands are variable. A recent National Institutes of Health (NIH)-sponsored double-blind, placebo-controlled study using the Indena brand showed no statistical difference between placebo and saw palmetto berry for treatment of BPH/LUTS. Permixon brand is the most widely studied product (see “Permixon” above). Minimal side effects are associated with saw palmetto. Saw palmetto berry extract (SPBE) compounds are also sold for “prostate health.” SPBE includes ingredients such as beta-sitosterol and stigmasterol with no reliable clinical data to support their use.

REFERENCE

Bent S, et al. Saw palmetto for benign prostatic hyperplasia. N Engl J Med 2006;354:557–566.

Habib FK, Wyllie MG. Not all brands are created equal: A comparison of selected components of different brands of Serenoa repens extract. Prostate Ca Prostatic Dis 2004;7:195–200.

SELENIUM

A trace mineral that may prevent the development of prostate cancer. Epidemiologic studies suggest a chemo-preventative effect. One study of patients with high-grade prostatic intraepithelial neoplasia 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 begin in 2001 of over 35,000 men studying the prostate cancer chemopreventive effects of selenium and vitamin E alone and in combination. The data monitoring safety board (DMSB) halted the trial in the fall of 2008. Their concerns were that the supplements did not appear to offer any benefit. In particular, there was a nonstatistically significant trend to increasing prostate cancer with vitamin E alone and increased diabetes risk in men

on selenium alone.

REFERENCE

Joniav S, et al. Effect of nutritional challenge in patients with isolated high-grade prostatic intra-epithelial neoplasia. Urology 2007;69:1102–1106.

Lippman SM, Klein EA, Goodman PJ, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2009;301(1):39–51.

SOUTH AFRICAN STAR GRASS (Hypoxis roperi)

This extract is taken for BPH/LUTS. The active compound is thought to be -sitosterols, which are thought to induce apoptosis by transforming growth factor (TGF)-1; this is unproven clinically. Initial studies showed dramatic improvements in symptom scores and flow rates; however, confirmatory studies are still needed. Adverse effects are believed to be minimal.

REFERENCE

Klippel KF, et al. A multi-center, placebo-controlled, double-blind clinical trial of -sitosterol (phytosterol) for the treatment of benign prostatic hyperplasia. Br J Urol 1997;80:427–432.

Wilt TJ, et al. Beta-sitosterol for the treatment of benign prostatic hyperplasia: A systematic review. BJU Int 1999;83:976–983.

STINGING NETTLE (Urtica dioca, Urticae radix)

Bazoton is a branded form of this extract; see above. The clinical evidence of the effectiveness of nettle root is based primarily on open studies, and the significance of this must be confirmed. Minimal toxicity is associated with stinging nettle use.

REFERENCE

Chrubasik JE, et al. A comprehensive review on the stinging nettle effect and efficacy profiles. Part II: Urticae radix. Phytomedicine 2007;14:568–579.

YOHIMBINE (Pausinystalia yohimbe) Yocon, Yohimex

An extract of the bark of the yohim tree has been used for erectile dysfunction and decreased libido. The mechanism of action is as an -adrenergic antagonist. Conflicting studies show both positive and no effect when compared to placebo. It appears to have greatest utility for men with psychogenic impotence. Despite the advent of phosphodiesterase 5 (PDE5) inhibitors, there is still widespread utilization of this over-the-counter product. Side effects include anxiety, tremors, dizziness, hypertension, and tachycardia. Do not use with antidepressants (eg, MAOIs or similar agents)

REFERENCE

Dinsmore WW. Available and future treatments for erectile dysfunction. Clin Cornerstone 2005;7:37–45.

Reid K, et al. Double-blind trial of yohimbine in the treatment of psychogenic impotence. Lancet 1987;2:421–423.

SECTION VI

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 tract system. Although some general information about the drug may be presented, this is not intended to be a complete 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 or website, 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 only on the medical literature, and these uses are not listed in the package insert. Double asterisks (**) designate 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 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]

MEDICATION KEY

Medications are listed in alphabetical order by generic name. Some of the more commonly recognized trade names in the US are listed for each medication (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. Uses: 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 and Peds. Where 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 modifica-

tions may be noted (ie, take with food, avoid antacids, etc.). Caution: [Pregnancy/fetal risk categories, breast-feeding (as noted below)] Cautions concerning the use of the drug in specific settings. CI: Contraindications. Disp: Common dosing forms. SE: Common or significant side effects. Notes: Other key useful information about the drug.

CONTROLLED SUBSTANCE CLASSIFICATION

Medications under the control of the US Drug Enforcement Agency (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) I: All nonresearch use forbidden (eg, heroin, etc.).

Schedule (C-II) II: High addictive potential; medical use accepted. No telephone call-in prescriptions; no refills.

Schedule (C-III) 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, acetaminophen plus codeine).

Schedule (C-IV) IV: Limited potential for dependence; prescription rules same as for schedule III (eg, benzodiazepines, propoxyphene).

Schedule (C-V) 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.

OR

Animal studies have shown an adverse effect, 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 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.

OR

No animal reproduction studies and no adequate studies in humans have been done.

Category D: There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

Category X: Studies in animals or humans or adverse reaction reports, or both, have demonstrated fetal abnormalities. The risk of use in pregnant women clearly outweighs any possible benefit.

Category ?: No data available (not a formal classification; included to provide complete dataset).

BREAST-FEEDING CLASSIFICATION

No formally recognized classification exists for drugs and breast-feeding. This shorthand is based on information the Clinician's Pocket Drug Reference, 2010.

+ Compatible with breast-feeding

M Monitor patient or use with caution

± Excreted, or likely excreted, with unknown effects or at unknown concentrations

?/– Unknown excretion, but effects likely to be of concern

– Contraindicated in breast-feeding

? No data available

ACETAMINOPHEN [APAP, N-ACETYL-P-AMINOPHENOL] (TYLENOL, OTHER GENERIC) [OTC]

USES: *Mild–mod pain, headache, fever*

ACTION: Nonnarcotic analgesic; CNS synthesis of prostaglandins and hypothalamic heat-regulating center

DOSE:

Adults: 650 mg PO or PR q4–6h or 1,000 mg PO q6h; max 4 g/24 hr.

Peds: <12 yr: 10–15 mg/kg/dose PO or PR q4–6h; max 2.6 g/24 hr. Administer q6h if CrCl 10–50 mL/min and q8h if CrCl <10 mL/min

CAUTION: [B, +]; hepatotoxic in elderly and w/EtOH use w/>4 g/d; EtOH liver disease, G6PD deficiency

CI: Hypersensitivity

DISP: Tablets melt-away/dissolving 160 mg; tablets: 325, 500, 650 mg; chew tablets 80, 160 mg; liquid 100 mg/mL, 120 mg/2.5 mL, 120 mg/5 mL, 160 mg/5 mL, 167 mg/5 mL, 325 mg/5 mL, 500 mg/15 mL, 80 mg/0.8 mL; suppository 80, 120, 125, 325, 650 mg

SE: Overdose hepatotoxic at 10 g; 15 g can be lethal; treat w/N-acetylcysteine

NOTES: No anti-inflammatory or platelet-inhibiting action; avoid EtOH

ACETAMINOPHEN + CODEINE (TYLENOL NO. 2, 3, NO. 4) [C-III, C-V]

USES: *Mild-mod pain (No. 2–3); mod–severe pain (No. 4)*

ACTION: Combined acetaminophen and narcotic analgesic

DOSE:

Adults: 1–2 tablets q3–4h PRN or 30–60 mg/codeine q4–6h based on codeine content (max dose acetaminophen = 4 g/d).

Peds: Acetaminophen 10–15 mg/kg/dose; codeine 0.5–1 mg/kg dose q4–6h (guide: 3–6 yr, 5 mL/dose; 7–12 yr, 10 mL/dose); max 2.6 g/d if <12 yr; in renal/hepatic impaired

CAUTION: [C, +]; EtOH liver disease; G6PD deficiency

CI: Hypersensitivity

DISP: Tablets 300 mg acetaminophen + codeine (No. 2 = 15 mg, No. 3 = 30 mg, No. 4 = 60 mg); capsules 325 mg acetaminophen + codeine; suspension (C-V) acetaminophen 120 mg + codeine 12 mg/5 mL

SE: Drowsiness, dizziness, N/V

ACETAZOLAMIDE (DIAMOX)

USES: *Diuresis, drug and CHF edema, glaucoma, to prevent high-altitude sickness, refractory epilepsy* metabolic alkalosis

ACTION: Carbonic anhydrase inhibitor; renal excretion of hydrogen and renal excretion of Na+, K+, HCO3-, and H2O

DOSE:

Adults: Diuretic: 250–375 mg IV or PO q24h. Metabolic alkalosis: 250 mg IV q6h × 4 or 500 mg IV × 1.

Peds: Epilepsy: 8–30 mg/kg/24 hr PO in divided doses; max 1 g/d. Diuretic: 5 mg/kg/24 hr PO or IV. Alkalinization of urine: 5 mg/kg/dose PO b.i.d.–t.i.d. Glaucoma: 8–30 mg/kg/24 hr PO in 3 divided doses; max 1 g/d; dose w/CrCl 10–50 mL/min; avoid if CrCl <10 mL/min.

CAUTION: [C, +]

CI: Renal/hepatic/adrenal failure, sulfa allergy, hyperchloremic acidosis

DISP: Tablets 125, 250 mg; ER capsules 500 mg; injectable 500 mg/vial, powder for reconstitution

SE: Malaise, metallic taste, drowsiness, photosensitivity, hyperglycemia

NOTES: Follow Na+ and K+; watch for metabolic acidosis; CBC and platelets; SR forms not for epilepsy

ACETOHYDROXAMIC ACID (LITHOSTAT)

USES: *Adjunct for chronic urea-splitting UTI*, struvite calculi

ACTION: Bacterial urease, ammonia in the urine by urea-splitting organisms

DOSE:

Adults: 250 mg PO 3–4 times/d, total 10–15 mg/kg/d.

Peds: 10 mg/kg/d PO

CAUTION: [X,–]; preexisting psych disorders

CI: Pregnancy, component hypersensitivity

DISP: Tablets 250 mg

SE: Hemolytic anemia (follow CBC), bone marrow suppression, hepatotoxicity (follow LFTs), flushing, rash, nervousness, tremor, anorexia, N/V

NOTES: Take on empty stomach

ACETYLCYSTEINE (ACETADOTE, MUCOMYST)

USES: *Mucolytic, antidote to acetaminophen hepatotoxicity/overdose* adjuvant treatment in chronic bronchopulmonary diseases and cystic fibrosis* to prevent contrast-induced renal dysfunction

ACTION: Splits mucoprotein disulfide linkages; restores glutathione in acetaminophen overdose to protect liver

DOSE:

Adults and Peds Antidote: PO or NG: 140 mg/kg load, then 70 mg/kg q4h × 17 doses (dilute 1:3 in carbonated beverage or orange juice), repeat if emesis within 1 hr of dosing. Acetadote: 150 mg/kg IV over 60 min, then 50 mg/kg over 4 hr, then 100 mg/kg over 16 hr; to prevent renal dysfunction: 600–1,200 mg PO b.i.d. × 2 days

CAUTION: [B, ?]

DISP: Solution, inhaled and oral 10%, 20%; acetadote IV solution 20%

SE: Bronchospasm (inhaled), N/V, drowsiness, anaphylactoid reactions w/IV

NOTES: Activated charcoal adsorbs PO acetylcysteine for acetaminophen ingestion; start treatment for acetaminophen overdose within 6–8 hr

ACYCLOVIR (ZOVIRAX)

USES: *Herpes simplex (HSV; genital/mucocutaneous, encephalitis, keratitis); varicella zoster, herpes zoster (shingles) infections*

ACTION: Interferes with viral DNA synthesis

DOSE:

Adults: Herpes CDC Recommended Regimens: 400 mg PO t.i.d. × 7–10 days or 200 mg PO q.i.d. × 7–10 days; Recurrence: 400 mg PO b.i.d.; Episodic within 1 day of lesion: 400 mg PO t.i.d. × 5 days OR 800 mg PO b.i.d. × 5 days OR 800 mg PO t.i.d. × 2 days; Topical: Initial herpes genitalis: Apply q3h (6×/d) for 7 days. HSV encephalitis: 10 mg/kg IV q8h × 10 days. Herpes zoster: 800 mg PO 5×/d for 7–10 days. IV: 5–10 mg/kg/dose IV q8h.

Peds: Genital HSV: 3 mo–2 yr: 15 mg/kg/d IV divided q8h × 5–7 d, 60 mg/kg/d max. 2–12 yr: 1,200 mg/d PO divided q8h × 7–10 days. >12 yr: 1,000–1,200 mg PO divided q8h × 7–10 days. HSV encephalitis: 3 mo–2 12 yr: 60 mg/kg/d IV divided q8h × 10 days. >12 yr: 30 mg/kg/d IV divided q8h × 10 days. Chickenpox: 2 yr: 20 mg/kg/dose PO q.i.d. × 5 days. Shingles: <12 yr: 30 mg/kg/d PO or 1,500 mg/m2/d IV divided q8h × 7–10 d; w/CrCl <50

mL/min

CAUTION: [B, +]

CI: Hypersensitivity to compound

DISP: Capsules 200 mg; tablets 400, 800 mg; suspension 200 mg/5 mL; injectable 500 and 1,000 mg/vial; injectable solution 25 mg/mL, 50 mg/mL ointment 5% and cream 5%

SE: Dizziness, lethargy, malaise, confusion, rash, IV site inflammation; transient Cr/BUN

NOTES: PO is better than topical for herpes genitalis; alternative CDC agents for herpes genitalis include famciclovir, valacyclovir

ALDESLEUKIN [IL-2] (PROLEUKIN)

WARNING: High dose is associated with capillary leak syndrome, hypotension, and organ perfusion; infection due to poor neutrophil activity; Discontinue w/mod–severe lethargy, may progress to coma.

USES: *Met RCC and melanoma*

ACTION: Acts via IL-2 receptor; many immunomodulatory effects

DOSE: 600,000 IU/kg q8h × 14 doses days 1–5 and days 15–19 of 28-day cycle (FDA-approved dose/schedule for RCC); other schedules (eg, high-dose 24 × 106 IU/m2 IV q8h on days 1–5 and 12–16)

CAUTION: [C, ?/–]

CI: Organ allografts

DISP: Powder for reconstitution 22 × 106 IU, when reconstituted 18 million IU/mL = 1.1 mg/mL

SE: Flu-like syndromes (malaise, fever, chills), N/V/D, bilirubin; capillary leak syndrome; BP, tachycardia, pulmonary and peripheral edema, fluid retention, and weight gain; renal and mild hematologic toxicity (HgB, platelet, WBC), eosinophilia; cardiac toxicity (ischemia, atrial arrhythmias); neurotoxicity (CNS depression, somnolence, delirium, rare coma); pruritic rashes, urticaria, and erythroderma are common

ALENDRONATE (FOSAMAX, FOSAMAX PLUS D)

USES: *Treat/prevent osteoporosis in male/postmenopausal female; treat steroid-induced osteoporosis, Paget disease*, hypercalcuria

ACTION: normal and abnormal bone resorption, osteoclast action; reduces serum and urinary Ca2+ levels

DOSE: Osteoporosis: 10 mg/d PO or 70 mg every week; Fosamax plus D 1 tablet every week. Steroid-induced osteoporosis: 5 mg/d PO, 10 mg/d postmenopausal not on estrogen. Prevention: 5 mg/d PO or 35 mg every week. Paget disease: 40 mg/d PO

CAUTION: [C, ?]; not OK if CrCl <35 mL/min, w/NSAID use

CI: Esophageal anomalies, inability to sit/stand upright for 30 min, Ca2+

DISP: Tablets 5, 10, 35, 40, 70 mg, solution 70 mg/75 mL; Fosamax plus D: Alendronate 70 mg w/cholecalciferol (vitamin D3) 2,800 or 5,600 IU

SE: Abdominal pain, acid regurgitation, constipation, D/N, dyspepsia, musculoskeletal pain, jaw osteonecrosis (w/dental procedures, chemo)

NOTES: Take upon rising in A.M. w/H2O (8 oz) >30 min before 1st food/beverage of the day; do not lie down for 30 min after. Ca2+ and vitamin D supplementation is necessary for regular tablet.

ALFUZOSIN (UROXATRAL)

WARNING: May prolong QTc interval.

USES: *Symptomatic benign prostatic hyperplasia*

ACTION: -Blocker

DOSE: 10 mg PO daily immediately after the same meal

CAUTION: [B, –]

CI: With/CYP3A4 inhibitors; mod–severe hepatic impair

DISP: Tablets 10 mg ER

SE: Postural BP, dizziness, headache, fatigue

NOTES: Do not cut or crush; ejaculatory disorders compared w/similar drugs

ALLOPURINOL (ZYLOPRIM, LOPURIN, ALOPRIM)

USES: *Gout, hyperuricemia of malignancy, uric acid urolithiasis*

ACTION: Xanthine oxidase inhibitor; uric acid production

DOSE:

Adults: PO: Initial 100 mg/d; usual 300 mg/d; max 800 mg/d; divided dose if >300 mg/d. IV: 200–400 mg/m2/d (max 600 mg/24 hr); (p.c. w/plenty of fluid).

Peds: Only for hyperuricemia of malignancy if <10 yr: 10 mg/kg/24 hr PO or 200 mg/m2/d IV divided q6–8h; max 600 mg/24 hr; in renal impairment

CAUTION: [C, M]

DISP: Tablets 100, 300 mg; injectable 500 mg/30 mL (Aloprim)

SE: Rash, N/V, renal impair, angioedema

NOTES: Aggravates acute gout; begin after acute attack resolves; IV dose of 6 mg/mL final concentration as single daily infusion or divided at 6-, 8-, or 12-hr intervals

ALPROSTADIL, INTRACAVERNOSAL (CAVERJECT, EDEX)

USES: *ED*

ACTION: Prostaglandin; relaxes smooth muscles, dilates cavernosal arteries, lacunar spaces w/blood entrapment

DOSE: 2.5–60 g intracavernosal; titrate in office

CAUTION: [X, –]

CI: Risk of priapism (eg, sickle cell); penile deformities/implants; men in whom sexual activity is inadvisable

DISP: Caverject: 5-, 10-, 20-, 40-g powder for injectable vials ± diluent syringes 10-, 20-, 40-g amp. Caverject Impulse: Self-contained syringe (29 gauge) 10 and 20 g. Edex: 10-, 20-, 40-g cartridges

SE: Local pain w/injection

NOTES: Counsel about priapism, penile fibrosis, and hematoma risks; titrate dose in office

ALPROSTADIL, URETHRAL SUPPOSITORY (MUSE)

USES: *ED*

ACTION: Urethral absorption; prostaglandin, vasodilator, relaxes smooth muscle of corpus cavernosa

DOSE: 125–1000-g system 5–10 min prior to sex; repeat × 1/24 hr; titrate in office

CAUTION: [X, –]

CI: Priapism risk (especially sickle cell, myeloma, leukemia) penile deformities/implants; men in whom sex is inadvisable

DISP: 125, 250, 500, 1,000 g w/transurethral system

SE: BP, dizziness, syncope, penile/testicular pain, urethral burning/bleeding, priapism

NOTES: Titrate dose in office; duration 30–60 min

AMIKACIN (AMIKIN)

USES: *Serious gram(–) bacterial infections* and mycobacteria

ACTION: Aminoglycoside; protein synthesis. Spectrum: Good gram(–) bacterial coverage: Pseudomonas and Mycobacterium sp

DOSE:

Adults and Peds Conventional: 5–7.5 mg/kg/dose q8h; once daily; 15–20 mg/kg q24h; interval w/renal impairment. Neonates <1,200 g, 0–4 wk: 7.5 mg/kg/dose q18h–24h. <7 days, 1,200–2,000 g: 7.5 mg/kg/dose q12h; >2,000 g: 10 mg/kg/dose q12h. >7 days, 1,200–2,000 g: 7 mg/kg/dose q8h; >2,000 g: 7.5–10 mg/kg/dose q8h

CAUTION: [C, ±]; avoid w/diuretics

DISP: 50 and 250 mg/mL injectable

SE: Nephro-/oto-/neurotoxicity, neuromuscular blockage, respiratory paralysis

NOTES: May be effective in gram(–) resistance to gentamicin and tobramycin; follow Cr. Levels: Peak: 30 min after infusion; Trough <0.5 hr before next dose; Therapeutic: Peak 20–30 g/mL; Trough: <8 g/mL; Toxic peak >35 g/mL; Half-life: 2 hr

AMILORIDE (MIDAMOR)

USES: *Hypertension, CHF, and thiazide-induced K+*

ACTION: K+-sparing diuretic; interferes w/K+/Na+ exchange in distal tubule

DOSE:

Adults: 5–10 mg PO daily.

Peds: 0.625 mg/kg/d; w/renal impairment

CAUTION: [B, ?]

CI: K+, SCr >1.5, BUN >30, diabetic neuropathy, w/other K+-sparing diuretics

DISP: Tablets 5 mg

SE: K+; headache, dizziness, dehydration, impotence.

NOTES: Monitor K+

AMINOCAPROIC ACID (AMICAR)

USES: *Excessive bleeding from systemic hyperfibrinolysis and urinary fibrinolysis*

ACTION: Fibrinolysis; inhibits TPA, inhibits conversion of plasminogen to plasmin

DOSE:

Adults: 5 g IV or PO (1st h) followed by 1–1.25 g/hr IV or PO × 8h or until bleeding controlled; 30 g/d max.

Peds: 100 mg/kg IV (1st h) then 1 g/m2/hr; max 18 g/m2/d; w/renal insufficiency

CAUTION: [C, ?]; upper urinary tract bleeding

CI: DIC

DISP: Tablets 500, syrup 250 mg/mL; injectable 250 mg/mL

SE: BP, bradycardia, dizziness, headache, fatigue, rash, GI disturbance, platelet function

NOTES: Administer × 8 hr or until bleeding controlled; not for upper urinary tract bleeding.

AMINO-CERV PH 5.5 CREAM

USES: *Mild cervicitis,* postpartum cervicitis/cervical tears, postcryosurgery, and postconization

ACTION: Hydrating agent; removes excess keratin in hyperkeratotic conditions

DOSE: 1 Applicator-full intravaginally h.s. × 2–4 wk

CAUTION: [C, ?]; w/viral skin infection

DISP: Vaginal cream

SE: Stinging, local irritation

NOTES: Also known as carbamide or urea; contains 8.34% urea, 0.5% sodium propionate, 0.83% methionine, 0.35% cystine, 0.83% inositol, and benzalkonium chloride

AMINOGLUTETHIMIDE (CYTADREN)

USES: *Cushing syndrome*, adrenocortical carcinoma, breast and prostate cancers

ACTION: Adrenal steroidogenesis and conversion of androgens to estrogens; 1st generation aromatase inhibitor

DOSE: Initial 250 mg PO 4 × d, titrate q 1–2 wk max 2 g/d; w/hydrocortisone 20–40 mg/d; w/renal insufficiency

CAUTION: [D, ?]

DISP: Tablets 250 mg

SE: Adrenal insufficiency (medical adrenalectomy), hypothyroidism, masculinization, BP, N/V, rare hepatotoxicity, rash, myalgia, fever, drowsiness, lethargy, anorexia

NOTES: Give q6h to reduce nausea

AMIODARONE (CORDARONE, PACERONE)

WARNING: Liver toxin, exacerbation of arrhythmias and lung damage reported.

USES: *Recurrent VF or hemodynamically unstable VT,* supraventricular arrhythmias, AF

ACTION: Class III antiarrhythmic

DOSE:

Adults: Typical dose: Ventricular arrhythmias: IV: 15 mg/min for 10 min, then 1 mg/min × 6 hr, maintenance 0.5–mg/min continuous infusion or PO: Load: 800–1,600 mg/d PO × 1–3 wk. Maintenance: 600–800 mg/d PO for 1 mo, then 200–400 mg/d

CAUTION: [D, –]; may require digoxin/warfarin dose; many drug interactions

CI: Sinus node dysfunction, 2nd-/3rd-degree AV block, sinus brady (w/o pacemaker), iodine sensitivity

DISP: Tablets 100, 200, 400 mg; injectable 50 mg/mL

SE: Pulmonary fibrosis, exacerbation of arrhythmias, QT interval; CHF, hypo-/hyperthyroidism, LFTs, liver failure, corneal microdeposits, optic neuropathy/neuritis, peripheral neuropathy, photosensitivity

NOTES: A rare, noninfective cause of epididymitis, as drug accumulates in high concentrations within the epididymis, causing inflammation. Can be unilateral or bilateral and resolves on discontinuation

AMITRIPTYLINE (ELAVIL)

WARNING: Antidepressants may suicide risk; consider risks/benefits of use. Monitor closely.

USES: *Depression (not bipolar depression)* peripheral neuropathy, chronic pain, tension headaches, enuresis, interstitial cystitis

ACTION: Tricyclic antidepressant; reuptake of serotonin and norepinephrine by presynaptic neurons; time in REM sleep, vasopressin secretion, relaxes the detrusor muscle

DOSE:

Adults: Initial: 30–50 mg PO h.s.; may to 300 mg h.s. Interstitial cystitis: 75 mg/d PO h.s.

Peds: Not for <12 yr unless for chronic pain. Initial: 0.1 mg/kg PO h.s., over 2–3 wk to 0.5–2 mg/kg PO h.s.; taper to discontinue

CAUTION: [D, ±]; CVD, seizures, narrow-angle glaucoma, hepatic impairment

CI: W/MAOIs or within 14 days of use, during acute MI recovery

DISP: Tablets 10, 25, 50, 75, 100, 150 mg; injectable 10 mg/mL

SE: Strong anticholinergic SEs; overdose may be fatal; urine retention, sedation, ECG changes, photosensitivity

NOTES: Levels: Therapeutic: 120 to 150 ng/mL; Toxic: >500 mg/mL; levels may not correlate w/effectiveness

AMLODIPINE (NORVASC)

USES: *Hypertension, stable or unstable angina*

ACTION: Calcium channel blocker; relaxes coronary vascular smooth muscle

DOSE: 2.5–10 mg/d PO; w/hepatic impairment

CAUTION: [C, ?]

DISP: Tablets 2.5, 5, 10 mg

SE: Peripheral edema, headache, palpitations, flushing, dizziness

NOTES: Take w/o regard to meals

AMMONIUM ALUMINUM SULFATE (ALUM) [OTC]

USES: *Hemorrhagic cystitis when saline bladder irrigation fails*

ACTION: Astringent

DOSE: 1–2% solution w/constant NS bladder irrigation

CAUTION: [±]

DISP: Powder for reconstitution

SE: Encephalopathy possible; aluminum levels, especially w/renal insufficiency; can precipitate and occlude catheters

NOTES: Safe w/o anesthesia and w/vesicoureteral reflux

AMOXICILLIN (AMOXIL, POLYMOX)

USES: *Ear, nose, and throat, lower respiratory, skin, UTIs from susceptible gram(+) bacteria* endocarditis prophylaxis, H. pylori eradication w/other agents (gastric ulcers)

ACTION: -Lactam antibiotic; cell wall synthesis. Spectrum: Gram(+) (Streptococcus sp, Enterococcus sp); some gram(–) (H. influenzae, E. coli, N. gonorrhoeae, H. pylori, P. mirabilis)

DOSE:

Adults: 250–500 mg PO t.i.d. or 500–875 mg b.i.d.

Peds: 25–100 mg/kg/24 hr PO divided q8h, 200–400 mg PO b.i.d. (equivalent to 125–250 mg t.i.d.); in renal impairment

CAUTION: [B, +]

DISP: Capsules 250, 500 mg; chewable tablets 125, 200, 250, 400 mg; suspension 50 mg/mL, 125, 200, 250, and 400 mg/5 mL; tablets 500, 875 mg

SE: D; skin rash

NOTES: Cross-hypersensitivity w/penicillin; many E. coli strains resistant; chew tablets contain phenylalanine

AMOXICILLIN AND CLAVULANIC ACID (AUGMENTIN, AUGMENTIN 600 ES, AUGMENTIN XR)

USES: *Ear, lower respiratory, sinus, urinary tract, skin infections caused by -lactamase–producing H. influenzae, S. aureus, and E. coli*

ACTION: -Lactam antibiotic w/-lactamase inhibitor Spectrum: Gram(+), same as amoxicillin alone, MSSA; gram(–) as w/amoxicillin alone, -lactamase–producing H. influenzae, Klebsiella sp, M. catarrhalis

DOSE:

Adults: 250–500 mg PO q8h or 875 mg q12h; XR 2,000 mg PO q12h.

Peds: 20–40 mg/kg/d as amoxicillin PO divided q8h or 45 mg/kg/d divided q12h; in renal impairment; take w/food

CAUTION: [B, enters breast milk]

DISP: Supplied (as amoxicillin/clavulanic): Tablets 250/125, 500/125, 875/125 mg; chewable tablets 125/31.25, 200/28.5, 250/62.5, 400/57 mg; suspension 125/31.25, 250/62.5, 200/28.5, 400/57 mg/5 mL; suspension ES 600/42.9 mg/5 mL; XR tablet 1,000/62.5 mg

SE: Abdominal discomfort, N/V/D, allergic reaction, vaginitis

NOTES: Do not substitute 2 250-mg tablets for 1 500-mg tablet (overdose of clavulanic acid); max clavulanic acid 125 mg/dose

AMPHOTERICIN B (AMPHOCIN)

USES: *Severe, systemic fungal infections; oral and cutaneous candidiasis*

ACTION: Binds ergosterol in the fungal membrane to alter permeability

DOSE:

Adults and Peds Test dose: 1 mg IV adults or 0.1 mg/kg to 1 mg IV in children; then 0.25–1.5 mg/kg/24 hr IV over 2–6 hr (25–50 mg/d or every other day); total varies w/indication. PO: 1 mL q.i.d.

CAUTION: [B, ?]

DISP: Powder (injectable) 50 mg/vial

SE: K+/Mg2+ from renal wasting; anaphylaxis, headache, fever, chills, nephrotoxicity, BP, anemia, rigors

NOTES: Monitor Cr/LFTs/K+/Mg2+; in renal impairment; pretreatment w/acetaminophen and antihistamines (Benadryl) reduces side effects

AMPHOTERICIN B CHOLESTERYL (AMPHOTEC)

USES: *Aspergillosis, if intolerant/refractory to conventional amphotericin B,* systemic candidiasis

ACTION: Binds ergosterol in fungal membrane, alters permeability

DOSE:

Adults and Peds Test dose: 1.6–8.3 mg, over 15–20 min, then 3–4 mg/kg/d; 1 mg/kg/hr infusion, 7.5 mg/kg/d max; w/renal insufficiency

CAUTION: [B, ?]

DISP: Powder for injectable 50 mg, 100 mg/vial

SE: Anaphylaxis; fever, chills, headache, K+, Mg2+, nephrotoxicity, BP, anemia

NOTES: Do not use in-line filter; LFTs/electrolytes

AMPHOTERICIN B LIPID COMPLEX (ABELCET)

USES: *Refractory invasive fungal infection in patients intolerant of conventional amphotericin B*

ACTION: Binds ergosterol in fungal membrane, alters permeability

DOSE:

Adults and Peds 5 mg/kg/d IV single daily dose

CAUTION: [B, ?]

DISP: Injectable 5 mg/mL

SE: Anaphylaxis; fever, chills, headache, K+, Mg2+, nephrotoxicity, BP, anemia

NOTES: Filter w/5-micron needle; do not mix in electrolyte-containing solutions; if infusion >2 hr, manually mix bag

AMPHOTERICIN B LIPOSOMAL (AMBISOME)

USES: *Refractory invasive fungal infection w/intolerance to conventional amphotericin B; cryptococcal meningitis in HIV; empiric for febrile neutropenia; visceral leishmaniasis*

ACTION: Binds ergosterol in fungal membrane, alters membrane permeability

DOSE:

Adults and Peds 3–6 mg/kg/d, infusion 60–120 min; dose varies by indication; in renal insufficiency

CAUTION: [B, ?]

DISP: Powder injectable 50 mg

SE: Anaphylaxis, fever, chills, headache, K+, Mg2+ nephrotoxicity, BP, anemia

NOTES: Use 1-micron filter

AMPICILLIN (AMCILL, OMNIPEN)

USES: *Respiratory, GU, or GI tract infections, meningitis due to gram(–) and (+) bacteria; SBE prophylaxis*

ACTION: -Lactam antibiotic; cell wall synthesis. Spectrum: Gram(+) (Streptococcus sp, Staphylococcus sp, Listeria); gram(–) (Klebsiella sp, E. coli, H. influenzae, P. mirabilis, Shigella sp, Salmonella sp)

DOSE:

Adults: 500 mg–2 g IM or IV q6h or 250–500 mg PO q6h; varies by indication.

Peds: Neonates <7 d: 50–100 mg/kg/24 hr IV divided q8h. Term infants: 75–150 mg/kg/24 hr divided q6–8h IV or PO. Peds:>1 mo: 100–200 mg/kg/24 hr divided q4–6h IM or IV; 50–100 mg/kg/24 h divided q6h PO up to 250 mg/dose. Meningitis: 200–400 mg/kg/24 hr divided q4–6h IV; w/renal impairment; take on empty stomach

CAUTION: [B, M]; cross-hypersensitivity w/penicillin

DISP: Capsules 250, 500 mg; suspension 100 mg/mL (reconstituted drops), 125 mg/5 mL, 250 mg/5 mL; powder (injectable) 125, 250, 500, 1, 2, 10 g/vial

SE: D, rash, allergic reaction

NOTES: Many E. coli are resistant

AMPICILLIN-SULBACTAM (UNASYN)

USES: *Gynecologic, intra-abdominal, skin infections due to -lactamase–producing S. aureus, Enterococcus, H. influenzae, P. mirabilis, and Bacteroides sp*

ACTION: -Lactam antibiotic and -lactamase inhibitor. Spectrum: Gram(+/–) as for ampicillin alone; also Enterobacter, Acinetobacter, Bacteroides

DOSE:

Adults: 1.5–3 g IM or IV q6h.

Peds: 100–400 mg ampicillin/kg/d (150–300 mg Unasyn) q6h; w/renal insufficiency

CAUTION: [B, M]

DISP: Powder for injectable 1.5, 3 g/vial, 15-g bulk package

SE: Allergic reactions, rash, diarrhea, injection site pain

NOTES: A 2:1 ratio ampicillin:sulbactam

ANIDULAFUNGIN (ERAXIS)

USES: *Candidemia, esophageal candidiasis, other Candida infection (peritonitis, intra-abdominal abscess)*

ACTION: Echinocandin; cell wall synthesis Spectrum: C. albicans, C. glabrata, C. parapsilosis, C. tropicalis

DOSE: Candidemia, others: 200 mg IV × 1, then 100 mg IV daily (treat for 14 days after last + culture)

CAUTION: [C, ?/–]

CI: Echinocandin hypersensitivity

DISP: Powder 50 mg/vial, 100 mg/vial

SE: Histamine-mediated infusion reactions (urticaria, flushing, ↓ BP, dyspnea, etc), fever, N/V/D, ↑ K+, headache, ↑ LFTs, worsening hepatic failure

NOTES: Infusion rate to <1.1 mg/min w/infusion reactions

ASPIRIN (BAYER, ECOTRIN, ST. JOSEPH'S) [OTC]

USES: *Angina, CABG, PTCA, carotid endarterectomy, ischemic stroke, TIA, MI, arthritis, pain,* headache, *fever,* inflammation, Kawasaki disease

ACTION: Prostaglandin inhibitor

DOSE:

Adults: Pain, fever: 325–650 mg q4–6h PO or PR (4 g/d max). RA: 3–6 g/d PO in divided doses. Platelet inhibitor: 81–325 mg PO daily. Prevent MI: 81 (preferred)–325 mg PO daily.

Peds: Antipyretic: 10–15 mg/kg/dose PO or PR q4–6h up to 80 mg/kg/24 hr. RA: 60–100 mg/kg/24 hr PO divided q4–6h (keep levels 15–30 mg/dL); for all uses 4 g/d max; avoid w/CrCl <10 mL/min, severe liver disease

CAUTION: [C, M]; linked to Reye syndrome; avoid w/viral illness in peds <16 yr

CI: Allergy to ASA, chickenpox/flu symptoms, syndrome of nasal polyps, angioedema, and bronchospasm to NSAIDs

DISP: Caplet: 81, 325, 500 mg; Tablets 325, 500 mg; chewable tablets 81 mg; EC tablets 81, 325, 500, 650 mg; SR tablets 650, 800, 975 mg;gum 227 mg; suppositories 300, 600 mg

SE: GI upset, erosion, and bleeding

NOTES: Discontinue 1 wk prior to surgery; avoid/limit EtOH. Salicylate levels: Therapeutic: 100–250 g/mL. Toxic: >300 g/mL

ASPIRIN + CODEINE (EMPIRIN NO 3, 4) [C-III]

USES: Mild to *mod pain,* symptomatic nonproductive cough

ACTION: Combined effects of ASA and codeine

DOSE:

Adults: 1–2 tablets PO q4–6h PRN.

Peds: ASA 10 mg/kg/dose; codeine 0.5–1 mg/kg/dose q4h

CAUTION: [D, M]

CI: Allergy to ASA/codeine, PUD, bleeding, anticoagulant treatment, children w/chickenpox or flu symptoms, syndrome of nasal polyps, angioedema, and bronchospasm to NSAIDs

DISP: Tablets 325 mg of ASA and codeine (codeine in No. 3 = 30 mg, No. 4 = 60 mg)

SE: Drowsiness, dizziness, GI upset, ulceration, bleeding

NOTES: Discontinue 1 wk prior to surgery; avoid/limit EtOH

ATROPINE, BENZOIC ACID, HYOSCYAMINE SULFATE, METHENAMINE, METHYLENE BLUE, PHENYL SALICYLATE (URISED)

USES: *Lower urinary tract discomfort*

ACTION: Methenamine in acidic urine releases formaldehyde (antiseptic), methylene blue/benzoic acid (mild antiseptic), phenyl salicylate (mild analgesic), hyoscyamine and atropine (parasympatholytic; muscle spasm)

DOSE:

Adults: 2 tablets PO q.i.d.

Peds: >6 yr: Individualize

CAUTION: [C, ?/–]; avoid w/sulfonamides

CI: Narrow-angle glaucoma, pyloric/duodenal obstruction, BOO, coronary artery spasm

DISP: Tablet; atropine 0.03 mg/benzoic acid 45 mg/hyoscyamine 0.03 mg/methenamine 40.8 mg/methylene blue 5.4 mg/phenyl salicylate 18.1 mg

SE: Rash, dry mouth, flushing, pulse, dizziness, blurred vision, urine/feces discoloration, voiding difficulty

NOTES: Take w/plenty of fluid; can cause crystalluria

AZATHIOPRINE (IMURAN)

WARNING: May neoplasia w/chronic use; mutagenic and hematologic toxicity possible

USES: *Adjunct to prevent renal transplant rejection, RA,* SLE, Crohn disease, ulcerative colitis

ACTION: Immunosuppressive; antagonizes purine metabolism

DOSE: Renal transplant: 3–5 mg/kg/d IV/PO single daily dose, taper by 0.5 mg/kg q4wk to lowest effective dose. RA: 1 mg/kg/d once daily or divided b.i.d. × 6–8 wk, 0.5 mg/kg/d q4wk to 2.5 mg/kg/d; w/renal insufficiency

CAUTION: [D, ?]

CI: Pregnancy

DISP: Tablets, 50, 75, 100 mg; powder for injectable 100 mg

SE: GI intolerance, fever, chills, leukopenia, thrombocytopenia

NOTES: Handle injectable w/cytotoxic precautions; interaction w/allopurinol; do not administer live vaccines on drug; CBC and LFTs; dose per local transplant protocol, usually start 1–3 days pretransplant

AZITHROMYCIN (ZITHROMAX)

USES: *Community-acquired pneumonia, pharyngitis, otitis media, skin infections, nongonococcal (chlamydial) urethritis, chancroid and PID; treat/prevent MAC in HIV*

ACTION: Macrolide antibiotic; bacteriostatic; protein synthesis. Spectrum: Chlamydia, H. ducreyi, H. influenzae, Legionella, M. catarrhalis, M. pneumoniae, M. hominis, N. gonorrhoeae, S. aureus, S. agalactiae, S. pneumoniae, S. pyogenes

DOSE:

Adults: Nongonococcal urethritis: 1 g PO × 1. Gonorrhea, uncomplicated: 2 g PO × 1. Chancroid: 1 g PO × 1; tablets OK w/ or w/o food; w/CrCl <10 mL/mg

CAUTION: [B, +]

DISP: Tablets 250, 500, 600 mg; Z-Pack (5-day, 250 mg); Tri-Pak (500-mg tablets × 3); suspension 1 g; single-dose packet (ZMAX) ER suspension (2 g); suspension 100, 200 mg/5 mL; injectable powder 500 mg; 2.5 mL ophthalmic solution 1%

SE: GI upset, metallic taste

AZTREONAM (AZACTAM)

USES: *Aerobic gram(–) UTIs, lower respiratory, intra-abdominal, skin, gynecologic infections, and septicemia*

ACTION: Monobactam: cell wall synthesis. Spectrum: Gram(–) (Pseudomonas, E. coli, Klebsiella, H. influenzae, Serratia, Proteus, Enterobacter, Citrobacter)

DOSE:

Adults: 1–2 g IV/IM q6–12h. UTI: 500–1 g IV q8–12h.

Peds: Premature: 30 mg/kg/dose IV q12h. Term and children: 30 mg/kg/dose q6–8h; in renal impairment

CAUTION: [B, +]

DISP: Injectable (solution), 1 g, 2 g/50 mL powder for reconstitution to 500 mg, 1 g, 2 g

SE: N/V/D, rash, pain at injection site

NOTES: No gram(+) or anaerobic activity; OK in penicillin-allergic patients

BACITRACIN, TOPICAL (BACIGUENT); BACITRACIN AND POLYMYXIN B, TOPICAL (POLYSPORIN); BACITRACIN, NEOMYCIN, AND POLYMYXIN B, TOPICAL (NEOSPORIN); BACITRACIN, NEOMYCIN, POLYMYXIN B, AND HYDROCORTISONE, TOPICAL (CORTISPORIN); BACITRACIN, NEOMYCIN, POLYMYXIN B, AND LIDOCAINE, TOPICAL (CLOMYCIN)

USES: Prevent/treat *minor skin infections*

ACTION: Topical antibiotic w/added components (anti-inflammatory and analgesic)

DOSE: Apply sparingly b.i.d.–q.i.d.

CAUTION: [C, ?]; not for deep wounds, puncture, or animal bites

DISP: Bacitracin 500 U/g ointment; bacitracin units/polymyxin B sulfate 10,000 U/g ointment and powder; bacitracin 400 U/neomycin 35 mg/polymyxin B 5,000 U/g ointment; bacitracin 400 U/neomycin 3.5 mg/polymyxin B 5,000 U/hydrocortisone 10 mg/g ointment; bacitracin 500 U/neomycin 3.5 mg/polymyxin b 5,000 U/lidocaine 40 mg/g ointment

NOTES: Ophthalmic, systemic, and irrigation forms are available, but not generally used due to potential toxicity

BACLOFEN (LIORESAL INTRATHECAL, GENERIC)

WARNING: Abrupt discontinuation of IT form can lead to organ failure, rhabdomyolysis, and death

USES: *Spasticity due to severe chronic disorders (eg, MS, ALS, or spinal cord lesions),* trigeminal neuralgia, intractable hiccups

ACTION: Centrally acting skeletal muscle relaxant; transmission of monosynaptic and polysynaptic cord reflexes

DOSE:

Adults: Initial, 5 mg PO t.i.d.; every 3 days to effect; max 80 mg/d. Intrathecal: Via implantable pump (see insert).

Peds: 2–7 yr: 10–15 mg/d divided q8h; titrate, max 40 mg/d. >8 yr: Max 60 mg/d IT: Via implantable pump (see insert); in renal impairment; take w/food or milk

CAUTION: [C, +]; epilepsy, neuropsychological disturbances

DISP: Tablets 10, 20 mg; IT injectable 50 g/mL, 10 mg/20 mL, 10 mg/5 mL

SE: Dizziness, drowsiness, insomnia, ataxia, weakness, BP

BASILIXIMAB (SIMULECT)

WARNING: Administer only under the supervision of a physician experienced in immunosuppression therapy in an appropriate facility

USES: *Prevent acute transplant rejection*

ACTION: IL-2 receptor antagonists

DOSE:

Adults and Peds: >35 kg: 20 mg IV 2 hr before transplant, then 20 mg IV for 4 days posttransplant.

Peds: <35 kg: 10 mg 2 hr prior to transplant; same dose IV for 4 days posttransplant

CAUTION: [B, ?/–]

CI: Hypersensitivity to murine proteins

DISP: Injectable powder 10, 20 mg

SE: Edema, hypertension, headache, dizziness, fever, pain, infection, GI effects, electrolyte disturbances

NOTES: A murine/human MoAb

BCG [BACILLUS CALMETTE-GUéRIN] (THERACYS, TICE BCG)

WARNING: Contains live, attenuated mycobacteria; risk for transmission; handle as a biohazard; nosocomial infections reported in immunosuppressed; fatal reactions reported

USES: *Bladder cancer (superficial),* TB prophylaxis

ACTION: Attenuated live BCG; immunomodulator

DOSE: Bladder cancer: 1 vial prepared and instilled into bladder for 2 hr. Repeat once/wk × 6 wk; then 1 treatment at 3, 6, 12, 18, and 24 mo after

CAUTION: [C, ?]; asthma

CI: Immunocompromised, steroid use, febrile illness, UTI, gross hematuria, w/traumatic catheterization or UTI

DISP: Powder for reconstitution to 81 mg (105 ± 87 × 108 CFU vial) (TheraCys), 50 mg (1–8 × 108 CFU/vial) (Tice BCG)

SE: Intravesical: Hematuria, urinary frequency, dysuria, bacterial UTI, rare BCG sepsis

NOTES: Routine US adult BCG immunization is not performed; occasionally used in high-risk children who are PPD(–) and cannot take INH; intravesical use, dispose/void in toilet with chlorine bleach

BELLADONNA AND OPIUM SUPPOSITORIES (BANDO SUPPRETTES) [C-II]

USES: *Bladder spasms; mod/severe pain*

ACTION: Antispasmodic, analgesic

DOSE: 1 suppository PR q6h PRN

CAUTION: [C, ?]

CI: Glaucoma, respiratory depression

DISP: 15A = 30 mg opium/16.2 mg belladonna extract; 16A = 60 mg opium/16.2 mg belladonna extract

SE: Anticholinergic (eg, sedation, urinary retention, constipation)

BENAZEPRIL (LOTENSIN)

USES: *Hypertension,* diabetic nephropathy, CHF

ACTION: ACE inhibitor

DOSE: 10–80 mg/d PO

CAUTION: [C (1st trimester), D (2nd and 3rd trimesters), +]

CI: Angioedema, history of edema, bilateral RAS

DISP: Tablets 5, 10, 20, 40 mg

SE: Symptomatic BP w/diuretics; dizziness, headache, K+, nonproductive cough

BETHANECHOL (URECHOLINE, DUVOID, OTHERS)

USES: *Acute postop/postpartum nonobstructive urinary retention; neurogenic bladder with retention*

ACTION: Stimulates cholinergic smooth muscle in bladder and GI tract

DOSE:

Adults: Initial 5–10 mg then repeat hourly until response or 50 mg, typical 10–50 mg t.i.d.–q.i.d., 200 mg/d max t.i.d.–q.i.d.; 2.5–5 mg SQ t.i.d.–q.i.d. and PRN.

Peds: 0.3–0.6 mg/kg/24 hr PO divided t.i.d.–q.i.d. or 0.15–2 mg/kg/d SQ divided 3–4 doses; take on empty stomach

CAUTION: [C, –]

CI: BOO, PUD, epilepsy, hyperthyroidism, bradycardia, COPD, AV conduction defects, Parkinsonism, BP, vasomotor instability

DISP: Tablets 5, 10, 25, 50 mg; injectable 5 mg/mL

SE: Abdominal cramps, diarrhea, salivation, BP

NOTES: Do not use IM/IV

BEVACIZUMAB (AVASTIN)

WARNING: Associated with GI perforation, wound dehiscence, and fatal hemorrhage, hemoptysis and GI bleeding

USES: *Breast, lung, colon, and rectum cancers, glioblastoma multiforme, with interferon alpha in metastatic RCC*

ACTION: Vascular endothelial GF (VGEF) inhibitor, recombinant humanized monoclonal antibody

DOSE: RCC: 10 mg/kg IV infusion every 2 wk in combination with interferon alfa 2b (Roferon-A) 9 million units 3 times a week

CAUTION: [C,] Do not use w/in 28 d of surgery; D/C with serious adverse effects

DISP: 100 mg/4 mL, 400 mg/16 mL vials

SE: Wound dehiscence, GI perforation, tracheoesophageal fistula, arterial thrombosis, hemoptysis, hemorrhage, hypertension, proteinuria, CHF, infections, diarrhea, leukopenia

NOTES: Monitor for—BP & proteinuria; Roferon-A discontinued in US in 2007

BICALUTAMIDE (CASODEX, GENERIC)

USES: *Advanced prostate cancer w/LHRH agonists (eg, leuprolide, goserelin*)

ACTION: Nonsteroidal antiandrogen

DOSE: 50 mg/d

CAUTION: [Not indicated in women X, ?]

CI: Women

DISP: Capsules 50 mg

SE: Hot flashes, loss of libido, impotence, D/N/V, gynecomastia, and LFT elevation

BLEOMYCIN SULFATE (BLENOXANE)

USES: *Testis cancer; Hodgkin disease and NHLs; cutaneous lymphomas; and SCC (head and neck, larynx, cervix, skin, penis); malignant pleural effusion sclerosing agent*

ACTION: Induces DNA breakage (scission)

DOSE: Typical (per protocols) 0.25–0.5 U/kg (10–20 units/m2) 1–2 times/week; IV infusion: 15 U/m2 × 4 days; w/renal impairment

CAUTION: [D, ?]

CI: Severe pulmonary disease (pulmonary fibrosis)

DISP: Powder (injectable) 15, 30 U

SE: Hyperpigmentation and allergy (rash to anaphylaxis); fever in 50%; lung toxicity (idiosyncratic and dose-related); pneumonitis w/fibrosis; Raynaud phenomenon, N/V

NOTES: Test dose is 1 U, especially in lymphoma patients; lung toxicity w/total dose >400 U or single dose >30 U; avoid high FiO2 in general anesthesia to toxicity

BOTULINUM TOXIN TYPE A (BOTOX, BOTOX COSMETIC, MYOBLOC, DYSPORT)

WARNING: Distant spread of toxin is possible.

USES: *Glabellar lines (cosmetic), blepharospasm, cervical dystomia, axillary hyperhidrosis, strabismus*, overactive bladder

ACTION: Neurotoxicity, acetylcholine release from nerve endings, neuromuscular transmission; denervates sweat glands and muscles

DOSE:

Adults: Glabellar lines (cosmetic): 0.1 mL IM × 5 sites q3–4mo; Blepharospasm: 1.25–2.5 U IM/site q3mo; max 200 U/30 days cumulative dose; Cervical dystonia 198–300 U IM divided <100 U into sternocleidomastoid

Peds: Blepharospasm: >12 yr: See adult. Cervical dystonia: >16 yr: 198–300 U IM divided among affected muscles; use <100 U in sternocleidomastoid

CAUTION: [C, ?]; different products have different dosing units; w/neurologic disease; do not exceed dosing recommended; caution sedentary patient to resume activity slowly after injection; aminoglycosides and nondepolarizing muscle blockers may effects; risk for distant spread at the time of injection

CI: Hypersensitivity to components, injection site infection

DISP: 100 U injectable powder; reconstitute in 10 mL NS (10 U/mL)

SE: Anaphylaxis, erythema multiforme, dysphagia, dyspnea, syncope, headache, narrow-angle glaucoma, injection site pain, botulism poisoning (muscle weakness, hoarseness or trouble talking, trouble saying words clearly, loss of bladder control, trouble breathing or swallowing, double vision, blurred vision, or drooping eyelids)

NOTES: Fatalities with distant spread mostly in children and not during cosmetic use. Not FDA approved in urinary tract; typical bladder regimen reported 10–30 injections of 10U/1 mL/site (posterior wall in midline, right and left lateral walls and dome); trigone is spared

BUMETANIDE (BUMEX)

USES: *Edema from CHF, hepatic cirrhosis, and renal disease*

ACTION: Loop diuretic; ↓ reabsorption of Na+ and Cl-, in ascending loop of Henle and distal tubule

DOSE:

Adults: 0.5–2 mg/d PO; 0.5–1 mg IV/IM q8–24h (max 10 mg/d).

Peds: 0.015–0.1 mg/kg PO q6–24h (max 10 mg/d)

CAUTION: [D, ?]

CI: Anuria, hepatic coma, severe electrolyte depletion

DISP: Tablets 0.5, 1, 2 mg; injectable 0.25 mg/mL

SE: ↓ K+, ↓ Na+, ↑ Cr, ↑ uric acid, dizziness, ototoxicity

NOTES: Monitor fluid and electrolytes

BUTABARBITAL, HYOSCYAMINE HYDROBROMIDE, PHENAZOPYRIDINE (PYRIDIUM PLUS)

USES: *Relieve urinary tract pain w/UTI, procedures, trauma*

ACTION: Phenazopyridine (topical anesthetic), hyoscyamine (parasympatholytic, ↓ spasm), and butabarbital (sedative)

DOSE: 1 PO q.i.d., p.c. and h.s.; w/antibiotic for UTI, 2 days max

CAUTION: [C, ?]

DISP: Tablet butabarbital/hyoscyamine/phenazopyridine 15 mg/0.3 mg/150 mg

SE: Headache, rash, itching, GI distress, methemoglobinemia, hemolytic anemia, anaphylactoid-like reactions, dry mouth, dizziness, drowsiness, blurred vision

NOTES: Colors urine orange and may tint skin, sclera; stains clothing/contact lenses

BUTORPHANOL (STADOL) [C-IV]

USES: *Anesthesia adjunct; pain* and migraine headache

ACTION: Opiate agonist–antagonist w/central analgesic actions

DOSE: 1–4 mg IM or IV q3–4h PRN. Migraine: 1 spray in 1 nostril, repeat × 1 60–90 min, then q3–4h; ↓ in renal impairment

CAUTION: [C (D if high dose or prolonged use at term), +]

DISP: Injectable 1, 2 mg/mL; nasal 1 mg/spray (10 mg/mL)

SE: Drowsiness, dizziness, nasal congestion

NOTES: May induce withdrawal in opioid dependency

CALCITONIN (FORTICAL, MIACALCIN)

USES: Miacalcin: *Paget disease, emergent treatment of hypercalcemia; postmenopausal osteoporosis*; Fortical: *Postmenopausal osteoporosis*; osteogenesis imperfecta

ACTION: Polypeptide hormone (salmon derived); inhibits osteoclasts

DOSE: Paget disease: 100 U/d IM/SQ initial, 50 U/d or 50–100 U q1–3d maintenance. Hypercalcemia: 4 U/kg IM/SQ q12h; to 8 U/kg q12h, max q6h. Osteoporosis: 100 U every other day IM/SQ; intranasal 200 U = 1 nasal spray/d

CAUTION: [C, ?]

DISP: Fortical, Miacalcin nasal spray 200 IU/activation; injectable, Miacalcin 200 U/mL (2 mL)

SE: Facial flushing, N, injection site edema, nasal irritation, polyuria; may granular casts in urine

NOTES: For nasal spray, alternate nostrils daily; ensure adequate calcium and vitamin D intake; Fortical is rDNA derived from salmon

CALCITRIOL (ROCALTROL, CALCIJEX)

USES: *Predialysis reduction of PTH levels to treat bone disease; Ca^{2+} on dialysis*

ACTION: 1,25-Dihydroxycholecalci-ferol (vitamin D analog); Ca^{2+} and phosphorus absorption; bone mineralization

DOSE:

Adults: Renal failure: 0.25 g/d PO, 0.25 g/d q4–6wk PRN; 0.5 g 3 × week IV, PRN. Hypoparathyroidism: 0.5–2 g/d.

Peds: Renal failure: 15 ng/kg/d, PRN; maintenance 30–60 ng/kg/d. Hypoparathyroidism: <5 yr: 0.25–0.75 g/d. >6 yr: 0.5–2 g/d

CAUTION: [C, ?]; Mg^{2+} possible w/antacids

CI: Ca^{2+}; vitamin D toxicity

DISP: Injectable 1 g/mL (in 1 mL); capsules 0.25, 0.5 g; solution 1 g/mL

SE: Ca^{2+} possible

NOTES: Monitor to keep Ca^{2+} WNL; use non–aluminum phosphate binders and low-phosphate diet to control serum phosphate

CALCIUM ACETATE (PHOSLO)

USES: *ESRD-associated hyperphosphatemia*

ACTION: Ca^{2+} supplement w/o aluminum to PO_4^{2-} absorption

DOSE: 2–4 tablets PO w/meals

CAUTION: [C, ?]

CI: Ca^{2+}

DISP: Gel-cap 667 mg

SE: Can Ca^{2+}; hypophosphatemia, constipation

NOTES: Monitor Ca^{2+}

CALCIUM CARBONATE (TUMS, ALKA-MINTS, CHILDREN'S MYLANTA) [OTC]

USES: *Hyperacidity-associated w/peptic ulcer disease, hiatal hernia, etc.*, calcium supplementation

ACTION: Neutralizes gastric acid

DOSE: 500 mg–2 g PO PRN, 7 g/d max; w/renal impairment

CAUTION: [C, ?]

DISP: Chewable tablets 350, 420, 500, 550, 750, 850 mg; suspension

SE: Ca^{2+}, PO_4^{2-}, constipation

CALCIUM CITRATE (CAL-C-CAPSULES, CAL-CEE, CAL-CITRATE-225, CITRACAL KOSHER [OTC])

USES: *Antacid; treat/prevent calcium deficiency or hyperphosphatemia; reduce risk of osteoporosis*, reduce intestinal oxalate absorption in urolithiasis

ACTION: Ca^{2+} supplement, PO_4^{2-} absorption; Ca^{2+} binds intestinal oxalate and reduces oxalate available for absorption; citrate supplementation is beneficial in diarrheal states to increase urinary pH and citrate level

DOSE: 500 mg to 2 g 2–4 times/d; urolithiasis prevention 1–2 tablet/a.c.

CAUTION: [C, ?]; may effect of quinidine; may effects of tetracyclines, atenolol, salicylates, iron salts, fluoroquinolones

CI: Ca^{2+}

DISP: Many OTC forms as elemental calcium caps: Cal-C-Capsules 180 mg, Cal-Citrate-225: 225 mg; granules: 760 mg/teaspoonful; tablets Cal-Cee: 250 mg, Citracal: 200 mg

SE: Can Ca^{2+}; hypophosphatemia, constipation

NOTES: Requires vitamin D for absorption; monitor Ca^{2+}

CALCIUM CITRATE WITH VITAMIN D (CITRACAL MAXIMUM CAPLET, CITRACAL® Petites with Vitamin D, Citracal® Regular 250 mg + D [OTC])

USES: *Reduce risk of osteoporosis*

ACTION: Ca^{2+} supplement, PO_4^{2-} absorption; vitamin D supplement to enhance Ca^{2+} absorption

DOSE: 1–2 tablets b.i.d.

CAUTION: [C, ?]; may effect of quinidine; may effects of tetracyclines, atenolol, salicylates, iron salts, fluoroquinolones

CI: Ca^{2+}

DISP: Mg of Ca2+/IU vitamin D: Citracal Maximum Caplet: 630 mg/500 IU; Citracal Petites with Vitamin D: 400 mg/500 IU; Citracal Regular 250 mg + D: 500 mg/400 IU

SE: Can Ca2+; hypophosphatemia, constipation

NOTES: Monitor Ca2+

CALCIUM GLUBIONATE (NEO-CALGLUCON) [OTC]

USES: *Treat and prevent calcium deficiency*

ACTION: Ca2+ supplement

DOSE:

Adults: 6–18 g/d divided doses.

Peds: 600–2,000 mg/kg/d divided q.i.d. (9 g/d max); in renal impairment

CAUTION: [C, ?]

CI: Ca2+

DISP: OTC syrup 1.8 g/5 mL = elemental Ca 115 mg/5 mL

SE: Ca2+, PO24, constipation

NOTES: Take with full glass juice or water 1–3 hr after other meds or meals, 2 hr before iron supplements.

CALCIUM SALTS (CHLORIDE, GLUCONATE, GLUCEPTATE)

USES: *Ca2+ replacement,* VF, Ca2+ blocker toxicity, Mg2+ intoxication, tetany, *hyperphosphatemia in ESRD*

ACTION: Ca2+ supplement/replacement

DOSE:

Adults: Replacement: 1–2 g/d PO. Tetany: 1 g CaCl over 10–30 min; repeat in 6 hr PRN; Hyperkalemia/calcium channel blocker overdose: 8–16 mg/kg (usually 5–10 mL) IV.

Peds: Replacement: 200–500 mg/kg/24 hr PO or IV divided q.i.d. Cardiac emergency: 100 mg/kg/dose IV gluconate salt q10min. Tetany: 10 mg/kg CaCl over 5–10 min; repeat in 6 hr or use infusion (200 mg/kg/d max).

Adults and Peds Ca2+ due to citrated blood infusion: 0.45 mEq Ca/100 mL citrated blood infusion (in renal impairment)

CAUTION: [C, ?]

CI: Ca2+

DISP: CaCl2 injectable 10% = 100 mg/mL = Ca2+; 27.2 mg/mL = 10-mL ampule; Ca2+ gluconate injection 10% = 100 mg/mL = Ca2+ 9 mg/mL; tablets 500 mg = 45-mg Ca2+, 650 mg = 58.5-mg Ca2+, 975 mg = 87.75-mg Ca2+, 1 g = 90-mg Ca2+; Ca2+ gluceptate injectable 220 mg/mL = 18-mg/mL Ca2+

SE: Bradycardia, cardiac arrhythmias, Ca2+, constipation

NOTES: $CaCl_2$ 270 mg (13.6 mEq) elemental Ca^{2+}/g, and calcium gluconate 90 mg (4.5 mEq) Ca^{2+}/g. RDA for Ca^{2+}:

Peds: <6 mo: 210 mg/d; 6 mo–1 yr: 270 mg/d; 1–3 yr: 500 mg/d; 4–9 yr: 800 mg/d; 10–18 yr: 1,200 mg/d. Adults. 1000 mg/d; >50 yr: 1,200 mg/d

CANDESARTAN (ATACAND)

USES: *Hypertension,* diabetic nephropathy, CHF

ACTION: Angiotensin II receptor antagonist

DOSE: 4–32 mg/d (usual 16 mg/d)

CAUTION: [C (1st trimester, D 2nd and 3rd trimesters), –]

CI: Primary hyperaldosteronism; bilateral RAS

DISP: Tablets 4, 8, 16, 32 mg

SE: Dizziness, headache, flushing, angioedema

CAPTOPRIL (CAPOTEN, OTHERS)

USES: *Hypertension (HTN), CHF, MI,* LVD, diabetic nephropathy

ACTION: ACE inhibitor

DOSE:

Adults: HTN: Initial, 25 mg PO b.i.d.–t.i.d.; to maintenance q1–2 wk by 25-mg increments/dose (max 450 mg/d) to effect. CHF: Initial, 6.25–12.5 mg PO t.i.d.; titrate PRN. LVD: 50 mg PO t.i.d. Diabetic nephropathy: 25 mg PO t.i.d.

Peds: Infants <2 mo: 0.05–0.5 mg/kg/dose PO q8–24h. Children: Initial, 0.3–0.5 mg/kg/dose PO; to 6 mg/kg/d max in 2–4 divided doses; 1 hr a.c.

CAUTION: [C (1st trimester D 2nd–3rd trimesters) +]; unknown effects in renal impairment.

CI: History angioedema, bilateral RAS

DISP: Tablets 12.5, 25, 50, 100 mg

SE: Rash, proteinuria, cough, K^+

CARBOPLATIN (PARAPLATIN)

WARNING: Administration only by physician experienced in cancer chemotherapy; bone marrow suppression possible; anaphylaxis may occur.

USES: *Ovarian,* lung, head and neck, testicular, urothelial, and brain*cancers, non-Hodgkin lymphoma* and allogeneic and bone marrow transplant in high doses

ACTION: DNA cross-linker; forms DNA–platinum adducts

DOSE: Ovarian carcinoma: 360 mg/m2; AUC dosing 4–8 mg/mL (Culvert formula: Mg = AUC × [25 + calculated GFR]); adjust based on platelet count, CrCl, and BSA (Egorin formula); up to 1,500 mg/m2 used in bone marrow transplant setting (per protocols)

CAUTION: [D, ?]

CI: Severe bone marrow suppression, excessive bleeding

DISP: Injectable 50, 150, 450 mg vial (10 mg/mL)

SE: Anaphylaxis, bone marrow, N/V/D, nephrotoxicity, hematuria, neurotoxicity, LFTs

NOTES: Physiologic dosing based on Culvert or Egorin formula allows doses w/ toxicity

CASPOFUNGIN (CANCIDAS)

USES: *Invasive aspergillosis refractory/intolerant to standard therapy, esophageal candidiasis*

ACTION: Echinocandin; fungal cell wall synthesis; highest activity in regions of active cell growth

DOSE: 70 mg IV load day 1, 50 mg/d IV; slow infusion; in hepatic impairment

CAUTION: [C, ?/–]; do not use w/cyclosporine; not studied as initial therapy

CI: Allergy to any component

DISP: Injectable 50, 70 mg powder for reconstitution

SE: Fever, headache, N/V, thrombophlebitis at site, LFTs

NOTES: Monitor during infusion; limited experience >2 wk of therapy

CEFACLOR (RANICLOR)

USES: *Bacterial infections of the upper and lower respiratory tract, skin, bone, urinary tract, abdomen*

ACTION: 2nd-generation cephalosporin; cell wall synthesis. Spectrum: More gram(–) activity than 1st-gen cephalosporins; effective against gram(+) (Streptococcus sp, S. aureus); good coverage against gram(–) H. influenzae, E. coli, Klebsiella, Proteus.

DOSE:

Adults: 250–500 mg PO t.i.d.; ER 375–500 mg b.i.d.

Peds: 20–40 mg/kg/d PO divided 8–12 hr; renal impairment

CAUTION: [B, +]; antacids absorption

CI: Cephalosporin/penicillin allergy

DISP: Capsules 250, 500 mg; tablets ER 375, 500 mg; chewable tablets (Raniclor) 250, 375 mg; suspension 125, 187, 250, 375 mg/5 mL

SE: N/D, rash, eosinophilia, LFTs, headache, rhinitis, vaginitis

CEFADROXIL (DURICEF)

USES: *Infections of skin, bone, upper and lower respiratory tract, urinary tract*

ACTION: 1st-generation cephalosporin; cell wall synthesis. Spectrum: Good gram(+) coverage (group A -hemolytic Streptococcus, Staphylococcus); gram(–) (E. coli, Proteus, Klebsiella)

DOSE:

Adults: 1–2 g/d PO, 2 divided doses

Peds: 30 mg/kg/d divided b.i.d.; in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Capsules 500 mg; tablets 1 g; suspension, 250, 500 mg/5 mL

SE: N/V/D, rash, eosinophilia, LFTs

CEFAZOLIN (ANCEF, KEFZOL)

USES: *Infections of skin, bone, upper and lower respiratory tract, urinary tract*

ACTION: 1st-generation cephalosporin; -lactam cell wall synthesis. Spectrum: Good coverage of gram(+) bacilli and cocci (Streptococcus, Staphylococcus [except Enterococcus]); some coverage of gram(–) (E. coli, Proteus, Klebsiella)

DOSE:

Adults: 1–2 g IV q8h.

Peds: 25–100 mg/kg/d IV divided q6–8h; in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Injectable: 500 mg, 1, 10, 20 g

SE: D, rash, eosinophilia, LFTs, injection site pain

NOTES: Widely used for surgical prophylaxis

CEFDINIR (OMNICEF)

USES: *Infections of the respiratory tract, skin, bone, and urinary tract*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: Many gram(+) and (–) organisms; more active than cefaclor and cephalexin against Streptococcus, Staphylococcus; some anaerobes

DOSE:

Adults: 300 mg PO b.i.d. or 600 mg/d PO.

Peds: 7 mg/kg PO b.i.d. or 14 mg/kg/d PO; in renal impairment

CAUTION: [B, +]; w/penicillin-sensitive patients, serum sickness–like reactions reported

CI: Hypersensitivity to cephalosporins

DISP: Capsules 300 mg; suspension 125, 250 mg/5 mL

SE: Anaphylaxis, diarrhea, rare pseudomembranous colitis

CEFDITOREN (SPECTRACEF)

USES: *Acute exacerbations of chronic bronchitis, pharyngitis, tonsillitis; skin infections*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: Good gram(+) coverage (Streptococcus, Staphylococcus); gram(–) (H. influenzae, M. catarrhalis)

DOSE:

Adults, Peds: >12 yr: Skin: 200 mg PO b.i.d. × 10 d; avoid antacids within 2 hr; take w/meals; in renal impairment

CAUTION: [B, ?]; renal/hepatic impairment

CI: Cephalosporin/penicillin allergy, milk protein, or carnitine deficiency

DISP: 200 mg tablets

SE: Headache, N/V/D, colitis, nephrotoxicity, hepatic dysfunction, Stevens-Johnson syndrome, toxic epidermal necrolysis, allergic reactions

NOTES: Causes renal excretion of carnitine; tablets contain milk protein

CEFEPIME (MAXIPIME)

USES: *Complicated/uncomp UTI, pneumonia, empiric febrile neutropenia, skin/soft-tissue infections, complicated intra-abdominal infections*

ACTION: 4th-generation cephalosporin; cell wall synthesis. Spectrum: Gram(+) coverage S. pneumoniae, S. aureus; gram(–) K. pneumoniae, E. coli, P. aeruginosa, Enterobacter sp

DOSE:

Adults: 1–2 g IV q8–12h.

Peds: 50 mg/kg q8h for febrile neutropenia; 50 mg/kg b.i.d. for skin/soft-tissue infections; in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Injectable 500 mg, 1, 2 g

SE: Rash, pruritus, N/V/D, fever, headache, (+) Coombs test w/o hemolysis

NOTES: Can give IM or IV

CEFIXIME (SUPRAX)

USES: *Respiratory tract, skin, bone, and urinary tract infections*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: S. pneumoniae, S. pyogenes, H. influenzae, enterobacteria

DOSE:

Adults: 400 mg PO divided daily–b.i.d. Uncomplicated urethral or endocervical gonorrhea (pregnant/nonpregnant): 400 mg PO ×1.

Peds: 8–20 mg/kg/d PO divided daily–b.i.d.; w/renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Suspension 100, 200 mg/5 mL

SE: N/V/D, flatulence, abdominal pain

NOTES: Monitor renal/hepatic function; use suspension for otitis media

CEFOPERAZONE (CEFOBID)

USES: *Infections of respiratory, skin, urinary tracts; sepsis*

ACTION: 3rd-generation cephalosporin; bacterial cell wall synthesis. Spectrum: Gram(–) coverage (eg, E. coli, Klebsiella), P. aeruginosa but less than ceftazidime; gram(+) coverage variable against Streptococcus, Staphylococcus sp

DOSE:

Adults: 2–4 g/d IM/IV divided q 8–12h (16 g/d max).

Peds: (Not approved) 100–150 mg/kg/d IM/IV divided b.i.d.–t.i.d. (12 g/d max); in renal/hepatic impairment

CAUTION: [B, +]; may bleeding risk

CI: Cephalosporin/penicillin allergy

DISP: Powder for injectable 1, 2, 10 g

SE: D, rash, eosinophilia, LFTs, hypoprothrombinemia, bleeding (due to MTT side chain)

NOTES: May interfere w/warfarin; disulfiram-like reaction

CEFOTAXIME (CLAFORAN)

USES: *Infections of lower respiratory tract, skin, bone and joint, urinary tract, meningitis, sepsis, PID, GC*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: Most gram(–) (not Pseudomonas), some gram(+) cocci S. pneumoniae, S. aureus (penicillinase/nonpenicillinase producing), H. influenzae (including ampicillin-resistant), not Enterococcus; many penicillin-resistant pneumococci

DOSE:

Adults: Uncomplicated infection: 2 g IV/IM q12h; Mod–severe infection 1–2 g IV/IM q8–12h; severe/septicemia 2 g IV/IM q4–8h; GC urethritis, cervicitis, rectal in female: 0.5 g IM × 1; rectal GC men 1 g IM × 1;

Peds: 50–200 mg/kg/d IV divided q6–8h; w/renal/hepatic impairment

CAUTION: [B, +]; arrhythmia w/rapid injection; w/colitis

CI: Cephalosporin/penicillin allergy

DISP: Powder for injection 500 mg, 1, 2, 10, 20 g; premixed infusion 20 mg/mL, 40 mg/mL

SE: D, rash, pruritus, colitis, eosinophilia, transaminases

CEFOTETAN (CEFOTAN)

USES: *Infections of upper/lower respiratory tract, skin, bone, urinary tract, abdomen, gynecologic system*

ACTION: 2nd-generation cephalosporin; cell wall synthesis. Spectrum: Less active against gram(+) anaerobes including B. fragilis; gram(–), including E. coli, Klebsiella, Proteus

DOSE:

Adults: 1–3 g IV q12h.

Peds: 20–40 mg/kg/d IV divided q12h (6 g/d max) w/renal impairment

CAUTION: [B, +]; may bleeding risk; w/history of penicillin allergies, w/other nephrotoxic drugs

CI: Cephalosporin/penicillin allergy

DISP: Powder for injectable 1, 2, 10 g

SE: D, rash, eosinophilia, transaminases, hypoprothrombinemia, bleeding (due to MTT side chain)

NOTES: May interfere w/warfarin

CEFOXITIN (MEFOXIN)

USES: *Infections of upper/lower respiratory tract, skin, bone, urinary tract, abdomen, gynecologic system*

ACTION: 2nd-generation cephalosporin; cell wall synthesis. Spectrum: Good gram(–) coverage against enteric bacilli (ie, E. coli, Klebsiella, Proteus); anaerobic B. fragilis.

DOSE:

Adults: 1–2 g IV q6–8h.

Peds: 80–160 mg/kg/d divided q4–6h (12 g/d max); w/renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Powder for injectable 1, 2, 10 g

SE: D, rash, eosinophilia, transaminases

CEFPODOXIME (VANTIN)

USES: *Respiratory, skin, urinary tract infections*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: S. pneumoniae or non–-lactamase-producing H. influenzae; acute uncomplicated N. gonorrhoeae; some uncomplicated gram(–) (E. coli, Klebsiella, Proteus)

DOSE:

Adults: 100–400 mg PO q12h. Uncomplicated urethral or endocervical gonorrhea: 400 mg PO × 1.

Peds: 10 mg/kg/d PO divided b.i.d.; in renal impairment, w/food.

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Tablets 100, 200 mg; suspension 50, 100 mg/5 mL

SE: D, rash, headache, eosinophilia, transaminases

NOTES: Drug interactions w/agents that gastric pH

CEFPROZIL (CEFZIL)

USES: *Respiratory tract, skin, and urinary tract infections*

ACTION: 2nd-generation cephalosporin; cell wall synthesis. Spectrum: Active against MRSA, Streptococcus, gram(–) bacilli (E. coli, Klebsiella, P. mirabilis, H. influenzae, Moraxella).

DOSE:

Adults: 250–500 mg PO daily–b.i.d.

Peds: 7.5–15 mg/kg/d PO divided b.i.d.; in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Tablets 250, 500 mg; suspension 125, 250 mg/5 mL

SE: D, dizziness, rash, eosinophilia, transaminases

NOTES: Use higher doses for otitis and pneumonia

CEFTAZIDIME (FORTAZ, CEPTAZ, TAZIDIME, TAZICEF)

USES: *Respiratory tract, skin, bone, urinary tract infections, meningitis, septicemia*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: P. aeruginosa sp, good gram(–) activity

DOSE:

Adults: 500–2 g IV/IM q8–12h.

Peds: 30–50 mg/kg/dose IV q8h; in renal impairment

CAUTION: [B, +]; penicillin sensitivity

CI: Cephalosporin/penicillin allergy

DISP: Powder for injectable 500 mg, 1, 2, 6 g

SE: D, rash, eosinophilia, transaminases

NOTES: Use only for proven or strongly suspected infection to development of drug resistance

CEFTIBUTEN (CEDAX)

USES: *Respiratory tract, skin, urinary tract infections, otitis media*

ACTION: 3rd-generation cephalosporin; cell wall synthesis. Spectrum: H. influenzae, M. catarrhalis; weak against S. pneumoniae

DOSE:

Adults: 400 mg/d PO.

Peds: 9 mg/kg/d PO; in renal impairment; take on empty stomach (suspension)

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Capsules 400 mg; suspension 90 mg/5 mL

SE: D, rash, eosinophilia, ↑ transaminases

CEFTIZOXIME (CEFIZOX)

USES: *Respiratory tract, skin, bone, and urinary tract infections, meningitis, septicemia*

ACTION: 3rd-generation cephalosporin; ↓ cell wall synthesis. Spectrum: Good gram(–) bacilli coverage (not Pseudomonas), some gram(+) cocci coverage (not Enterococcus), and some anaerobes

DOSE:

Adults: 1–4 g IV q8–12h.

Peds: 150–200 mg/kg/d IV divided q6–8h; ↓ in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Injectable 1, 2, 10 g

SE: D, fever, rash, eosinophilia, thrombocytosis, ↑ transaminases

CEFTRIAXONE (ROCEPHIN)

WARNING: Avoid in hyperbilirubinemic neonates or co-infused w/calcium-containing products.

USES: *Respiratory tract (pneumonia), skin, bone, abdominal, urinary tract infections; meningitis, septicemia*

ACTION: 3rd-generation cephalosporin; ↓ cell wall synthesis. Spectrum: Moderate coverage of gram(+); excellent against -lactamase producers

DOSE:

Adults: 1–2 g IV/IM q12–24h. Chancroid: 25 mg IM × 1. Uncomplicated urethral or endocervical gonorrhea (pregnant/nonpregnant): 125 mg IM × 1.

Peds: 50–100 mg/kg/d IV/IM divided q12–24h; neonatal conjunctivitis (ophthalmia neonatorum): 25–50 mg/kg/d IV (125 mg max in single dose); ↓ w/renal impairment

CAUTION: [B, +]

CI: Cephalosporin allergy; hyperbilirubinemic neonates

DISP: Powder for injectable 250 mg, 500 mg, 1, 2, 10 g; premixed 20, 40 mg/mL

SE: D, rash, leukopenia, thrombocytosis, eosinophilia, ↑ LFTs

CEFUROXIME (CEFTIN [PO], ZINACEF [PARENTERAL])

USES: *Upper/lower respiratory tract, skin, bone, urinary tract, abdomen, gynecologic infections*

ACTION: 2nd-generation cephalosporin; ↓ cell wall synthesis. Spectrum: Staphylococci, group B streptococci, H. influenzae, E. coli, Enterobacter, Salmonella, Klebsiella

DOSE:

Adults: 750 mg–1.5 g IV q6h or 250–500 mg PO b.i.d.

Peds: 75–150 mg/kg/d IV divided q8h or 20–30 mg/kg/d PO divided b.i.d.; w/renal impairment; take PO w/food

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Tablets 250, 500 mg; suspension 125, 250 mg/5 mL; powder for injectable 750 mg, 1.5, 7.5 g

SE: D, rash, eosinophilia, LFTs

NOTES: Cefuroxime film-coated tablets and suspension not bioequivalent; do not substitute on a mg/mg basis; IV crosses blood–brain barrier

CELECOXIB (CELEBREX)

WARNING: Risk of serious cardiovascular thrombotic events, MI, and stroke, can be fatal; risk of serious GI adverse events including bleeding, ulceration, and perforation of the stomach or intestines; can be fatal.

USES: *Osteoarthritis, RA, ankylosing spondylitis, acute pain, primary dysmenorrhea; preventive in FAP*

ACTION: NSAID; COX-2 pathway

DOSE: 100–200 mg/d or b.i.d. FAP: 400 mg PO b.i.d.; w/hepatic impairment; take w/food/milk

CAUTION: [C/D (3rd trimester), ?]; w/renal impairment

CI: Sulfonamide allergy, perioperative CABG

DISP: Capsules 100, 200, 400 mg

SE: See warning; GI upset, hypertension, edema, renal failure, headache

NOTES: Watch for symptoms of GI bleed; no effect on platelet/bleeding time; can affect drugs metabolized by P450 pathway

CEPHALEXIN (KEFLEX, PANIXINE DISPERDOSE)

USES: *Skin, bone, upper/lower respiratory tract (streptococcal pharyngitis), otitis media, uncomplicated cystitis infections*

ACTION: 1st-generation cephalosporin; cell wall synthesis. Spectrum: Streptococcus (including -hemolytic), Staphylococcus, E. coli, Proteus, Klebsiella

DOSE:

Adults and Peds: 15 yr: 250–1,000 mg PO q.i.d.; Cystitis: 7–14 days (4 g/d max).

Peds: <15 yr: 25–100 mg/kg/d PO divided b.i.d.–q.i.d.; in renal impairment; on empty stomach

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Capsules 250, 500 mg; (Panixine DisperDose) tablets for oral suspension 100, 125, 250 mg; suspension 125, 250 mg/5 mL

SE: D, rash, eosinophilia, gastritis, dyspepsia, LFTs, C. difficile colitis, vaginitis

CEPHRADINE (VELOSEF)

USES: *Respiratory, GU, GI, skin, soft-tissue, bone, joint infections*

ACTION: 1st-generation cephalosporin; cell wall synthesis. Spectrum: Gram(+) bacilli and cocci coverage (not Enterococcus); some gram(–) (E. coli, Proteus, Klebsiella)

DOSE:

Adults: 250–500 mg q6–12h (8 g/d max).

Peds: >9 mo: 25–100 mg/kg/d divided b.i.d.–q.i.d. (4 g/d max); in renal impairment

CAUTION: [B, +]

CI: Cephalosporin/penicillin allergy

DISP: Capsules: 250, 500 mg; powder for suspension 125, 250 mg/5 mL

SE: Rash, eosinophilia, LFTs, N/V/D

CHLOROTHIAZIDE (DIURIL)

USES: *Hypertension, edema*

ACTION: Thiazide diuretic

DOSE:

Adults: 500 mg–1 g PO daily–b.i.d.; 100–1,000 mg/d IV (for edema only).

Peds: >6 mo: 10–20 mg/kg/24 hr PO divided b.i.d.; 4 mg/kg/d IV; OK w/food

CAUTION: [D,+]

CI: Sensitivity to thiazides/sulfonamides, anuria

DISP: Tablets 250, 500 mg; suspension 250 mg/5 mL; injectable 500 mg/vial

SE: K+, Na+, dizziness, hyperglycemia, hyperuricemia, hyperlipidemia, photosensitivity

NOTES: Do not use IM/SQ; take early in the day to avoid nocturia; use sunblock; monitor electrolytes

CHLORTHALIDONE (HYGROTON, OTHERS)

USES: *Hypertension*

ACTION: Thiazide diuretic

DOSE:

Adults: 25–100 mg PO daily.

Peds: Not approved; 2 mg/kg/dose PO 3 × wk or 1–2 mg/kg/d PO; in renal impairment; OK w/food/milk

CAUTION: [D, +]

CI: Cross-sensitivity w/thiazides or sulfonamides; anuria

DISP: Tablets 15, 25, 50 mg

SE: K+, dizziness, photosensitivity, hyperglycemia, hyperuricemia, sexual dysfunction

CHOLECALCIFEROL [VITAMIN D3] (Delta D)

USES: Dietary supplement to treat vitamin D deficiency

ACTION: Intestinal Ca2+ absorption

DOSE: 400–1,000 IU/d PO

CAUTION: [A (D doses above the RDA), +]

CI: Ca2+, hypervitaminosis, allergy

DISP: Tablets 400, 1,000 IU

SE: Vitamin D toxicity (renal failure, hypertension, psychosis)

NOTES: 1 mg cholecalciferol = 40,000 IU vitamin D activity

CHOLESTYRAMINE (QUESTRAN, QUESTRAN LIGHT, PREVALITE)

USES: *Hypercholesterolemia; hyperlipidemia, pruritus associated w/partial biliary obstruction; D associated w/excess fecal bile acids,* pseudomembranous colitis, dig tox, hyperoxaluria

ACTION: Binds intestinal bile acids, and intestinal oxylate to form insoluble complexes; diarrhea associated with enteric hyperoxaluria

DOSE:

Adults: Titrate: 1–4 g/d PO b.i.d. to max 24 g/d divided 1–6 doses/d.

Peds: 240 mg/kg/d in 3 divided doses

CAUTION: [C, ?]; constipation, phenylketonuria; may interfere with other drug absorption; consider supplement w/fat-soluble vitamins

CI: Complete biliary or bowel obstruction; w/mycophenolate hyperlipoproteinemia types III, IV, V

DISP: (Questran) 4 g cholestyramine resin/9 g powder; (Prevalite) w/aspartame: 4 g resin/5.5 g powder; (Questran Light) 4 g resin/6.4 g powder

SE: Constipation, abdominal pain, bloating, headache, rash, vitamin K deficiency

NOTES: Overdose may cause GI obstruction/steatorrhea; mix 4 g in 2–6 oz of noncarbonated beverage; take other meds 1–2 hr before or 6 hr after; lipids

CICLOPIROX (LOPROX, PENLAC)

USES: *Tinea pedis/cruris/corporis/versicolor/rubrum; cutaneous candidiasis*

ACTION: Antifungal antibiotic; cellular depletion of essential substrates and/or ions

DOSE:

Adults and Peds: >10 yr: Massage into affected area b.i.d.

CAUTION: [B, ?]

CI: Component sensitivity

DISP: Cream 0.77%; gel 0.77%; topical suspension 0.77%; shampoo 1%; nail lacquer 8%

SE: Pruritus, local irritation, burning

NOTES: Discontinue w/irritation; avoid dressings; gel best for athlete's foot

CINACALCET (SENSIPAR)

USES: *Secondary hyperparathyroidism in patients on dialysis; hypercalcemia in parathyroid carcinoma*

ACTION: Calcimimetic; activation of calcium receptors on parathyroid cells inhibits PTH secretion; hypercalciuria is not significantly affected

DOSE: Secondary hyperparathyroidism: 30 mg QD initial, increase PRN to maintain iPTH level 150–300 pg/mL

CAUTION: [C/?]; multiple drug interactions, w/severe hepatic failure, w/impaired cardiac function

CI: Hypersensitivity to compound

DISP: Tablets 30, 60, 90 mg

SE: Decreases testosterone and calcium levels; adynamic bone disease if iPTH levels <100 pg/mL

NOTES: Follow serum calcium, phosphorus, iPTH levels

CIPROFLOXACIN (CIPRO, CIPRO XR, PROQUIN XR)

WARNING: Risk of tendonitis and tendon rupture.

USES: *Lower respiratory tract, sinus, skin and skin structure, bone/joint, and UT infections, including prostatitis, anthrax*

ACTION: Quinolone antibiotic; DNA gyrase. Spectrum: Broad gram(±) coverage; aerobics; little Streptococcus; good Pseudomonas, E. coli, B. fragilis, P. mirabilis, K. pneumoniae, C. jejuni, Shigella

DOSE:

Adults: 250–750 mg PO q12h; XR 500–1,000 mg PO q24h; or 200–400 mg IV q12h; Chancroid: 500 mg PO b.i.d. × 3 days; Uncomplicated urethral or endocervical gonorrhea if penicillin allergy (resistant strains in Asia, Hawaii, California); 500 mg PO × 1; avoid in pregnancy; in renal impairment

CAUTION: [C, ?/–]; children <18 yr

CI: Component sensitivity

DISP: Tablets 100, 250, 500, 750 mg; tablets XR 500, 1,000 mg; suspension 5 g/100 mL, 10 g/100 mL; injectable 200, 400 mg; premixed piggyback 200, 400 mg/100 mL

SE: Restlessness, N/V/D, rash, ruptured tendons, LFTs

NOTES: Avoid antacids; reduce/restrict caffeine intake; interactions w/theophylline, caffeine, sucralfate, warfarin, antacids. Most tendon problems in Achilles, rarely, shoulder and hand

CISPLATIN (PLATINOL, PLATINOL AQ)

WARNING: Anaphylactic-like reaction, ototoxicity, cumulative renal toxicity; doses >100 mg/m2 q3–4wk rarely used; do not confuse w/carboplatin.

USES: *Testicular, bladder, ovarian cancers,* SCLC, NSCLC, breast, head and neck, penile cancers; osteosarcoma; ped brain tumors

ACTION: DNA-binding; denatures double helix; intrastrand cross-linking

DOSE: 10–20 mg/m2/d for 5 days q3wk; 50–120 mg/m2 q3–4wk (per protocols); w/renal impairment

CAUTION: [D, –]; cumulative renal toxicity may be severe; bone marrow, hearing impairment, preexisting renal insufficiency

CI: W/anthrax or live vaccines, platinum-containing compound allergy; w/cidofovir

DISP: Injectable 1 mg/mL

SE: Allergic reactions, N/V, nephrotoxicity (w/administration of other nephrotoxic drugs; minimize by NS infusion and mannitol diuresis), high-frequency hearing loss in 30%, peripheral stocking/glove-type neuropathy, cardiotoxicity (ST, T-wave changes), Mg2+, mild bone marrow, hepatotoxicity; renal impairment is dose-related and cumulative

NOTES: Give taxanes before platinum derivatives; Mg2+, electrolytes before and within 48 hr after cisplatin

CITRIC ACID, GLUCONO-DELTA-LACTONE, AND MAGNESIUM CARBONATE (RENACIDIN)

USES: *Chemolysis of calculi/incrustations in the urinary tract composed of apatite (calcium carbonate-phosphate) or struvite (magnesium ammonium phosphates) in nonsurgical candidates; adjunctive therapy to dissolve residual apatite/struvite fragments postop; partial dissolution of calculi to facilitate surgical removal*

WARNING: Not FDA approved for use above the bladder due to reports of death.

ACTION: Dissolution of calculi by exchange of Mg2+ from irrigating solution for insoluble Ca2+ in calcification. Mg2+ salts are soluble in the citrate irrigating solution, dissolving calculus

DOSE: Intermittent bladder irrigation: 30–50 mL via Foley, clamped for 30 minutes, repeated t.i.d. for encrustations and 4–6 times/d for bladder stones; irrigation via dual nephrostomy tube (inflow/outflow) or into ureteral catheter with nephrostomy drainage; essential to keep pressure <80 cm H2O by manometer

CAUTION: [C, ?]

CI: Obstructed urinary tract, active UTI not treated

DISP: Solution

SE: Irritation, sepsis, other infections.

NOTES: Suby solution G was modified by addition of magnesium salts to create Renacidin

CLARITHROMYCIN (BIAXIN, BIAXIN XL)

USES: *Upper/lower respiratory tract, skin/skin structure infections, H. pylori infections, infections caused by non-Tuberculosis (atypical) mycobacterium; prevention of MAC infections in HIV-infection*

ACTION: Macrolide antibiotic, protein synthesis. Spectrum: H. influenzae, M. catarrhalis, S. pneumoniae, M. pneumoniae, H. pylori

DOSE:

Adults: 250–500 mg PO b.i.d. or 1,000 mg (2 × 500 mg XL tablet)/d Mycobacterium: 500 mg PO b.i.d.

Peds: >6 mo: 7.5 mg/kg/dose PO b.i.d.; w/renal impairment

CAUTION: [C, ?]; antibiotic-associated colitis; rare QT prolongation and ventricular arrhythmias, including torsade de pointes

CI: Macrolide allergy; w/ranitidine in patients w/history of porphyria or CrCl <25 mL/min

DISP: Tablets 250, 500 mg; suspension 125, 250 mg/5 mL; 500 mg XL tablet

SE: QT interval, metallic taste, N/D, abdominal pain, headache, rash

NOTES: Multiple drug interactions, theophylline and carbamazepine levels; do not refrigerate suspension

CLINDAMYCIN (CLEOCIN, CLEOCIN-T, OTHERS)

WARNING: Pseudomembranous colitis may range from mild to life-threatening.

USES: *Aerobic/anaerobic infections; topical for severe acne and vaginal infections*

ACTION: Bacteriostatic; interferes w/protein synthesis. Spectrum: Streptococci, pneumococci, staphylococci, and gram(+) and (–) anaerobes; no activity against gram(–) aerobes

DOSE:

Adults: PO: 150–450 mg PO q6–8h. IV: 300–600 mg IV q6h or 900 mg IV q8h. Vaginal: 1 applicator h.s. for 7 days. Topical: Apply 1% gel, lotion, or solution b.i.d.

Peds: Neonates: (Avoid use; contains benzyl alcohol) 10–15 mg/kg/24 hr divided q8–12h. >1 mo: 10–30 mg/kg/24 hr divided q6–8h, to a max of 1.8 g/d PO or 4.8 g/d IV. Topical: Apply 1%, gel, lotion, or solution b.i.d.; in severe hepatic impairment

CAUTION: [B, +]; can cause fatal colitis

CI: History pseudomembranous colitis

DISP: Capsules 75, 150, 300 mg; suspension 75 mg/5 mL; injectable 300 mg/2 mL; vaginal cream 2%; topical solution 1%; gel 1%; lotion 1%; vaginal suppository 100 mg

SE: Diarrhea may be C. difficile pseudomembranous colitis, rash, LFTs

NOTES: Discontinue drug with diarrhea, evaluate for C. difficile

CLONIDINE, ORAL (CATAPRES)

USES: *Hypertension*; opioid, EtOH, and tobacco withdrawal, ADHD.

ACTION: Centrally acting -adrenergic stimulant

DOSE:

Adults: 0.1 mg PO b.i.d., adjust daily by 0.1- to 0.2-mg increments (max 2.4 mg/d).

Peds: 5–10 g/kg/d divided q8–12h (max 0.9 mg/d); in renal impairment

CAUTION: [C, ±]; avoid w/-blocker, in elderly, severe CVD, renal impairment

CI: Component sensitivity

DISP: Tablets 0.1, 0.2, 0.3 mg

SE: Drowsiness, orthostatic BP, xerostomia, constipation, bradycardia, dizziness

NOTES: More effective for hypertension if combined w/diuretics; withdraw slowly, rebound hypertension w/abrupt discontinuation of doses >0.2 mg b.i.d.; ADHD use in peds needs cardiovascular assessment before starting epidural clonidine (Duraclon) used for chronic cancer pain

CLONIDINE, TRANSDERMAL (CATAPRES TTS)

USES: *Hypertension*

ACTION: Centrally acting -adrenergic stimulant

DOSE: 1 patch q7d to hairless area (upper arm/torso); titrate to effect; w/severe renal impairment

CAUTION: [C, ±]; avoid w/-blocker; withdraw slowly, in elderly, severe CVD, w/renal impairment

CI: Component sensitivity

DISP: TTS-1, TTS-2, TTS-3 (delivers 0.1, 0.2, 0.3 mg, respectively, of clonidine/d for 1 wk)

SE: Drowsiness, orthostatic BP, xerostomia, constipation, bradycardia

NOTES: Do not discontinue abruptly (rebound hypertension); doses >2 TTS-3 usually not associated w/ efficacy; steady state in 2–3 d

CLOTRIMAZOLE (LOTRIMIN, MYCELEX, OTHERS) [OTC]

USES: *Candidiasis and tinea infections*

ACTION: Antifungal; alters cell wall permeability. Spectrum: Oropharyngeal candidiasis, dermatophytoses, superficial mycoses, cutaneous candidiasis, vulvovaginal candidiasis

DOSE: PO: Prophylaxis: 1 troche dissolved in mouth t.i.d. Treat: 1 troche dissolved in mouth 5 times a day × 14 days. Vaginal 1% cream: 1 applicator-full h.s. for 7 days. 2% cream: 1 applicator-full h.s. for 3 days. Tablets: 100 mg vaginally h.s. for 7 days or 200 mg (2 tablets) vaginally h.s. for 3 days or 500-mg tablets vaginally h.s. once. Topical: Apply b.i.d. 10–14 days

CAUTION: [B (C if PO), ?]; not for systemic fungal infection; safety in children <3 yr not established

CI: Component allergy

DISP: 1% cream; solution; lotion; troche 10 mg; vaginal tablets 100, 200, 500 mg; vaginal cream 1%, 2%

SE: Topical: Local irritation; PO: N/V, LFTs.

NOTES: PO prophylaxis immunosuppressed patients.

CLOTRIMAZOLE AND BETAMETHASONE (LOTRISONE)

USES: *Fungal skin infections*

ACTION: Imidazole antifungal and anti-inflammatory. Spectrum: Tinea pedis/cruris/corpora

DOSE: 17 yr: Massage into area b.i.d. for 2–4 wk

CAUTION: [C, ?]; varicella infection

CI: Children <12 yr

DISP: Cream 1/0.05% 15, 45 g; lotion 1/0.05% 30 mL

SE: Local irritation, rash

NOTES: Not for diaper dermatitis or under occlusive dressings

COCAINE [C-II]

USES: *Topical anesthetic for mucous membranes*

ACTION: Narcotic analgesic, local vasoconstrictor

DOSE: Lowest topical amount that provides relief; 1 mg/kg max

CAUTION: [C, ?]

CI: Pregnancy, ocular anesthesia

DISP: Topical solution and viscous preparations 4–10%; powder

SE: CNS stimulation, nervousness, loss of taste/smell, chronic rhinitis, cardiovascular toxicity, abuse potential

NOTES: Use only on PO, laryngeal, and nasal mucosa; do not use on extensive areas of broken skin

CODEINE [C-II]

USES: *Mild–mod pain; symptomatic relief of cough*

ACTION: Narcotic analgesic; cough reflex

DOSE:

Adults: Analgesic: 15–20 mg PO or IM q.i.d. PRN. Antitussive: 10–20 mg PO q4h PRN; max 120 mg/d.

Peds: Analgesic: 0.5–1 mg/kg/dose PO q4–6h PRN. Antitussive: 1–1.5 mg/kg/24 hr PO divided q4h; max 30 mg/24 hr; in renal/hepatic impairment

CAUTION: [C (D if prolonged use or high dose at term), +]; CNS depression, history drug abuse, severe hepatic impairment

CI: Component sensitivity

DISP: Tablets 15, 30, 60 mg; solution 15 mg/5 mL; injectable 15, 30 mg/mL

SE: Drowsiness, constipation, BP

NOTES: Usually combined w/acetaminophen for pain or w/agents (eg, terpin hydrate) as an antitussive; 120 mg IM = 10 mg IM morphine

CONIVAPTAN (VAPRISOL)

USES: *Euvolemic and hypervolemic hyponatremia*

ACTION: Dual arginine vasopressin V1A/V2 receptor antagonist

DOSE: 20 mg IV × 1 over 30 min, then 20 mg continuous IV infusion over 24 hr; 20 mg/d continuos IV infusion for 1–3 more d; may to 40 mg/d if Na+ not responding; 4 day max use; use large vein, change site q24h

CAUTION: [C; ?/–]; rapid Na+ (>12 mEq/L/24 hr) may cause osmotic demyelination syndrome; impaired renal/hepatic function; may digoxin levels; CYP3A4 inhibitor

CI: Hypovolemic hyponatremia; w/CYP3A4 inhibitors

DISP: Ampule 20 mg/4 mL.

SE: Infusion site reactions, headache, N/V/D, constipation, K+, orthostatic BP, thirst, dry mouth, pyrexia, polyuria, infection

NOTES: Monitor Na+, volume, neurologic status; discontinue w/very rapid Na+; mix only w/5% dextrose

CYANOCOBALAMIN [VITAMIN B12] (Nascobal)

USES: *Pernicious anemia and other vitamin B12 deficiency states; requirements due to pregnancy; thyrotoxicosis; liver or kidney disease*; supplementation may be necessary with urinary diversion if distal terminal ileum resected

ACTION: Vitamin B12 supplement; coenzyme cell replication and hematopoiesis

DOSE:

Adults: 30 g/d × 5–10 d; 100 g IM or SQ daily; intranasal: 500 g once a week for patients in remission, for 5–10 d, then 100 g IM 2 × wk for 1 mo, then 100 g IM monthly.

Peds: Use 0.2 g/kg × 2 days test dose; if OK, 30–50 g/d for 2 wks (total 10 g) then maintenance: 100 mg/mo

CAUTION: [A (C if dose exceeds RDA), +]

CI: Allergy to cobalt; hereditary optic nerve atrophy; Leber disease

DISP: Tablets 50, 100, 250, 500, 1,000, 2,500, 5,000 g; injectable 100, 1,000 g/mL; intranasal (Nascobal) gel 500 g/0.1 mL

SE: Itching, diarrhea, headache, anxiety

NOTES: PO absorption erratic; not for use w/hyperalimentation

CYCLOPHOSPHAMIDE (CYTOXAN, NEOSAR)

USES: *Hodgkin disease/NHLs; multiple myeloma; small cell lung, breast, and ovarian cancers; mycosis fungoides; neuroblastoma; retinoblastoma; acute leukemias; allogeneic and bone marrow transplant in high doses; severe rheumatologic disorders (SLE, JRA)*

ACTION: Alkylating agent

DOSE:

Adults: (Per protocol) 500–1,500 mg/m2; single dose at 2–4-wk intervals; 1.8 g/m2–160 mg/kg (or at 12 g/m2 in 75-kg individual) in the bone marrow transplant setting (per protocols)

CAUTION: [D, ?]; w/bone marrow suppression, hepatic insufficiency

CI: Component sensitivity

DISP: Tablets 25, 50 mg; injectable 500 mg, 1, 2 g

SE: Bone marrow; hemorrhagic cystitis, SIADH, alopecia, anorexia; N/V; hepatotoxicity; rare interstitial pneumonitis; irreversible testicular atrophy possible; cardiotoxicity rare; 2nd malignancies (bladder, ALL) risk 3.5% at 8 yr, 10.7% at 12 yr

NOTES: Hemorrhagic cystitis prophylaxis: Continuous bladder irrigation and mesna uroprotection; encourage hydration, long-term bladder cancer screening. Reported neuroblastoma regimens include: Low-dose cyclophosphamide, Adriamycin, and cisplatin in setting of surgery failures. Intermediate risk: Induction with cyclophosphamide and Adriamycin cycles w or w/o radiation and cisplatin maintenance. High risk: Cyclophosphamide, Adriamycin, VM-26, doxorubicin, cisplatin, etoposide in various combinations

CYCLOSPORINE (SANDIMMUNE, NEORAL, GENGRAF)

WARNING: Risk neoplasm, risk skin malignancies, risk hypertension and nephrotoxicity.

USES: *Organ rejection in kidney, liver, heart, bone marrow transplant w/steroids; RA; psoriasis*

ACTION: Immunosuppressant; reversible inhibition of immunocompetent lymphocytes; prevents IL-2 production via calcineurin inhibition (binds cyclophilin protein)

DOSE:

Adults and Peds PO: 15 mg/kg/d12h pretransplant; after 2 wk, taper by 5 mg/wk to 5–10 mg/kg/d. IV: If NPO, give 1/3 PO dose IV; in renal/hepatic impairment

CAUTION: [C, ?]; dose-related risk of nephro-/hepatotoxicity; live, attenuated vaccines may be less effective

CI: Renal impairment; uncontrolled hypertension

DISP: Capsules 25, 100 mg; PO solution 100 mg/mL; injectable 50 mg/mL

SE: May BUN and Cr and mimic transplant rejection; hypertension; headache; hirsutism

NOTES: Administer in glass container; many drug interactions; Neoral and Sandimmune are not interchangeable; monitor BP, Cr, CBC, LFTs, interaction w/St. John's wort. Levels: Trough: Just before next dose: Therapeutic: Variable 150–300 ng/mL by RIA

CYTOMEGALOVIRUS IMMUNE GLOBULIN [CMV-IG IV] (CYTOGAM)

USES: *Attenuation CMV disease associated w/transplantation*

ACTION: Exogenous IgG antibodies to CMV

DOSE: 150 mg/kg/dose within 72 hr of transplant, for 16 wk posttransplant; see insert

CAUTION: [C, ?]; anaphylactic reactions; renal dysfunction

CI: Allergy to immunoglobulins; IgA deficiency

DISP: Injectable 50 mg/mL

SE: Flushing, N/V, muscle cramps, wheezing, headache, fever

NOTES: IV only; administer by separate line; do not shake

DACARBAZINE (DTIC)

WARNING: Causes hematopoietic depression, hepatic necrosis; may be carcinogenic, teratogenic

USES: *Melanoma, Hodgkin disease, sarcoma*

ACTION: Alkylating agent; antimetabolite as a purine precursor; protein synthesis, RNA, and especially DNA

DOSE: 2–4.5 mg/kg/d for 10 consecutive days or 250 mg/m2/d for 5 days (per protocols); in renal impairment

CAUTION: [C, ?]; in bone marrow suppression; renal/hepatic impairment

CI: Component sensitivity

DISP: Injectable 100, 200 mg

SE: Bone marrow, N/V, hepatotoxicity, flu-like syndrome, BP, photosensitivity, alopecia, facial flushing, facial paresthesias, urticaria, phlebitis at injection site

NOTES: Avoid extravasation, follow CBC, platelets

DACLIZUMAB (ZENAPAX)

WARNING: Administer under skilled supervision in equipped facility

USES: *Prevent acute organ rejection*

ACTION: IL-2 receptor antagonist

DOSE: 1 mg/kg/dose IV; 1st dose pretransplant, then 1 mg/kg q 14d × 4 doses

CAUTION: [C, ?]

CI: Component sensitivity

DISP: Injectable 5 mg/mL

SE: Hyperglycemia, edema, hypertension, BP, constipation, headache, dizziness, anxiety, nephrotoxicity, pulmonary edema, pain, anaphylaxis/hypersensitivity

NOTES: Administer within 4 hr of preparation

DACTINOMYCIN (COSMEGEN)

WARNING: Administer under skilled supervision in equipped facility; powder and solution toxic, corrosive, mutagenic, carcinogenic, and teratogenic; avoid exposure and use precautions

USES: *Choriocarcinoma, Wilms tumor, Kaposi and Ewing sarcomas, rhabdomyosarcoma, uterine and testicular cancers*

ACTION: DNA-intercalating agent

DOSE:

Adults: 0.5 mg/d for 5 d; 2 mg/wk for 3 consecutive wk; 15 g/kg or 0.45 mg/m2/d (max 0.5 mg) for 5 days q3–8wk.

Peds: Sarcoma: (Per protocols) in renal impairment

CAUTION: [C, ?]

CI: Concurrent/recent chickenpox or herpes zoster; infants <6 mo

DISP: Injectable 0.5 mg

SE: Myelo-/immunosuppression, severe N/V/D, alopecia, acne, hyperpigmentation, radiation recall phenomenon, tissue damage w/extravasation, hepatotoxicity

NOTES: Classified as antibiotic but not used as antimicrobial

DALTEPARIN (FRAGMIN)

WARNING: Risk of spinal/epidural hematoma with LP

USES: *Unstable angina, non–Q-wave MI; prevent and treat DVT following surgery (hip, abdominal) in patients w/restricted mobility; extended therapy for PE DVT in cancer patients*

ACTION: LMW heparin

DOSE: DVT prophylaxis: 2,500–5,000 U SQ 1–2 hr preop, then daily for 5–10 days. Systemic anticoagulation: 200 U/kg/d SQ or 100 U/kg b.i.d. SQ

CAUTION: [B, ?]; in renal/hepatic impairment, active hemorrhage, cerebrovascular disease, cerebral aneurysm, severe hypertension

CI: HIT; pork-product allergy; w/mifepristone

DISP: Injectable 2,500 U (16 mg/0.2 mL), 5,000 U (32 mg/0.2 mL), 7,500 U (48 mg/0.3 mL), 10,000 U (64 mg/mL), 25,000 U/mL (3.8 mL); prefilled vials 10,000 U/mL (9.5 mL)

SE: Bleeding, pain at site, platelet

NOTES: Predictable effects eliminate lab monitoring; not for IM/IV use

DANTROLENE (DANTRIUM)

WARNING: Hepatotoxicity reported; discontinue after 45 days if no benefit observed

USES: *Spasticity due to upper motor neuron disorders (eg, spinal cord injuries, stroke, CP, MS); malignant hyperthermia*

ACTION: Skeletal muscle relaxant

DOSE:

Adults: Spasticity: 25 mg PO daily; 25 mg to effect to 100 mg max PO q.i.d. PRN.

Peds: 0.5 mg/kg/dose b.i.d.; by 0.5 mg/kg to effect, to 3 mg/kg/dose max q.i.d. PRN.

Adults and Peds Malignant hyperthermia: Treat: Continuous rapid IV, start 1 mg/kg until symptoms subside or 10 mg/kg is reached. Post-crisis follow-up: 4–8 mg/kg/d in 3–4 divided doses for 1–3 days to prevent recurrence

CAUTION: [C, ?]; impaired cardiac/pulmonary/hepatic function

CI: Active hepatic disease; in patients in whom spasticity is needed to maintain posture or balance

DISP: Capsules 25, 50, 100 mg; powder for injectable 20 mg/vial

SE: Hepatotoxicity, LFTs, drowsiness, dizziness, rash, muscle weakness, D/N/V, pleural effusion w/pericarditis, diarrhea, blurred vision, photosensitivity

NOTES: Monitor LFTs; avoid sunlight/EtOH/CNS depressants

DARIFENACIN (ENABLEX)

USES: *Overactive bladder (urge incontinence, urgency, and frequency)*

ACTION: Muscarinic receptor antagonist

DOSE: 7.5 mg/d PO; 15 mg/d max (7.5 mg/d w/mod hepatic impairment or w/CYP3A4 inhibitors); w/drugs metabolized by CYP2D; swallow whole

CAUTION: [C, ?/–]; w/hepatic impairment

CI: Urinary/gastric retention, uncontrolled narrow-angle glaucoma, paralytic ileus

DISP: Tablets ER 7.5 mg, 15 mg

SE: Xerostomia/eyes, constipation, dyspepsia, abdominal pain, retention, abnormal vision, dizziness, asthenia

DEGARELIX (FIRMAGON)

USES: *Advanced prostate cancer*

ACTION: Reversible LHRH antagonist, decreases LH and testosterone with no flare as with LHRH agonists

DOSE: Initial 240 mg SQ of 2 divided doses of 120 mg (40 mg/mL); maintenance dose 80 mg SQ every 28 days (20 mg/mL)

CAUTION: Not for women

CI: Female

DISP: 120 mg vial (initial); 80 mg vial (maintenance) for reconstitution

SE: Injection site reactions, hot flashes, ↑ weight, ↑ serum GGT

NOTES: Requires 2 injections initially due to large volume; 44% testosterone castration (< 50 ng/dL) at day 1, 96% day 3

DESMOPRESSIN (DDAVP, STIMATE)

WARNING: Not for hemophilia B or w/factor VIII antibody; not for hemophilia A w/factor VIII levels <5%

USES: *DI (intranasal and parenteral); bleeding due to uremia, hemophilia A, and type I von Willebrand disease (parenteral), nocturnal enuresis*

ACTION: Synthetic analog of vasopressin (human ADH); ↑ factor VIII

DOSE:

Adults and Peds: >6 yr: Nocturnal enuresis: 0.2 mg PO h.s.; titrated up to 0.6 mg PRN.

CAUTION: [B, M]; avoid overhydration

CI: Hemophilia B; CrCl <50 mL/min, severe classic von Willebrand disease; patients w/factor VIII antibodies; hyponatremia

DISP: Tablets 0.1, 0.2 mg; injectable 4, 15 g/mL; nasal solution 0.1, 1.5 mg/mL

SE: Facial flushing, headache, dizziness, vulval pain, nasal congestion, pain at injection site, ↓ Na+ with potentially life-threatening hyponatremia, H2O intoxication

NOTES: FDA notice December 2007: Intranasal form no longer indicated for enuresis (severe hyponatremia). Discontinuation of therapy associated w/60–70% relapse. In very young and old, ↑ fluid intake to avoid H2O intoxication and ↓ Na+

DIAZEPAM (VALIUM, DIASTAT) [C-IV]

USES: *Anxiety, EtOH withdrawal, muscle spasm, status epilepticus, panic disorders, amnesia, preop sedation*

ACTION: Benzodiazepine

DOSE:

Adults: Anxiety, muscle spasm: 2–10 mg PO b.i.d.–q.i.d. or IM/IV q3–4h PRN. Preop: 5–10 mg PO or IM 20–30 min or IV just prior to procedure.

Peds: Sedation, muscle relaxation: 0.04–0.3 mg/kg/dose q2–4h IM or IV to max of 0.6 mg/kg in 8 hr, or 0.12–0.8 mg/kg/24 hr PO divided t.i.d.–q.i.d.; ↓ w/hepatic impairment

CAUTION: [D, ?/–]

CI: Coma, CNS depression, respiratory depression, narrow-angle glaucoma, severe uncontrolled pain, pregnancy

DISP: Tablets 2, 5, 10 mg; solution 1, 5 mg/mL; injectable 5 mg/mL; rectal gel 2.5, 5, 10, 20 mg/mL

SE: Sedation, amnesia, bradycardia, BP, rash, respiratory rate

NOTES: 5 mg/min IV max in adults or 1–2 mg/min in peds (respiratory arrest possible); IM absorption erratic; avoid abrupt discontinuation.

DIBUCAINE (NUPERCAINAL)

USES: *Hemorrhoids and minor skin conditions*

ACTION: Topical anesthetic

DOSE: Insert PR w/applicator b.i.d. and after each bowel movement; apply sparingly to skin

CAUTION: [C, ?]; topical use only

CI: Component sensitivity

DISP: 1% ointment w/rectal applicator; 0.5% cream

SE: Local irritation, rash

DICLOXACILLIN (DYNAPEN, DYCILL)

USES: *Pneumonia, skin, and soft-tissue infections, and osteomyelitis caused by penicillinase-producing staphylococci*

ACTION: Bactericidal; cell wall synthesis. Spectrum: S. aureus, Streptococcus

DOSE:

Adults: 150–500 mg q.i.d. (2 g/d max).

Peds: <40 kg: 12.5–100 mg/kg/d divided q.i.d.; take on empty stomach

CAUTION: [B, ?]

CI: Component or penicillin sensitivity

DISP: Capsules 125, 250, 500 mg; solution 62.5 mg/5 mL

SE: N/D, abdominal pain

NOTES: Monitor PTT on warfarin

DIFLUNISAL (DOLOBID)

WARNING: May risk of cardiovascular events and GI bleeding; contraindicated in postop CABG

USES: *Mild–mod pain; osteoarthritis*

ACTION: NSAID

DOSE: Pain: 500 mg PO b.i.d.; in renal impairment, take w/food/milk

CAUTION: [C (D 3rd trimester or near delivery), ?]; CHF, hypertension, renal/hepatic dysfunction, and history PUD

CI: Allergy to NSAIDs or aspirin, active GI bleed, post-CABG

DISP: Tablets 250, 500 mg

SE: May bleeding time; headache, abdominal cramps, heartburn, GI ulceration, rash, interstitial nephritis, fluid retention

DIMETHYL SULFOXIDE [DMSO] (RIMSO-50)

USES: *Interstitial cystitis*

ACTION: Unknown

DOSE: Intravesical, 50 mL, retain for 15 min; repeat q2wk until relief

CAUTION: [C, ?]

CI: Component sensitivity

DISP: 50% and 100% solution

SE: Cystitis, eosinophilia, GI, and taste disturbance.

NOTES: Often used as cocktail with triamcinolone, heparin, sodium bicarbonate

DOCETAXEL (TAXOTERE)

WARNING: Do not administer if neutrophil count <1,500 cell/mm3; severe reactions possible in hepatic dysfunction.

USES: *Breast (anthracycline-resistant), ovarian, lung, prostate cancers*

ACTION: Antimitotic agent; promotes microtubular aggregation; semisynthetic taxoid

DOSE: 100 mg/m2 over 1 hr IV q3wk (per protocols); dexamethasone 8 mg b.i.d. prior and continue for 3–4 d; dose w/ bilirubin levels

CAUTION: [D, –]

CI: Sensitivity to meds w/polysorbate 80, component sensitivity

DISP: Injectable 20 mg/0.5 mL, 80 mg/2 mL

SE: Bone marrow, neuropathy, N/V, alopecia, fluid retention syndrome; cumulative doses of 300–400 mg/m2 w/o steroid preparation and posttreatment; 600–800 mg/m2 w/steroid preparation; allergy possible (rare w/steroid preparation)

NOTES: Bilirubin, SGOT and SGPT prior to each cycle; frequent CBC during therapy

DORIPENEM (DORIBAX)

USES: *Complicated intra-abdominal and UTI including pyelo*

ACTION: Carbapenem, a -lactam, cell wall synthesis; Spectrum: Excellent gram(+) coverage (except MRSA and Enterococcus sp.), excellent gram(–) coverage including -lactamase producers, good anaerobic coverage

DOSE: 500 mg IV q8h, w/renal impairment

CAUTION: [B, ?]

CI: Carbapenem, -lactam hypersensitivity

DISP: 500 mg single-use vial

SE: Headache, N/D, rash, phlebitis

NOTES: May valproic acid levels; overuse may bacterial resistance; monitor for C. difficile-associated D

DOXAZOSIN (CARDURA, CARDURA XL)

USES: *Hypertension and symptomatic benign prostatic hyperplasia (BPH)*

ACTION: 1-Adrenergic blocker; relaxes bladder neck smooth muscle

DOSE: Hypertension: Initial 1 mg/d PO; may to 16 mg/d PO. BPH: Initial 1 mg/d PO, may to 8 mg/d; XL 2–8 mg q A.M.

CAUTION: [B, ?]; w/liver impairment

CI: Component sensitivity

DISP: Tablets 1, 2, 4, 8 mg; XL 4, 8 mg

SE: Dizziness, headache, drowsiness, fatigue, malaise, sexual dysfunction, doses >4 mg postural BP risk

NOTES: 1st dose h.s.; syncope may occur within 90 min of initial dose

DOXORUBICIN (ADRIAMYCIN, RUBEX)

USES: *Acute leukemias; Hodgkin disease/NHLs; soft-tissue, osteosarcoma, Ewing sarcoma; Wilms tumor; neuroblastoma; bladder, breast, ovarian, gastric, thyroid, and lung cancers*

ACTION: Intercalates DNA; DNA topoisomerase I and II

DOSE: 60–75 mg/m2 q3wk; w/hepatic impairment; IV use only cardiotoxicity w/weekly (20 mg/m2/wk) or continuous infusion (60–90 mg/m2 over 96 hr; per protocols)

CAUTION: [D, ?]

CI: Severe CHF, cardiomyopathy, preexisting bone marrow, previous treatment w/total cumulative doses of doxorubicin, idarubicin, daunorubicin

DISP: Injectable 10, 20, 50, 75, 150, 200 mg

SE: Bone marrow, venous streaking and phlebitis, N/V/D, mucositis, radiation recall phenomenon, cardiomyopathy rare (dose-related)

NOTES: Limit of 550 mg/m2 cumulative dose (400 mg/m2 w/prior mediastinal irradiation); dexrazoxane may limit cardiac toxicity; tissue damage w/extravasation; red/orange urine; vesicant w/extravasation, treat with dexrazoxane

DOXYCYCLINE (ADOXA, PERIOSTAT, ORACEA, VIBRAMYCIN, VIBRA-TABLETS)

USES: *Broad-spectrum antibiotic* acne vulgaris, uncomplicated GC, chlamydia, PID, Lyme disease, skin infections, anthrax, malaria prophylaxis

ACTION: Tetracycline; bacteriostatic; protein synthesis. Spectrum: Limited gram(+/–) coverage, Rickettsia sp, Chlamydia, M. pneumoniae, B. anthracis

DOSE:

Adults: 100 mg PO q12h on 1st d, then 100 mg PO daily–b.i.d. or 100 mg IV q12h; Chlamydia: × 7 d. Lyme: × 21 d. PID: × 14 days.

Peds: >8 yr: 5 mg/kg/24 hr PO, 200 mg/d max divided daily–b.i.d.

CAUTION: [D, +]; hepatic impairment

CI: Children <8 yr, severe hepatic dysfunction

DISP: Tablets 20, 50, 75, 100, 150 mg; capsules 50, 100 mg; Oracea 40 mg capsules (30 mg timed-release, 10 mg DR); syrup 50 mg/5 mL; suspension 25 mg/5 mL; injectable 100, 200 mg/vial

SE: Diarrhea, GI disturbance, photosensitivity

NOTES: Effect w/antacids; tetracycline of choice in renal impairment; for inhalational anthrax use w/1–2 additional antibiotics, not for CNS anthrax

DUTASTERIDE (AVODART)

USES: *Symptomatic benign prostatic hyperplasia (BPH) to improve symptoms, risk of retention and BPH surgery alone or in combo w/tamsulosin*

ACTION: 5-Reductase inhibitor (dual type I and 2); intracellular DHT

DOSE: Monotherapy: 0.5 mg PO/d. Combo: 0.5 mg/d PO w/tamsulosin 0.4 mg/d

CAUTION: [Not indicated in women X, –]; hepatic impairment; pregnant women should not handle pills

CI: Women, peds

DISP: Capsules 0.5 mg

SE: Testosterone, TSH , PSA levels, impotence, libido, gynecomastia, ejaculatory disturbance

NOTES: No blood donation until 6 mo after discontinuation; new baseline PSA at 6 mo; corrected PSA × 2; under study for prostate cancer chemotherapy prevention; recent clinical trial shows 24% reduction in prostate cancer risk

ECONAZOLE (SPECTAZOLE)

USES: *Tinea, cutaneous Candida, tinea versicolor infections*

ACTION: Topical antifungal

DOSE: Apply to areas b.i.d. (daily for tinea versicolor) for 2–4 wk

CAUTION: [C, ?]

CI: Component sensitivity

DISP: Topical cream 1%

SE: Local irritation, pruritus, erythema

NOTES: Early symptoms/clinical improvement; complete course to avoid recurrence

ENALAPRIL (VASOTEC)

WARNING: ACE inhibitors used during pregnancy can cause fetal injury and death

USES: *Hypertension, CHF, LVD,* diabetic nephropathy

ACTION: ACE inhibitor

DOSE:

Adults: 2.5–40 mg/d PO; 1.25 mg IV q6h.

Peds: 0.05–0.08 mg/kg/d PO q12–24h; w/renal impairment

CAUTION: [C (1st trimester; D 2nd and 3rd trimester), +]; discontinue immediately w/pregnancy, w/NSAIDs, K+ supplements

CI: Bilateral RAS, angioedema

DISP: Tablets 2.5, 5, 10, 20 mg; IV 1.25 mg/mL (1, 2 mL)

SE: BP w/initial dose (especially w/diuretics), K+, Cr, nonproductive cough, angioedema

NOTES: Monitor Cr; discontinue diuretic for 2–3 days prior to start

ENOXAPARIN (LOVENOX)

WARNING: Recent or anticipated epidural/spinal anesthesia risk of spinal/epidural hematoma w/subsequent paralysis

USES: *Prevention/treatment of DVT; treatment of PE, unstable angina, non–Q-wave MI*

ACTION: LMW heparin; inhibits thrombin by complexing w/antithrombin III

DOSE:

Adults: Prevention: 30 mg SQ b.i.d. or 40 mg SQ q24h. DVT/PE Treatment: 1 mg/kg SQ q12h or 1.5 mg/kg SQ q24h; CrCl <30 mL/min to 1 mg/kg/d SQ.

Peds: Prevention: 0.5 mg/kg SQ q12h. DVT/PE Treatment: 1 mg/kg SQ q12h; dose w/CrCl <30 mL/min

CAUTION: [B, ?]; not for prophylaxis in prosthetic heart valves

CI: Active bleeding, heparin-induced thrombocytopenia (HIT)

DISP: Injectable 10 mg/0.1 mL (30, 40, 60, 80, 100, 120, 150-mg syringes); 300-mg/mL multidose vial

SE: Bleeding, hemorrhage, bruising, thrombocytopenia, fever, pain/hematoma at site, AST/ALT

NOTES: No effect on bleeding time, platelet function, PT, or aPTT; monitor platelet for HIT, clinical bleeding; may monitor antifactor Xa; not for IM use

EPHEDRINE

USES: *Acute bronchospasm, bronchial asthma, nasal congestion,* hypotension, narcolepsy, enuresis, myasthenia gravis, retrograde ejaculation

ACTION: Sympathomimetic; stimulates - and -receptors; bronchodilator, close bladder neck

DOSE:

Adults: Retrograde ejaculation: 50 mg PO q.i.d. Congestion: 25–50 mg PO q6h PRN; BP: 25–50 mg IV q5–10min, 150 mg/d max.

Peds: 0.2–0.3 mg/kg/dose IV q4–6h PRN

CAUTION: [C, ?/–]

CI: Arrhythmias; narrow-angle glaucoma

DISP: Nasal solution 0.48%, 0.5%; capsules 25 mg; injectable 50 mg/mL; nasal spray 0.25%

SE: CNS stimulation (nervousness, anxiety, trembling), tachycardia, arrhythmia, hypertension, xerostomia, dysuria

NOTES: Protect IV from light; monitor BP, HR, urinary output; can cause false-pos amphetamine drug test; take last dose 4–6 hr before h.s.; abuse potential, OTC sales mostly banned/restricted

EPIRUBICIN (ELLENCE)

WARNING: Do not give IM or SQ. Extravasation causes tissue necrosis; potential cardiotoxicity; severe myelosuppression; dose w/hepatic impairment.

USES: *Adjuvant therapy for positive axillary nodes after resection of primary breast cancer,* intravesical for bladder cancer.

ACTIONS

Anthracycline cytotoxic agent

DOSE: Per protocols; intravesical 50 mg epirubicin/50 mL NaCl; systemic dose w/hepatic impairment

CAUTION: [D, –]

CI: Baseline neutrophil count <1,500 cells/mm3, severe cardiac insufficiency, recent MI, severe arrhythmias, severe hepatic dysfunction, previous anthracyclines treatment to max cumulative dose

DISP: Injectable 50 mg/25 mL, 200 mg/100 mL

SE: Mucositis, N/V/D, alopecia, bone marrow, cardiotoxicity, secondary AML, tissue necrosis w/extravasation (see Adriamycin for dose), lethargy

NOTES: CBC, bilirubin, AST, Cr, cardiac function before/during each cycle

EPLERENONE (INSPRA)

USES: *Hypertension*

ACTION: Selective aldosterone antagonist

DOSE:

Adults: 50 mg PO daily–b.i.d., doses >100 mg/d no benefit w/ K+; to 25 mg/d PO if giving w/CYP3A4 inhibitors

CAUTION: [B, ±]; w/CYP3A4 inhibitors; monitor K+ with ACE inhibitor, ARBs, NSAIDs, K+-sparing diuretics; grapefruit juice, St. John's wort

CI: K+ >5.5 mEq/L; NIDDM w/microalbuminuria; SCr >2 mg/dL (males), >1.8 mg/dL (females); CrCl <30 mL/min; w/K+ supplements/K+-sparing diuretics, ketoconazole

DISP: Tablets 25, 50 mg

SE: Cholesterol/triglycerides, K+, headache, dizziness, gynecomastia, diarrhea, orthostatic BP

NOTES: May take 4 wks for full effect

EPOETIN ALFA [ERYTHROPOIETIN, EPO] (EPOGEN, PROCRIT)

WARNING: Mortality, serious cardiovascular/thromboembolic events, and tumor progression. Renal failure patients experienced greater risks (death/cardiovascular events) on ESAs to target higher Hgb levels. Maintain Hgb 10–12g/dL. In some cancers, ESAs survival/time-to-progression when dosed Hgb 12 g/dL. Use lowest dose needed. Use only for myelosuppressive chemotherapy. Discontinue following chemotherapy. Preop ESA DVT. Consider DVT prophylaxis.

USES: *CRF-associated anemia, zidovudine treatment in HIV, cancer chemotherapy; transfusions associated w/surgery*

ACTION: Induces erythropoiesis

DOSE:

Adults and Peds 50–150 U/kg IV/SQ 3 × wk; adjust dose q4–6wk PRN. Surgery: 300 U/kg/d × 10 days before to 4 days after; dose if Hct ~36% or Hgb 12 g/dL or Hgb >1 g/dL in 2-wk period; hold dose if Hgb >12 g/dL

CAUTION: [C, +]

CI: Uncontrolled hypertension

DISP: Injectable 2,000; 3,000; 4,000; 10,000; 20,000; 40,000 U/mL

SE: Hypertension, headache, fatigue, fever, tachycardia, N/V

NOTES: Refrigerate; monitor baseline and posttreatment Hct/Hgb, BP, ferritin; used at some centers to blood counts before radical prostatectomy

EPROSARTAN (TEVETEN)

USES: *Hypertension,* diabetic nephropathy, CHF.

ACTION: Angiotensin receptor blocker

DOSE: 400–800 mg/d single dose or b.i.d.

CAUTION: [C (1st trimester); D (2nd and 3rd trimester); discontinue immediately when pregnancy detected]; w/lithium, K+ with K+-sparing diuretics/supplements/high-dose trimethoprim

CI: Bilateral RAS, 1st-degree aldosteronism

DISP: Tablets 400, 600 mg

SE: Fatigue, depression, URI, UTI, abdominal pain, rhinitis/pharyngitis/cough, hypertriglyceridemia

ERTAPENEM (INVANZ)

USES: *Complicated intra-abdominal, acute pelvic, skin infections; pyelonephritis, prostate cancer*

ACTION: A carbapenem; -lactam antibiotic, cell wall synthesis. Spectrum: Good gram (±)/anaerobic coverage; not Pseudomonas, penicillin-resistant pneumococci, MRSA, Enterococcus, -lactamase (+) H. influenzae, Mycoplasma, Chlamydia

DOSE:

Adults: 1 g/d IM/IV; 500 mg/d in CrCl <30 mL/min.

Peds: 3 mo–12 yr: 15 mg/kg b.i.d. IM/IV, max 1 g/d

CAUTION: [B, ?/–]; seizure history, CNS disorders, -lactam and multiple allergies, probenecid, renal clearance

CI: Component hypersensitivity or amide anesthetics

DISP: Injectable 1 g/vial

SE: Headache, N/V/D, injection site reactions, thrombocytosis, LFTs

NOTES: Can give IM × 7 d, IV × 14 d; 137 mg Na+ (6 mEq)/g ertapenem

ERYTHROMYCIN (E-MYCIN, EES, ERY-TABLET, ERYPED, ILOTYCIN)

USES: *Bacterial infections; bowel preparation*; GI motility (prokinetic); *acne vulgaris*

ACTION: Bacteriostatic; interferes w/protein synthesis. Spectrum: Group A streptococci (S. pyogenes), S. pneumoniae, N. meningitidis, N. gonorrhoeae (if penicillin-allergic), Legionella, M. pneumoniae

DOSE:

Adults: Base 250–500 mg PO q6–12h or ethylsuccinate 400–800 mg q6–12h; 500 mg–1 g IV q6h. Chancroid: 500 mg PO t.i.d. × 7 d. Prokinetic: 250 mg PO t.i.d. 30 min a.c.

Peds: 30–50 mg/kg/d PO divided q6–8h or 20–40 mg/kg/d IV divided q6h, max 2 g/d

CAUTION: [B, +]; toxicity of carbamazepine, cyclosporine, digoxin, methylprednisolone, theophylline, felodipine, warfarin, simvastatin/lovastatin; sildenafil dose w/use

CI: Hepatic impairment, preexisting liver disease (estolate), use with pimozide

DISP: Lactobionate (Ilotycin): Powder for injectable 500 mg, 1 g. Base: Tablets 250, 333, 500 mg; capsules 250 mg. Estolate (Ilosone): Suspension 125, 250 mg/5 mL. Stearate

(Erythrocin): Tablets 250, 500 mg. Ethylsuccinate (EES, EryPed): Chewable tablets 200 mg; tablets 400 mg; suspension 200, 400 mg/5 mL

SE: Headache, abdominal pain, N/V/D; [QT prolongation, torsade de pointes, VA/VT(rarely)]; cholestatic jaundice (estolate)

NOTES: 400 mg ethylsuccinate = 250 mg base/estolate; w/food minimizes GI upset; lactobionate contains benzyl alcohol (caution in neonates)

ERYTHROMYCIN AND SULFISOXAZOLE (ERYZOLE, PEDIAZOLE)

USES: *Upper/lower respiratory tract; bacterial infections; H. influenzae otitis media in children*; infections in penicillin-allergic patients

ACTION: Macrolide antibiotic w/sulfonamide

DOSE:

Adults: Based on erythromycin content; 400 mg erythromycin/1,200 mg sulfisoxazole PO q6h.

Peds: >2 mo: 40–50 mg/kg/d erythromycin and 150 mg/kg/d sulfisoxazole PO divided q6h; max 2 g/d erythromycin or 6 g/d sulfisoxazole × 10 d; in renal impairment

CAUTION: [C (D if near term), +]; w/PO anticoagulants, hypoglycemics, phenytoin, cyclosporine

CI: Infants <2 mo

DISP: Suspension erythromycin ethylsuccinate 200 mg/sulfisoxazole 600 mg/5 mL (100, 150, 200 mL)

SE: GI upset

ESTERIFIED ESTROGENS (ESTRATAB, MENEST)

WARNING: Risk endometrial cancer. Do not use in prevention of CVD or dementia; risk of MI, stroke, breast cancer, PE, DVT, in postmenopausal women.

USES: *Vasomotor symptoms or vulvar/vaginal atrophy w/menopause*; female hypogonadism, prostate cancer, osteoporosis prevention

ACTION: Estrogen supplement

DOSE: Menopausal vasomotor symptoms: 0.3–1.25 mg/d, cyclically 3 wk on, 1 wk off; add progestin 10–14 days w/28–d cycle w/uterus intact. Vulvovaginal atrophy: Same regimen except use 0.3–1.25 mg. Hypogonadism: 2.5–7.5 mg/d PO × 20 d, off × 10 d; add progestin 10–14 days w/28-d cycle w/uterus intact

CAUTION: [X, –]

CI: Undiagnosed genital bleeding, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis, recent MI, pregnancy, severe hepatic disease

DISP: Tablets 0.3, 0.625, 1.25, 2.5 mg

SE: N, headache, bloating, breast enlargement/tenderness, edema, venous thromboembolism, hypertriglyceridemia, gallbladder disease

NOTES: Use lowest dose for shortest time; see WHI data (www.whi.org)

ESTERIFIED ESTROGENS + METHYLTESTOSTERONE (ESTRATEST, ESTRATEST HS, SYNTEST DS, HS)

WARNING: Risk endometrial cancer. Avoid in pregnancy. Do not use in prevention of CVD or dementia; risk of MI, stroke, breast cancer, PE, DVT in postmenopausal women

USES: *Vasomotor symptoms*; postpartum breast engorgement.

ACTION: Estrogen and androgen supplement

DOSE: 1 tablet/d × 3 wk, 1 wk off

CAUTION: [X, –]

CI: Genital bleeding of unknown cause, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis, recent MI, pregnancy

DISP: Tablets (estrogen/methyltestosterone) 0.625 mg/1.25 mg, 1.25 mg/2.5 mg.

SE: N, headache, bloating, breast enlargement/tenderness, edema, triglycerides, venous thromboembolism, gallbladder disease

NOTES: Use lowest dose for shortest time; see WHI data (www.whi.org)

ESTRADIOL, GEL (DIVIGEL)

WARNING: Risk of endometrial cancer. Do not use in prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women (50–79). Dementia risk in postmenopausal women (65).

USES: *Vasomotor symptoms in menopause*

ACTION: Estrogen

DOSE: 0.25 g every day on right or left upper thigh

CAUTION: [X, ±]; may PT/PTT/platelet aggregation w/thyroid disease

CI: Undiagnosed genital bleeding, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis, recent MI, pregnancy, severe hepatic disease

DISP: 0.1% gel 0.25/0.5/1 g single-dose foil packets w/0.25, 0.5, 1-mg estradiol, respectively

SE: N, headache, bloating, breast enlargement/tenderness, edema, venous thromboembolism, BP, hypertriglyceridemia, gallbladder disease

NOTES: If person other than patient applies, glove should be used, keep dry immediately after, rotate site; contains alcohol, caution around flames until dry, not for vaginal use

ESTRADIOL, GEL (ELESTRIN)

WARNING: Do not use in the prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women.

USES: *Postmenopausal vasomotor symptoms*

ACTION: Estrogen

DOSE: Apply 0.87–1.7 g/d to skin; add progestin × 10–14 d/28–d cycle w/intact uterus; use lowest effective estrogen dose

CAUTION: [X, ?]

CI: AUB, breast cancer, estrogen-dependent tumors, thromboembolic disorders, recent MI, pregnancy, severe hepatic disease

DISP: Gel 0.06%

SE: Thromboembolic events, MI, stroke, BP, breast/ovarian/endometrial cancers, site reactions, vaginal spotting, breast changes, abdominal bloating, cramps, headache, fluid retention

NOTES: Apply to upper arm, wait >25 min before sunscreen; avoid concomitant use for >7 d; BP, breast exams

ESTRADIOL, ORAL (ESTRACE, DELESTROGEN, FEMTRACE)

WARNING: Risk of endometrial cancer; avoid in pregnancy.

USES: *Atrophic vaginitis, menopausal vasomotor symptoms, low estrogen levels, palliation breast/prostate cancers*

ACTION: Estrogen

DOSE: PO: 1–2 mg/d, adjust PRN to control symptoms. Vaginal cream: 2–4 g/d × 2 wk, then 1 g 1–3 × wk. Vasomotor symptoms/vaginal atrophy: 10–20 mg IM q4wk; discontinue or taper at 3–6-mo intervals. Hypoestrogenism: 10–20 mg IM q4wk. Prostate cancer: 30 mg IM q12wk

CAUTION: [X, –]

CI: Genital bleeding of unknown cause, breast cancer, porphyria, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis; recent MI; hepatic impairment

DISP: Ring 0.05, 0.1, 2 mg; gel 0.061%; tablets 0.5, 1, 2 mg; vaginal cream 0.1 mg/g; depot injection (Delestrogen) 10, 20, 40 mg/mL

SE: N, headache, bloating, breast enlargement/tenderness, edema, triglycerides, venous thromboembolism, gallbladder disease

ESTRADIOL, TRANSDERMAL (ESTRADERM, CLIMARA, VIVELLE, VIVELLE DOT)

WARNING: Risk of endometrial cancer. Do not use in prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women (50–79). Dementia risk in postmenopausal women (65)

USES: *Severe menopausal vasomotor symptoms; female hypogonadism*

ACTION: Estrogen supplement

DOSE: Start 0.0375–0.05 mg/d patch 2 × wk based on product; adjust PRN to control symptoms; w/intact uterus cycle 3 wk on 1 wk off or use cyclic progestin 10–14 days

CAUTION: [X, –]; see “Estradiol”

CI: Pregnancy, AUB, porphyria, breast cancer, estrogen-dependent tumors, history thrombophlebitis, thrombosis

DISP: Transdermal patches (mg/24 hr) 0.025, 0.0375, 0.05, 0.06, 0.075, 0.10

SE: N, bloating, breast enlargement/tenderness, edema, headache, hypertriglyceridemia, gallbladder disease

NOTES: Do not apply to breasts; place on trunk, rotate sites

ESTRADIOL, VAGINAL (ESTRING, FEMRING, VAGIFEM)

WARNING: Risk of endometrial cancer. Do not use in prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women (50–79)

USES: *Postmenopausal vaginal atrophy (Estring)* *vasomotor symptoms and vulvar/vaginal atrophy associated with menopause (Femring)* *atrophic vaginitis (Vagifem)*

ACTION: Estrogen

DOSE: Estring: Insert ring into upper 3rd of vaginal vault; remove and replace after 90 d; reassess 3–6 mo. Femring: Use lowest effective dose, insert vaginally, replace q3mo. Vagifem: 1 tablet vaginally every day × 2 wk, then maintenance 1 tablet 2 × wk, discontinue or taper at 3–6 mo

CAUTION: [X, –]; may PT/PTT/platelet aggregation w/thyroid disease, toxic shock reported

CI: Undiagnosed genital bleeding, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombophlebitis, recent MI, pregnancy, severe hepatic disease

DISP: Estring ring: 0.0075 mg/24 hr; Femring ring: 0.05 and 0.1 mg/d; Vagifem tablet (vaginal): 25 g

SE: Headache, leukorrhea, back pain, candidiasis, vaginitis, vaginal discomfort/hemorrhage, arthralgia, insomnia, abdominal pain

ESTRAMUSTINE PHOSPHATE (EMCYT)

USES: *Advanced prostate cancer*

ACTION: Estradiol w/nornitrogen mustard; exact mechanism unknown

DOSE: 14 mg/kg/d in 3–4 divided doses; on empty stomach, no dairy products

CAUTION: Do not use in females

CI: Active thrombophlebitis or thromboembolic disorders

DISP: Capsules 140 mg

SE: N/V, exacerbation of preexisting CHF, edema, hepatic disturbances, thrombophlebitis, MI, PE, gynecomastia in 20–100%

NOTES: Low-dose breast irradiation before may gynecomastia

ESTROGEN, CONJUGATED (PREMARIN)

WARNING: Risk of endometrial cancer. Do not use in prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women (50–79). Dementia risk in postmenopausal women (65)

USES: *Mod–severe menopausal vasomotor symptoms; atrophic vaginitis; palliative advanced prostate cancer; prevention/treatment of estrogen-deficiency osteoporosis*

ACTION: Estrogen hormonal replacement

DOSE: 0.3–1.25 mg/d PO cyclically. Prostate cancer: 1.25–2.5 mg PO t.i.d.

CAUTION: [X, –]

CI: Severe hepatic impairment, genital bleeding of unknown cause, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombosis, thrombophlebitis, recent MI

DISP: Tablets 0.3, 0.45, 0.625, 0.9, 1.25, 2.5 mg; vaginal cream 0.625 mg/g

SE: Risk of endometrial cancer, gallbladder disease, thromboembolism, headache, possibly breast cancer.

NOTES: Generic products not equivalent

ESTROGEN, CONJUGATED SYNTHETIC (CENESTIN, ENJUVIA)

WARNING: Risk of endometrial cancer. Do not use in prevention of CVD or dementia; risk MI, stroke, breast cancer, PE, DVT in postmenopausal women (50–79). Dementia risk in postmenopausal women (65).

USES: *Vasomotor menopausal symptoms, vulvovaginal atrophy, prevent postmenopausal osteoporosis*

ACTION: Multiple estrogen hormonal replacement

DOSE: W/intact uterus, progestin × 10–14 d/28–d cycle. Vasomotor symptoms: 0.3–1.25 mg/d (Enjuvia), 0.625–1.25 mg/d (Cenestin) PO. Vaginal atrophy: 0.3 mg/d. Osteoporosis (Cenestin): 0.625 mg/d

CAUTION: [X, –]

CI: See “Estrogen, Conjugated.”

DISP: Tablets (Cenestin) 0.3, 0.45, 0.625, 0.9 mg; (Enjuvia ER) 0.3, 0.45, 0.625, 1.25 mg

SE: Risk endometrial/breast cancers, gallbladder disease, thromboembolism

ESTROGEN, CONJUGATED + MEDROXYPROGESTERONE (PREMPRO, PREMPHASE)

WARNING: Do not use for prevention of CVD or dementia; risk of MI, stroke, breast cancer, PE, DVT; risk of dementia in postmenopausal women.

USES: *Mod–severe menopausal vasomotor symptoms; atrophic vaginitis; prevent postmenopausal osteoporosis*

ACTION: Hormonal replacement

DOSE: Prempro 1 tablet PO daily; Premphase 1 tablet PO daily

CAUTION: [X, –]

CI: Severe hepatic impairment, genital bleeding of unknown cause, breast cancer, estrogen-dependent tumors, thromboembolic disorders, thrombosis, thrombophlebitis

DISP: As estrogen/medroxyprogesterone. Prempro: Tablets 0.625/2.5, 0.625/5 mg; Premphase: Tablets 0.625/0 (d 1–14) and 0.625/5 mg (d 15–28)

SE: Gallbladder disease, thromboembolism, headache, breast tenderness

NOTES: See WHI (www.whi.org)

ETHAMBUTOL (MYAMBUTOL)

USES: *Pulmonary TB* and other mycobacterial infections, macobacterium avium complex (MAC)

ACTION: RNA synthesis

DOSE:

Adults and Peds: >12 yr: 15–25 mg/kg/d PO single dose; in renal impairment, take w/food, avoid antacids

CAUTION: [C, +]

CI: Unconscious patients, optic neuritis

DISP: Tablets 100, 400 mg

SE: Headache, hyperuricemia, acute gout, abdominal pain, LFTs, optic neuritis, GI upset

ETODOLAC

WARNING: May risk of cardiovascular events and GI bleeding; may worsen BP.

USES: *Osteoarthritis and pain,* RA

ACTION: NSAID

DOSE: 200–400 mg PO b.i.d.–q.i.d. (max 1,200 mg/d)

CAUTION: [C (D 3rd trimester), ?]; bleeding risk w/aspirin, warfarin; nephrotoxicity w/cyclosporine; history CHF, hypertension, renal/hepatic impairment, PUD

CI: Active GI ulcer

DISP: Tablets 400, 500 mg; ER tablets 400, 500, 600 mg; capsules 200, 300 mg

SE: N/V/D, gastritis, abdominal cramps, dizziness, headache, depression, edema, renal impairment

NOTES: Do not crush tablets

ETOPOSIDE [VP-16] (VEPESID, TOPOSAR)

USES: *Testicular, non-small cell lung cancer (NSCLC), Hodgkin disease, NHLs, peds ALL, allogeneic/autologous bone marrow transplant in high doses*

ACTION: Topoisomerase II inhibitor

DOSE: 50 mg/m2/d IV for 3–5 d; 50 mg/m2/d PO for 21 days (PO availability = 50% of IV); 2–6 g/m2 or 25–70 mg/kg in bone marrow transplant (per protocols); in renal/hepatic impairment

CAUTION: [D, –]

CI: IT administration

DISP: Capsules 50 mg; injectable 20 mg/mL

SE: N/V (emesis in 10–30%), bone marrow, alopecia, BP w/rapid IV, anorexia, anemia, leukopenia, risk secondary leukemias

EVEROLIMUS (AFINITOR)

USES: *Advanced RCC after failure of sunitinib or sorafenib*

ACTION: MTOR inhibitor

DOSE: 10 mg/d PO, to 5 mg with side effects or hepatic impairment

CAUTION: [D/–]; avoid live vaccines/contact with those who have received live vaccines; avoid w/CYP3A4 inhibitors

CI: Hypersensitivity to compound or other rapamycin derivatives

DISP: Tablets 5, 10 mg

SE: Noninfectious pneumonitis, increased infection risk, oral ulcers, asthenia, cough, fatigue diarrhea, serum glucose, creatinine, lipids; hemoglobin, WBC, platelets

NOTES: Follow CBC, LFT, glucose lipids

FAMCICLOVIR (FAMVIR)

USES: *Acute herpes zoster (shingles), genital herpes*

ACTION: Viral DNA synthesis

DOSE: Zoster: 500 mg PO q8h × 7 days. Genital herpes simplex CDC recommended regimens: 250 mg PO t.i.d. × 7–10 days or 200 mg PO q.i.d. × 7–10 days. Recurrence: 250 mg PO b.i.d. Episodic within 1 day of lesion: 125 mg PO t.i.d. × 5 days OR 1,000 mg PO b.i.d. × 1 days; w/renal impairment

CAUTION: [B, –]

CI: Component sensitivity

DISP: Tablets 125, 250, 500 mg

SE: Fatigue, dizziness, headache, pruritus, N/D

NOTES: Best within 72 hr of initial lesion; CDC alternative regimens for genital herpes includes acyclovir and valacyclovir

FENOPROFEN (NALFON)

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID

DOSE: 200–600 mg q4–8h, to 3,200 mg/d max; w/food

CAUTION: [B (D 3rd trimester), ±] CHF, hypertension, renal/hepatic impairment, history PUD

CI: NSAID sensitivity

DISP: Capsules 200, 300, 600 mg

SE: GI disturbance, dizziness, headache, rash, edema, renal/hepatic impairment

NOTES: Swallow whole

FENTANYL (SUBLIMAZE) [C-II]

USES: *Short-acting analgesic* in anesthesia and prostate cancer

ACTION: Narcotic analgesic

DOSE:

Adults: 25–100 g/kg/dose IV/IM titrated. Anesthesia: 5–15 g/kg. Pain: 200 g over 15 min, titrate to effect.

Peds: 1–2 g/kg IV/IM q1–4h titrate; in renal impairment

CAUTION: [B, +]

CI: Paralytic ileus ICP, respiratory depression, severe renal/hepatic impairment

DISP: Injectable 0.05 mg/mL

SE: Sedation, BP, bradycardia, constipation, N, respiratory depression, miosis

NOTES: 0.1 mg fentanyl = 10 mg morphine IM

FENTANYL IONTOPHORETIC TRANSDERMAL SYSTEM (IONSYS)

WARNING: Use only w/hospitalized patients; discontinue on discharge; fentanyl may result in potentially life-threatening respiratory depression and death

USES: *Short-term in-hospital analgesia*

ACTION: Opioid narcotic, iontophoretic transdermal

DOSE: 40 g/activation by patient; dose given over 10 min; max over 24 hr 3.2 mg (80 doses)

CAUTION: [C, –]

CI: See fentanyl

DISP: Battery-operated self-contained transdermal system, 40 g/activation, 80 doses

SE: See “Fentanyl, Site Reaction.”

NOTES: Choose normal skin site chest or upper outer arm; titrate to comfort, patient must have access to supplemental analgesia; instruct in device use; dispose of properly at discharge

FENTANYL, TRANSDERMAL (DURAGESIC) [C-II]

WARNING: Potential for abuse and fatal overdose

USES: *Persistent mod–severe chronic pain in patients already tolerant to opioids*

ACTION: Narcotic

DOSE: Apply patch to upper torso q72h; dose based on narcotic requirements in previous 24 hr; start 25 g/hr patch q72h; in renal impairment

CAUTION: [B, +]; w/CYP3A4 inhibitors may fentanyl effect, w/history substance abuse

CI: Not opioid tolerant, short-term pain management, postop pain in outpatient surgery, mild pain, PRN use ICP, respiratory depression, severe renal/hepatic impairment, peds <2 yr

DISP: Patches 12.5, 25, 50, 75, 100 g/hr

SE: Respiratory depression (fatal), sedation, BP, bradycardia, constipation, N, miosis

NOTES: 0.1 mg fentanyl = 10 mg morphine IM; do not cut patch; peak level 24–72 hr

FENTANYL, TRANSMUCOSAL SYSTEM (ACTIQ, FENTORA) [C-II]

WARNING: Potential for abuse and fatal overdose; use only in cancer patients with chronic pain who are opioid tolerant; buccal formulation bioavailability over transmucosal; do not substitute on a g-per-g basis; use w/strong CYP3A4 inhibitors may fentanyl levels

USES: *Breakthrough cancer pain*

ACTION: Narcotic analgesic, transmucosal absorption

DOSE: Start 100 g buccal (Fentora) × 1, may repeat in 30 min, 4 tablets/dose max; titrate; start 200 g PO (Actiq) × 1, may repeat × 1 after 30 min; titrate

CAUTION: [B, +]

CI: ICP, respiratory depression, severe renal/hepatic impairment, management of postop or awake pain

DISP: (Actiq) Lozenges on stick 200, 400, 600, 800, 1,200, 1,600 g; (Fentora) buccal tablets 100, 200, 300, 400, 600, 800 g

SE: Sedation, BP, bradycardia, constipation, N, respiratory depression, miosis

NOTES: 0.1 mg fentanyl = 10 mg IM morphine; for use in patients already tolerant to opioid therapy

FESOTERODINE FUMARATE (TOVIAZ)

USES: *Overactive bladder with symptoms of urge urinary incontinence, urgency, frequency*.

ACTION: Competitive muscarinic receptor antagonist, bladder muscle contractions

DOSE: 4 mg PO QD, to 8 mg PO QD if necessary

CAUTION: [C/–]; doses >4 mg not recommended w/severe renal insufficiency or w/potent CYP3A4 inhibitors (eg, ketoconazole, itraconazole, clarithromycin); BOO, decreased GI motility and constipation, treated narrow-angle glaucoma, myasthenia gravis

CI: Urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma, hypersensitivity to components

DISP: Tablets 5, 10 mg

SE: Dry mouth, constipation; decreased sweating can lead to heat prostration

FINASTERIDE (PROSCAR, PROPECIA)

USES: *Benign prostatic hyperplasia (BPH) and androgenetic alopecia*

ACTION: 5-Reductase to reduce DHT

DOSE: BPH: 5 mg/d PO. Alopecia: 1 mg/d PO; food absorption

CAUTION: [X, –]; hepatic impairment

CI: Pregnant women should avoid handling pills, teratogen to male fetus

DISP: Tablets 1 mg (Propecia), 5 mg (Proscar)

SE: Libido, ejaculate volume, ED, gynecomastia

NOTES: Both Proscar and Propecia PSA by ~50%; reestablish PSA baseline 6 mo (double PSA for true reading); 3–6 mo to affect urinary symptoms; continue to maintain new hair, Prostate Cancer Prevention Trial demonstrated 25% in prostate cancer risk over 7 yr

FLAVOXATE (URISPAS)

USES: *Relief of dysuria, urgency, nocturia, suprapubic pain, urinary frequency, incontinence symptoms*

ACTION: Antispasmodic

DOSE: 100–200 mg PO t.i.d.–q.i.d.

CAUTION: [B, ?]

CI: GI obstruction, GI hemorrhage, ileus, achalasia, benign prostatic hyperplasia

DISP: Tablets 100 mg

SE: Drowsiness, blurred vision, xerostomia

FLUCONAZOLE (DIFLUCAN)

USES: *Candidiasis (esophageal, oropharyngeal, urinary tract, vaginal, prophylaxis); cryptococcal meningitis, prophylaxis w/bone marrow transplant*

ACTION: Antifungal; cytochrome P450 sterol demethylation. Spectrum: All Candida sp except C. krusei

DOSE:

Adults: 100–400 mg/d PO or IV. Vaginitis: 150 mg PO daily. Crypto: Doses up to 800 mg/d reported; 400 mg days 1, then 200 mg × 10–12 wk after CSF (–).

Peds: 3–6 mg/kg/d PO or IV; 12 mg/kg/d/systemic infection; in renal impairment

CAUTION: [C, –]

CI: None

DISP: Tablets 50, 100, 150, 200 mg; suspension 10, 40 mg/mL; injectable 2 mg/mL

SE: Headache, rash, GI upset, K+, LFTs

NOTES: PO (preferred) = IV levels

FLUDROCORTISONE ACETATE (FLORINEF)

USES: *Adrenocortical insufficiency, Addison disease, salt-wasting syndrome*

ACTION: Potent mineralocorticoid with high glucocorticoid activity; reabsorption of Na+/loss of K+ from distal renal tubules

DOSE:

Adults: 0.05–0.2 mg/d (typical ranges 0.1 mg 3 × week to 0.2 mg/d.

Peds: 0.05–0.1 mg/d PO

CAUTION: [C, ?]

CI: Systemic fungal infections; known allergy

DISP: Tablets 0.1 mg

SE: Hypertension, edema, CHF, headache, dizziness, convulsions, acne, rash, bruising, hyperglycemia, hypothalamic–pituitary–adrenal suppression, cataracts

NOTES: For adrenal insufficiency, use w/glucocorticoid; dose changes based on plasma renin activity, follow electrolytes

FLUOROURACIL [5-FU] (ADRUCIL)

WARNING: Administration by experienced chemotherapy physician only; patients should be hospitalized for 1st course due to risk of severe reaction

USES: *Colorectal, gastric, pancreatic, breast, basal cell,* head, neck, bladder cancers

ACTION: Inhibits thymidylate synthetase (DNA synthesis, S-phase specific)

DOSE: Per protocols, 370–1,000 mg/m2/d × 1–5 days IV push or 24-hr continuous infusion; protracted venous infusion of 200–300 mg/m2/d; 800 mg/d max

CAUTION: [D, ?]; toxicity w/allopurinol; do not give MRX before 5-FU

CI: Poor nutritional status, bone marrow function, thrombocytopenia, major surgery within past mo, G6PD enzyme deficiency, pregnancy, serious infection, bilirubin >5 mg/dL

DISP: Injectable 50 mg/mL

SE: Stomatitis, esophagopharyngitis, N/V/D, anorexia, bone marrow, rash/dry skin/photosensitivity, tingling in hands/feet w/pain (palmar–plantar erythrodysesthesia), phlebitis/discoloration at injection sites

NOTES: Thiamine intake; contraception OK

FLUOROURACIL, TOPICAL [5-FU] (EFUDEX)

USES: *Basal cell carcinoma; actinic/solar keratosis,* penile cancer

ACTION: Inhibits thymidylate synthetase (DNA synthesis, S-phase specific)

DOSE: 5% cream b.i.d. × 2–6 wk

CAUTION: [D, ?]; irritant chemotherapy

CI: Component sensitivity

DISP: Cream 0.5, 1, 5%; solution 1, 2, 5%

SE: Rash, dry skin, photosensitivity

NOTES: Healing may not be evident for 1–2 mo; wash hands thoroughly; avoid occlusive dressings; do not overuse; limited experience with small SCC of penis

FLUOXETINE (PROZAC, SARAFEM)

WARNING: Closely monitor for worsening depression or emergence of suicidality, particularly in ped patients

USES: *Depression, OCD, panic disorder, bulimia (Prozac)* Premenstural dysphoric disorder (PMDD) (Sarafem),* premature ejaculation

ACTION: SSRI

DOSE: 20 mg/d PO (max 80 mg/d divided dose); weekly 90 mg/wk after 1–2 wk of standard dose. Bulimia: 60 mg q AM Panic disorder: 20 mg/d. OCD: 20–80 mg/d. PMDD: 20 mg/d or 20 mg intermittently, start 14 days prior to menses, repeat with each cycle; in hepatic failure

CAUTION: [C, ?/–]; serotonin syndrome w/MAOI, SSRI, serotonin agonists, linezolid; QT prolongation w/phenothiazines

CI: MAOI/thioridazine (wait 5 wk after discontinuation before MAOI)

DISP: Prozac: Capsules 10, 20, 40 mg; scored tablets 10, 20 mg; SR capsules 90 mg; solution 20 mg/5 mL. Sarafem: Capsules 10, 20 mg

SE: N, nervousness, weight loss, headache, insomnia

FLUOXYMESTERONE (HALOTESTIN, ANDROXY) [C-III]

USES: *Androgen-responsive metastatic breast cancer, hypogonadism*

ACTION: Synthetic testosterone derivative with significant androgen activity

DOSE: Hypogonadism: 5–20 mg/d; Delayed puberty in males: 2.5–20 mg/d for 4–6 mo

CAUTION: [X, ?/–]; effect w/anticoagulants, cyclosporine, insulin, lithium, narcotics

CI: Serious cardiac, liver, or kidney disease; pregnancy

DISP: Tablets 10 mg

SE: Priapism; edema; virilization; amenorrhea/menstrual irregularities; hirsutism; alopecia; acne; N; cholestasis; suppression of factors II, V, VII, and X; polycythemia; libido; headache; anxiety

NOTES: Radiographic exam of hand/wrist q6mo in prepubertal children; total T4 levels

FLUTAMIDE (EULEXIN)

WARNING: Liver failure and death reported. Measure LFTs before, monthly, and periodically after; discontinue immediately if ALT 2 × upper limits of normal or jaundice develops

USES: Advanced *prostate cancer* (w/LHRH agonists; eg, leuprolide or goserelin); w/radiation and LHRH for localized prostate cancer

ACTION: Nonsteroidal antiandrogen

DOSE: 250 mg PO t.i.d. (750 mg total)

CAUTION: [D, ?]

CI: Severe hepatic impairment

DISP: Capsules 125 mg

SE: Hot flashes, loss of libido, impotence, N/V/D, gynecomastia, hepatic failure

NOTES: LFTs, avoid EtOH

FONDAPARINUX (ARIXTRA)

WARNING: When epidural/spinal anesthesia or spinal puncture is used, patients anticoagulated or scheduled to be anticoagulated with LMW heparins, heparinoids, or fondaparinux are at risk for epidural or spinal hematoma, which can result in long-term or permanent paralysis

USES: *DVT prophylaxis* w/hip fracture, hip or knee replacement, abdominal surgery; w/DVT or PE in combination w/warfarin

ACTION: Synth inhibitor of activated factor X; a pentasaccharide

DOSE: 2.5 mg/d SQ, up to 5–9 d; start >6 hr postop; w/renal impairment

CAUTION: [B, ?]; bleeding risk w/anticoagulants, antiplatelets, drotrecogin alfa, NSAIDs

CI: <50 kg, CrCl <30 mL/min, active bleeding, SBE platelet w/antiplatelet antibodies

DISP: Prefilled syringes w/27-gauge needle: 2.5/0.5, 5/0.4, 7.5/0.6, 10/0.8, mg/mL

SE: Thrombocytopenia, anemia, fever, N

NOTES: Discontinue if platelets <100,000 mm3; only give SQ; may monitor antifactor Xa levels

FOSFOMYCIN (MONUROL)

USES: *Uncomplicated UTI*

ACTION: Cell wall synthesis. Spectrum: Gram(+) coverage Enterococcus, staphylococci, pneumococci; gram(–) coverage of E. coli, Salmonella, Shigella, H. influenzae, Neisseria, indole-negative Proteus, Providencia; B. fragilis and anaerobic gram(–) cocci are resistant

DOSE: 3 g PO in 90–120 mL of H2O single dose; in renal impairment

CAUTION: [B, ?]; absorption w/antacids/Ca salts

CI: Component sensitivity

DISP: Granule packets 3 g

SE: Headache, GI upset

NOTES: May take 2–3 days for symptoms to improve

FOSINOPRIL (MONOPRIL)

USES: *Hypertension, CHF,* diabetic nephropathy

ACTION: ACE inhibitor

DOSE: 10 mg/d PO initial; max 40 mg/d PO; in elderly; in renal impairment

CAUTION: [D, +]; K+ w/K+ supplements, ARBs, K+-sparing diuretics; renal after-effects w/NSAIDs, diuretics, hypovolemia

CI: Hereditary/idiopathic angioedema or angioedema w/ACE inhibitor, bilateral RAS

DISP: Tablets 10, 20, 40 mg

SE: Cough, dizziness, angioedema, K+

FUROSEMIDE (LASIX)

USES: *CHF, hypertension, edema,* ascites

ACTION: Loop diuretic; Na and Cl reabsorption in ascending loop of Henle and distal tubule

DOSE:

Adults: 20–80 mg PO or IV b.i.d.

Peds: 1 mg/kg/dose IV q6–12h; 2 mg/kg/dose PO q12–24h (max 6 mg/kg/dose); doses w/renal impairment

CAUTION: [C, +]; K+, risk digoxin toxicity and ototoxicity w/aminoglycosides, cisplatin (especially in renal dysfunction)

CI: Sulfonylurea allergy; anuria; hepatic coma; electrolyte depletion

DISP: Tablets 20, 40, 80 mg; solution 10 mg/mL, 40 mg/5 mL; injectable 10 mg/mL

SE: BP, hyperglycemia, K+

NOTES: Follow electrolytes, renal function; high doses IV may cause ototoxicity

GABAPENTIN (NEURONTIN)

USES: Adjunct in *partial seizures; PHN*; chronic pain and pelvic pain syndromes

ACTION: Anticonvulsant; GABA analog

DOSE:

Adults and Peds: >12 yr: Anticonvulsant: 300 mg PO t.i.d., max 3,600 mg/d. PHN: 300 mg day 1, 300 mg b.i.d. day 2, 300 mg t.i.d. day 3, titrate (1,800–3,600 mg/d); w/renal impairment

CAUTION: [C, ?]; use in peds 3–12 yr w/epilepsy may CNS-related adverse events

CI: Component sensitivity

DISP: Capsules 100, 300, 400; solution 250 mg/5 mL; scored tablet 600, 800 mg

SE: Somnolence, dizziness, ataxia, fatigue

NOTES: Not necessary to monitor levels; taper / over 1 wk

GALLIUM NITRATE (GANITE)

WARNING: Risk of severe renal insufficiency w/concurrent use of nephrotoxic drugs (eg, aminoglycosides, amphotericin B). Discontinue if use of potentially nephrotoxic drug is indicated; hydrate several days after administration. Discontinue w/Cr >2.5 mg/dL

USES: * Hypercalcemia of malignancy*; bladder cancer

ACTION: Bone resorption of Ca2+

DOSE: Ca2+: 100–200 mg/m2/d × 5 days. Cancer: 350 mg/m2 continuous infusion × 5 days to 700 mg/m2 rapid IV infusion q2wk in antineoplastic settings (per protocols)

CAUTION: [C, ?]; do not give w/live or rotavirus vaccine

CI: SCr >2.5 mg/dL

DISP: Injectable 25 mg/mL

SE: Renal insufficiency, Ca2+, hypophosphatemia, bicarb, <1% acute optic neuritis

NOTES: In bladder cancer, use in combo w/vinblastine and ifosfamide

GEMCITABINE (GEMZAR)

USES: *Pancreatic cancer, brain mets, NSCLC,* gastric and bladder cancers

ACTION: Antimetabolite; ribonucleotide reductase; produces false nucleotide base-inhibiting DNA synthesis

DOSE: 1,000–1,250 mg/m2 over 30 min–1 hr IV infusion/wk × 3–4 wk or 6–8 wk; modify dose based on hematologic function (per protocol)

CAUTION: [D, ?/–]

CI: Pregnancy

DISP: Injectable 200 mg, 1 g

SE: Bone marrow, N/V/D, drug fever, skin rash

NOTES: Reconstituted solution 38 mg/mL; monitor hepatic/renal function

GENTAMICIN (GARAMYCIN, G-MYTICIN, OTHERS)

USES: *Septicemia; serious bacterial infection of CNS, urinary, respiratory, GI tracts, including peritonitis, skin, bone; soft-tissue, including burns; severe P. aeruginosa infection w/carbenicillin; group D streptococci endocarditis w/penicillin-type drug; serious staphylococcal infections (but not antibiotic of 1st choice); mixed infection w/staphylococci and gram(–)*

ACTION: Aminoglycoside, bactericidal; protein synthesis. Spectrum: Gram(–), but not Neisseria, Legionella, Acinetobacter; weaker gram(+) but synergy w/penicillins

DOSE:

Adults: Standard: 1–2 mg/kg IV q8–12h or daily dosing 4–7 mg/kg q24h IV. Gram(+) synergy: 1 mg/kg q8h.

Peds: Infants <7 days <1,200 g: 2.5 mg/kg/dose q18–24h. Infants >1,200 g: 2.5 mg/kg/dose q12–18h. Infants >7 days: 2.5 mg/kg/dose IV q8–12h. Children: 2.5 mg/kg/d IV q8h; w/renal insufficiency; if obese, dose based on IBW

CAUTION: [C, ±]; avoid other nephrotoxins

CI: Aminoglycoside sensitivity

DISP: Premixed infusions 40, 60, 70, 80, 90, 100, 120 mg; ADD-Vantage injectable vials 10 mg/mL; injectable 40 mg/mL; IT preservative-free 2 mg/mL

SE: Nephro-/oto-/neurotoxicity

NOTES: Follow CrCl, SCr, serum conc for dose adjustments; use IBW to dose (use adjusted if obese >30% IBW); OK to use intraperitoneal for peritoneal dialysis-related infections. Levels: Peak: 30 min after infusion; Trough <0.5 hr before next dose; Therapeutic: Peak 5–8 g/mL, Trough <2 g/mL, if >2 associated w/renal toxicity

GOSERELIN (ZOLADEX)

USES: *Advanced prostate cancer (CAP)* and w/radiation for localized high-risk disease, *endometriosis, breast cancer*

ACTION: LHRH agonist, transient then in LH, w/ testosterone

DOSE: 3.6 mg SQ (implant) q28d or 10.8 mg SQ q3mo; usually upper abdominal wall

CAUTION: [X, –]

CI: Pregnancy, breast-feeding, 10.8-mg implant not for women

DISP: SQ implant 3.6 (1 mo), 10.8 mg (3 mo)

SE: Hot flashes, libido, gynecomastia, transient exacerbation of cancer-related bone pain (flare reaction 7–10 days after 1st dose)

NOTES: Inject SQ into fat in abdominal wall; do not aspirate; use antiandrogens to block flare

HEPARIN

USES: *Treat/prevent DVT and PE,* unstable angina, AF w/emboli, acute arterial occlusion

ACTION: Acts w/antithrombin III to inactivate thrombin and thromboplastin formation

DOSE:

Adults: Prophylaxis: 3,000–5,000 U SQ q8–12h. DVT/PE Treatment: Load 50–80 U/kg IV (max 10,000 U), then 10–20 U/kg IV qh (adjust based on PTT); bolus 60 units/kg (max 4,000 U); then 12 U/kg/hr (max 1,000 U/hr); round to nearest 50 U; keep PTT 1.5–2.0 (control).

Peds: Infants: Load 50 U/kg IV bolus, then 20 U/kg/hr IV by continuos infusion. Children: Load 50 U/kg IV, then 15–25 U/kg continuous infusion or 100 U/kg/dose q4h IV intermittent bolus (adjust based on PTT)

CAUTION: [B, +]; risk of hemorrhage w/anticoagulants, aspirin, antiplatelets, cephalosporins w/MTT side chain

CI: Uncontrolled bleeding, severe thrombocytopenia, suspected ICH

DISP: Injectable 10, 100, 1,000, 2,000, 2,500, 5,000, 7,500, 10,000, 20,000, 40,000 U/mL

SE: Bruising, bleeding, thrombocytopenia

NOTES: Follow PTT, thrombin time, or activated clotting time; little PT effect; therapeutic PTT 1.5–2 × control for most conditions; monitor for HIT w/platelet counts

HISTRELIN (VANTAS)

USES: *Palliative treatment of advanced prostate cancer*

ACTION: LHRH antagonist; transiently LH and testosterone followed by suppression to castrate levels of testosterone by ~4 wk

DOSE: Implant with local anesthesia in optimum site (subcutaneous insertion ~1/2-way between shoulder and elbow, in line with crease between biceps and triceps muscles) every 12 mo; remove old implant

CAUTION: [Not indicated in women D, +]

CI: Women and children, component hypersensitivity

DISP: Implant w/50 mg histrelin (50 g/d release) and sterile implantation kit

SE: Hot flashes, fatigue, weight, ED, gynecomastia, testicular atrophy, implant site reactions

NOTES: Monitor PSA and testosterone levels

HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE (GARDASIL)

USES: *Prevent cervical cancer, precancerous genital lesions, genital warts due to HPV 6, 11, 16, 18 in females 9–26 yr*

ACTION: Recombinant vaccine, passive humoral immunity

DOSE: 0.5 mL IM initially, then at 2 and 6 mo

CAUTION: [B, ?/–]

DISP: Single-dose vial and prefilled syringe, 0.5 mL

SE: Site reaction (pain, erythema, swelling, pruritus), fever, syncope

NOTES: 1st approved cancer prevention vaccine; report adverse events to VAERS (800–822–7967); IM in upper thigh or deltoid; continue cervical cancer screening

HYDROCHLOROTHIAZIDE (HYDRODIURIL, ESIDRIX, OTHERS)

USES: *Edema, hypertension*; prevent stones in hypercalcuria

ACTION: Thiazide diuretic; distal tubule Na+ reabsorption and calcium excretion

DOSE:

Adults: 25–100 mg/d PO single or divided doses; 200 mg/d max.

Peds: <6 mo: 2–3.3 mg/kg/d in 2 divided doses. 6 mo–12 yr: 2–2.2 mg/kg/d in 2 divided doses. >12 yr: 25–100 mg/d or divided b.i.d.

CAUTION: [D, +]

CI: Anuria, sulfonamide allergy, renal insufficiency

DISP: Tablets 25, 50, mg; capsules 12.5 mg; PO solution 50 mg/5 mL

SE: ↑ K+, hyperglycemia, hyperuricemia, ↓ Na+; sun sensitivity; lassitude, sleepiness in 30–35% upon initiation but subsides

NOTES: Monitor serum K+; monitor urinary calcium for urolithiasis effect; not considered primary therapy for absorptive hypercalcuria

HYDROCHLOROTHIAZIDE AND AMILORIDE (MODURETIC)

USES: *Hypertension*, with a thiazide diuretic (eg, hydrochlorothiazide) in hypercalcuria

ACTION: Combined thiazide and K+-sparing diuretic

DOSE: 1–2 tablets/d PO

CAUTION: [D, ?]

CI: Renal failure, sulfonamide allergy

DISP: Tablets (amiloride/HCTZ) 5 mg/50 mg

SE: ↑ BP, photosensitivity, ↓ K+/ ↑ K+, hyperglycemia, ↓ Na+, hyperlipidemia, hyperuricemia

NOTES: Not used alone in hypercalcuria; used in combination with thiazide diuretic when hypokalemia is problematic and urinary citrate levels are adequate

HYDROCHLOROTHIAZIDE AND SPIRONOLACTONE (ALDACTAZIDE)

USES: *Edema, hypertension*

ACTION: Thiazide and K+-sparing diuretic

DOSE: 25–200 mg each component/d, divided doses

CAUTION: [D, +]

CI: Sulfonamide allergy

DISP: Tablets (HCTZ/spironolactone) 25 mg/25 mg, 50 mg/50 mg

SE: Photosensitivity, ↑ BP, / ↑ K+, ↓ Na+, hyperglycemia, hyperlipidemia, hyperuricemia

HYDROCHLOROTHIAZIDE AND TRIAMTERENE (DYAZIDE, MAXZIDE)

USES: *Edema and hypertension*

ACTION: Combo thiazide and K+-sparing diuretic

DOSE: Dyazide: 1–2 capsules PO daily–b.i.d. Maxzide: 1 tablet/d PO

CAUTION: [D, ±]

CI: Sulfonamide allergy

DISP: Capsules (triamterene/HCTZ) 37.5 mg/25 mg, 75 mg/50 mg

SE: Photosensitivity, BP, / K+, Na+, hyperglycemia, hyperlipidemia, hyperuricemia.

NOTES: HCTZ component in Maxzide more bioavailable than in Dyazide; do not use in hypercalcuria due to triamterene stone risk

HYDROCODONE AND ACETAMINOPHEN (LORCET, VICODIN, HYCET, OTHERS) [C-III]

USES: *Mod–severe pain*

ACTION: Narcotic w/nonnarcotic analgesic

DOSE:

Adults: 1–2 capsules or tablets PO q4–6h PRN; solution 15 mL q4–6h.

Peds: Solution (Hycet) 0.27 mL/kg q4–6h

CAUTION: [C, M]

CI: CNS depression, severe respiratory depression

DISP: Many formulations; specify hydrocodone/acetaminophen dose on treatment; capsules 5/500; tablets 2.5/500, 5/325, 5/400, 5/500, 7.5/325, 7.5/400, 7.5/500, 7.5/650, 7.5/750, 10/325, 10/400, 10/500, 10/650, 10/660, 10/750; solution Hycet (fruit punch) 7.5 mg hydrocodone/325 mg acetaminophen/15 mL

SE: GI upset, sedation, fatigue

NOTES: Do not exceed >4 g acetaminophen/d

HYDROCODONE AND ASPIRIN (LORTAB ASA, OTHERS) [C-III]

USES: *Mod–severe pain*

ACTION: Narcotic analgesic with NSAID

DOSE: 1–2 PO q4–6h PRN, w/food/milk

CAUTION: [C, M]; renal function, gastritis/PUD

CI: Component sensitivity; children w/chickenpox (Reye syndrome)

DISP: 5 mg hydrocodone/500 mg ASA/tablet

SE: GI upset, sedation, fatigue

NOTES: Monitor for GI bleed

HYDROCODONE AND IBUPROFEN (VICOPROFEN) [C-III]

USES: *Mod–severe pain (<10 d)*

ACTION: Narcotic analgesic w/NSAID

DOSE: 1–2 tablets q4–6h PRN

CAUTION: [C, M]; renal insufficiency; effect w/ACE inhibitors and diuretics; effect w/CNS depressants, EtOH, MAOI, aspirin, TCAs, anticoagulants

CI: Component sensitivity

DISP: Tablets 7.5 mg hydrocodone/200 mg ibuprofen

SE: Sedation, fatigue, GI upset

HYDROCORTISONE, RECTAL (ANUSOL-HC SUPPOSITORY, CORTIFOAM RECTAL, PROCTOCORT, OTHERS)

USES: *Painful anorectal conditions,* radiation proctitis, ulcerative colitis

ACTION: Anti-inflammatory steroid

DOSE:

Adults: 10–100 mg PR daily–b.i.d. for 2–3 wk

CAUTION: [B, ?/–]

CI: Component sensitivity

DISP: Hydrocortisone acetate: Rectal aerosol 90 mg/applicator; suppository 25 mg. Hydrocortisone base: Rectal 0.5, 1, 2.5%; rectal suspension 100 mg/60 mL

SE: Minimal systemic effect

HYDROMORPHONE (DILAUDID) [C-II]

WARNING: A potent Schedule II opioid agonist; highest potential for abuse and risk of respiratory depression. HP formula is highly concentrated; do not confuse w/standard formulations, overdose and death could result. Alcohol, other opioids, CNS depressants respiratory depressant effects

USES: *Mod–severe pain*

ACTION: Narcotic analgesic

DOSE: 1–4 mg PO, IM, IV, or PR q4–6h PRN; 3 mg PR q6–8h PRN; w/hepatic failure

CAUTION: [B (D if prolonged use or high doses near term), ?]; respiratory depression and CNS effects; CNS depressants, phenothiazines, TCAs

CI: CNS lesion w/ ICP, COPD, cor pulmonale, emphysema, kyphoscoliosis, status asthmaticus; HP-injectable form in OB analgesia

DISP: Tablets 2, 4 mg, 8 mg scored; liquid 5 mg/5 mL or 1 mg/mL; injectable 1, 2, 4; HP is 10 mg/mL; suppository 3 mg

SE: Sedation, dizziness, GI upset

NOTES: Morphine 10 mg IM = hydromorphone 1.5 mg IM

HYDROXYZINE (ATARAX, VISTARIL)

USES: *Anxiety, sedation, itching* interstitial cystitis

ACTION: Antihistamine, antianxiolytic

DOSE:

Adults: Anxiety/sedation: 50–100 mg PO or IM q.i.d. or PRN (max 600 mg/d). Itching: 25–50 mg PO or IM t.i.d.–q.i.d. Interstitial cystitis: 25–75 mg/d.

Peds: 0.5–1.0 mg/kg/24 hr PO or IM q6h; w/hepatic impairment

CAUTION: [C, ±]; effects w/CNS depressants, anticholinergics, EtOH

CI: Component sensitivity

DISP: Tablets 10, 25, 50 mg; capsules 25, 50 mg; syrup 10 mg/5 mL; suspension 25 mg/5 mL; injectable 25, 50 mg/mL

SE: Drowsiness, anticholinergic effects

NOTES: Used to potentiate narcotic effects; not for IV/SQ (thrombosis and digital gangrene possible)

HYOSCYAMINE (ANASPAZ, CYSTOSPAZ, LEVSIN, OTHERS)

USES: *Spasm w/GI and bladder disorders*

ACTION: Anticholinergic

DOSE:

Adults: 0.125–0.25 mg (1–2 tablets) SL/PO t.i.d.–q.i.d., a.c. and h.s.; 1 SR capsules q12h

CAUTION: [C, +]; effects w/amantadine, antihistamines, antimuscarinics, haloperidol, phenothiazines, TCAs, MAOIs

CI: BOO, GI obstruction, narrow-angle glaucoma, myasthenia gravis, paralytic ileus, ulcerative colitis, MI

DISP: Cystospaz-M, Levsinex time-release capsules 0.375 mg; elixir (EtOH); solution 0.125 mg/5 mL; injectable 0.5 mg/mL; tablet 0.125 mg; tablet (Cystospaz) 0.15 mg; XR tablet (Levbid) 0.375 mg; SL (Levsin SL) 0.125 mg

SE: Dry skin, xerostomia, constipation, anticholinergic SE, heat prostration w/hot weather

NOTES: Administer tablets a.c.

HYOSCYAMINE, ATROPINE, SCOPOLAMINE, AND PHENOBARBITAL (DONNATAL, OTHERS)

USES: *Irritable bowel, spastic colitis, peptic ulcer,* spastic bladder

ACTION: Anticholinergic, antispasmodic

DOSE: 0.125–0.25 mg (1–2 tablets) t.i.d.–q.i.d., 1 capsule q12h (SR); 5–10 mL elixir t.i.d.–q.i.d. or q8h

CAUTION: [D, M]

CI: Narrow-angle glaucoma

DISP: Many combos/manufacturers. Capsules (Donnatal, others): Hyoscyamine 0.1037 mg/atropine 0.0194 mg/scopolamine 0.0065 mg/phenobarbital 16.2 mg. Tablets (Donnatal, others): Hyoscyamine 0.1037 mg/atropine 0.0194 mg/scopolamine 0.0065 mg/phenobarbital 16.2 mg. LA (Donnatal): Hyoscyamine 0.311 mg/atropine 0.0582 mg/scopolamine 0.0195 mg/phenobarbital 48.6 mg. Elixirs (Donnatal, others): Hyoscyamine 0.1037 mg/atropine 0.0194 mg/scopolamine 0.0065 mg/phenobarbital 16.2 mg/5 mL

SE: Sedation, xerostomia, constipation

IBANDRONATE (BONIVA)

USES: *Treat/prevent osteoporosis in postmenopausal women,* hypercalcuria

ACTION: Bisphosphonate, osteoclast-mediated bone-resorption, serum and urinary Ca2+

DOSE: 2.5 mg/d PO or 150 mg once a month on same day (do not lie down for 60 min after); 3 mg IV over 15–30 s q3mo

CAUTION: [C, ?/–]; avoid w/CrCl <30 mL/min

CI: Uncorrected Ca2+; inability to stand/sit upright for 60 min (PO)

DISP: Tablets 2.5, 150 mg; injectable IV 3 mg/3 mL

SE: Jaw osteonecrosis (avoid extensive dental procedures), N/D, headache, dizziness, asthenia, hypertension, infection, dysphagia, esophagitis, esophageal/gastric ulcer, musculoskeletal pain

NOTES: Take upon rising w/H2O (6–8 oz) >60 min before 1st food/beverage and any meds w/multivalent cations; give adequate Ca2+ and vitamin D supplements; possible association between bisphosphonates and severe muscle/bone/joint pain

IBUPROFEN (MOTRIN, MOTRIN IB, RUFEN, ADVIL, OTHERS) [OTC]

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis, pain, fever*

ACTION: NSAID

DOSE:

Adults: 200–800 mg PO b.i.d.–q.i.d. (max 2.4 g/d).

Peds: 30–40 mg/kg/d in 3–4 divided doses (max 40 mg/kg/d); w/food

CAUTION: [B, +]; may interfere w/aspirin's antiplatelet effect if given <8 hr before

CI: 3rd trimester pregnancy, severe hepatic impairment, allergy, use w/other NSAIDs, upper GI bleeding, ulcers

DISP: Tablets 100, 200, 400, 600, 800 mg; chew tablets 50, 100 mg; capsules 200 mg; suspension 100 mg/2.5 mL, 100 mg/5 mL, 40 mg/mL (Motrin IB and Advil OTC 200 mg are the OTC forms)

SE: Dizziness, peptic ulcer, platelet inhibition, worsening of renal insufficiency

IFOSFAMIDE (IFEX, HOLOXAN)

USES: Lung, breast, pancreatic, gastric cancers Hodgkin lymphoma/NHL, soft-tissue sarcoma

ACTION: Alkylating agent

DOSE: (Per protocol) 1.2 g/m2/d for 5 days bolus or continuous infusion; 2.4 g/m2/d for 3 d; w/mesna uroprotection; in renal/hepatic impairment

CAUTION: [D, M]; effect w/phenobarbital, carbamazepine, phenytoin; St. John's wort may levels

CI: Bone marrow function, pregnancy

DISP: Injectable 1, 3 g

SE: Hemorrhagic cystitis, nephrotoxicity, N/V, mild–mod leukopenia, lethargy/confusion, alopecia, hepatic enzyme

NOTES: Administer w/mesna to prevent hemorrhagic cystitis

IMIPENEM–CILASTATIN (PRIMAXIN)

USES: *Serious infections* due to susceptible bacteria

ACTION: Bactericidal; cell wall synthesis. Spectrum: Gram(+) (S. aureus, group A and B streptococci), gram(–) (not Legionella), anaerobes

DOSE:

Adults: 250–1,000 mg (imipenem) IV q6–8h, 500–750 mg IM.

Peds: 60–100 mg/kg/24 hr IV divided q6h; CrCl <70 mL/min

CAUTION: [C, ±]; probenecid toxicity

CI: Peds w/CNS infection (seizure risk) and <30 kg w/renal impairment

DISP: Injectable (imipenem/cilastatin) 250/250 mg, 500/500 mg

SE: Seizures if drug accumulates, GI upset, thrombocytopenia

IMIPRAMINE (TOFRANIL, TOFRANIL-PM)

WARNING: Close observation for suicidal thinking or unusual changes in behavior.

USES: *Depression, enuresis,* panic attack, chronic pain, retrograde ejaculation

ACTION: TCA; CNS synaptic serotonin or norepinephrine; time in REM sleep, vasopressin secretion, relaxes detrusor muscle

DOSE:

Adults: Hospitalized: Initial 100 mg/24 hr PO in divided doses; over several wks, 300 mg/d max. Outpatient: Maintenance 50–150 mg PO h.s., 300 mg/24 hr max. Retrograde ejaculation: 50 mg/d PO h.s.

Peds: Antidepressant: 1.5–5 mg/kg/24 hr divided daily–q.i.d. Enuresis: >6 yr: 0.9–1.5 mg/kg/d h.s.; typical dose 25 mg (5–8 yr); 50 mg for older children (max 50 mg for 6–12 yr, 75 mg for >12 yr); treat for 2–3 mo, then taper

CAUTION: [D, ?/–]

CI: MAOIs, narrow-angle glaucoma, acute recovery from MI, pregnancy, CHF, angina, CVD, arrhythmias

DISP: Tofranil: Tablets 10, 25, 50 mg; Tofranil-PM: Capsules 75, 100, 125, 150 mg

SE: Cardiovascular symptoms, dizziness, xerostomia, discolored urine

NOTES: Sedation than amitriptyline; discontinue if enuresis not better in 3 wk

IMIQUIMOD CREAM, 5% (ALDARA)

USES: *Anogenital warts, HPV, condylomata acuminata*, molluscum contagiosum

ACTION: Unknown; ? cytokine induction

DOSE: Apply 3 × week, leave on 6–10 hr and wash off w/soap and water, continue to 16 wks max

CAUTION: [B, ?]

CI: Component sensitivity

DISP: Single-dose packets 5% (250-mg cream)

SE: Local skin reactions

NOTES: Not a cure; may weaken condoms/vaginal diaphragms, wash hands before/after use

INDAPAMIDE (LOZOL)

USES: * Edema, hypertension,* hypercalcuria

ACTION: Similar action to thiazides; reduces urinary calcium levels

DOSE: 1.25–2.5 mg/d PO

CAUTION: [D, ?]; may hypotensive effects of ACE inhibitors, may prolong QTc intervals when used with other drugs (ciprofloxacin)

CI: Allergy to thiazides or sulfonamide drugs; anuria; renal insufficiency; pregnancy

DISP: Tablet 1.25, 2.5 mg

SE: Irritation, sepsis, other infections

NOTES: Once daily dosing, follow electrolytes and urinary calcium levels

INDIGO CARMINE INJECTION [INDIGOTINDISULFONATE]

USES: *Localization of ureteral orifices during cystoscopy,* identification of urinary tract injury intraoperatively

ACTION: Excreted and appears in urine as blue color usually within 10 min of injection

DOSE: 5 mL IV (preferred) or IM

CAUTION: [C, ?]

CI: Allergy to compound

DISP: 5 mg vials for injection; do not dilute or inject with other solutions

SE: Mild pressor, rare idiosyncratic reaction

NOTES: May transiently alter pulse oximeter; originally used as a renal function test

INTERFERON ALFA 2B (INTRON-A)

WARNING: Can cause or aggravate fatal or life-threatening neuropsychological, autoimmune, ischemic, and infectious disorders. Monitor closely.

USES: *Hairy cell leukemia, Kaposi sarcoma, melanoma, CML, chronic hep B and C, follicular NHL, condylomata acuminata,* RCC, superficial bladder cancer

ACTION: Antiproliferative; modulates host immune response; viral replication in infected cells

DOSE: Per protocols; IM and IV.

Adults: Condyloma (Intron A): 1 million U/lesion (max 5 lesions) 3 × wk for 3 wk. Bladder carcinoma in situ: High dose (50–100 MU) intravesically weekly; different regimens described; typically 6 wk. Bladder carcinoma, superficial BCG refractory: Used in combination with intravesical BCG (either standard or reduced dose BCG) with 50–100 million U interferon-2b for 6 wk; maintenance regimens described

CAUTION: [C/–]

CI: Benzyl alcohol sensitivity, decompensated liver disease, autoimmune disease, immunosuppressed, neonates, infants

DISP: Injectable powder 10, 18, 50 million U; multidose pen 3, 5, 10 million U/0.2 mL; multidose vial 6 million U/3 mL; 10 million U 2.5 mL (see also polyethylene glycol [PEG]-interferon)

SE: Flu-like symptoms, fatigue, anorexia, neurotoxicity at high doses; up to 40% neutralizing antibodies w/systemic therapy

NOTES: Not FDA approved for intravesical use; with systemic therapy follow baseline CXR and ECG; CBC w/diff/platelets (baseline and routinely), LFTs, creatinine, electrolytes, triglycerides, thyroid function tests (baseline and periodically during treatment). Interferon alpha-2a (Roferon), not interferon alpha 2b used in Avastin plus interferon trial of RCC (see “Bevacizumab”).

IRBESARTAN (AVAPRO)

USES: *Hypertension, diabetic nephropathy,* CHF

ACTION: Angiotensin II receptor antagonist

DOSE: 150 mg/d PO, may to 300 mg/d

CAUTION: [C (1st trimester; D 2nd/3rd), ?/–]

DISP: Tablets 75, 150, 300 mg

SE: Fatigue, BP, K

ISONIAZID (INH)

USES: *Treatment/prophylaxis of TB*

ACTION: Bactericidal; interferes w/mycolic acid synthesis, disrupts cell wall

DOSE:

Adults: Active TB: 5 mg/kg/24 hr PO or IM (usually 300 mg/d) or DOT: 15 mg/kg (max 900 mg) 3×/wk. Prophylaxis: 300 mg/d PO for 6–12 mo or 900 mg 2×/wk.

Peds: Active TB: 10–15 mg/kg/d daily–b.i.d. PO or IM 300 mg/d max. Prophylaxis: 10 mg/kg/24 hr PO; in hepatic/renal dysfunction

CAUTION: [C, +]; liver disease, dialysis; avoid EtOH

CI: Acute liver disease, history INH hepatitis

DISP: Tablets 100, 300 mg; syrup 50 mg/5 mL; injectable 100 mg/mL

SE: Hepatitis, peripheral neuropathy, GI upset, anorexia, dizziness, skin reaction

NOTES: Use w/2–3 other drugs for active TB, based on INH resistance patterns, when TB was acquired, and sensitivity results; prophylaxis usually w/INH alone. IM rarely used. Peripheral neuropathy w/pyridoxine 50–100 mg/d. See CDC guidelines (MMWR) for current recommendations.

ITRACONAZOLE (SPORANOX)

WARNING: Contraindicated w/cisapride, pimozide, quinidine, dofetilide, or levacetylmethadol. Serious cardiovascular events (eg, QT, torsade de pointes, VT, cardiac arrest, and/or sudden death) reported w/these meds and other CYP3A4 inhibitors. Do not use for onychomycosis w/ventricular dysfunction.

USES: *Fungal infections (aspergillosis, blastomycosis, histoplasmosis, candidiasis)*

ACTION: Azole antifungal, ergosterol synthesis

DOSE: 200 mg PO daily–b.i.d. (capsules w/meals or cola/grapefruit juice); PO solution on empty stomach; avoid antacids

CAUTION: [C, ?]; numerous interactions

CI: See warning; pregnancy or considering pregnancy; ventricular dysfunction

DISP: Capsules 100 mg; solution 10 mg/mL

SE: N/V, rash, hepatotoxic, K+, CHF, BP, neuropathy

NOTES: Solution and capsules are not interchangeable; useful in patients who cannot take amphotericin B; follow LFTs

IXABEPILONE (IXEMPRA)

WARNING: Contraindicated in combo w/capecitabine w/AST/ALT >2.5× ULN or bilirubin >1 × ULN due to toxicity and neutropenia-related death.

USES: *Metastatic/locally advanced breast cancer after failure of an anthracycline, a taxane, and capecitabine,* prostate cancer on protocol

ACTION: Microtubule inhibitor

DOSE: 40 mg/m2 IV over 3 hr q3wk

CAUTION: [D, ?/–]

CI: Hypersensitivity to Cremophor EL; baseline ANC <1,500 cells/mm3 or platelet <100,000 cells/mm3; AST or ALT >2.5 × ULN, bilirubin >1 × ULN

DISP: Injectable 15, 45 mg

SE: Neutropenia, leukopenia, anemia, thrombocytopenia, peripheral sensory neuropathy, fatigue/asthenia, myalgia/arthralgia, alopecia, N/V/D, stomatitis/mucositis

NOTES: Substrate CYP3A4; dose must be adjusted with strong CYP3A4 inhibitor/inducers

KETOCONAZOLE (NIZORAL)

WARNING: Oral use has risk of fatal hepatotoxicity. Concomitant terfenadine, astemizole, and cisapride are CI due to serious cardiovascular adverse events.

USES: *Systemic fungal infections (Candida, blastomycosis, histoplasmosis, etc.); refractory topical dermatophyte infection*; carcinoma of the prostate (CAP) when rapid testosterone needed or 2nd-line in hormone refractory CAP

ACTION: Azole, fungal cell wall synthesis; high dose blocks P450, testosterone production

DOSE: PO: 200 mg/d PO; to 400 mg/d PO for serious infection. CAP: 400 mg PO t.i.d. w/hydrocortisone 20–40 mg divided b.i.d.; best on empty stomach

CAUTION: [C, ±]; any agent that gastric pH absorption; may enhance anticoagulants; w/EtOH (disulfiram-like reaction); numerous interactions including statins, niacin

CI: CNS fungal infections, w/astemizole, triazolam

DISP: Tablets 200 mg

SE: N, rashes, hair loss, headache, weight gain, dizziness, disorientation, fatigue, impotence, hepatoxicity, adrenal suppression, acquired cutaneous adherence (sticky skin syndrome)

NOTES: Monitor LFTs; can rapidly testosterone levels; reduces circulating vitamin D3 levels by 30–40%

KETOCONAZOLE, TOPICAL (EXTINA, KURIC, NIZORAL AD SHAMPOO, XOLEGEL) [SHAMPOO—OTC]

USES: *Topical for seborrheic dermatitis, shampoo for dandruff,* local fungal infections due to dermatophytes and yeast

ACTION: Azole, fungal cell wall synthesis

DOSE: Topical: Apply once or twice daily

CAUTION: [C, ±]

CI: Broken/inflamed skin

DISP: Topical cream 2%; (Xolegel) gel 2%, (Extina) foam 2%, shampoo 1% and 2%

SE: Irritation, pruritus, stinging

NOTES: Do not dispense foam into hands.

KETOPROFEN (ORUDIS, ORUVAIL)

WARNING: May risk of cardiovascular events and GI bleeding; CI for perioperative pain in CABG surgery.

USES: *Arthritis (RA/OA), pain*

ACTION: NSAID; prostaglandins

DOSE: 25–75 mg PO t.i.d.–q.i.d., 300 mg/d/max; SR 200 mg/d; w/food; w/hepatic/renal impairment, elderly

CAUTION: [C (D 3rd trimester), –] w/ACE, diuretics; warfarin, lithium, MTX

CI: NSAID/ASA sensitivity

DISP: Capsules 50, 75 mg; capsules SR 200 mg

SE: GI upset, peptic ulcers, dizziness, edema, rash, BP, LFTs, renal dysfunction

KETOROLAC (TORADOL)

WARNING: For short-term (5 d) treatment of mod–severe acute pain; CI w/PUD, GI bleed, post-CABG, anticipated major surgery, severe renal insufficiency, bleeding diathesis, labor and delivery, nursing, and w/ASA/NSAIDs. NSAIDs may cause an increased risk of cardiovascular thrombotic events (MI, stroke). PO CI in peds <16 yr.

USES: *Pain*

ACTION: NSAID; prostaglandins

DOSE:

Adults: 15–30 mg IV/IM q6h; 10 mg PO q.i.d. only as continuation of IM/IV; max IV/IM 120 mg/d, max PO 40 mg/d.

Peds: 2–16 yr: 1 mg/kg IM × 1 dose; 30 mg max; IV: 0.5 mg/kg, 15 mg max; do not use for >5 d; if >65 yr, elderly, w/renal impairment, <50 kg

CAUTION: [C (D 3rd trimester), –]; w/ACE inhibitor, diuretics, BP meds, warfarin

CI: See “Warning.”

DISP: Tablets 10 mg; injectable 15 mg/mL, 30 mg/mL

SE: Bleeding, peptic ulcer disease, Cr and LFTs, BP, edema, dizziness, allergy

KUNECATECHINS [SINECATECHINS] (VEREGEN)

USES: *External genital/perianal warts*

ACTION: Unknown; green tea extract

DOSE: Apply 0.5-cm ribbon to each wart 3 × day until all warts clear; no >16 wk

CAUTION: [C; ?]

DISP: Ointment 15%

SE: Erythema, pruritus, burning, pain, erosion/ulceration, edema, induration, rash, phimosis

NOTES: Wash hands before/after use; not necessary to wipe off prior to next use; avoid on open wounds

LANTHANUM CARBONATE (FOSRENOL)

USES: *Hyperphosphatemia in renal disease*

ACTION: Phosphate binder

DOSE: 750–1,500 mg PO daily divided doses, w/or immediately p.c.; titrate q2–3wk based on PO42 levels

CAUTION: [C, ?/–]; no data in GI disease; not for peds

DISP: Chewable tablets 250, 500, 750, 1,000 mg

SE: N/V, graft occlusion, headache, BP

NOTES: Chew tablets before swallowing; separate from meds that interact with antacids by 2 hr

LEUCOVORIN (WELLCOVORIN)

USES: *Overdose of folic acid antagonist; megaloblastic anemia, augment 5-FU impaired MTX elimination; w/5-FU in colon cancer*

ACTION: Reduced folate source; circumvents action of folate reductase inhibitors (eg, MTX)

DOSE: Leucovorin rescue: 10 mg/m2 PO/IM/IV q6h; start within 24 hr after dose or 15 mg PO/IM/IV q6h, 25 mg/dose max PO. Folate antagonist overdose (eg, Pemetrexed): 100 mg/m2 IM/IV × 1 then 50 mg/m2 IM/IV q6h × 8 days 100 mg/m2 × 1. 5-FU adjuvant treatment, colon cancer per protocol; low dose: 20 mg/m2/d IV × 5 days w/5-FU 425 mg/m2/d IV × 5 d, repeat q4–5wk × 6; high dose: 500 mg/m2 IV every wk × 6, w/5-FU 500 mg/m2 IV every wk × 6 wk, repeat after 2 wk off × 4. Megaloblastic anemia: 1 mg IM/IV daily

CAUTION: [C, ?/–]

CI: Pernicious anemia

DISP: Tablets 5, 10, 15, 25 mg; injectable 50, 100, 200, 350, 500 mg

SE: Allergic reaction, N/V/D, fatigue, wheezing, platelet

NOTES: Monitor Cr, methotrexate levels q24h w/leucovorin rescue; do not use intrathecally/intraventricularly; w/5-FU CBC w/diff, platelet, LFTs, electrolytes

LEUPROLIDE (LUPRON, LUPRON DEPOT, LUPRON DEPOT-PED, VIADUR, ELIGARD)

USES: *Advanced carcinoma of the prostate (CAP) (all except Depot-Ped), endometriosis (Lupron), uterine fibroids (Lupron), and precocious puberty (Lupron-Ped)*

ACTION: LHRH agonist; paradoxically release of LHRH w/ LH from anterior pituitary; in men testosterone

DOSE:

Adults: CAP: Lupron DEPOT: 7.5 mg IM q28d or 22.5 mg IM q3mo or 30 mg IM q4mo. Eligard: 7.5 mg SQ q28d or 22.5 mg SQ q3mo or 30 mg SQ q4mo or 45 mg SQ 6 mo. Endometriosis (Lupron DEPOT): 3.75 mg IM every mo × 6 mo or 11.25 IM q3mo × 2 mo. Fibroids: 3.75 mg IM every mo × 3 mo or 11.25 mg IM × 1 mo.

Peds: CPP (Lupron DEPOT-Ped): 50 g/kg/d SQ injection; by 10 g/kg/d until total down-regulation achieved. <25 kg: Lupron DEPOT: 7.5 mg IM q4wk; >25–37.5 kg: 11.25 mg IM q4wk; >37.5 kg: 15 mg IM q4wk, by 3.75 mg q4wk until response

CAUTION: [X, –]; w/impending cord compression in CAP

CI: Abnormal uterine bleeding (AUB), implant in women/peds; pregnancy

DISP: Injectable 5 mg/mL; Lupron DEPOT 3.75 (1 mo for fibroids, endometriosis); Lupron DEPOT (for CAP) 7.5 mg (1 mo), 11.25 (3 mo), 22.5 (3 mo), 30 mg (4 mo); Eligard depot (for CAP; requires refrigerated storage) 7.5 (1 mo); 22.5 (3 mo), 30 (4 mo), 45 mg (6 mo); Viadur 65 mg 12-mo SQ implant (unavailable to new patients after April 2008); Lupron DEPOT-Ped 7.5, 11.25, 15 mg

SE: Hot flashes, gynecomastia, N/V, alopecia, anorexia, dizziness, headache, insomnia, paresthesias, depression exacerbation, peripheral edema, and bone pain (transient flare reaction at 7–14 days after the 1st dose [LH/testosterone surge before suppression]); bone marrow w/ >6 mo use; bone loss possible

NOTES: Nonsteroidal antiandrogen (eg, bicalutamide) may block flare in men w/CAP

LEVOFLOXACIN (LEVAQUIN)

WARNING: Risk Achilles tendon rupture and tendonitis

USES: *Skin/skin structure infection, UTI, chronic bacterial prostatitis, acute pyelo, acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, prostate cancer, including multidrug-resistant S. pneumoniae, nosocomial pneumonia; treat inhalational anthrax in adults and peds 6 mo*

ACTION: Quinolone, DNA gyrase. Spectrum: Excellent gram(+) coverage except MRSA and E. faecium; excellent gram(–) coverage except Stenotrophomonas maltophilia and Acinetobacter sp; poor anaerobic coverage

DOSE:

Adults: 18 yr: IV/PO: Bronchitis: 500 mg/d × 7 days. Anthrax: 500 mg/d × 60 d; Uncomp UTI: 250 mg/d × 3 days. Comp UTI/Acute pyelo: 250 mg/d × 10 days or 750 mg/d × 5 days. CrCl 10–19 mL/min: 250 mg, then 250 mg q48h or 750 mg, then 500 mg q48h. Hemodialysis: 750 mg, then 500 mg q48h. Uncomplicated urethral or endocervical gonorrhea if penicillin allergy (resistant strains in Asia, Hawaii, and California); 250 mg PO × 1 avoid in pregnancy.

Peds: 6 mo: Anthrax only >50 kg: 500 mg q 24h × 60 d. <50 kg: 8 mg/kg (250 mg/dose max) q12h for 60 days w/renal impairment; avoid antacids w/PO; PO solution 1 hr before, 2 hr p.c.

CAUTION: [C, –]; w/cation-containing products (eg, antacids), w/drugs that QT interval

CI: Quinolone sensitivity

DISP: Tablets 250, 500, 750 mg; premixed IV 250, 500, 750 mg; injectable 25 mg/mL; Leva-Pak 750 mg × 5 days

SE: N/D, dizziness, rash, GI upset, photosensitivity, CNS stimulant w/IV use, C. difficile enterocolitis; rare fatal hepatoxicity

NOTES: Use w/steroids tendon risk; only for anthrax in peds

LIDOCAINE; LIDOCAINE WITH EPINEPHRINE (ANESTACON TOPICAL, XYLOCAINE, XYLOCAINE VISCOUS, XYLOCAINE MPF OTHERS)

USES: *Local anesthetic, epidural/caudal anesthesia, regional nerve blocks, topical on mucous membranes (mouth/pharynx/urethra)*

ACTION: Anesthetic; stabilizes neuronal membranes; inhibits ionic fluxes required for initiation and conduction

DOSE:

Adults: Local injection anesthetic: 4.5 mg/kg max total dose or 300 mg; w/epinephrine 7 mg/kg or total 500 mg max dose. PO: 15 mL viscous swish and spit or pharyngeal gargle and swallow, do not use <3-hr intervals or >8 × in 24 hr. Urethra: 10–15 mL (200–300 mg) jelly in men, 5 mL female urethra; 600 mg/24 hr max.

Peds: Topical: Apply max 3 mg/kg/dose. Local injection anesthetic: Max 4.5 mg/kg

CAUTION: [B, +]; corn allergy; epi-containing solution may interact w/TCA or MAOI and cause severe BP

CI: Do not use lidocaine w/epi on digits, ears, or nose (vasoconstriction and necrosis)

DISP: Injectable local 0.5, 1, 1.5, 2, 4, 10, 20%; injectable w/epinephrine 0.5%/1:200,000, 1%/1:100,000, 2%/1:100,000; MPF 1%/1:200,000, 1.5%/1:200,000, 2%/1:200,000; dental formulations 2%/1:50,000, 2%/1:100,000; cream 2%; gel 2, 2.5%; ointment 2.5, 5%; liquid 2.5%; solution 2, 4%; viscous 2%

SE: Dizziness, paresthesias, convulsions associated w/toxicity

LIDOCAINE POWDER INTRADERMAL INJECTION SYSTEM (ZINGO)

USES: *Local anesthesia before venipuncture or IV in peds 3–18 yr*

ACTION: Local amide anesthetic

DOSE: Apply 3 min before procedure

CAUTION: [N/A, N/A] only on intact skin

CI: Lidocaine allergy

DISP: 6.5-inch device to administer under pressure 0.5 mg lidocaine powder in 2-cm area, single use

SE: Skin reaction, edema, petechiae

LIDOCAINE/PRILOCAINE (EMLA, LMX)

USES: *Topical anesthetic for intact skin or genital mucous membranes*; adjunct to phlebotomy or dermal procedures

ACTION: Amide local anesthetics

DOSE:

Adults: EMLA cream, anesthetic disc (1 g/10 cm2): Thick layer 2–2.5 g to intact skin, cover w/occlusive dressing (eg, Tegaderm) for at least 1 hr. Anesthetic disc: 1 g/10 cm2 for at least 1 hr.

Peds: Max dose: <3 mo or <5 kg: 1 g/10 cm2 for 1 hr. 3–12 mo and >5 kg: 2 g/20 cm2 for 4 hr. 1–6 yr and >10 kg: 10 g/100 cm2 for 4 hr. 7–12 yr and >20 kg: 20 g/200 cm2 for 4 hr

CAUTION: [B, +] Methemoglobinemia

CI: Use on mucous membranes, broken skin, eyes; allergy to amide-type anesthetics

DISP: Cream 2.5% lidocaine/2.5% prilocaine; anesthetic disc (1 g); periodontal gel 2.5/2.5%

SE: Burning, stinging, methemoglobinemia

NOTES: Longer contact time effect

LINDANE (KWELL, OTHERS)

WARNING: Only for patients intolerant of failed 1st-line therapy w/safer agents. Seizures and deaths reported w/repeat/prolonged use. Caution due to increased risk of neurotoxicity in infants, children, elderly, w/other skin conditions, and if <50 kg. Instruct on proper use and inform that itching occurs after successful killing of scabies or lice.

USES: *Head lice, pubic crab lice, body lice, scabies*

ACTION: Ectoparasiticide and ovicide

DOSE:

Adults and Peds Cream or lotion: Thin layer to dry skin after bathing, leave for 8–12 hr, pour on laundry. Shampoo: Apply 30 mL to dry hair, develop a lather w/warm water for 4 min, comb out nits

CAUTION: [C, ±]

CI: Premature infants, uncontrolled seizure disorders, open wounds

DISP: Lotion 1%; shampoo 1%

SE: Arrhythmias, seizures, local irritation, GI upset, ataxia, alopecia, N/V, aplastic anemia

NOTES: Caution w/overuse (may be absorbed); may repeat treatment in 7 d; try OTC 1st w/pyrethrins (Pronto, Rid, others)

LINEZOLID (ZYVOX)

USES: *Infections caused by gram(+) bacteria (including VRE), pneumonia, skin infections*

ACTION: Unique; binds ribosomal bacterial RNA; bacteriocidal for streptococci, bacteriostatic for enterococci and staphylococci. Spectrum: Excellent gram(+) coverage including VRE and MRSA

DOSE:

Adults: 400–600 mg IV or PO q12h.

Peds: 10 mg/kg IV or PO q8h (q12h in preterm neonates)

CAUTION: [C, ?/–]; w/reversible MAOI, avoid foods w/tyramine and cough/cold products w/pseudoephedrine; w/ bone marrow

DISP: Injectable 200, 600 mg; tablets 600 mg; suspension 100 mg/5 mL

SE: Lactic acidosis, peripheral/optic neuropathy, hypertension, N/D, headache, insomnia, GI upset, bone marrow, tongue discoloration

NOTES: Weekly CBC; not for gram() infection, deaths in catheter-related infections

LISINOPRIL (PRINIVIL, ZESTRIL)

WARNING: ACE inhibitors can cause fetal injury/death in 2nd/3rd trimester; discontinue w/pregnancy.

USES: *Hypertension, CHF, prevent diabetic nephropathy and acute MI*

ACTION: ACE inhibitor

DOSE: 5–40 mg/24 hr PO daily–b.i.d., CHF target 40 mg/d. AMI: 5 mg within 24 hr of MI, then 5 mg after 24 hr, 10 mg after 48 hr, then 10 mg/d; in renal insufficiency; use low dose, slowly in elderly

CAUTION: [D, –]

CI: Bilateral RAS, pregnancy, ACE inhibitor sensitivity (angioedema)

DISP: Tablets 2.5, 5, 10, 20, 30, 40 mg

SE: Dizziness, headache, cough, BP, angioedema, K+, Cr, rare bone marrow

NOTES: To prevent diabetic nephropathy, start when urinary microalbuminuria begins; BUN, Cr, K+, WBC

LOMEFLOXACIN (MAXAQUIN)

USES: *UTI, acute exacerbation of chronic bronchitis; prophylaxis in transurethral procedures*

ACTION: Quinolone antibiotic; DNA gyrase. Spectrum: Good gram(–) coverage including H. influenzae except Stenotrophomonas maltophilia, Acinetobacter sp, and some P. aeru-

ginosa

DOSE: 400 mg/d PO; w/renal insufficiency, avoid antacids

CAUTION: [C, –]; interactions w/cation-containing products

CI: Quinolone allergy, children <18 yr, QT interval, K+

DISP: Tablets 400 mg

SE: N/V/D, abdominal pain, photosensitivity, seizures, headache, dizziness, tendon rupture, peripheral neuropathy, pseudomembranous colitis, anaphylaxis

LOSARTAN (COZAAR)

WARNING: Can cause fatal injury and death if used in 2nd/3rd trimesters. Discontinue therapy if pregnancy detected.

USES: *Hypertension (HTN), diabetic nephropathy, prevent CVA in HTN and LVH*

ACTION: Angiotensin II receptor antagonist

DOSE:

Adults: 25–50 mg PO daily–b.i.d., max 100 mg; in elderly/hepatic impairment.

Peds: 6 yr: HTN: Initial 0.7 mg/kg/d, to 50 mg/d PRN; 1.4 mg/kg/d or 100 mg/d max

CAUTION: [C (1st trimester, D 2nd and 3rd trimester), ?/–]; w/NSAIDs; w/K+-sparing diuretics, supplement may cause K+; w/renal artery stenosis (RAS), hepatic impairment

CI: Pregnancy, component sensitivity

DISP: Tablets 25, 50, 100 mg

SE: BP in patients on diuretics; K+; GI upset, facial/angioedema, dizziness, cough, weakness, renal function

LYMPHOCYTE IMMUNE GLOBULIN [ANTITHYMOCYTE GLOBULIN, ATG] (ATGAM)

WARNING: Should only be used by physician experienced in immunosuppressive treatments or management of solid-organ and/or bone marrow transplant. Adequate lab and supportive medical resources must be readily available in the facility for patient management.

USES: *Allograft rejection in renal transplant; aplastic anemia if not candidates for bone marrow transplant,* prevent rejection of other solid-organ transplants, graft vs. host disease (GVHD) after bone marrow transplant

ACTION: Circulating T lymphocytes; human/equine product

DOSE:

Adults: Prevent rejection: 15 mg/kg/d IV × 14 d, then every other day × 14 d; initial dose within 24 hr before/after transplant. Treat rejection: Same except use 10–15 mg/kg/d; max 21 doses in 28 days.

Peds: Prevent rejection: 5–25 mg/kg/d IV

CAUTION: [C, –]

CI: History reaction to other equine -globulin preparation, leukopenia, thrombocytopenia

DISP: Injectable 50 mg/mL

SE: Discontinue w/severe thrombocytopenia/leukopenia; rash, fever, chills, BP, headache, K+, CP, edema, N/V/D, lightheadedness

NOTES: Test dose: 0.1 mL 1:1,000 dilution in NS, a systemic reaction precludes use; give via central line; consider pretreatment w/antipyretic, antihistamine, and/or corticosteroids

MAGNESIUM OXIDE (MAG-OX 400, OTHERS) [OTC]

USES: *Replace low Mg2+ levels,* reduce urinary oxylate taken with pyridoxine, hypomagnesuria

ACTION: Mg supplement, urinary oxylate

DOSE: 400–800 mg/d or divided w/food in full glass of H2O; urolithiasis 20–40 mEq (1–2 tablets Mag-Ox 400) PO b.i.d.–t.i.d.; w/renal impairment

CAUTION: [B, +]; w/neuromuscular disease and renal impairment, w/bisphosphonates, calcitriol, calcium channel blockers, neuromuscular blockers, tetracyclines, quinolones

CI: Ulcerative colitis, diverticulitis, ileostomy/colostomy, heart block

DISP: Capsules 140, 250, 500, 600 mg; tablets (Mag-Ox 400) 400 mg (Mg 20 mEq; equivalent to elemental magnesium 242 mg)

SE: D, N

NOTES: Hypermagnesemia and toxicity may occur w/renal impairment w/>50 mEq/d Mg2+ due to decreased clearance; ~5–20% of PO administered Mg2+ salts can be systemically absorbed; hypomagnesuria is an uncommon cause of urolithiasis but can be associated with inflammatory bowel disease.

MAGNESIUM SULFATE (VARIOUS)

USES: *Replace low Mg2+; preeclampsia, eclampsia, and premature labor, cardiac arrest, acute MI arrhythmias, cerebral edema, barium poisoning, seizures, pediatric acute nephritis*; refractory K+ and Ca2+

ACTION: Mg2+ supplement, bowel evacuation, acetylcholine in nerve terminals, rate of sinoatrial node firing

DOSE:

Adults: 3 g PO q6h × 4 PRN. Supplement: 1–2 g IM or IV; repeat PRN.

Peds: 25–50 mg/kg/dose IM, IV, IO q4–6h for 3–4 doses; repeat PRN; q8–12h in neonates; max 2 g single dose; dose w/low urinary output or renal insufficiency

CAUTION: [A/C (manufacturer specific), +]; w/neuromuscular disease; interactions see “Magnesium Oxide and Aminoglycosides”

CI: Heart block, renal failure

DISP: Premixed injectable: 10, 20, 40, 80 mg/mL; injectable 125, 500 mg/mL; oral/topical powder 227, 454, 480, 1,810, 1,920, 2,721 g

SE: CNS depression, diarrhea, flushing, heart block, BP, vasodilation

NOTES: Different formulation may contain Al2+

MANNITOL (VARIOUS)

USES: *Cerebral edema, intraocular pressure, renal impairment, poisonings, GU irrigation*

ACTION: Osmotic diuretic

DOSE: Test dose: 0.2 g/kg/dose IV over 3–5 min; if no diuresis within 2 hr, discontinue. Oliguria: 50–100 g IV over 90 min. IOP: 0.5–2 g/kg IV over 30 min

CAUTION: [C, ?/M]; w/CHF or volume overload, w/nephrotoxic drugs and lithium

CI: Anuria, dehydration, heart failure, PE

DISP: Injectable 5, 10, 15, 20, 25%; GU solution 5%

SE: May exacerbate CHF, N/V/D, / BP, HR

NOTES: Monitor for volume depletion; useful for partial nephrectomy renal artery clamping to protect kidney short-term

MEGESTROL ACETATE (MEGACE, MEGACE-ES)

USES: *Breast/endometrial cancers; appetite stimulant in cachexia (cancer/HIV)*

ACTION: Hormone; antileuteinizing; progesterone analog

DOSE: Cancer: 40–320 mg/d PO in divided doses. Appetite: 800 mg/d PO divided dose or Megace ES 625 mg/d

CAUTION: [X, –]; thromboembolism; handle w/care

CI: Pregnancy

DISP: Tablets 20, 40 mg; suspension 40 mg/mL; Megace ES 125 mg/mL

SE: DVT, edema, menstrual bleeding, photosensitivity, N/V/D, headache, mastodynia, CA, glucose, insomnia, rash, bone marrow, BP, CP, palpitations

NOTES: Do not discontinue abruptly; Megace ES not equivalent to others mg/mg; Megace ES approved only for anorexia

MEPERIDINE (DEMEROL, MEPERITAB) [C-II]

USES: *Mod–severe pain,* postop shivering, rigors from amphotericin B

ACTION: Narcotic analgesic

DOSE:

Adults: 50–150 mg PO or IV/IM/SQ q3–4h PRN.

Peds: 1–1.5 mg/kg/dose PO or IM/SQ q3–4h PRN, up to 100 mg/dose; in elderly/hepatic impairment, avoid in renal impairment

CAUTION: [C/D (prolonged use or high dose at term), +]; seizure threshold, adrenal insufficiency, head injury, ICP, hepatic impairment, not OK in sickle cell disease

CI: W/MAOIs, renal failure, pregnancy

DISP: Tablets 50, 100 mg; syrup/solution 50 mg/5 mL; injectable 10, 25, 50, 75, 100 mg/mL

SE: Respiratory/CNS depression, seizures, sedation, constipation, BP, rash N/V, biliary/urethral spasms, dyspnea

NOTES: Analgesic effects potentiated w/hydroxyzine; 75 mg IM = 10 mg morphine IM; not best in elderly; do not use PO for acute pain; not OK for repetitive use in ICU setting

MEROPENEM (MERREM)

USES: *Intra-abdominal infections, bacterial meningitis, skin infection*

ACTION: Carbapenem; cell wall synthesis. Spectrum: Excellent gram(+) coverage (except MRSA, methicillin-resistant S. epidermidis [MRSE] and E. faecium); excellent gram(–) coverage including extended-spectrum -lactamase producers; good anaerobic coverage

DOSE:

Adults: Abdominal infection: 1 to 2 g IV q8h. Skin infection: 50 mg IV q8h. Meningitis: 2 g IV q8h.

Peds: 3 mo, <50 kg Abdominal infection: 20 mg/kg IV q8h. Skin infection: 20 mg/kg IV q8h. Meningitis: 40 mg/kg IV q8h.

Peds: >50 kg Use adult dose; max 2 g IV q8h; in renal insufficiency (see insert)

CAUTION: [B, ?]; w/probenecid, VPA

CI: -Lactam sensitivity

DISP: Injectable 1 g, 500 mg

SE: Less seizure potential than imipenem; C. difficile enterocolitis, diarrhea, platelet

NOTES: Overuse bacterial resistance

MESNA (MESNEX)

USES: *Prevent hemorrhagic cystitis due to ifosfamide or cyclophosphamide*

ACTION: Antidote; reacts with acrolein and other metabolites to form stable compounds

DOSE: Per protocol; dose as% of ifosfamide or cyclophosphamide dose. IV bolus: 20% (eg, 10–12 mg/kg) IV at 0, 4, and 8 hr, then 40% at 0, 1, 4, and 7 hr. IV infusion: 20% pre-chemotherapy, 50–100% w/chemotherapy, then 25–50% for 12 hr following chemotherapy. Oral: 100% ifosfamide dose given as 20% IV at hour 0 then 40% PO at hours 4 and 8; if PO dose vomited, repeat or give dose IV; mix PO w/juice

CAUTION: [B; ?/–]

CI: Thiol sensitivity

DISP: Injectable 100 mg/mL; tablets 400 mg

SE: BP, platelet, HR, RR allergic reactions, headache, GI upset, taste perversion

NOTES: Hydration helps hemorrhagic cystitis; higher dose for bone marrow transplant; IV contains benzyl alcohol

METHENAMINE HIPPURATE (HIPREX), METHENAMINE MANDELATE (UROQUID-ACID NO. 2)

USES: *Suppress recurrent UTI long-term. Use only after infection cleared by antibiotics*

ACTION: Converted to formaldehyde and ammonia in acidic urine; nonspecific bactericidal action

DOSE:

Adults: Hippurate: 1 g PO b.i.d. Mandelate: Initial 1 g q.i.d.; PO p.c. and h.s., maintenance 1–2 g/d.

Peds: 6–12 yr: Hippurate: 0.5–1 g PO b.i.d.; PO divided b.i.d. >2 yr: Mandelate: 50–75 mg/kg/d PO divided q.i.d.; take w/food, ascorbic acid w/hydration

CAUTION: [C, +]

CI: Renal insufficiency, severe hepatic disease, severe dehydration

DISP: Methenamine hippurate (Hiprex, Urex): Tablets 1 g. Methenamine mandelate 500 mg, 1 g EC tablets

SE: Rash, GI upset, dysuria, LFTs, superinfection w/prolonged use, C. difficile-associated diarrhea

NOTES: Use w/sulfonamides may precipitate in urine. Hippurate not indicated in peds <6 yr. Not for patients w/indwelling catheters, as dwell time is required for action

METHOTREXATE (RHEUMATREX DOSE PACK, TREXALL)

WARNING: Administration only by experienced physician; do not use in women of childbearing age unless absolutely necessary (teratogenic); impaired elimination w/impaired renal function, ascites, pleural effusion; severe bone marrow w/NSAIDs; hepatotoxic, occasionally fatal; can induce life-threatening pneumonitis. Diarrhea and ulcerative stomatitis require discontinuation; lymphoma risk; may cause tumor lysis syndrome; can cause severe skin reaction, opportunistic infections; w/RT can tissue necrosis risk. Preservatives make this agent unsuitable for intrathecal or higher-dose use.

USES: *ALL; AML; leukemic meningitis; trophoblastic tumors (choriocarcinoma, hydatidiform mole); breast, lung, head, neck cancers; Burkitt lymphoma; mycosis fungoides; osteosarcoma; Hodgkin disease/NHL; psoriasis; RA/JRA,* chronic disease

ACTION: Dihydrofolate reductase-mediated product of tetrahydrofolate, causes DNA synthesis

DOSE:

Adults: Cancer: Per protocol. RA: 7.5 mg/wk PO 1/wk 1 or 2.5 mg q12h PO for 3 doses/wk.

Peds: 10 mg/m2 PO/IM every wk, then 5–14 mg/m2 × 1 or as 3 divided doses 12 hr apart; elderly, w/renal/hepatic impairment

CAUTION: [D, –]; w/other nephro-/hepatotoxic meds, multiple interactions, w/seizure, profound bone marrow other than cancer-related

CI: Severe renal/hepatic impairment, pregnancy/lactation

DISP: Dose pack 2.5 mg in 8, 12, 16, 20, or 24 doses; tablets 2.5, 5, 7.5, 10, 15 mg; injectable 25 mg/mL; injectable powder 20 mg, 1 g

SE: Bone marrow, N/V/D, anorexia, mucositis, hepatotoxicity (transient and reversible; may progress to atrophy, necrosis, fibrosis, cirrhosis), rashes, dizziness, malaise, blurred vision, alopecia, photosensitivity, renal failure, pneumonitis; rare pulmonary fibrosis; chemical arachnoiditis and headache w/IT delivery

NOTES: Monitor CBC, LFTs, Cr, MTX levels and CXR; high dose >500 mg/m2 requires leucovorin rescue to toxicity; w/intrathecal, use preservative-/alcohol-free solution. Systemic levels: Therapeutic: >0.01 micromole; Toxic >10 micromoles over 24 hr

METHYLENE BLUE INJECTION 1%

USES: *Drug-induced methemoglobinuria,* visualization of fistula and urinary tract injury intraoperatively, local injection to dye to facilitate intraoperative identification

ACTION: Low IV dose converts methemoglobin to hemoglobin; excreted and appears in urine as green/green blue color

DOSE: 0.1–0.2 mL/kg body weight IV; direct instillation into fistulous tract or into urinary tract

CAUTION: [?/?]

CI: Allergy to compound

DISP: 1, 10 mL ampules for injection

SE: IV use: Nausea, abdominal, chest pain, sweating

NOTES: Stains tissue blue, limiting repeat use when used for surgical visualization; limited experience to treat ifosfamide neurotoxicity

METRONIDAZOLE (FLAGYL, METROGEL)

WARNING: Carcinogenic in rats.

USES: *Bone/joint, endocarditis, intra-abdominal, meningitis, and skin infections; amebiasis and amebic liver abscess; trichomoniasis in patient/partner; bacterial vaginosis; PID; giardiasis; antibiotic-associated pseudomembranous colitis (C. difficile), eradicate H. pylori w/combo therapy, rosacea, prophylactic in postop colorectal surgery*

ACTION: Interferes w/DNA synthesis. Spectrum: Excellent anaerobic, C. difficile coverage

DOSE:

Adults: Anaerobic infections: 500 mg IV q6–8h. Trichomonas: 250 mg PO t.i.d. for 7 days or 2 g PO × 1 (treat partner). C. difficile: 500 mg PO or IV q8h for 7–10 days (PO preferred; IV only if NPO); if no response, change to PO vancomycin. Vaginosis: 1 applicator intravaginally every day or b.i.d. × 5 d, or 500 mg PO b.i.d. × 7 days or 750 mg PO every day × 7 days.

Peds: 30 mg/kg PO/IV/d divided q6H, 4 g/d max divided. Trichomonas: 15–30 mg/kg/d PO divided q8h × 7 days. C. difficile: 20 mg/kg/d PO divided q6h × 10 d, max 2 g/d; w/severe hepatic/renal impairment

CAUTION: [B, ±]; avoid EtOH, w/warfarin, CYP3A4 substrates, lithium levels

CI: 1st trimester of pregnancy

DISP: Tablets 250, 500 mg; XR tablets 750 mg; capsules 375 mg; IV 500 mg/100 mL; lotion 0.75%; gel 0.75, 1%; intravaginal gel 0.75% (5 g/applicator 37.5 mg in 70-g tube), cream 0.75, 1%

SE: Disulfiram-like reaction; dizziness, headache, GI upset, anorexia, urine discoloration, flushing, metallic taste

NOTES: For trichomoniasis, treat patient's partner; no aerobic bacteria activity; use in combo for serious mixed infections; wait 24 hr after 1st dose to breast-feed or 48 hr if extended therapy, take ER on empty stomach

MICONAZOLE (MONISTAT 1 COMBO, MONISTAT 3, MONISTAT 7) [OTC] (MONISTAT-DERM)

USES: *Candidal infections, dermatomycoses (tinea pedis/cruris/corporis/versicolor, Candidiasis)*

ACTION: Azole antifungal, alters fungal membrane permeability

DOSE: Intravaginally: 100 mg/d suppository or 2% cream intravaginally h.s. × 7 days or 200 mg suppository or 4% cream intravaginally h.s. × 3 days. Derm: Apply b.i.d., AM/PM Tinea versicolor: Apply once daily. Treat tinea pedis for 1 mo and other infections for 2 wk.

Peds: 12 yr: 100 mg suppository or 2% cream intravaginally h.s. × 7 days or 200 mg suppository or 4% cream intravaginally h.s. × 3

CAUTION: [C, ?]; azole sensitivity

DISP: Monistat-Derm: (Rx) cream 2%; Monistat 1 Combo: 2% cream w/1,200 mg suppository, Monistat 3: vaginal cream 4%, suppository 200 mg; Monistat 7: cream 2%, suppository 100 mg; lotion 2%; powder 2%; effervescent tablet 2%, ointment 2%, spray 2%; vaginal suppository 100, 200, 1,200 mg; vaginal cream 2%, 4%; [OTC]

SE: Vaginal burning; skin contact dermatitis, irritation, burning

NOTES: May interfere w/condom and diaphragm, do not use w/tampons

MICONAZOLE/ZINC OXIDE/PETROLATUM (VUSION)

USES: *Candidal diaper rash*

ACTION: Combo antifungal

DOSE:

Peds: >4 wk: Apply at each diaper change × 7 days

CAUTION: [C, ?]

CI: None

DISP: Miconazole/zinc oxide/petrolatum ointment 0.25/15/81.35%, 50-, 90-g tube

SE: None

NOTES: Keep diaper dry, not for prevention

MINERAL OIL-PRAMOXINE HCL-ZINC OXIDE (TUCKS OINTMENT, [OTC])

USES: *Temporary relief of anorectal disorders (itching, etc.)*

ACTION: Topical anesthetic

DOSE:

Adults and Peds: 12 yr. Cleanse, rinse, and dry, apply externally or into anal canal w/tip 5 × d for 7 days max.

CAUTION: [?/?]; do not place into rectum

CI: None

DISP: Ointment 30-g tube

SE: Local irritation

NOTES: Discontinue w/or if rectal bleeding occurs or if condition worsens or does not improve within 7 d

MINOCYCLINE (DYNACIN, MINOCIN, SOLODYN)

USES: *Mod–severe non-nodular acne (Solodyn), anthrax, rickettsiae, gonococcus, skin infection, URI, UTI, nongonococcal urethritis, amebic dysentery, asymptomatic meningococcal carrier, Mycobacterium marinum*

ACTION: Tetracycline, bacteriostatic, protein synthesis

DOSE:

Adults and Peds: >12 yr: Usual: 200 mg, then 100 mg q12h or 100–200 mg, then 50 mg q.i.d. Gonococcal urethritis, men: 100 mg q12h × 5 days. Syphilis: Usual dose × 10–15 days. Meningococcal carrier: 100 mg q12h × 5 days. M. marinum: 100 mg q12h × 6–8 wk. Uncomp urethral, endocervical, or rectal infection: 100 mg q12h × 7 days minimum.

Adults and Peds: >12 yr Acne: (Solodyn): 1 mg/kg/d PO day × 12 wk. >8 yr: 4 mg/kg initially then 2 mg/kg q12h w/food to irritation, hydrate well, dose or extend interval w/renal impairment

CAUTION: [D, –]; associated w/pseudomembranous colitis, w/renal impairment, may OCP, or w/warfarin may INR

CI: Allergy, women of childbearing potential

DISP: Tablets 50, 75, 100 mg; tablets ER (Solodyn) 45, 90, 135 mg, capsules (Minocin) 50, 100 mg; suspension 50 mg/mL

SE: D, headache, fever, rash, joint pain, fatigue, dizziness, photosensitivity, hyperpigmentation, SLE syndrome, pseudotumor cerebri

NOTES: Do not cut/crush/chew; keep away from children, tooth discoloration in <8 yr or w/use during last half of pregnancy

MITOMYCIN (MUTAMYCIN)

WARNING: Administer only by physician experienced in chemotherapy; myelosuppressive; can induce HUS with irreversible renal failure.

USES: *Stomach, pancreas,* breast, colon cancers; SCC of the anus; non-small cell lung cancer, head and neck, cervical; bladder cancer (intravesically)

ACTION: Alkylating agent; generates oxygen-free radicals w/DNA strand breaks

DOSE: (Per protocol) 20 mg/m2 q6–8wk IV or 10 mg/m2 combo w/other myelosuppressive drugs q6–8wk. Bladder cancer: 20–40 mg in 40 mL NS via a urethral catheter once a week × 8 wk, followed by monthly × 12 mo for 1 yr; in renal/hepatic impairment

CAUTION: [D, –]

CI: Plt, WBC, coagulation disorders, Cr >1.7 mg/dL, cardiac toxicity w/vinca alkaloids/doxorubicin

DISP: Injectable 5, 20, 40 mg

SE: Bone marrow (persists for 3–8 wk, may be cumulative; minimize w/lifetime dose <50–60 mg/m2), N/V, anorexia, stomatitis, renal toxicity, microangiopathic hemolytic anemia w/renal failure (HUS), venoocclusive liver disease, interstitial pneumonia, alopecia, extravasation reactions, contact dermatitis; CHF

NOTES: Avoid urine contact with skin due to contact dermatitis risk

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: *Inoperable adrenocortical carcinoma (functioning/nonfunctioning)

ACTION: Adrenal cytotoxic agent, exact mechanism not known; may alter mitochondria and decreases cortisol production (ortho-para-DDD)

DOSE: 2–6 gm/d in divided dose t.i.d.–q.i.d.; increase as tolerated to maximum tolerated dose (generally 2–18 gm/d); decrease dose with side effects; administer with glucocorticoid

and if needed mineralocorticoid replacement

CAUTION: [C/?]; increases warfarin metabolism

CI: Hypersensitivity to compound

DISP: Tablets 500 mg

SE: Adrenal insufficiency, GI distress, depression, lethargy, somnolence, dizziness, vertigo, orthostasis

NOTES: Neuropsychiatric testing with use >2 yr; higher doses of glucocorticoid required due to metabolism; treat until there is no clinical benefit

MITOXANTRONE (NOVANTRONE)

WARNING: Administer only by physician experienced in chemotherapy; except for acute leukemia, do not use w/ANC count of <1,500 cells/mm3; severe neutropenia can result in infection, follow CBC; cardiotoxic (CHF), secondary AML reported.

USES: *AML (w/cytarabine), ALL, CML, prostate/lung cancers, MS*, breast cancer, NHL

ACTION: DNA-intercalating agent; DNA synthesis by interacting with topoisomerase II

DOSE: Per protocol; w/hepatic impairment, leukopenia, thrombocytopenia

CAUTION: [D, –]; reports of secondary AML, w/MS cardiovascular risk, do not treat MS patients w/low LVEF

CI: Pregnancy, significant in LVEF

DISP: Injectable 2 mg/mL

SE: Bone marrow, N/V, stomatitis, alopecia (infrequent), cardiotoxicity, urine discoloration; secretions and scleras may be blue-green

NOTES: Maintain hydration; baseline cardiovascular evaluation w/ECG and LVEF; cardiac monitoring prior to each dose; not for intrathecal use

MOEXIPRIL (UNIVASC)

WARNING: ACE inhibitors can cause fatal injury/death in 2nd/3rd trimester; discontinue w/pregnancy.

USES: *Hypertension, post-MI,* diabetic nephropathy

ACTION: ACE inhibitor

DOSE: 7.5–30 mg in 1–2 divided doses 1 hr a.c.; in renal impairment

CAUTION: [C (1st trimester, D 2nd and 3rd trimester), ?]

CI: ACE inhibitor sensitivity

DISP: Tablets 7.5, 15 mg

SE: BP, edema, angioedema, headache, dizziness, cough, K+

MORPHINE (AVINZA XR, ASTRAMORPH/PF, DURAMORPH, INFUMORPH, MS CONTIN, KADIAN SR, ORAMORPH SR, ROXANOL) [C-II]

WARNING: Do not crush/chew SR/CR forms.

USES: *Severe pain*, AMI

ACTION: Narcotic analgesic; SR/CR forms for chronic use

DOSE:

Adults: Short-term use PO: 5–30 mg q4h PRN. IV/IM: 2.5–15 mg q2–6h. Suppository: 10–30 mg q4h. SR formulations 15–60 mg q8–12h (do not chew/crush). IT/epidural (Duramorph, Infumorph, Astramorph/PF): Per protocol in infusion device.

Peds: >6 mo: 0.1–0.2 mg/kg/dose IM/IV q2–4h PRN to 15 mg/dose max; 0.2–0.5 mg/kg PO q4–6h PRN; 0.3–0.6 mg/kg SR tablets PO q12h; 2–4 mg IV (over 1–5 min) q5–30 min (ECC 2005)

CAUTION: [C, ±]; severe respiratory depression possible, w/head injury

CI: Severe asthma, respiratory depression, GI obstruction

DISP: IR tablets 15, 30 mg; solution 10, 20, 100 mg/5 mL; suppository 5, 10, 20, 30 mg; injectable 2, 4, 5, 8, 10, 15, 25, 50 mg/mL; MS Contin CR tablets 15, 30, 60, 100, 200 mg; Oramorph SR tablets 15, 30, 60, 100 mg; Kadian SR capsules 10, 20, 30, 50, 60, 80, 100 mg; Avinza XR capsules 30, 60, 90, 120 mg; Duramorph/Astramorph PF injectable 0.5, 1 mg/mL; Infumorph 10, 25 mg/mL

SE: Narcotic SE (respiratory depression, sedation, constipation, N/V, pruritus, diaphoresis, urinary retention, biliary colic), granulomas w/IT

NOTES: May require scheduled dosing to relieve severe chronic pain

MOXIFLOXACIN (AVELOX)

WARNING: Increase risk of tendon rupture and tendonitis.

USES: *Acute sinusitis/bronchitis, skin/soft-tissue/intra-abdominal infections, conjunctivitis, community-acquired pneumonia

ACTION: 4th-generation quinolone; DNA gyrase. Spectrum: Excellent gram(+) coverage except MRSA and E. faecium; good gram(–) coverage except P. aeruginosa, Stenotrophomonas maltophilia, Acinetobacter sp; good anaerobic coverage

DOSE: 400 mg/d PO/IV; avoid cation products, antacids; t.i.d.

CAUTION: [C, ?/–]; quinolone sensitivity; interactions w/Mg, Ca, Al, Fe-containing products, and class IA and III antiarrhythmic agents

CI: Quinolone/component sensitivity

DISP: Tablets 400 mg; ABC Pak 5 tablets; injectable

SE: Dizziness, N, QT prolongation, seizures, photosensitivity, tendon rupture

MUPIROCIN (BACTROBAN, BACTROBAN NASAL)

USES: *Impetigo (ointment); skin lesion infect w/S. aureus or S. pyogenes; eradicate MRSA in nasal carriers*

ACTION: Bacterial protein synthesis

DOSE: Topical: Apply small amount t.i.d × 5–14 days. Nasal: Apply 1/2 single-use tube b.i.d. in nostrils × 5 days

CAUTION: [B, ?]

CI: Do not use w/other nasal products

DISP: Ointment 2%; cream 2%; nasal ointment 2% 1-g single-use tubes

SE: Local irritation, rash

NOTES: Patient to contact health-care provider if no improvement in 3–5 d

MUROMONAB-CD3 (ORTHOCLONE OKT3)

WARNING: Can cause anaphylaxis; monitor fluid status; cytokine release syndrome.

USES: *Acute rejection following organ transplantation*

ACTION: Murine antibody, blocks T-cell function

DOSE: Per protocol

Adults: 5 mg/d IV for 10–14 days.

Peds: <30 kg: 2.5 mg/d. >30 kg: 5 mg/d IV for 10–14 days

CAUTION: [C, ?/–]; w/history of seizures, pregnancy, uncontrolled hypertension

CI: Murine sensitivity, fluid overload

DISP: Injectable 5 mg/5 mL

SE: Anaphylaxis, pulmonary edema, fever/chills w/1st dose (premedicate w/steroid/acetaminophen/antihistamine); cytokine release syndrome (BP, fever, rigors)

NOTES: Monitor during infusion; use 0.22–micron filter

MYCOPHENOLIC ACID (MYFORTIC)

WARNING: Risk of infections, lymphoma, other cancers; PML, risk of pregnancy loss and malformation, women of childbearing potential must use contraception.

USES: *Prevent rejection after renal transplant*

ACTION: Cytostatic to lymphocytes

DOSE:

Adults: 720 mg PO b.i.d.

Peds: BSA 1.19–1.58 m2: 540 mg b.i.d. BSA >1.8 m2: Adult dose; used w/steroids and cyclosporine w/renal insufficiency/neutropenia; take on empty stomach

CAUTION: [D, ?/–]

CI: Component allergy

DISP: Delayed-release tablets 180, 360 mg

SE: N/V/D, pain, fever, headache, infection, hypertension, anemia, leukopenia, edema

MYCOPHENOLATE MOFETIL (CELLCEPT), MYCOPHENOLATE ACID (MYFORTIC)

WARNING: Risk of infections, lymphoma, other cancers; PML; risk of pregnancy loss and malformation; women of childbearing potential must use contraception.

USES: *Prevent organ rejection after transplant*

ACTION: Impairs B- and T-cell proliferation

DOSE:

Adults: Renal transplantation: CellCept: 1 g PO b.i.d. (dose > 2 g/d not recommended) or 1 g IV b.i.d. Myfortic: 720 mg PO b.i.d.

Peds: Renal transplantation: CellCept: 600 mg/m2/dose b.i.d.; 1 g b.i.d. max. Alternative dosing: BSA 1.25–1.5 m2: 750 mg PO b.i.d. BSA >1.5 m2: 1 g PO b.i.d. Myfortic: 400 mg/m2/dose b.i.d.; 720 mg PO b.i.d. max. BSA <1.19 m2: This formulation not recommended. BSA 1.19–1.58 m2: 540 mg PO b.i.d. 1,080 mg/d max. BSA >1.58 m2: 720 mg PO b.i.d. 1,440 mg/d max; dose in renal insufficiency or neutropenia

CAUTION: [D, ?/–]

CI: Component allergy; IV use in polysorbate 80 allergy

DISP: CellCept capsules 250, tablet 500 mg; suspension 200 mg/mL, injectable 500 mg; Myfortic delayed-release tablet 180, 360 mg

SE: N/V/D, pain, fever, headache, infection, hypertension, anemia, leukopenia, edema

NOTES: Used w/steroids and cyclosporine; use up to 14 days IV, then switch to PO. IV: Infuse over >2 hr. PO taken on empty stomach, do not open capsules

NABUMETONE (RELAFEN)

WARNING: May risk of cardiovascular events and GI bleeding, perforation; CI w/postop CABG.

USES: *Osteoarthritis and rheumatoid arthritis,* pain

ACTION: NSAID; prostaglandins

DOSE: 1,000–2,000 mg/d divided daily–b.i.d. w/food

CAUTION: [C, –]; severe hepatic disease

CI: W/peptic ulcer, NSAID sensitivity, after CABG

DISP: Tablets 500, 750 mg

SE: Dizziness, rash, GI upset, edema, peptic ulcer, BP

NAFCILLIN (NALLPEN, UNIPEN)

USES: *Infections due to susceptible strains of Staphylococcus, Streptococcus*

ACTION: Bactericidal; -lactamase-resistant penicillin; cell wall synthesis. Spectrum: Good gram(+) coverage, except MRSA and enterococcus; no gram(–) and poor anaerobe coverage

DOSE:

Adults: 1–2 g IV q4–6h.

Peds: 50–200 mg/kg/d divided q4–6h

CAUTION: [B, ?]; penicillin allergy

CI: Penicillin allergy

DISP: Injectable powder l, 2 g

SE: Interstitial nephritis, N/D, fever, rash, allergic reaction

NOTES: No adjustment for renal function

NAFTIFINE (NAFTIN)

USES: *Tinea pedis/cruris/corporis*

ACTION: Allylamine antifungal, cell membrane ergosterol synthesis

DOSE: Apply daily (cream) or b.i.d. (gel)

CAUTION: [B, ?]

CI: Component sensitivity

DISP: 1% cream; gel

SE: Local irritation

NALBUPHINE (NUBAIN)

USES: *Mod–severe pain; preop and obstetric analgesia*

ACTION: Narcotic agonist–antagonist; ascending pain pathways

DOSE:

Adults: Pain: 10 mg/70 kg IV/IM/SQ q3–6h; adjust PRN; 20 mg/dose or 160 mg/d max. Anesthesia: Induction: 0.3–3 mg/kg IV over 10–15 min; maintenance 0.25–0.5 mg/kg IV.

Peds: 0.2 mg/kg IV or IM, 20 mg max; w/renal/in hepatic impairment

CAUTION: [B, M]; w/opiate use

CI: Component sensitivity

DISP: Injectable 10, 20 mg/mL

SE: CNS depression, drowsiness; caution, BP

NAPROXEN (ALEVE [OTC], NAPROSYN, ANAPROX)

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID; prostaglandins

DOSE:

Adults and Peds: >12 yr: 200–500 mg b.i.d.–t.i.d. to 1,500 mg/d max. >2 yr: JRA: 5 mg/kg/dose b.i.d.; in hepatic impairment

CAUTION: [C, (D 3rd trimester), +]

CI: NSAID or ASA triad sensitivity, peptic ulcer, post-CABG pain, 3rd-trimester pregnancy

DISP: Tablets 220, 250, 375, 500 mg; DR tablets 375 mg, 500 mg; CR tablets 375 mg, 550 mg; suspension 125 mL/5 mL

SE: Dizziness, pruritus, GI upset, peptic ulcer, edema

NOTES: Take w/food to GI upset

NEOMYCIN-POLYMYXIN BLADDER IRRIGANT [NEOSPORIN GU IRRIGANT]

USES: *Continuous irrigant to prevent bacteriuria and gram(–) bacteremia associated w/indwelling catheter*

ACTION: Bactericidal; not for Serratia sp or streptococci

DOSE: 1 mL irrigant in 1 L of 0.9% NaCl; continuous bladder irrigation w/1 L of solution/24 hr 10 days max

CAUTION: [D]

CI: Component allergy

DISP: Solution neomycin sulfate 40 mg and polymyxin B 200,000 U/mL; ampule 1, 20 mL

SE: Rash, neomycin oto-/nephrotoxicity (rare)

NOTES: Potential for bacterial/fungal superinfection; not for injection; use only 3-way catheter for irrigation

NEOMYCIN SULFATE (NEO-FRADIN, GENERIC)

WARNING: Systemic absorption of PO route may cause neuro-/oto-/nephrotoxicity; respiratory paralysis possible with any route of administration

USES: *Hepatic coma, bowel preparation*

ACTION: Aminoglycoside, poorly absorbed PO; GI bacterial flora

DOSE:

Adults: 3–12 g/24 hr PO in 3–4 divided doses.

Peds: 50–100 mg/kg/24 hr PO in 3–4 divided doses

CAUTION: [C, ?/–]; renal failure, neuromuscular disorders, hearing impairment

CI: Intestinal obstruction

DISP: Tablets 500 mg; PO solution 125 mg/5 mL

SE: Hearing loss w/long-term use; rash, N/V

NOTES: Do not use parenterally (toxicity); part of the Condon bowel preparation; also topical form

NIFEDIPINE (PROCARDIA, PROCARDIA XL, ADALAT CC)

USES: *Vasospastic or chronic stable angina and hypertension*; tocolytic; expulsion therapy for a symptomatic ureteral stone

ACTION: Calcium channel blocker

DOSE:

Adults: SR tablets 30–90 mg/d. Ureteral calculi: Common regimen 30 mg SR PO × up to 10 days

Peds: 0.25–0.9 mg/kg/24 hr divided t.i.d.–q.i.d.

CAUTION: [C, +]; heart block, aortic stenosis

CI: IR preparation for urgent or emergent hypertension; acute MI

DISP: Capsules 10, 20 mg; SR tablets 30, 60, 90 mg

SE: HA common on initial treatment; reflex tachycardia may occur w/regular-release dosage forms; peripheral edema, BP, flushing, dizziness

NOTES: Adalat CC and Procardia XL not interchangeable; SL administration not OK

NILUTAMIDE (NILANDRON)

WARNING: Interstitial pneumonitis possible; most cases in 1st 3 mo; check CXR before and during treatment.

USES: *Combo w/surgical castration for metastatic prostate cancer*

ACTION: Nonsteroidal antiandrogen

DOSE: 300 mg/d PO in divided doses × 30 d, then 150 mg/d

CAUTION: [Not used in females]

CI: Severe hepatic impairment, respiratory insufficiency

DISP: Tablets 150 mg

SE: Interstitial pneumonitis, hot flashes, libido, impotence, N/V/D, gynecomastia, hepatic dysfunction

NOTES: May cause reaction when taken w/EtOH; follow LFTs

NITROFURANTOIN (FURADANTIN, MACRODANTIN, MACROBID)

WARNING: Pulmonary fibrosis possible

USES: *Prophylaxis/treat UTI*

ACTION: Bacteriocidal; interferes w/carbohydrate metabolism. Spectrum: Some gram(±) bacterial coverage; Pseudomonas, Serratia, and most Proteus resistant

DOSE:

Adults: Prophylaxis: 50–100 mg/d PO. Treat: 50–100 mg PO q.i.d. × 7 d. Macrobid 100 mg PO b.i.d. × 7 days.

Peds: Prophylaxis: 1–2 mg/kg/d divided 1–2 doses, max 100 mg/d. Treat: 5–7 mg/kg/24 hr in 4 divided doses (w/food/milk/antacid)

CAUTION: [B, +/not OK if child <1 mo]; avoid w/CrCl <60 mL/min

CI: Renal failure, infants <1 mo, pregnancy at term

DISP: Capsules 25, 50, 100 mg; suspension 25 mg/5 mL

SE: GI effects, dyspnea, various acute/chronic pulmonary reactions, peripheral neuropathy, hemolytic anemia w/G6PD deficiency, rare aplastic anemia

NOTES: Macrocrystals (Macrodantin) less nausea than other forms; not for comp UTI; may turn urine brown; depresses spermatogenesis

NORFLOXACIN (NOROXIN)

WARNING: Use associated with tendon rupture and tendonitis

USES: *Comp and uncomp UTI due to gram(–) bacteria, prostatitis, gonorrhea,* infectious diarrhea, conjunctivitis

ACTION: Quinolone, DNA gyrase, bactericidal. Spectrum: Broad gram(±) coverage, E. faecalis, E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, S. epidermidis, S. saprophyticus

DOSE: Uncomp UTI (E. coli, K. pneumoniae, P. mirabilis): 400 mg PO b.i.d. × 3 d; other uncomp UTI treatment, × 7–10 days. Comp UTI: 400 mg q12h for 10–21 days PO b.i.d. Gonorrhea: 800 mg × 1 dose. Prostatitis: 400 mg PO b.i.d. × 28 days. Gastroenteritis, traveler's diarrhea: 400 mg PO × 1–3 d; take 1 hr a.c. or 2 hr p.c.; CrCl <30 mL/min use 400 mg/d

CAUTION: [C, –]; quinolone sensitivity, w/some antiarrhythmics

CI: History allergy or tendon problems

DISP: Tablets 400 mg; ophthalmic ointment 3 mg/mL

SE: Photosensitivity, headache, dizziness, asthenia, GI upset, pseudomembranous colitis; ocular burning w/ophthalmic use

NOTES: Interactions w/antacids, theophylline, caffeine; good concentration in the kidney and urine, poor blood levels; not for urosepsis; CDC suggests do not use for GC

NYSTATIN (MYCOSTATIN)

USES: *Mucocutaneous Candida infections (oral, skin, vaginal)*

ACTION: Alters membrane permeability. Spectrum: Susceptible Candida sp

DOSE:

Adults and Peds PO: 400,000–600,000 U PO swish and swallow q.i.d. Vaginal: 1 tablet vaginally h.s. × 2 wk. Topical: Apply b.i.d.–t.i.d. to area.

Peds: Infants 200,000 U PO q6h.

CAUTION: [B (C, PO), +]

DISP: PO suspension 100,000 U/mL; PO tablets 500,000 U; troches 200,000 U; vaginal tablets 100,000 U; topical cream/ointment 100,000 U/g; powder 100,000 U/g

SE: GI upset, Stevens-Johnson syndrome

NOTES: Not absorbed PO; not for systemic infections

OFLOXACIN (FLOXIN)

WARNING: Use associated with tendon rupture and tendonitis

USES: *Lower respiratory tract, skin and skin structure, and UTI, prostatitis, uncomp gonorrhea, and Chlamydia infections*

ACTION: Bactericidal; DNA gyrase. Broad spectrum gram(±) coverage: S. pneumoniae, S. aureus, S. pyogenes, H. influenzae, P. mirabilis, N. gonorrhoeae, C. trachomatis, E. coli

DOSE:

Adults: 200–400 mg PO b.i.d. or IV q12h. Uncomplicated urethral or endocervical gonorrhea if penicillin allergy (resistant strains in Asia, Hawaii, and California): 400 mg PO × 1. Avoid in pregnancy; take on empty stomach

CAUTION: [C, –]; ↓ absorption w/antacids, sucralfate, Al-, Ca-, Mg-, Fe-, Zn-containing drugs

CI: Quinolone allergy

DISP: Tablets 200, 300, 400 mg; injectable 20, 40 mg/mL; ophthalmic and otic ointment 0.3%

SE: N/V/D, photosensitivity, insomnia, headache, local irritation

OXACILLIN (PROSTAPHLIN)

USES: *Infections due to susceptible S. aureus and Streptococcus*

ACTION: Bactericidal; ↓ cell wall synthesis. Spectrum: Excellent gram(+), poor gram(–) coverages

DOSE:

Adults: 250–500 mg (2 g severe) IM/IV q4–6h.

Peds: 150–200 mg/kg/d IV divided q4–6h

CAUTION: [B, M]

CI: Penicillin sensitivity

DISP: Powder for injectable 500 mg, 1, 2, 10 g

SE: GI upset, interstitial nephritis, blood dyscrasias

OXAPROZIN (DAYPRO, DAYPRO ALTA)

WARNING: May ↑ risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID; ↓ prostaglandin synthesis

DOSE:

Adults: 600–1,200 mg/d (divided dose helps GI tolerance); ↓ w/renal/hepatic impairment.

Peds: JRA (Daypro): 22–31 kg: 600 mg/d. 32–54 kg: 900 mg/d

CAUTION: [C (D in 3rd trimester), ?]; peptic ulcer, bleeding disorders

CI: ASA/NSAID sensitivity perioperative pain w/CABG

DISP: Daypro ALTA tablet 600 mg; caplets 600 mg

SE: CNS inhibition, sleep disturbance, rash, GI upset, peptic ulcer, edema, renal failure, anaphylactoid reaction w/ASA triad (asthmatic w/rhinitis, nasal polyps, bronchospasm w/NSAID use)

OXICONAZOLE (OXISTAT)

USES: *Tinea cruris/corporis/pedis/versicolor*

ACTION: ? Ergosterols in fungal cell membrane. Spectrum: Most Epidermophyton floccosum, Trichophyton mentagrophytes, Trichophyton rubrum, Malassezia furfur

DOSE: Apply thin layer daily–b.i.d.

CAUTION: [B, M]

CI: Component allergy

DISP: Cream, lotion 1%

SE: Local irritation

OXYBUTYNIN (DITROPAN, DITROPAN XL, GENERIC)

USES: *Symptomatic relief of urgency, nocturia, incontinence w/neurogenic or reflex neurogenic bladder*

ACTION: Anticholinergic/antimuscarinic, relaxes bladder smooth muscle, bladder capacity

DOSE:

Adults: 5 mg PO b.i.d.–t.i.d., 5 mg q.i.d. max. XL: 5–10 mg/d, 30 mg/d max.

Peds: >5 yr: 5 mg PO b.i.d.–t.i.d.; 15 mg/d max.

Peds: 1–5 yr 0.2 mg/kg/dose b.i.d.–q.i.d. (syrup 5 mg/5 mL); 15 mg/d max; in elderly; periodic drug holidays OK

CAUTION: [B, ?]

CI: Narrow-angle glaucoma, myasthenia gravis, GI/GU obstruction, ulcerative colitis, megacolon

DISP: Tablets 5 mg; XL tablets 5, 10, 15 mg; syrup 5 mg/5 mL

SE: Anticholinergic (drowsiness, xerostomia, constipation, tachycardia), extended release form shell expelled in stool

OXYBUTYNIN GEL (GELNIQUE)

USES: *Overactive bladder*

ACTION: Anticholinergic/antimuscarinic, relaxes bladder smooth muscle, bladder capacity

DOSE: Apply 1 sachet to dry, intact skin on the abdomen, upper arms/shoulders, or thighs; rotate sites

CAUTION: [B, ?/–]

CI: GI/GU obstruction, narrow-angle glaucoma

DISP: Packs (sachet) 1 g unit dose (1.14 mL,100 mg/g)

SE: Anticholinergic, itching/redness at site

NOTES: Do not apply to same site within 7 d

OXYBUTYNIN TRANSDERMAL SYSTEM (OXYTROL)

USES: *Overactive bladder*

ACTION: Anticholinergic/antimuscarinic, relaxes bladder smooth muscle, bladder capacity

DOSE: 1 3.9 mg/d system apply twice weekly (q3–4d) to abdomen, hip, or buttock

CAUTION: [B, ?/–]

CI: GI/GU retention, narrow-angle glaucoma

DISP: 3.9 mg/d transdermal patch

SE: Anticholinergic (eg, dry mouth), itching/redness at site

NOTES: Do not apply to same site within 7 d

OXYCHLOROSENE (CLORPACTIN WCS-90)[OTC]

USES: Topical treatment of wounds; intravesical for interstitial cystitis

ACTION: Topical antibiotic (hypochloric acid)

DOSE: 0.1– 0.4% sterile water or isotonic saline

CAUTION: [?,?]; given intravesically only with general or regional anesthesia

CI: Hypersensitivity to oxychlorosene

DISP: Powder for solution 2 g

SE: Irritation

NOTES: Not commonly used for interstitial cystitis

OXYCODONE [DIHYDROHYDROXY-CODEINONE] (OXYCONTIN, OXYIR, ROXICODONE) [C-II]

WARNING: High abuse potential; controlled-release only for extended chronic pain, not for PRN use; 60-, 80-, 160-mg tablet for opioid-tolerant patients.

USES: *Mod–severe pain, usually in combo w/nonnarcotic analgesics*

ACTION: Narcotic analgesic

DOSE:

Adults: 5 mg PO q6h PRN (IR). Mod–severe chronic pain: 10–160 mg PO q12h (ER).

Peds: 6–12 yr: 1.25 mg PO q6h PRN. >12 yr: 2.5 mg q6h PRN; w/severe liver/renal disease, elderly; w/food

CAUTION: [B (D if prolonged use/near term), M]

CI: Allergy, respiratory depression, acute asthma, ileus w/microsomal morphine

DISP: IR capsules (OxyIR) 5 mg; CR Roxicodone tablets 15, 30 mg; ER (OxyContin) 10, 15, 20, 30, 40, 60, 80 mg; liquid 5 mg/5 mL; solution concentrate 20 mg/mL

SE: BP, sedation, respiratory depression, dizziness, GI upset, constipation, risk of abuse

NOTES: OxyContin for chronic cancer pain; do not crush/chew/cut ER product; sought after as drug of abuse

OXYCODONE AND ACETAMINOPHEN (PERCOCET, TYLOX) [C-II]

USES: *Mod–severe pain*

ACTION: Narcotic analgesic

DOSE:

Adults: 1–2 tablets/capsules PO q4–6h PRN (acetaminophen max dose 4 g/d).

Peds: Oxycodone 0.05–0.15 mg/kg/dose q 4–6h PRN, 5 mg/dose max

CAUTION: [C (D prolonged use or near term), M]

CI: Allergy, paralytic ileus, respiratory depression

DISP: Percocet tablets, mg oxycodone/mg acetaminophen: 2.5/325, 5/325, 7.5/325, 10/325, 7.5/500, 10/650; Tylox capsules 5 mg oxycodone, 500 mg acetaminophen; solution 5 mg oxycodone and 325 mg acetaminophen/5 mL

SE: BP, sedation, dizziness, GI upset, constipation

OXYCODONE AND ASPIRIN (PERCODAN) [C-II]

USES: *Mod–severe pain*

ACTION: Narcotic analgesic w/NSAID

DOSE:

Adults: 1–2 tablets/capsules PO q4–6h PRN.

Peds: Oxycodone 0.05–0.15 mg/kg/dose q 4–6h PRN, up to 5 mg/dose; in severe hepatic failure

CAUTION: [D, –]; peptic ulcer

CI: Component allergy, children (<16 yr) with viral infection, respiratory depression, ileus

DISP: Generics: 4.83 mg oxycodone hydrochloride, 0.38 mg oxycodone terephthalate, 325 mg ASA; Percodan 4.83 mg oxycodone hydrochloride, 325 mg ASA

SE: Sedation, dizziness, GI upset/ulcer, constipation, allergy

OXYCODONE/IBUPROFEN (COMBUNOX) [C-II]

WARNING: May risk of serious cardiovascular events; CI in perioperative CABG pain; risk of GI events such as bleeding

USES: *Short-term (not >7 d) management of acute mod–severe pain*

ACTION: Narcotic w/NSAID

DOSE: 1 tablet q6h PRN; 4 tablet max/24 hr; 7 day max

CAUTION: [C, –]; w/impaired renal/hepatic function; COPD, CNS depression, avoid in pregnancy

CI: Paralytic ileus, 3rd trimester pregnancy, allergy to ASA or NSAIDs, where opioids are CI

DISP: Tablets 5 mg oxycodone/400 mg ibuprofen

SE: N/V, somnolence, dizziness, sweating, flatulence, ↑LFTs

NOTES: Renal function; abuse potential w/oxycodone

OXYMORPHONE (OPANA, OPANA ER) [C-II]

WARNING: (Opana ER) Abuse potential, controlled-release only for chronic pain; do not consume EtOH-containing beverages, may cause fatal overdose.

USES: *Mod–severe pain, sedative*

ACTION: Narcotic analgesic

DOSE: 10–20 mg PO q4–6h PRN if opioid-naïve or 1–1.5 mg SQ/IM q4–6h PRN or 0.5 mg IV q4–6h PRN; start 20 mg/dose max PO. Chronic pain: ER 5 mg PO q12h; if opioid-naïve ↑PRN 5–10 mg PO q12h q3–7d; take 1 hr p.c. or 2 hr a.c.; ↓dose w/elderly, renal/hepatic impairment

CAUTION: [B, ?]

CI: ↑ICP, severe respiratory depression, w/EtOH or liposomal morphine, severe hepatic impairment

DISP: Tablets 5, 10 mg; ER 5, 10, 20, 40 mg

SE: ↓BP, sedation, GI upset, constipation, histamine release

NOTES: Related to hydromorphone

PACLITAXEL (TAXOL, ABRAXANE)

WARNING: Administration only by physician experienced in chemotherapy; fatal anaphylaxis and hypersensitivity possible; severe myelosuppression possible.

USES: *Ovarian/breast/prostate cancers,* Kaposi sarcoma, non-small cell lung cancer

ACTION: Mitotic spindle poison; promotes microtubule assembly and stabilization against depolymerization

DOSE: Per protocols; use glass or polyolefin containers (eg, nitroglycerin tubing set); PVC sets leach plasticizer; ↓in hepatic failure

CAUTION: [D, –]

CI: Neutropenia <1,500 WBC/mm3; solid tumors, component allergy

DISP: Injectable 6 mg/mL, 5 mg/mL albumin bound (Abraxane)

SE: ↓Bone marrow, peripheral neuropathy, transient ileus, myalgia, bradycardia, ↓BP, mucositis, N/V/D, fever, rash, headache, phlebitis; hematologic toxicity schedule-dependent; leukopenia dose-limiting by 24-hr infusion; neurotoxicity limited w/short (1–3 hr) infusion; allergic reactions (dyspnea, ↓BP, urticaria, rash)

NOTES: Maintain hydration; allergic reaction usually within 10 min of infusion; minimize w/corticosteroid, antihistamine pretreatment

PAMIDRONATE (AREDIA)

USES: *Hypercalcemia of malignancy, Paget disease, palliate symptomatic bone metastases*

ACTION: Bisphosphonate; ↓ normal/abnormal bone resorption

DOSE: Hypercalcemia: 60–90 mg IV over 2–24 hr or 90 mg IV over 24 hr if severe; may repeat in 7 days. Paget disease: 30 mg/d IV slow infusion over 4 hr × 3 days. Osteolytic bone mets in myeloma: 90 mg IV over 4 hr every mo. Osteolytic bone mets breast cancers: 90 mg IV over 2 hr q3–4wk; 90 mg/max single dose

CAUTION: [D, ?/–]; avoid invasive dental procedures w/use

CI: Pregnancy, bisphosphonate sensitivity

DISP: Injectable 30, 60, 90 mg

SE: Fever, malaise, convulsions, injection site reaction, uveitis, fluid overload, hypertension, abdominal pain, N/V, constipation, UTI, bone pain, ↓ K+, ↓ Ca2+, ↓ Mg2+, hypophosphatemia, jaw osteonecrosis, renal toxicity

NOTES: Perform dental exam pretherapy; follow Cr, hold dose if Cr ↑ by 0.5 mg/dL w/normal baseline or by 1 mg/dL w/abnormal baseline; restart when Cr returns within 10% of baseline

PAROXETINE (PAXIL, PAXIL CR, PEXEVA)

WARNING: Closely monitor for worsening depression or emergence of suicidality, particularly in children, adolescents, and young adults; not for use in peds.

USES: *Depression, obsessive–compulsive disorder, panic disorder, social anxiety disorder,* premenstural dysphoric disorder (PMDD)

ACTION: SSRI

DOSE: 10–60 mg PO single daily dose in AM; CR 25 mg/d PO; ↑ 12.5 mg/wk (max range 26–62.5 mg/d)

CAUTION: [D, ?/]; ↑ bleeding risk

CI: W/MAOI, thioridazine, pimozide

DISP: Tablets 10, 20, 30, 40 mg; suspension 10 mg/5 mL; CR 12.5, 25, 37.5 mg

SE: HA, somnolence, dizziness, GI upset, N/D, ↓ appetite, sweating, xerostomia, tachycardia, ↓ libido

NOTES: May impair fertility; associated with a 5× increase in risk of abnormal sperm DNA fragmentation as measured by TUNEL score

PENBUTOLOL (LEVATOL)

USES: *Hypertension*

ACTION: 1, 2-Adrenergic receptor blocker,

DOSE: 20–40 mg/d; ↓ in hepatic insufficiency

CAUTION: [C 1st trimester; D if 2nd/3rd trimester, M]

CI: Asthma, cardiogenic shock, cardiac failure, heart block, bradycardia, COPD, PE

DISP: Tablets 20 mg

SE: Flushing, BP, fatigue, hyperglycemia, GI upset, sexual dysfunction, bronchospasm

PENCICLOVIR (DENAVIR)

USES: *Herpes simplex (herpes labialis/cold sores)*

ACTION: Competitive inhibitor of DNA polymerase

DOSE: Apply at 1st sign of lesions, then q2h while awake × 4 day

CAUTION: [B, ?/–]

CI: Allergy, previous reaction to famciclovir

DISP: Cream 1%

SE: Erythema, headache

NOTES: Do not apply to mucous membranes

D-PENICILLAMINE (CUPRIMINE, DEPEN)

WARNING: Significant side effects possible; patients should be warned to report promptly any symptoms suggesting toxicity (fever, sore throat, chills, bruising, or bleeding); toxicity may be dose related; should only be administered by experienced physician.

USES: *Rheumatoid arthritis, Wilson disease, cystinuria*

ACTION: Chelating agent

DOSE:

Adult Cystinuria: Titrate to keep cystine excretion 100–200 mg/d (<100 mg/d with history of urolithiasis), 1–4 g/d PO in divided doses q6h, typical dose 2 g/d.

Peds: Titrate to keep cystine excretion 100–200 mg/d (<100 mg/d with history of urolithiasis), 30 mg/kg/d in 4 divided doses

CAUTION: [D, –]; w/other meds that act as hematopoietic depressants

CI: Hypersensitivity to components, renal insufficiency, previous aplastic anemia due to drug, pregnancy

DISP: Cream 1%

SE: Allergic reactions in up to 33%; agranulocytosis, aplastic anemia, diarrhea, anorexia, abdominal pain, dermatologic manifestations, nephrotic syndrome

NOTES: Do not discontinue therapy in cystinuria; interruptions of a few days can cause hypersensitivity with resumption of therapy; monitor CBC, UA (proteinuria, hematuria), urinary cysteine levels; use THIOLA if intolerant of d-penicillamine

PENICILLIN G, AQUEOUS (POTASSIUM OR SODIUM) (PFIZERPEN, PENTIDS)

USES: *Bacteremia, endocarditis, pericarditis, respiratory tract infections, meningitis, neurosyphilis, skin/skin structure infections*

ACTION: Bactericidal; cell wall synthesis. Spectrum: Most gram(+) (not staphylococci), streptococci, N. meningitidis, syphilis, clostridia, and anaerobes (not Bacteroides)

DOSE:

Adults: Based on indication, 0.6–24 million U/d in divided doses q4h.

Peds: Newborns <1 wk: 25,000–50,000 U/kg/dose IV q12h. Infants 1 wk–<1 mo: 25,000–50,000 U/kg/dose IV q8h. Children: 100,000–300,000 U/kg/24h IV divided q4h; in renal impairment

CAUTION: [B, M]

CI: Allergy

DISP: Powder for injection

SE: Allergic reactions; interstitial nephritis, diarrhea, seizures

NOTES: Contains 1.7 mEq of K+/million units

PENICILLIN G BENZATHINE (BICILLIN)

USES: *Single-dose regimen for streptococcal pharyngitis, rheumatic fever, glomerulonephritis prophylaxis, and syphilis*

ACTION: Bactericidal; cell wall synthesis. Spectrum: See “Penicillin G.”

DOSE:

Adults: 1.2–2.4 million U deep IM injection q2–4wk.

Peds: 50,000 U/kg/dose, 2.4 million U/dose max; deep IM injection q2–4 wk

CAUTION: [B, M]

CI: Allergy

DISP: Injectable 300,000, 600,000 U/mL; Bicillin L-A benzathine salt only; Bicillin C-R combined benzathine and procaine (300,000 U procaine w/300,000 U benzathine/mL or 900,000 U benzathine w/300,000 U procaine/2 mL)

SE: Injection site pain, acute interstitial nephritis, anaphylaxis

NOTES: IM use only; sustained action, w/levels up to 4 wk; drug of choice for noncongenital syphilis

PENICILLIN G PROCAINE (WYCILLIN, OTHERS)

USES: *Infections of respiratory tract, skin/soft tissue, scarlet fever, syphilis*

ACTION: Bactericidal; cell wall synthesis. Spectrum: Penicillin G-sensitive organisms that respond to low, persistent serum levels

DOSE:

Adults: 0.6–4.8 million U/d in divided doses q12–24h; give probenecid at least 30 min prior to penicillin to prolong action.

Peds: 25,000–50,000 U/kg/d IM divided daily–b.i.d.

CAUTION: [B, M]

CI: Allergy

DISP: Injectable 300,000, 500,000, 600,000 U/mL

SE: Pain at injection site, interstitial nephritis, anaphylaxis

NOTES: LA parenteral penicillin; levels up to 15 hr

PENICILLIN V (PEN-VEE K, VEETIDS, OTHERS)

USES: Susceptible streptococcal infections, otitis media, URIs, skin/soft-tissue infections (penicillin-sensitive staphylococci)

ACTION: Bactericidal; cell wall synthesis. Spectrum: Most gram(+), including streptococci

DOSE:

Adults: 250–500 mg PO q6h, q8h, q12h.

Peds: 25–50 mg/kg/d PO in 4 doses; in renal impairment; take on empty stomach

CAUTION: [B, M]

CI: Allergy

DISP: Tablets 125, 250, 500 mg; suspension 125, 250 mg/5 mL

SE: GI upset, interstitial nephritis, anaphylaxis, convulsions

NOTES: Well-tolerated PO penicillin; 250 mg = 400,000 U of penicillin G

PENTAZOCINE (TALWIN, TALWIN COMPOUND, TALWIN NX) [C-IV]

WARNING: PO use only; severe and potentially lethal reactions from misuse by injection.

USES: *Mod–severe pain*

ACTION: Partial narcotic agonist–antagonist

DOSE:

Adults: 30 mg IM or IV; 50–100 mg PO q3–4h PRN.

Peds: 5–8 yr: 15 mg IM q4h PRN. 8–14 yr: 30 mg IM q4h PRN; in renal/hepatic impairment

CAUTION: [C (1st trimester, D w/prolonged use/high dose near term), ±]

CI: Allergy, ICP (unless ventilated)

DISP: Talwin Compound tablet 12.5 mg + 325 mg ASA; Talwin NX 50 mg + 0.5 mg naloxone; injectable 30 mg/mL

SE: Considerable dysphoria; drowsiness, GI upset, xerostomia, seizures

NOTES: 30–60 mg IM = 10 mg of morphine IM; Talwin NX has naloxone to curb abuse by nonoral route

PENTOSAN POLYSULFATE SODIUM (ELMIRON)

USES: *Relieve pain/discomfort w/interstitial cystitis*

ACTION: Bladder wall buffer; negatively charged synthetic sulfated polysaccharide w/affinity for mucosal membranes. Repletes defect in glycosaminoglycan layer; this may also

calcium oxalate crystallization and stone formation by reducing crystal aggregation; may intestinal oxalate transport and urinary oxalate excretion

DOSE: 100 mg PO t.i.d.; on empty stomach w/H2O 1 hr a.c. or 2 hr p.c.

CAUTION: [B, ?/–]

CI: Allergy

DISP: Capsules 100 mg

SE: Alopecia, N/D, headache, LFTs, anticoagulant effects, platelets, rectal bleeding

NOTES: Reassess after 3 mo; may have role in refractory calcium urolithiasis

PENTOXIFYLLINE (TRENTAL)

USES: *Symptoms of PVD*

ACTION: Blood cell viscosity, restores RBC flexibility

DOSE:

Adults: 400 mg PO t.i.d. p.c.; treat min 8 wk for effect; to b.i.d. w/GI/CNS side effects

CAUTION: [C, ±]

CI: Cerebral/retinal hemorrhage, methylxanthine (caffeine) intolerance

DISP: Tablets CR 400 mg; tablets ER 400 mg

SE: Dizziness, headache, GI upset

PERINDOPRIL ERBUMINE (ACEON)

WARNING: ACE inhibitors can cause death to developing fetus; discontinue immediately w/pregnancy.

USES: *Hypertension, reduce mortality in patients with CAD,* prevent progression of nephropathy in diabetes and hypertension

ACTION: ACE inhibitor; prevents conversion of angiotensin I to angiotensin II

DOSE: 4–8 mg/d divided dose; 16 mg/d max; avoid w/food; w/elderly/renal impairment

CAUTION: [C (1st trimester; D 2nd and 3rd trimester), ?/–] ACE inhibitor–induced angioedema

CI: Bilateral RAS, primary hyperaldosteronism

DISP: Tablets 2, 4, 8 mg

SE: Weakness, headache, BP, dizziness, GI upset, cough

NOTES: OK w/diuretics

PERMETHRIN (NIX, ELIMITE) [OTC]

USES: *Lice/scabies*

ACTION: Pediculicide

DOSE:

Adults and Peds Lice: Saturate hair and scalp; allow 10 min before rinsing. Scabies: Apply cream head to toe; leave for 8–14 hr, wash w/H2O

CAUTION: [B, ?/–]

CI: Allergy

DISP: Topical lotion 1%; cream 5%

SE: Local irritation

NOTES: Sprays available (Rid, A200, Nix) to disinfect clothing, bedding, combs, and brushes; lotion not OK in peds <2 yr; may repeat after 7 d

PHENAZOPYRIDINE (PYRIDIUM, AZO-STANDARD, UROGESIC, OTHERS)

USES: *Lower urinary tract irritation,* interstitial cystitis

ACTION: Anesthetic on urinary tract mucosa

DOSE:

Adults: 100–200 mg PO t.i.d.; 2 day max w/antibiotics for UTI; w/renal insufficiency

CAUTION: [B, ?]; hepatic disease

CI: Renal failure

DISP: Tablets 100, 200 mg

SE: GI disturbances, red-orange urine color (can stain clothing, contact lenses), headache, dizziness, acute renal failure, methemoglobinemia, tinting of sclera/skin

NOTES: Take w/food

PIMECROLIMUS (ELIDEL)

WARNING: Associated with rare skin malignancies and lymphoma, limit to area, not for age <2 yr

USES: *Atopic dermatitis* refractory, severe perianal itching

ACTION: Inhibits T-lymphocytes

DOSE:

Adults and Peds: >2 yr: Apply b.i.d.; use at least 1 wk following resolution

CAUTION: [C, ?/–]; w/local infection, lymphadenopathy; immunocompromise; avoid in patients <2 yr

CI: Allergy component, <2 yr

DISP: Cream 1%

SE: Phototoxicity, local irritation/burning, flu-like symptoms, may malignancy

NOTES: Use on dry skin only; wash hands after; 2nd-line/short-term use only

PIPERACILLIN (PIPRACIL)

USES: *Infections of skin, bone, respiratory, urinary tracts, abdomen, sepsis*

ACTION: 4th-generation penicillin; bactericidal; cell wall synthesis. Spectrum: Primarily gram(+) coverage, better Enterococcus, H. influenzae, not staphylococci; gram(–) E. coli, Proteus, Shigella, Pseudomonas, not -lactamase–producing

DOSE:

Adults: 2–4 g IV q4–6h.

Peds: 200–300 mg/kg/d IV divided q4–6h; in renal failure

CAUTION: [B, M]

CI: Penicillin/-lactam sensitivity

DISP: Powder for injectable 2, 3, 4, 40 g

SE: Platelet aggregation, interstitial nephritis, renal insufficiency, anaphylaxis, hemolytic anemia

NOTES: Often used w/aminoglycoside

PIPERACILLIN–TAZOBACTAM (ZOSYN)

USES: *Infections of skin, bone, respiratory, urinary tracts, abdomen, sepsis*

ACTION: 4th-generation penicillin plus -lactamase inhibitor; bactericidal; cell wall synthesis. Spectrum: Good gram(+), excellent gram(–) coverages; anaerobes and -lactamase producers

DOSE:

Adults: 3.375–4.5 g IV q6h; in renal insufficiency

CAUTION: [B, M]

CI: Penicillin or -lactam sensitivity

DISP: Powder for injection; frozen, premix injectable 3.25, 3.375, 4.5 g

SE: D, headache, insomnia, GI upset, serum sickness-like reaction, pseudomembranous colitis

NOTES: Often used in combo w/aminoglycoside

PIROXICAM (FELDENE)

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID; prostaglandins

DOSE: 10–20 mg/d

CAUTION: [B (1st trimester; D if 3rd trimester or near term), +]; GI bleeding

CI: ASA/NSAID sensitivity

DISP: Capsules 10, 20 mg

SE: Dizziness, rash, GI upset, edema, acute renal failure, peptic ulcer

PODOPHYLLIN (PODOCON-25, CONDYLOX GEL 0.5%, CONDYLOX)

USES: *Topical therapy of benign growths (genital and perianal warts [condylomata acuminata],* papillomas, fibromas)

ACTION: Direct antimitotic effect; exact mechanism unknown

DOSE: Condylox gel and Condylox: Apply b.i.d. for 3 consecutive days a week for 4 wk; 0.5 mL/d max. Podocon-25: Use sparingly on the lesion, leave on for 1–4 hr, thoroughly wash off

CAUTION: [X, ?]; immunosuppression

CI: DM, bleeding lesions

DISP: Podocon-25 (w/benzoin) 15–mL bottles; Condylox gel 0.5% 35-g clear gel; Condylox solution 0.5% 35-g clear

SE: Local reactions, significant absorption; anemias, tachycardia, paresthesias, GI upset, renal/hepatic damage

NOTES: Podocon-25 applied by the clinician; do not dispense directly to patient

POLYETHYLENE GLYCOL [PEG]/ELECTROLYTE SOLUTION (GOLYTELY, COLYTE)

USES: *Bowel preparation prior to exam or surgery*

ACTION: Osmotic cathartic

DOSE:

Adults: Following 3–4–h fast, drink 240 mL of solution q10min until 4 L consumed or until bowel movements are clear.

Peds: 25–40 mL/kg/h for 4–10 hr

CAUTION: [C, ?]

CI: GI obstruction, bowel perforation, megacolon, ulcerative colitis

DISP: Powder for reconstitution to 4 L

SE: Cramping or N, bloating

NOTES: 1st bowel movement should occur in ~1 hr; chilled solution more palatable

POLYETHYLENE GLYCOL [PEG] 3350 (MIRALAX)

USES: *Occasional constipation,* bowel prep

ACTION: Osmotic laxative

DOSE: 17-g powder (1 heaping Tbsp) in 8 oz (1 cup) of H2O and drink; max 14 day

CAUTION: [C, ?]; rule out bowel obstruction before use

CI: GI obstruction, allergy to PEG

DISP: Powder for reconstitution; bottle cap holds 17 g

SE: Upset stomach, bloating, cramping, gas, severe D, hives

NOTES: Can add to H2O, juice, soda, coffee, or tea

POTASSIUM P-AMINOBENZOATE (POTABA)

USES: *Possibly effective in Peyronie disease and other conditions such as scleroderma*

ACTION: Vitamin B family, may have antifibrotic effect

DOSE: 12 g/d in 4–6 divided doses

CAUTION: [C, M]

CI: Component allergy; use with sulfonamides

DISP: Capsules 500 mg; powder 2 g/pack

SE: Fever, rash, GI upset

NOTES: Many improve pain and lessen penile curvature

POTASSIUM CITRATE (UROCIT-K)

USES: *Alkalinize urine, prevention of nephrolithiasis in patients with RTA w/calcium stones, hypocitraturic calcium oxalate lithiasis, and uric acid lithiasis, w/wo uric acid stones*

ACTION: Urinary alkalinizer, increase urinary citrate (intracellular pH, which citrate production)

DOSE: 1 packet dissolved in H2O or 15–30 mL p.c. and h.s. 10–20 mEq PO t.i.d. w/meals, max 100 mEq/d

CAUTION: [A, +]

CI: Severe renal impairment, dehydration, K+, peptic ulcer, w/K+-sparing diuretics, salt substitutes, active UTI (bacteria may effectiveness of citrate and pH may encourage bacterial growth)

DISP: 540 (5 mEq), 1,080 (10 mEq) mg tablets

SE: GI upset, Ca2+, K+, metabolic alkalosis

NOTES: Test urine pH with Nitrazine paper; monitor periodic serum K+

POTASSIUM CITRATE AND CITRIC ACID (CYTRA K, POLYCITRA-K)

USES: *Alkalinize urine, prevent urinary stones (uric acid, Ca stones if hypocitraturic)*

ACTION: Urinary alkalinizer, urinary citrate levels

DOSE:

Adults: 1 powder packet in water p.c. and h.s.; solution 15–30 mL p.c. and h.s.

Peds: Solution 5–15 mL p.c. and h.s.; adjust dose based on urine pH

CAUTION: [A, +]; drug effect with K+-containing medications, K+-sparing diuretics, ACE inhibitors, or cardiac glycosides, meds that slow GI transit adverse GI effects

CI: Severe renal impairment, dehydration, K+, peptic ulcer; w/use of K+-sparing diuretics or salt substitutes

DISP: Solution 10 mEq/5 mL; powder 30 mEq/packet

SE: GI upset, Ca2+, K+, metabolic alkalosis

POTASSIUM PHOSPHATE AND SODIUM PHOSPHATE (K-PHOS NEUTRAL, NEUTRA-PHOS K, PHOS-NAK, URO-KP-NEUTRAL, OTHERS)

USES: *Conditions w/excessive renal phosphate loss or inadequate phosphate absorption; acidify the urine to Ca+2 concentrations; antibacterial activity of methenamine; odor and rash due to urinary ammonia*

ACTION: Neutral orthophosphates; phosphate supplementation; urinary pyrophosphate, complexes w/Ca+2 with urinary Ca+2; vitamin D3 levels

DOSE:

Adult Urolithiasis: 250–500 mg phosphorus (8–16 mmol) (1–2 tablets) PO q.i.d. w/meals and h.s. with glass of water.

Peds: >4 yr: Urolithiasis: 1 tablet PO q.i.d.; w/meals and h.s. with glass of water

CAUTION: [A, +]; drug effect with K+-containing medications, K+-sparing diuretics, ACE inhibitors, or cardiac glycosides, meds that slow GI transit adverse GI effects

CI: Addison disease, K+, hyperphosphatemia, infected urolithiasis, severe renal impairment, dehydration, peptic ulcer

DISP: Caplet (Uro-KP-Neutral) dipotassium phosphate, disodium phosphate, and monobasic sodium phosphate; [equivalent to elemental phosphorus 258 mg, sodium 262.4 mg (10.8 mEq), and potassium 49.4 mg (1.3 mEq)]; powder, for PO solution (Phos-NaK) dibasic potassium phosphate, monobasic potassium phosphate, dibasic sodium phosphate, and monosodium phosphate/packet [equivalent to elemental phosphorus 250 mg, sodium 160 mg (6.9 mEq), and potassium 280 mg (7.1 mEq)]; tablets (K-Phos MF) potassium phosphate 155 mg and sodium phosphate 350 mg; (K-Phos Neutral) monobasic potassium phosphate 155 mg, dibasic sodium phosphate 852 mg, and monobasic sodium phosphate 130 mg; (K-Phos No. 2) potassium phosphate 305 mg and sodium phosphate 700 mg; (Phospha 250 Neutral) monobasic potassium phosphate 155 mg, dibasic sodium phosphate 852 mg, and monobasic sodium phosphate 130 mg

SE: GI upset, Ca2+, K+, metabolic alkalosis

NOTES: Take all dosage forms with, or powders mixed in, 6–8 oz of water; an effective therapy for hypercalcuria when thiazides cannot be used; particularly useful in hypercalcuria type III (renal phosphate leak)

POTASSIUM SUPPLEMENTS (KAON, KAOCHLOR, K-LOR, SLOW-K, MICRO-K, KLORVESS, OTHERS)

USES: *Prevent/treat K+* (eg, diuretic use)

ACTION: K+ supplement

DOSE:

Adults: 20–100 mEq/d PO divided daily–b.i.d.; IV 10–20 mEq/hr, max 40 mEq/hr and 150 mEq/d (monitor K+ levels frequently and in presence of continuous ECG monitoring w/high-dose IV).

Peds: Calculate K+ deficit; 1–3 mEq/kg/d PO divided daily–q.i.d.; IV max dose 0.5–1 mEq/kg/hr

CAUTION: [A, +]; renal insufficiency, use w/NSAIDs and ACE inhibitors

CI: K+

DISP: PO forms; see Table. Injectable

SE: GI irritation; bradycardia, K+, heart block

NOTES: Mix powder and liquid w/beverage (unsalted tomato juice, etc.); follow K+; Cl- salt OK w/alkalosis; w/acidosis use acetate, bicarbonate, citrate, or gluconate salt

Some Common Oral Potassium Supplements

Brand Name

Salt

Form

mEq Potassium/Dosing Unit

Glu-K

Gluconate

Tablet

2 mEq/tablet

Kaochlor 10%

KCl

Liquid

20 mEq/15 mL

Kaochlor S-F 10% (sugar-free)

KCl

Liquid

20 mEq/15 mL

Kaochlor Eff

Bicarbonate/KCl/citrate

Effervescent tablet

20 mEq/tablet

Kaon elixir

Gluconate

Liquid

20 mEq/15 mL

Kaon

Gluconate

Tablet

5 mEq/tablet

Kaon-Cl
KCl
Tablet, SR
6.67 mEq/tablet
Kaon-Cl 20
KCl
Liquid
40 mEq/15 mL
KayCiel
KCl
Liquid
20 mEq/15 mL
K-Lor
KCl
Powder
15 or 20 mEq/packet
Klorvess
Bicarbonate/KCl
Liquid
20 mEq/15 mL
Klotrix
KCl
Tablet, SR
10 mEq/tablet
K-Lyte
Bicarbonate/citrate
Effervescent tablet
25 mEq/tablet
K-Tablet
KCl
Tablet, SR
10 mEq/tablet
Micro-K
KCl
Capsule, SR

8 mEq/capsule
Slow-K
KCl
Tablet, SR
8 mEq/tablet
Tri-K
Acetate/bicarbonate/citrate
Liquid
45 mEq/15 mL
Twin-K
Citrate/gluconate
Liquid
20 mEq/5 mL
(SR = sustained release)

PRAMOXINE (ANUSOL OINTMENT, PROCTOFOAM-NS, OTHERS)

USES: *Relief of pain and itching from hemorrhoids, anorectal surgery*; topical for burns and dermatosis

ACTION: Topical anesthetic

DOSE: Apply freely to anal area q3h

CAUTION: [C, ?]

DISP: [OTC] All 1%; foam (ProctoFoam-NS), cream, ointment, lotion, gel, pads, spray

SE: Contact dermatitis, mucosal thinning w/chronic use

PRAMOXINE + HYDROCORTISONE (ENZONE, PROCTOFOAM-HC)

USES: *Relief of pain and itching from hemorrhoids*

ACTION: Topical anesthetic, anti-inflammatory

DOSE: Apply freely to anal area t.i.d.–q.i.d.

CAUTION: [C, ?/–]

DISP: Cream pramoxine 1% acetate 0.5/1%; foam pramoxine 1% hydrocortisone 1%; lotion pramoxine 1% hydrocortisone 0.25/1/2.5%, pramoxine 2.5% and hydrocortisone 1%

SE: Contact dermatitis, mucosal thinning with chronic use

PRAZOSIN (MINIPRESS)

USES: *Hypertension*

ACTION: Peripherally acting -adrenergic blocker

DOSE:

Adults: 1 mg PO t.i.d.; can to 20 mg/d max PRN.

Peds: 0.05–0.1 mg/kg/d in 3 divided doses; max 0.5 mg/kg/d

CAUTION: [C, ?]

CI: Component allergy, concurrent use of PDE5 inhibitors

DISP: Capsules 1, 2, 5 mg; tablets ER 2.5, 5 mg

SE: Dizziness, edema, palpitations, fatigue, GI upset

NOTES: Can cause orthostatic BP, take the 1st dose h.s.; tolerance develops to this effect; tachyphylaxis may result

PREGABALIN (LYRICA)

WARNING: Increased risk of suicidal behavior ideation

USES: *DM peripheral neuropathy pain; PHN; fibromyalgia; adjunct w/adult partial-onset seizures*

ACTION: Nerve transmission modulator, antinociceptive, antiseizure effect; mechanism?; related to gabapentin

DOSE: Neuropathic pain: 50 mg PO t.i.d., to 300 mg/d within 1 wk based on response, 300 mg/d max. Postherpetic neuralgia: 75–150 mg b.i.d., or 50–100 mg t.i.d.; start 75 mg b.i.d. or 50 mg t.i.d.; to 300 mg/d within 1 wk PRN; if pain persists after 2–4 wk, to 600 mg/d. Epilepsy: Start 150 mg/d (75 mg b.i.d. or 50 mg t.i.d.); may to max 600 mg/d; w/renal insufficiency; w/wo food

CAUTION: [C, –]; w/significant renal impairment (see insert), w/elderly and severe CHF avoid abrupt discontinuation

CI: Pregnancy

DISP: Capsules 25, 50, 75, 100, 150, 200, 225, 300 mg

SE: Dizziness, drowsiness, xerostomia, edema, blurred vision, weight gain, difficulty concentrating

NOTES: With discontinuation, taper over at least 1 wk

PROBENECID (BENEMID, OTHERS)

USES: *Prevent gout and hyperuricemia; prolongs levels of penicillins and cephalosporins*

ACTION: Uricosuric, renal tubular blocker of organic anions

DOSE:

Adults: Gout: 250 mg b.i.d. × 1 wk, then 0.5 g PO b.i.d.; can by 500 mg/mo to 2–3 g/d max. Antibiotic effect: 1–2 g PO 30 min before dose.

Peds: >2 yr: 25 mg/kg, then 40 mg/kg/d PO divided q.i.d.

CAUTION: [B, ?]

CI: High-dose ASA, mod–severe renal impairment, age <2 yr

DISP: Tablets 500 mg

SE: Headache, GI upset, rash, pruritus, dizziness, blood dyscrasias

NOTES: Do not use during acute gout attack.

PROPANTHELINE (PRO-BANTHINE)

USES: *Peptic ulcer disease,* symptomatic treatment of small intestine hypermotility, spastic colon, ureteral spasm, bladder spasm, pylorospasm

ACTION: Antimuscarinic

DOSE:

Adults: 15 mg PO a.c. and 30 mg PO h.s.; in elderly.

Peds: 2–3 mg/kg/24 hr PO divided t.i.d.–q.i.d.

CAUTION: [C, ?]

CI: Narrow-angle glaucoma, ulcerative colitis, toxic megacolon, GI/GU obstruction

DISP: Tablets 7.5, 15 mg

SE: Anticholinergic (eg, xerostomia, blurred vision)

PROPOXYPHENE (DARVON); PROPOXYPHENE AND ACETAMINOPHEN (DARVOCET); PROPOXYPHENE AND ASPIRIN (DARVON COMPOUND-65, DARVON-N + ASPIRIN) [C-IV]

WARNING: Excessive doses alone or in combo w/other CNS depressants can be cause of death; use w/caution in depressed or suicidal patients.

USES: *Mild–mod pain*

ACTION: Narcotic analgesic

DOSE: 1–2 PO q4h PRN; in hepatic impairment, elderly

CAUTION: [C (D if prolonged use), M]; hepatic impairment (acetaminophen), peptic ulcer (ASA); severe renal impairment, history EtOH abuse

CI: Allergy, suicide risk, history drug abuse

DISP: Darvon: Propoxyphene HCl capsules 65 mg. Darvon-N: Propoxyphene napsylate 100–mg tablets. Darvocet-N: Propoxyphene napsylate 50 mg/acetaminophen 325 mg. Darvocet-N 100: Propoxyphene napsylate 100 mg/acetaminophen 650 mg. Darvon Compound-65: Propoxyphene HCl capsules 65-mg/ASA 389 mg/caffeine 32 mg. Darvon-N w/ASA: Propoxyphene napsylate 100 mg/ASA 325 mg

SE: Overdose can be lethal; BP, dizziness, sedation, GI upset, LFTs

PROPRANOLOL (INDERAL)

USES: *Hypertension (HTN), angina, MI, hyperthyroidism, essential tremor, hypertrophic subaortic stenosis, pheochromocytoma; prevents migraines and atrial arrhythmias*

ACTION: 1-, 2-Adrenergic receptor blocker; only -blocker to block conversion of T4 to T3

DOSE:

Adults: Hypertension: 40 mg PO b.i.d. or 60–80 mg/d SR, weekly to max 640 mg/d. Pheochromocytoma: 30–60 mg/d divided t.i.d.–q.i.d.

Peds: Arrhythmia: 0.5–1.0 mg/kg/d divided t.i.d.–q.i.d., PRN q3–7d to 60 mg/d max; 0.01–0.1 mg/kg IV over 10 min, 1 mg max. HTN: 0.5–1.0 mg/kg divided b.i.d.–q.i.d., PRN q3–7d to 2 mg/kg/d max; in renal impairment

CAUTION: [C (1st trimester; D if 2nd or 3rd trimester), +]

CI: Uncompensated CHF, cardiogenic shock, bradycardia, heart block, PE, severe respiratory disease

DISP: Tablets 10, 20, 40, 80 mg; SR capsules 60, 80, 120, 160 mg; PO solution 4, 8, mg/mL; injectable 1 mg/mL

SE: Bradycardia, BP, fatigue, GI upset, ED

PROTAMINE (GENERIC)

USES: *Reverse heparin effect*

ACTION: Neutralizes heparin by forming a stable complex

DOSE: Based on degree of heparin reversal; give IV slowly; 1 mg reverses ~100 U of heparin given in the preceding 3–4 hr, 50 mg max

CAUTION: [C, ?]

CI: Allergy

DISP: Injectable 10 mg/mL

SE: Follow coagulants; anticoagulant effect if given w/o heparin; BP, bradycardia, dyspnea, hemorrhage

NOTES: aPTT ~15 min after use to assess response

PSEUDOEPHEDRINE (SUDAFED, NOVAFED, AFRINOL, OTHERS) [OTC]

WARNING: Not for use in peds <2 yr

USES: *Decongestant,* retrograde ejaculation

ACTION: Stimulates -adrenergic receptors w/vasoconstriction; close bladder neck

DOSE:

Adults: 30–60 mg PO q6–8h. Retrograde ejaculation: Up to 60 mg, PO q.i.d. for 2 to 14 days.

Peds: 2–5 yr: 15 mg q 4–6h, 60 mg/24h max. 6–12 yr: 30 mg q4–6h, 120 mg/24 hr max; w/renal insufficiency

CAUTION: [C, +]; w/bladder outlet obstruction

CI: Poorly controlled hypertension or CAD, w/MAOIs

DISP: Tablets 30, 60 mg; capsules 60 mg; SR tablets 120, 240 mg; liquid 7.5 mg/0.8 mL, 15, 30 mg/5 mL

SE: Hypertension, insomnia, tachycardia, arrhythmias, nervousness, tremor

NOTES: Found in many OTC cough/cold preparations; OTC restricted distribution

PYRAZINAMIDE (GENERIC)

USES: *Active TB in combo w/other agents*

ACTION: Bacteriostatic; unknown mechanism

DOSE:

Adults: 15–30 mg/kg/24 hr PO divided t.i.d.–q.i.d.; max 2 g/d; dosing based on lean body weight; dose in renal/hepatic impairment.

Peds: 15–30 mg/kg/d PO divided daily–b.i.d.; w/renal/hepatic impairment

CAUTION: [C, ±]

CI: Severe hepatic damage, acute gout

DISP: Tablets 500 mg

SE: Hepatotoxicity, malaise, GI upset, arthralgia, myalgia, gout, photosensitivity

NOTES: Use in combo w/other anti-TB drugs; consult MMWR for latest TB recommendations; dosage regimen differs for directly observed therapy

PYRIDOXINE [VITAMIN B6] (Aminoxin, Nestrex, Neuro-K, Pyri-500 [OTC])

USES: *Treat/prevent vitamin B6 deficiency,* supplement when on INH, idiopathic hyperoxaluria

ACTION: Vitamin B6 supplement; pyridoxal precursor

DOSE:

Adults: Deficiency: 10–20 mg/d PO. Drug-induced neuritis (eg, isoniazid, hydralazine, penicillamine, cycloserine): 100–200 mg/d; 25–100 mg/d prophylaxis. Idiopathic hyperoxaluria: 150–500 mg/d.

Peds: Deficiency: 5–25 mg/d × 3 wk then 1.5–2.5 mg/d. Drug-induced neuritis treatment: 10–50 mg/24h. Prophylaxis: 1–2 mg/kg/24h

CAUTION: [A (C if doses exceed RDA), +]; may levodopa, phenytoin, and phenobarbital levels

CI: Component allergy

DISP: Capsules, 20, 50, 250 mg; tablets 25, 50, 100, 250, 500 mg; tablet SR 500 mg; liquid 200 mg/5mL; injectable 100 mg/mL

SE: Allergic reactions, headache, N

NOTES: Peripheral INH neuropathy w/pyridoxine 50–100 mg/d

QUINAPRIL (ACCUPRIL)

WARNING: ACE inhibitors used during pregnancy can cause fetal injury and death.

USES: *Hypertension, CHF, diabetic nephropathy, post-MI*

ACTION: ACE inhibitor

DOSE: 10–80 mg PO daily; in renal impairment

CAUTION: [D, +] w/RAS, volume depletion

CI: ACE inhibitor sensitivity, angioedema, pregnancy

DISP: Tablets 5, 10, 20, 40 mg

SE: Dizziness, headache, BP, impaired renal function, angioedema, taste perversion, cough

QUINUPRISTIN–DALFOPRISTIN (SYNERCID)

USES: *Vancomycin-resistant infections due to E. faecium and other gram(+) organisms*

ACTION: Ribosomal protein synthesis. Spectrum: Vancomycin-resistant E. faecium, methicillin-susceptible S. aureus, S. pyogenes; not against E. faecalis

DOSE:

Adults and Peds 7.5 mg/kg IV q8–12h (central line preferred); incompatible w/NS or heparin; flush IV w/dextrose; w/hepatic failure

CAUTION: [B, M]; multiple drug interactions w/drugs metabolized by CYP3A4 (eg, cyclosporine)

CI: Component allergy

DISP: Injectable 500 mg (150 mg quinupristin/350 mg dalfopristin), 600 mg (180 quinupristin/420 mg dalfopristin)

SE: Hyperbilirubinemia, infusion site reactions and pain, arthralgia, myalgia

RALOXIFENE (EVISTA)

WARNING: Increased risk of venous thromboembolism and death from stroke.

USES: *Prevent osteoporosis, breast cancer prevention*

ACTION: Partial antagonist of estrogen, behaves like estrogen

DOSE: 60 mg/d

CAUTION: [X, –]

CI: Thromboembolism, pregnancy

DISP: Tablets 60 mg

SE: Chest pain, insomnia, rash, hot flashes, GI upset, hepatic dysfunction, leg cramps

RAMIPRIL (ALTACE)

WARNING: ACE inhibitors used during pregnancy can cause fetal injury and death.

USES: *Hypertension, CHF, diabetic nephropathy, post-MI*

ACTION: ACE inhibitor

DOSE: 2.5–20 mg/d PO divided daily–b.i.d.; in renal failure

CAUTION: [D, +]

CI: ACE inhibitor-induced angioedema

DISP: Capsules 1.25, 2.5, 5, 10 mg

SE: Cough, headache, dizziness, ↓ BP, renal impairment, angioedema

NOTES: OK in combination w/diuretics

RASBURICASE (ELITEK)

WARNING: Can cause hypersensitivity and anaphylaxis; severe hemolysis with G6PD deficiency and methemoglobinemia

USES: *Reduce ↑ uric acid due to tumor lysis (peds),* malignancy-related hyperuricemia in adults

ACTION: Catalyzes uric acid to water-soluble allantoin

DOSE:

Adults: 0.2 mg/kg/d × 3–7 days started prechemotherapy or 0.15–0.2 mg/kg × 1; repeat PRN based on uric acid levels; OR 3–6 mg × 1, repeated (1.5–6 mg) PRN based on uric acid levels

Peds: 0.15 or 0.20 mg/kg IV over 30 min, daily × 5

CAUTION: [C, ?/–]; falsely ↓ uric acid values

CI: Anaphylaxis, screen for G6PD deficiency to avoid hemolysis, methemoglobinemia

DISP: 1.5 mg injectable

SE: Fever, neutropenia, GI upset, headache, rash

NOTES: Place blood test tube for uric acid level on ice to stop enzymatic reaction; removed by dialysis

RIFAMPIN (RIFADIN)

USES: *TB; treatment/prophylaxis of N. meningitidis, H. influenzae, or S. aureus carriers*; adjunct w/severe S. aureus

ACTION: ↓ DNA-dependent RNA polymerase

DOSE:

Adults: TB: 600 mg PO or IV daily or twice weekly w/combo regimen.

Peds: 10–20 mg/kg/dose PO or IV daily–b.i.d.; ↑ in hepatic failure

CAUTION: [C, +]; w/amprenavir; multiple drug interactions

CI: Component allergy, active N. meningitidis infection, w/saquinavir/ritonavir

DISP: Capsules 150, 300 mg; injectable 600 mg

SE: Red-orange–colored bodily fluids, ↑ LFTs, flushing, headache

NOTES: Never use as single agent w/active TB

RISEDRONATE (ACTONEL, ACTONEL W/CALCIUM)

USES: *Paget disease; treat/prevent glucocorticoid-induced or postmenopausal osteoporosis; ↑ bone mass in osteoporotic men; w/calcium only is FDA-approved for female osteo-

porosis,* hypercalcuria

ACTION: Bisphosphonate; osteoclast-mediated bone resorption, serum and urine Ca2+

DOSE: Postmenopausal osteoporosis treatment: 5 mg/d or 35 mg every wk or 75 mg 2 consecutive days each month or 150 mg once a month. Postmenopausal prevention: 5 mg/d or 35 mg every wk. Men w/osteoporosis: 35 mg every wk; 30 min before 1st food/drink of the day. Glucocorticoid-induced: 5 mg/d. Paget disease: 30 mg/d × 2 mo; stay upright for 30 min after taking

CAUTION: [C, ?/–]; w/Ca2+ supplements and antacids absorption; may interfere with bone-imaging agents

CI: Component allergy, Ca2+, esophageal abnormalities, unable to stand/sit for 30 min, CrCl <30 mL/min

DISP: Actonel tablets 5, 30, 35, 75 mg; Actonel w/calcium: risedronate 35 mg (4 tablets)/calcium carbonate 1,250 mg (24 tablets)

SE: Headache, diarrhea, abdominal pain, severe bone/joint/muscle pain, flu-like symptoms, rash, esophagitis, jaw osteonecrosis

NOTES: Monitor LFTs, Ca2+, PO3+, K+

SERTACONAZOLE (ERTACZO)

USES: *Topical interdigital tinea pedis*

ACTION: Imidazole antifungal. Spectrum: Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum

DOSE:

Adults and Peds: >12: Apply between toes and immediate surrounding healthy skin b.i.d. × 4 wk

CAUTION: [C, ?]

CI: Component allergy

DISP: 2% cream

SE: Contact dermatitis, dry/burning skin, tenderness

NOTES: Use in immunocompetent patients; not for PO, intravaginal, ophthalmic use

SEVELAMER CARBONATE (RENVELA)

USES: *Control PO42 in ESRD*

ACTION: Phosphate binder

DOSE: Initial: PO42 >5.5 and <7.5 mg/dL: 800 mg PO; 7.5 mg/dL: 16,00 mg PO t.i.d. Switching from Sevelamer HCl: On a g-per-g basis; titrate / 1 tablet/meal 2-wk intervals PRN; take w/food

CAUTION: [C, ?]; w/swallowing disorders, bowel problems; may absorption of vitamins D, E, K; ciprofloxacin and other medicine levels

CI: PO4, bowel obstruction

DISP: Tablet 800 mg

SE: N/V/D, dyspepsia, abdominal pain, flatulence, constipation

NOTES: Separate other meds 1 hr before or 3 hr after

SEVELAMER HCL (RENAGEL)

USES: * PO42 in ESRD*

ACTION: Binds intestinal PO42

DOSE: 2–4 capsules PO t.i.d. w/meals; adjust based on PO42; max 4 g/dose

CAUTION: [C, ?]; may absorption of vitamins D, E, K; ciprofloxacin and other medicine levels

CI: PO42, bowel obstruction

DISP: Tablet 400, 800 mg

SE: BP changes, N/V/D, dyspepsia, thrombosis

NOTES: Do not open/chewable capsules; separate other meds 1 hr before or 3 hr after; 800 mg sevelamer = 667 mg Ca acetate

SILDENAFIL (VIAGRA, REVATIO)

USES: *ED (Viagra)*; *pulmonary artery hypertension (Revatio)*

ACTION: Phosphodiesterase type 5 (responsible for cGMP breakdown); cGMP activity to relax smooth muscles and flow to corpus cavernosum and pulmonary vasculature; ? antiproliferative on pulmonary artery smooth muscle

DOSE: ED: 25–100 mg PO 1 hr before sexual activity, max 1/d; if >65 yr; avoid fatty foods w/dose; postpone for 4 hr after taking -adrenergic antagonist

CAUTION: [B, ?]; w/CYP3A4 inhibitors, dose w/ritonavir; retinitis pigmentosa; hepatic/severe renal impairment; w/significant hypo-/hypertension

CI: W/nitrates or if sex not advised or with priapism risk

DISP: Tablets (Viagra) 25, 50, 100 mg; tablets (Revatio) 20 mg

SE: Headache; flushing; dizziness; blue haze visual change, hearing loss, priapism, nonarteritic anterior ischemic optic neuropathy (NAION).

NOTES: Cardiac events in absence of nitrates debatable; transient global amnesia reports; onset 15 min–1 hr, duration of action 4 hr

SILODOSIN (RAPAFLO)

USES: *Benign prostatic hyperplasia*

ACTION: Antagonist of prostatic 1 smooth muscle receptors (mostly 1A)

DOSE: 8 mg/d; 4 mg/d w/CrCl 30–50 mL/min; take w/food

CAUTION: [B, ?]; not for use in females; do not use w/other -blockers or w/cyclosporine; rule out prostate cancer before use; intraoperative floppy iris syndrome possible w/cataract

surgery; avoid

CI: Severe hepatic/renal impairment (CrCl <30 mL/min), w/CYP3A4 inhibitors (eg, ketoconazole, clarithromycin, itraconazole, ritonavir)

DISP: Capsules 4, 8 mg

SE: Retrograde ejaculation, dizziness, diarrhea, syncope, somnolence, orthostatic BP, nasopharyngitis, nasal congestion

NOTES: Not for use as antihypertensive; no effect on QT interval

SILVER SULFADIAZINE (SILVADENE, OTHERS)

USES: *Prevent/treat infection in 2nd- and 3rd-degree burns*

ACTION: Bactericidal

DOSE:

Adults and Peds Aseptically cover the area w/1/16–inch coating b.i.d.

CAUTION: [B unless near term, ?/–]

CI: Infants <2 mo, pregnancy near term

DISP: Cream 1%

SE: Itching, rash, skin discoloration, blood dyscrasias, hepatitis, allergy

NOTES: Systemic absorption w/extensive application

SIROLIMUS [RAPAMYCIN] (RAPAMUNE)

WARNING: Use only by physicians experienced in immunosuppression; immunosuppression is associated w/lymphoma, infection risk; do not use in lung transplant (fatal bronchial anastomotic dehiscence).

USES: *Prophylaxis of organ rejection in newly treated patients*

ACTION: T-lymphocyte activation

DOSE:

Adults: >40 kg: 6 mg PO on day 1, then 2 mg/d PO.

Peds: <40 kg and 13 yr: 3 mg/m2 load, then 1 mg/m2/d (in H2O/orange juice; no grapefruit juice w/sirolimus); take 4 hr after cyclosporine; in hepatic impairment

CAUTION: [C, ?/–]; grapefruit juice, ketoconazole

CI: Component allergy

DISP: Solution 1 mg/mL; tablet 1, 2 mg

SE: Hypertension, edema, CP, fever, headache, insomnia, acne, rash, cholesterol, GI upset, / K+, infections, blood dyscrasias, arthralgia, tachycardia, renal impairment, hepatic artery thrombosis, graft loss and death in de novo liver transplant (hepatic artery thrombosis), delayed wound healing

NOTES: Levels: Trough: 4–20 ng/mL; can vary based on assay and use of other immunosuppression agents; mortality in stable liver transplant patients after conversion from a CNI

regimen to sirolimus

SODIUM BICARBONATE [NAHCO3]

USES: *Alkalinization of urine,* RTA, *metabolic acidosis, K+, tricyclic antidepressant overdose*

ACTION: Alkalinizing agent

DOSE:

Adults: Metabolic acidosis: 2–5 mEq/kg IV over 8 hr and PRN based on acid–base status. Hyperkalemia: 1 mg/kg IV over 5 min. Alkalinize urine: 4 g (48 mEq) PO, then 1–2 g q4h; adjust based on urine pH; 2 amp (100 mEq/1 L D5W at 100–250 mL/hr IV, monitor urine pH and serum bicarbonate. Chronic renal failure: 1–3 mEq/kg/d. Distal RTA: 1 mEq/kg/d PO.

Peds: Chronic renal failure: See adult dosage. Distal RTA: 2–3 mEq/kg/d PO. Proximal RTA: 5–10 mEq/kg/d; titrate based on serum bicarbonate. Urine alkalinization: 84–840 mg/kg/d (1–10 mEq/kg/d) in divided doses; adjust based on urine pH

CAUTION: [C, ?]

CI: Alkalosis, Na+, severe PE, Ca2+

DISP: Powder, tablets 300 mg = 3.6 mEq, 325 mg = 3.8 mEq, 520 mg = 6.3 mEq, 600 mg = 7.3 mEq, 650 mg = 7.6 mEq; injectable 1 mEq/1 mL, 4.2% (5 mEq/10 mL), 7.5% (8.92 mEq/mL), 8.4% (10 mEq/10 mL) vial or ampule

SE: Belching, edema, flatulence, Na+, metabolic alkalosis

NOTES: Baking soda 1 tsp = 42 mEq HCO3); 1 g neutralizes 12 mEq of acid; 50 mEq bicarb = 50 mEq Na; can make 3 amps in 1 L D5W to = D5NS w/150 mEq bicarbonate

SODIUM CELLULOSE PHOSPHATE (CALCIBIND)

USES: *Adjunct to dietary restriction to reduce renal calculi formation in absorptive hypercalciuria type I*

ACTION: Reduces urinary Ca2+ excretion by intestinal binding of Ca2+

DOSE:

Adults: 5 g t.i.d. w/meals; decrease 5 g w/main meal and 2.5 g w/2 other meals when urinary Ca2+ declines to <150 mg/d

Peds: 25–35 mg/kg/d in 4 divided doses

CAUTION: [C, +]; avoid use with vitamin C

CI: Nonabsorptive hypercalcuria, bone diseases (eg, osteoporosis), hyperparathyroidism, hypocalcemic states

DISP: Powder, 2.5 g/scoop

SE: Can cause severe metabolic abnormalities, including hypomagnesemia, hyperoxaluria, Ca2+ and Fe malabsorption, osteoporosis

NOTES: Side-effect profile limits long-term use; use only if urinary Ca^{2+} > 500 mg/d; may increase urinary oxylate excretion since Ca^{2+} is not available to bind oxylate in intestine; must use with oxylate restriction and Mg supplementation to prevent Mg deficiency.

SODIUM CITRATE/CITRIC ACID (BICITRA, ORACIT)

USES: *Chronic metabolic acidosis, alkalinize urine; dissolve uric acid and cysteine stones*

ACTION: Urinary alkalinizer

DOSE:

Adults: 10–30 mL in 1–3 oz H_2O p.c. and h.s.

Peds: 5–15 mL in 1–3 oz H_2O p.c. and h.s.; best p.c.

CAUTION: [C, +]

CI: Aluminum-based antacids; severe renal impairment or Na-restricted diets

DISP: 15- or 30-mL unit dose: 16 (473 mL) or 4 (118 mL) fl oz

SE: Tetany, metabolic alkalosis, K^+, GI upset; avoid use of multiple 50-mL amps; can cause Na^+/hyperosmolality

NOTES: 1 mL = 1 mEq Na and 1 mEq bicarbonate

SODIUM PHOSPHATE (VISICOL)

WARNING: Acute phosphate nephropathy possible

USES: *Bowel prep prior to colonoscopy,* short-term constipation

ACTION: Hyperosmotic laxative

DOSE: 3 tablets PO w/at least 8 oz clear liquid q15 min (20 tablets total night before procedure; 3–5 hr before colonoscopy, repeat)

CAUTION: [C, ?]; renal impairment, electrolyte disturbances

CI: Megacolon, bowel obstruction, CHF, ascites, unstable angina, gastric retention, bowel perforation, colitis, hypomotility

DISP: Tablets 0.398, 1.102 g

SE: QT, PO24, K^+, N/D, flatulence, cramps, abdominal bloating/pain

NOTES: Acute phosphate nephropathy is associated with calcium-phosphate crystal deposits in the renal tubules and may result in permanent renal dysfunction. Risk factors for acute phosphate nephropathy: Age >55 yr, hypovolemia, pre-existing renal impairment, bowel obstruction, or active colitis; w/meds that may affect renal perfusion/function (eg, diuretics, ACE inhibitors, ARBs, and possibly NSAIDs).

SODIUM POLYSTYRENE SULFONATE (KAYEXALATE)

USES: *Treat K^+*

ACTION: Na^+/K^+ ion-exchange resin

DOSE:

Adults: 15–60 g PO or 30–60 g PR q6h based on serum K+.

Peds: 1 g/kg/dose PO or PR q6h based on serum K+ (given w/agent [eg, sorbitol], to promote movement through the bowel)

CAUTION: [C, M]

CI: Na+

DISP: Powder; suspension 15 g/60 mL sorbitol

SE: Na+, K+, Na retention, GI upset, fecal impaction

NOTES: Enema acts more quickly than PO; PO most effective, onset action >2 hr

SOLIFENACIN (VESICARE)

USES: *Overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence*

ACTION: Antimuscarinic, detrusor contractions

DOSE: 5 mg PO daily, 10 mg/d max; w/renal/hepatic impairment

CAUTION: [C, ?/–]; BOO or GI obstruction, ulcerative colitis, myasthenia gravis, renal/hepatic impairment, QT prolongation risk

CI: Narrow-angle glaucoma, urinary/gastric retention

DISP: Tablets 5, 10 mg

SE: Constipation, xerostomia, dyspepsia, blurred vision, drowsiness

NOTES: CYP3A4 substrate; azole antifungals levels; recent concern over cognitive effects

SORAFENIB (NEXAVAR)

USES: *Advanced renal cell carcinoma,* metastatic liver cancer

ACTION: Multi-kinase inhibitor; tumor growth and angiogenesis by inhibiting Raf kinases and cell surface kinase receptors (VEGFR-2, VEGFR-3, PDGFR-, cKIT, FLT-3)

DOSE:

Adults: 400 mg PO b.i.d. on empty stomach

CAUTION: [D, –]; w/irinotecan, doxorubicin, warfarin; avoid conception (male/female)

DISP: Tablets 200 mg

SE: Hand–foot syndrome; treatment-emergent hypertension; bleeding, INR, cardiac infarction/ischemia; pancreatic enzymes, hypophosphatemia, lymphopenia, anemia, fatigue, alopecia, pruritus, diarrhea, GI upset, headache, neuropathy

NOTES: Monitor BP 1st 6 wk; may require dose (daily or every other day); impaired metabolism in patients of Asian descent; unknown effect on wound healing; discontinue before major surgery.

SORBITOL (GENERIC)

USES: *Constipation*

ACTION: Laxative

DOSE: 30–60 mL PO of 20–70% solution PRN

CAUTION: [B, +]

CI: Anuria

DISP: Liquid 70%

SE: Edema, electrolyte loss, lactic acidosis, GI upset, xerostomia

NOTES: May be vehicle for many liquid formulations (eg, zinc, Kayexalate)

SPIRONOLACTONE (ALDACTONE)

USES: *Hyperaldosteronism, hypertension, ascites from cirrhosis*

ACTION: Aldosterone antagonist; K+-sparing diuretic

DOSE:

Adults: CHF (NYHA class III–IV) 12.5–25 mg/d (w/ACE and loop diuretic); hypertension 25–50 mg/d.

Peds: 1–3.3 mg/kg/24 hr PO divided b.i.d.–q.i.d. Neonates: 0.5–1 mg/kg/dose q8h; take w/food

CAUTION: [D, +]

CI: K+, acute renal failure, anuria

DISP: Tablets 25, 50, 100 mg

SE: K+ and gynecomastia, arrhythmia, sexual dysfunction, confusion, dizziness, D/N/V, abnormal menstruation

NOTES: Mild antiandrogenic properties

STARCH, TOPICAL, RECTAL (TUCKS SUPPOSITORIES [OTC])

USES: *Temporary relief of anorectal disorders (itching, etc)*

ACTION: Topical protectant

DOSE:

Adults and Peds: 12 yr: Cleanse, rinse and dry, insert 1 suppository rectally 6×/d × 7 day max

CAUTION: [?, ?]

CI: None

DISP: Suppository

SE: Discontinue w/or if rectal bleeding occurs or if condition worsens or does not improve within 7 d.

STEROIDS, SYSTEMIC

USES: *Endocrine disorders* (adrenal Insufficiency), *rheumatoid disorders, collagen–vascular diseases, derm diseases, allergic states, cerebral edema,* nephritis, nephrotic syndrome, immunosuppression for transplantation, Ca^{2+}, malignancies (breast, lymphomas), preop (in any pt who has been on steroids in the previous year, known hypoadrenalism, preop for adrenalectomy); inject into joints/tissue

ACTION: Glucocorticoid with some mineralocorticoid activity based on compound

DOSE: Varies w/use and institutional protocols. General guidelines:

Adrenal insufficiency, acute: Adults: Hydrocortisone: 100 mg IV; then 300 mg/d divided q6h; convert to 50 mg PO q8h × 6 doses, taper to 30–50 mg/d divided b.i.d. Peds: Hydrocortisone: 1–2 mg/kg IV, then 150–250 mg/d divided t.i.d.

Adrenal insufficiency, chronic (physiologic replacement): May need mineralocorticoid supplement such as Florinef. Adults: Hydrocortisone 20 mg PO every AM, 10 mg PO every PM; cortisone 0.5–0.75 mg/kg/d divided b.i.d.; cortisone 0.25–0.35 mg/kg/d IM; dexamethasone 0.03–0.15 mg/kg/d or 0.6–0.75 mg/m2/d divided q6–12h PO, IM, IV. Peds: Hydrocortisone 0.5–0.75 mg/kg/d PO t.i.d.; hydrocortisone succinate 0.25–0.35 mg/kg/d IM

Congenital adrenal hyperplasia: Peds: Initial hydrocortisone: 30–36 mg/m2/d PO divided 1/3 dose every AM, 2/3 dose every PM; maintenance 20–25 mg/m2/d divided b.i.d.

Immunosuppressive/anti-inflammatory: Adults and Older Peds: Hydrocortisone 15–240 mg PO, IM, IV q12h; methylprednisolone 4–48 mg/d PO, taper to lowest effective dose; methylprednisolone Na succinate 10–80 mg/d IM. Adults: Prednisone or prednisolone 5–60 mg/d PO divided daily–q.i.d. Infants and Younger Children: Hydrocortisone 2.5–10 mg/kg/d PO divided q6–8h; 1–5 mg/kg/d IM/IV divided b.i.d.

Nephrotic syndrome: Peds: Prednisolone or prednisone 2 mg/kg/d PO t.i.d.–q.i.d. until urine is protein-free for 5 d, use up to 28 d; for persistent proteinuria, 4 mg/kg/dose PO every other day max 120 mg/d for an additional 28 d; maintenance 2 mg/kg/dose every other day for 28 d; taper over 4–6 wk (max 80 mg/d).

Septic shock (controversial): Adults: Hydrocortisone 500 mg–1 g IM/IV q2–6h. Peds: Hydrocortisone 50 mg/kg IM/IV, repeat q4–24h PRN.

Perioperative steroid coverage: Hydrocortisone 100 mg IV night before surgery, 1 hr preop, intraop, and 4, 8, and 12 hr postop; postop day 1 = 100 mg IV q6h; postop day 2 = 100 mg IV q8h; postop day 3 = 100 mg IV q12h; postop day 4 = 50 mg IV q12h; postop day 5 = 25 mg IV q12h; resume prior PO dosing if chronic use or discontinue if only perioperative coverage required

CAUTION: [C, ?/–]

CI: Active varicella infection, serious infection except TB, fungal infections

DISP: See table

SE: Appetite, hyperglycemia, K+, osteoporosis, nervousness, insomnia, steroid psychosis, adrenal suppression

NOTES: Hydrocortisone succinate for systemic, acetate for intraarticular; never abruptly discontinue steroids, taper dose

STREPTOKINASE (STREPTASE, KABIKINASE)

USES: *Coronary artery thrombosis, acute massive PE, DVT, and some occluded vascular grafts*

ACTION: Activates plasminogen to plasmin that degrades fibrin

DOSE:

Adults: PE: Load 250,000 U peripheral IV over 30 min, then 100,000 U/hr IV for 24–72 hr. DVT or arterial embolism: Load as w/PE, then 100,000 U/hr for 72 hr.

Peds: 3,500–4,000 U/kg over 30 min, then 1,000–1,500 U/kg/hr. Occluded catheter (controversial): 10,000–25,000 U in NS to final volume of catheter (leave in for 1 hr, aspirate and flush w/NS)

CAUTION: [C, +]

CI: Streptococcal infection or streptokinase in last 6 mo, active bleeding, CVA, TIA, spinal surgery/trauma in last month, vascular anomalies, severe hepatic/renal disease, endocarditis, pericarditis, severe uncontrolled hypertension

DISP: Powder for injectable 250,000, 750,000, 1,500,000 U

SE: Bleeding, BP, fever, bruising, rash, GI upset, hemorrhage, anaphylaxis

NOTES: If infusion inadequate to keep clotting time 2–5× control, see package for adjustments; antibodies remain 3–6 mo following dose

STREPTOMYCIN

WARNING: Neuro-/oto-/renal toxicity possible; neuromuscular blockage w/respiratory paralysis possible

USES: *TB combo therapy* streptococcal or enterococcal endocarditis

ACTION: Aminoglycoside; protein synthesis

DOSE:

Adults: TB: 15 mg/kg/d (up to 1 g), directly observed therapy (DOT) 2× wk 20–30 mg/kg/dose (max 1.5 g), DOT 3× wk 25–30 mg/kg/dose (max 1 g).

Peds: 15 mg/kg/d; DOT 2× wk 20–40 mg/kg/dose (max 1 g); DOT 3× wk 25–30 mg/kg/dose (max 1 g); w/renal insufficiency, either IM or IV over 30–60 min

CAUTION: [D, +]

CI: Pregnancy

DISP: Injectable 400 mg/mL (1-g vial)

SE: Incidence of vestibular and auditory toxicity, neurotoxicity risk in patients w/impaired renal function

NOTES: Monitor levels: Peak: 20–30 g/mL, Trough: <5 g/mL; Toxic peak: >50, Trough: >10; IV over 30–60 min

STRONTIUM-89 CHLORIDE (METASTRON)

USES: Bone pain in patients with osseous metastasis

ACTION: Ca2+ analogue taken up by bone in areas of active osteogenesis with selective radiation of metastasis

DOSE: 148 MBq (4 mCi) IV slowly, or 15 to 22 MBq/kg

CAUTION: [D,]

CI: Pregnancy

DISP: Injectable

SE: Platelets nadir about 12–16 wk after treatment

NOTES: Administered by radiation oncology; caution with platelet counts <60,000 or WBC of <2,400

SULINDAC (CLINORIL)

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID; prostaglandins

DOSE: 150–200 mg b.i.d., 400 mg/d max; w/food

CAUTION: [B (D if 3rd trimester or near term), ?]

CI: NSAID or ASA sensitivity, w/ketorolac, ulcer, GI bleeding, postop pain in CABG

DISP: Tablets 150, 200 mg

SE: Dizziness, rash, GI upset, pruritus, edema, renal blood flow, renal failure (? fewer renal effects than other NSAIDs), peptic ulcer, GI bleeding

SUNITINIB (SUTENT)

USES: *Advanced GIST refractory/intolerant of imatinib; advanced RCC*

ACTION: Antitumor and antiangiogenic; multityrosine kinase inhibitor (eg, PDGFR and), VEGFs, others.

DOSE:

Adults: 50 mg PO daily × 4 wk, followed by 2 wk holiday = 1 cycle; to 37.5 mg w/CYP3A4 inhibitors, to 87.5 mg w/CYP3A4 inducers

CAUTION: [D, –]; multiple interactions require dose modification (eg, St. John’s wort)

CI: W/atazanavir

DISP: Capsules 12.5, 25, 50 mg

SE: WBC and platelet, bleeding, BP, ejection fraction, QT interval, pancreatitis, DVT, seizures, adrenal insufficiency, N/V/D, skin discoloration, oral ulcers, taste perversion, hypothyroidism

NOTES: Monitor LVEF, ECG, CBC/platelets, chemistries (K+/Mg2+/phosphate), TFT and LFTs periodically; dose in 12.5-mg increments if not tolerated

TACROLIMUS [FK506] (PROGRAF, PROTOPIC)

WARNING: Risk of infection and lymphoma

USES: *Prevent organ rejection,* eczema

ACTION: Macrolide immunosuppressant; prevents IL-2 production via calcineurin inhibition

DOSE:

Adults: Renal transplantation: Initial dose: 0.2 mg/kg/d PO in 2 divided doses, q12h; initial dose may be given within 24 hr of transplant, but held until renal function recovers; OR 0.03–0.05 mg/kg/d continuous IV infusion.

Peds: IV: 0.03–0.05 mg/kg/d as continuous IV infusion. PO: 0.15–0.4 mg/kg/d PO divided q12h.

Adults and Peds Eczema: Apply b.i.d., continue 1 wk after clearing; take on empty stomach; w/hepatic/renal impairment

CAUTION: [C, –]; w/cyclosporine; avoid topical if <2 yr of age

CI: Component allergy, castor oil allergy w/IV form

DISP: Capsules 0.5, 1, 5 mg; injectable 5 mg/mL; ointment 0.03, 0.1%

SE: Neuro-/nephrotoxic, BP, edema, headache, insomnia, fever, pruritus, / K+, hyperglycemia, GI upset, anemia, leukocytosis, tremors, paresthesias, pleural effusion, seizures, lymphoma

NOTES: Monitor levels. Trough: 5–20 ng/mL based on indication and time since transplant. Reports of cancer risk; topical use for short-term/2nd-line; African Americans may require larger doses to maintain trough levels.

TADALAFIL (CIALIS, ADCIRCA)

USES: *ED (Cialis), pulmonary artery hypertension (Adcirca)*

ACTION: PDE5 inhibitor, cyclic guanosine monophosphate and NO levels; relaxes smooth muscles, dilates cavernosal arteries

DOSE:

Adults: ED PRN dosing: (Cialis) 10 mg PO before sexual activity (5–20 mg max) 1 dose/24 hr. Daily dosing: 2.5 mg/d w/o regard to timing of sex, may to 5 mg/d; w/o regard to meals; w/renal/hepatic insufficiency

CAUTION: [Not indicated in women B, ?]; w/-blockers (except tamsulosin) may cause hypotension, start with lowest dose possible; use w/CYP3A4 inhibitor (eg, ritonavir, ketoconazole, itraconazole) 2.5 mg/d dose or 5 mg PRN dose; CrCl <30 mL/min, hemodialysis, severe hepatic impairment do not use daily dosing; w/priapism risk

CI: Nitrates, severe hepatic impairment

DISP: Cialis Tablets 2.5, 5, 10, 20–mg. Adcirca 40 mg

SE: Headache, flushing, dyspepsia, back/limb pain, myalgia, nasal congestion, urticaria, Stevens-Johnson syndrome, dermatitis, visual field defect, NIAON, sudden /loss of hearing, tinnitus, priapism

NOTES: Onset 15 min–2 hr, duration of action 24–36 hr (longest acting of class); daily dosing may drug interactions; excessive EtOH may orthostasis; transient global amnesia reported

TAMSULOSIN (FLOMAX)

USES: *Benign prostatic hyperplasia,* expulsion therapy for a symptomatic ureteral stone

ACTION: Antagonist of prostatic -receptors, relaxation of smooth muscles in lower urinary tract

DOSE: 0.4 mg/d, may to 0.8 mg/d PO

CAUTION: [B, ?]

CI: Female gender

DISP: Capsules 0.4 mg

SE: Headache, dizziness, syncope, somnolence, libido, GI upset, retrograde ejaculation, rhinitis, rash, angioedema, intraoperative floppy iris syndrome

NOTES: Not for use as antihypertensive; do not open/crush/chew; approved for use w/dutasteride for benign prostatic hyperplasia

TELMISARTAN (MICARDIS)

USES: *Hypertension, CHF*

ACTION: Angiotensin II receptor antagonist

DOSE: 40–80 mg/d

CAUTION: [C (1st trimester; D, 2nd and 3rd trimester), ?/–]

CI: Angiotensin II receptor antagonist sensitivity

DISP: Tablets 20, 40, 80 mg

SE: Edema, GI upset, headache, angioedema, renal impairment, orthostatic BP

TEMAZEPAM (RESTORIL) [C-IV]

USES: *Insomnia,* anxiety, depression, panic attacks

ACTION: Benzodiazepine

DOSE: 15–30 mg PO h.s. PRN; in elderly

CAUTION: [X, ?/–]; potentiates CNS depressive effects of opioids, barbiturates, EtOH, antihistamines, MAOIs, TCAs

CI: Narrow-angle glaucoma

DISP: Capsules 7.5, 15, 22.5, 30 mg

SE: Confusion, dizziness, drowsiness, hangover

NOTES: Abrupt discontinuation after >10 day use may cause withdrawal.

TEMSIROLIMUS (TORISEL)

USES: *Advanced RCC*

ACTION: Active metabolite is sirolimus; multikinase inhibitor, MTOR, hypoxic-induced factors (HIF 1 and 2), VEGF

DOSE: 25 mg IV 30–60 min 1 × wk. Hold w/ANC <1,000/mm3, platelet <75,000/mm3, or NCI grade 3 tox. Resume when tox grade 2 or less, restart w/dose 5 mg/wk not <15 mg/wk. w/CYP3A4 inhibitors: 12.5 mg/wk. w/CYP3A4 inducers: 50 mg/wk

CAUTION: [D, –]; avoid live vaccines, wound healing, avoid perioperatively

CI: None

DISP: Injectable 25 mg/mL w/250 mL diluent

SE: Rash, asthenia, mucositis, N, bowel perforation, anorexia, edema, lipids, glucose, triglycerides, LFTs, Cr, WBC, HCT, platelet, PO4

NOTES: Premedicate w/antihistamine; lipids, CBC, platelet, Cr, glucose; w/sunitinib dose-limiting toxicity likely; females use w/contraception

TERAZOSIN (HYTRIN)

USES: *Benign prostatic hyperplasia and hypertension*

ACTION: 1-Blocker (blood vessel and bladder neck/prostate)

DOSE: Initial, 1 mg PO h.s.; 20 mg/d max; may w/diuretic or other BP medicine

CAUTION: [C, ?] w/-blocker, calcium channel blocker, ACE inhibitor

CI: -Antagonist sensitivity

DISP: Tablets 1, 2, 5, 10 mg; capsules 1, 2, 5, 10 mg

SE: BP, and syncope following 1st dose; dizziness, weakness, nasal congestion, peripheral edema, palpitations, GI upset

NOTES: Caution w/1st dose syncope; if for hypertension, combine w/thiazide diuretic

TERBINAFINE (LAMISIL, LAMISIL AT)

USES: *Onychomycosis, tinea/pedis/cruris/corporus/versicolor* cutaneous candidiasis, pityriasis versicolor

ACTION: Squalene epoxidase resulting in fungal death

DOSE: PO: 250 mg/d PO for 6–12 wk. Topical: Apply to area; tinea pedis b.i.d., tinea cruris and corporus once a day–b.i.d., tinea versicolor solution b.i.d.; ↓ PO in renal/hepatic impairment

CAUTION: [B, –]; PO ↑ effects of drug metabolism by CYP2D6, w/liver/renal impairment

CI: CrCl <50 mL/min, WBC <1,000, severe liver disease

DISP: Tablets 250 mg; Lamisil AT [OTC] cream, gel, solution 1%

SE: Headache, dizziness, rash, pruritus, alopecia, GI upset, taste perversion, neutropenia, retinal damage, Stevens-Johnson syndrome, ↑ LFTs

NOTES: Effect may take months due to need for new nail growth; topical not for nails; do not use occlusive dressings; PO follow CBC/LFTs.

TERCONAZOLE (TERAZOL 7)

USES: *Vaginal fungal infections*

ACTION: Topical triazole antifungal

DOSE: 1 applicator-full or 1 suppository intravaginally h.s. × 3–7 day

CAUTION: [C, ?]

CI: Component allergy

DISP: Vaginal cream 0.4, 0.8%, vaginal suppository 80 mg

SE: Vulvar/vaginal burning

NOTES: Insert high into vagina.

TERIPARATIDE (FORTEO)

WARNING: Osteosarcoma risk in animals, therefore only use in patients for whom the potential benefits outweigh risks.

USES: *Severe/refractory osteoporosis*

ACTION: PTH (recombinant)

DOSE: 20 g SQ daily in thigh or abdomen

CAUTION: [C, ?/–]

CI: W/Paget disease, prior radiation, bone metastases, ↑ Ca2+; caution in urolithiasis

DISP: 3-mL prefilled device (discard after 28 d)

SE: Orthostatic ↓ BP on administration, N/D, ↑ Ca2+; leg cramps

NOTES: 2 yr max use; osteosarcoma in animals

TESTOSTERONE (ANDROGEL, ANDRODERM, DELATESTRYL, DEPO-TESTOSTERONE, STRIANT, TESTIM, TESTOPEL) [C-III]

USES: *Male hypogonadism, delayed male puberty,* postmenopausal women w/estrogen to increase sexual desire; female breast cancer

ACTION: Testosterone replacement; ↑ lean body mass, libido

DOSE: AndroGel: 5-g gel every A.M. to clean dry area on shoulder, upper arm, abdomen;10g/d max. Androderm: 2 2.5-mg or 1 5-mg patch daily h.s. to clean dry area on back, arm, etc. Delatestryl, Depo-Testosterone: 50–400 mg every 2–4 wk. Striant: 30-mg buccal tablets b.i.d. (apply to gum over incisor; do not chew or swallow). Testim: 1 5-g gel tube every AM to clean dry area on shoulder, upper arm. Testopel: 150–450 mg (2–6 pellets) SQ implant every 3–6 mo (implant 2 75-mg pellets for each 25 mg testosterone required weekly; example: For 75 mg/wk, implant 450 mg (6 pellets).

CAUTION: [N/A, N/A]; cover topical gel sites and wash hands to prevent transfer of drug to others; alcohol-based gels flammable; avoid fire or smoking until gel dried; patch contains metal, remove for MRI exam; may potentiate sleep apnea

CI: Known or suspected prostate cancer, male breast cancer

DISP: AndroGel 1.25 g/actuation; 2.5, 5-g packet; Testim 5-g gel (delivers 50 mg testosterone); Androderm 2.5, 5-mg patches; Delatestryl (as enanthate) 200 mg/mL (1, 5 mL); Depo-Testosterone (as cypionate) 100 mg/mL (10 mL), 200 mg/mL (1,10 mL); Striant: 30-mg buccal tablets; Testopel 75 mg/implant

SE: Site reactions, acne, edema, weight gain, gynecomastia, hypertension, sleep apnea, prostate enlargement

NOTES: Do not apply topical agents to genitalia; dose-adjust based on serum testosterone levels; PO agents associated w/hepatic tumors and not sold in US; transdermal/mucosal forms preferred. Testopel is implanted 3–4 inches below belt line in superior gluteal region; close site w/Steri-Strip and apply cold compress after.

TETRACYCLINE (ACHROMYCIN V, SUMYCIN)

USES: *Broad-spectrum antibiotic*

ACTION: Bacteriostatic; protein synthesis. Spectrum: Gram(+): Staphylococcus, Streptococcus. Gram(–): H. pylori. Atypicals: Chlamydia, Rickettsia, Mycoplasma

DOSE:

Adults: 250–500 mg PO b.i.d.–q.i.d.

Peds: >8 yr: 25–50 mg/kg/24 hr PO q6–12h; w/renal/hepatic impairment, w/o food preferred

CAUTION: [D, +]

CI: Pregnancy, antacids, w/dairy products, children <8 yr

DISP: Capsules 100, 250, 500 mg; tablets 250, 500 mg; PO suspension 250 mg/5 mL

SE: Photosensitivity, GI upset, renal failure, pseudotumor cerebri, hepatic impairment

NOTES: Can stain tooth enamel and depress bone formation in children; may serum testosterone by up to 20%

TICARCILLIN/POTASSIUM CLAVULANATE (TIMENTIN)

USES: *Infections of the skin, bone, respiratory, urinary tracts, abdomen, sepsis*

ACTION: Carboxy-penicillin; bactericidal; cell wall synthesis; clavulanic acid blocks -lactamase. Spectrum: Good gram(+) coverage, not MRSA; good gram(–) and anaerobe coverage

DOSE:

Adults: 3.1 g IV q4–6h, max 24 g ticarcillin component/d.

Peds: 200–300 mg/kg/d IV divided q4–6h; in renal failure

CAUTION: [B, ±]; penicillin sensitivity

DISP: Injectable ticarcillin/clavulanate acid 3.1 g/0.1 g vial

SE: Hemolytic anemia, false + proteinuria

NOTES: Often used in combo w/aminoglycosides; penetrates CNS with meningeal irritation

TICLOPIDINE (TICLID)

WARNING: Neutropenia/agranulocytosis, TTP, aplastic anemia reported.

USES: * Risk of thrombotic stroke,* protect grafts status post-CABG, diabetic microangiopathy, ischemic heart disease, DVT prophylaxis, graft prophylaxis after renal transplant

ACTION: Platelet aggregation inhibitor

DOSE: 250 mg PO b.i.d. w/food

CAUTION: [B, ?/–]; toxicity of ASA, anticoagulation, NSAIDs, theophylline

CI: Bleeding, hepatic impairment, neutropenia, thrombocytopenia

DISP: Tablets 250 mg

SE: Bleeding, GI upset, rash, on LFTs

NOTES: Follow CBC 1st 3 mo

TIGECYCLINE (TYGACIL)

USES: *Complicated skin and soft-tissue infections; complicated intra-abdominal infections*

ACTION: Newer class, related to tetracycline; Spectrum: Broad gram(+), gram(–), anaerobic, some mycobacterial coverage; E. coli, E. faecalis (vancomycin-susceptible isolates), S. aureus (methicillin-susceptible/resistant), Streptococcus (agalactiae, anginosus, pyogenes), Citrobacter freundii, Enterobacter cloacae, B. fragilis group, C. perfringens, Peptostreptococcus

DOSE:

Adults: 100 mg, then 50 mg q12h IV over 30–60 min q12h

CAUTION: [D, ?]; hepatic impairment, monotherapy w/intestinal perforation; not OK in peds, w/tetracycline allergy

CI: Component sensitivity

DISP: Injectable 50 mg vial

SE: N/V, injection site reaction

TINIDAZOLE (TINDAMAX)

WARNING: Off-label use discouraged (animal carcinogenicity w/other drugs in class)

USES: Adults/children >3 yr: *Trichomoniasis and giardiasis; intestinal amebiasis or amebic liver abscess*

ACTION: Antiprotozoal nitroimidazole. Spectrum: Trichomonas vaginalis, Giardia duodenalis, Entamoeba histolytica

DOSE:

Adults: Trichomoniasis: 2 g PO; treat partner.

Peds: Trichomoniasis: 50 mg/kg PO, 2 g/d max; take w/food

CAUTION: [C, D in 1st trimester; –]; may be cross-resistant with metronidazole; seizure/peripheral neuropathy may require discontinuation; w/CNS/hepatic impairment

CI: Metronidazole allergy, 1st-trimester pregnancy, w/EtOH use

DISP: Tablets 250, 500

SE: CNS disturbances; blood dyscrasias, taste disturbances, N/V, darkens urine

NOTES: Discontinue EtOH during and 3 day after treatment; potentiates warfarin and lithium; clearance w/other drugs; crush and disperse in cherry syrup for peds; removed by HD

TIOCONAZOLE (VAGISTAT)

USES: *Vaginal fungal infections*

ACTION: Topical antifungal

DOSE: 1 Applicator-full intravaginally h.s. (single dose)

CAUTION: [C, ?]

CI: Component allergy

DISP: Vaginal ointment 6.5%

SE: Local burning, itching, soreness, polyuria

NOTES: Insert high into vagina.

TIOPRONIN (THIOLA)

USES: *Prevent cystine urolithiasis in patients with severe homozygous cystinuria with urinary cystine >500 mg/d, who are resistant to conservative measures (high fluid intake, alkali and diet modification), or have adverse reactions to d-penicillamine*

ACTION: Combines with cystine to increase solubility

DOSE:

Adults and Peds: >9 yr: Encourage conservative hydration therapy with 3 L fluid/d (>2 L urine output) before initiating therapy. 800 mg/d initially (peds 15/mg/kg/d) divided t.i.d., 1 hr

a.c. or 2 hr p.c.; titrate based on urinary cysteine levels; typical adult dose 1,000 mg/d

CAUTION: [D, –]

CI: Component allergy

DISP: Tablets 100 mg

SE: Fever, rash, arthralgia, lymphadenopathy, hypogeusia, wrinkling and friable skin

NOTES: Maintain urine pH 6.5–7.0 (potassium alkali supplements over sodium alkali due to reduced hypercalcuria risks); check urinary cysteine after 1 mo and then every 3 mo to adjust dose

TOBRAMYCIN (NEBCIN)

USES: *Serious gram(–) infections*

ACTION: Aminoglycoside; protein synthesis. Spectrum: Gram(–) bacteria (including Pseudomonas)

DOSE:

Adults: Conventional dosing: 1–2.5 mg/kg/dose IV q8–12h. Once-daily dosing: 5–7 mg/kg/dose q24h.

Peds: 2.5 mg/kg/dose IV q8h; w/renal insufficiency

CAUTION: [C, M]

CI: Aminoglycoside sensitivity

DISP: Injectable 10, 40 mg/mL

SE: Nephro-/ototoxic

NOTES: Follow CrCl and levels. Levels: Peak: 30 min after infusion; Trough <0.5 hr before next dose; Therapeutic conventional: Peak 5–10 g/mL, Trough <2 g/mL

TOLMETIN (TOLECTIN)

WARNING: May risk of cardiovascular events and GI bleeding

USES: *Arthritis and pain*

ACTION: NSAID; prostaglandins

DOSE: 200–600 mg PO t.i.d.; 2,000 mg/d max

CAUTION: [C (D in 3rd trimester or near term), +]

CI: NSAID or ASA sensitivity; use for pain post-CABG

DISP: Tablets 200, 600 mg; capsules 400 mg

SE: Dizziness, rash, GI upset, edema, GI bleeding, renal failure

TOLNAFTATE (TINACTIN) [OTC]

USES: *Tinea pedis/cruris/corporis/manus/versicolor*

ACTION: Topical antifungal

DOSE: Apply to area b.i.d. for 2–4 wk

CAUTION: [C, ?]

CI: Nail and scalp infections

DISP: OTC 1% liquid, gel, powder, topical cream, ointment, powder, spray solution

SE: Local irritation

NOTES: Avoid ocular contact, infection should improve in 7–10 d

TOLTERODINE (DETROL, DETROL LA)

USES: *Overactive bladder with frequency, urgency, incontinence*

ACTION: Anticholinergic/antimuscarinic, relaxes bladder smooth muscle, bladder capacity

DOSE: Detrol 1–2 mg PO b.i.d., Detrol LA 2–4 mg/d

CAUTION: [C, ?/–]; w/CYP2D6 and 3A3/4 inhibitor

CI: Urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma

DISP: Detrol tablets 1, 2 mg; Detrol LA tablets 2, 4 mg

SE: Xerostomia, blurred vision, headache, constipation

NOTES: LA form may see intact pill in stool.

TRAMADOL (ULTRAM, ULTRAM ER)

USES: *Mod–severe pain*

ACTION: Centrally acting analgesic

DOSE:

Adults: 50–100 mg PO q4–6h PRN, start 25 mg PO every AM, q3d to 25 mg PO q.i.d.; 50 mg q3d, 400 mg/d max (300 mg if >75 yr); ER 100–300 mg PO daily.

Peds: 0.5–1 mg/kg PO q4–6h PRN; w/renal insufficiency

CAUTION: [C, ?/–]

CI: Opioid dependency; w/MAOIs; sensitivity to codeine

DISP: Tablets 50 mg; ER 10, 20, 30 mg

SE: Dizziness, headache, somnolence, GI upset, respiratory depression, anaphylaxis

NOTES: Seizure threshold; tolerance/dependence may develop

TRAMADOL/ACETAMINOPHEN (ULTRACET)

USES: *Short-term treatment of acute pain (<5 d)*

ACTION: Centrally acting analgesic; nonnarcotic analgesic

DOSE: 2 tablets PO q4–6h PRN; 8 tablets/d max. Elderly/renal impairment: Lowest possible dose; 2 tablets q12h max if CrCl <30

CAUTION: [C, –]; seizures, hepatic/renal impairment, or history addictive tendencies

CI: Acute intoxication

DISP: Tablet 37.5 mg tramadol/325 mg acetaminophen

SE: SSRIs, TCAs, opioids, MAOIs risk of seizures; dizziness, somnolence, tremor, headache, N/V/D, constipation, xerostomia, liver toxicity, rash, pruritus, sweating, physical dependence

NOTES: Avoid EtOH

TRIAMCINOLONE AND NYSTATIN (MYCOLOG-II)

USES: *Cutaneous candidiasis*

ACTION: Antifungal and anti-inflammatory

DOSE: Apply lightly to area b.i.d.; max 25 mg/d

CAUTION: [C, ?]

CI: Varicella; systemic fungal infections

DISP: Cream and ointment 15, 30, 60, 120 mg

SE: Local irritation, hypertrichosis, pigmentation changes

NOTES: For short-term use (<7 d)

TRIAMTERENE (DYRENIUM)

USES: *Edema associated w/CHF, cirrhosis*

ACTION: K+-sparing diuretic

DOSE:

Adults: 100–300 mg/24 hr PO divided daily–b.i.d.

Peds: Hypertension: 2–4 mg/kg/d in 1–2 divided doses; w/renal/hepatic impairment

CAUTION: [B (manufacturer; D, editor opinion), ?/–]

CI: K+, renal impairment; caution w/other K+-sparing diuretics

DISP: Capsules 50, 100 mg

SE: K+, blood dyscrasias, liver damage, other reactions

NOTES: Do not use in hypercalcuria due to triamterene stone risk.

TRICHLORMETHIAZIDE (NAQUA)

USES: *Hypertension,* alternative therapy to other diuretics in hypercalcuria (except resorptive hypercalcuria)

ACTION: Long-acting thiazide diuretic, reduces urinary Ca2+ excretion

DOSE: 2–4 mg/d PO

CAUTION: [D, ?]; w/hepatic impairment; NSAIDs may reduce effectiveness; diabetic control may become lost, potentiates digoxin and lithium toxicity

CI: Drug hypersensitivity; anuria; renal impairment (CrCl <30 mL/min)

DISP: Tablets 2, 4 mg

SE: Photosensitivity; increased levels of cholesterol and triglycerides; azotemia can occur; fluid/electrolyte imbalances (eg, hyponatremia, hypercalcemia, hyperuricemia, hypokalemia, hypomagnesemia, hyperchloremic acidosis, hyperglycemia, hypocitraturia)

NOTES: Follow serum K+ levels; not 1st choice for hypercalcuria

TRIETHYLENETHIOPHOS-PHORAMIDE (THIO-TEPA, TESPA, TSPA)

USES: *Hodgkin disease/NHLs; leukemia; breast, ovarian cancers; preparative regimens for allogeneic and bone marrow transplant w/high doses; intravesical for superficial bladder cancer*

ACTION: Poly-functional alkylating agent

DOSE: 0.5 mg/kg q1–4wk, 6 mg/m2 IM or IV × 4 day q2–4wk, 15–35 mg/m2 by continuous IV infusion over 48 hr; 60 mg in bladder and retained 2 hr q1–4wk

CAUTION: [D, –]

CI: Component allergy

DISP: Injectable 15, 30 mg

SE: Bone marrow, N/V, dizziness, headache, allergy, paresthesias, alopecia, dysuria

NOTES: Intravesical use in bladder cancer is infrequent today.

TRIMETHOPRIM (PRIMSOL, PROLOPRIM)

USES: *UTI due to susceptible gram(+) and gram(–) organisms; treat PCP w/dapsone* suppression of UTI

ACTION: Dihydrofolate reductase. Spectrum: Many gram(±) except Bacteroides, Branhamella, Brucella, Chlamydia, Clostridium, Mycobacterium, Mycoplasma, Nocardia, Neisseria, Pseudomonas, Treponema

DOSE:

Adults: 100 mg PO b.i.d. or 200 mg/d PO; PCP 5 mg/kg t.i.d. × 21 day w/dapsone.

Peds: 4 mg/kg/d in 2 divided doses; w/renal failure

CAUTION: [C, +]

CI: Megaloblastic anemia due to folate deficiency

DISP: Tablets 100 mg; PO solution 50 mg/5 mL

SE: Rash, pruritus, megaloblastic anemia, hepatic impairment, blood dyscrasias

NOTES: Take w/plenty of H2O

TRIMETHOPRIM (TMP)–SULFAMETHOXAZOLE (SMX) [CO-TRIMOXAZOLE] (BACTRIM, SEPTRA)

USES: *UTI treatment/prophylaxis, otitis media, sinusitis, bronchitis*

ACTION: SMX synthesis of dihydrofolic acid, TMP dihydrofolate reductase to impairment protein synthesis. Spectrum: Includes Shigella, PCP, and Nocardia infections, Mycoplasma, Enterobacter sp, Staphylococcus, Streptococcus, and more

DOSE:

Adults: 1 DS tablet PO b.i.d. or 5–20 mg/kg/24 hr (based on TMP) IV in 3–4 divided doses. PCP: 15–20 mg/kg/d IV or PO (TMP) in 4 divided doses. Nocardia: 10–15 mg/kg/d IV

or PO (TMP) in 4 divided doses. UTI prophylaxis: 1 PO daily.

Peds: 8–10 mg/kg/24 hr (TMP) PO divided into 2 doses or 3–4 doses IV; do not use in newborns; in renal failure; maintain hydration

CAUTION: [B (D, if near term), +]

CI: Sulfonamide sensitivity, porphyria, megaloblastic anemia w/folate deficiency, significant hepatic impairment; newborns

DISP: Regular tablets 80 mg TMP/400 mg SMX; DS tablets 160 mg TMP/800 mg SMX; PO suspension 40 mg TMP/200 mg SMX/5 mL; injectable 80 mg TMP/400 mg SMX/5 mL

SE: Allergic skin reactions, photosensitivity, GI upset, Stevens-Johnson syndrome, blood dyscrasias, hepatitis

NOTES: Synergistic combo, interacts w/warfarin

TRIPTORELIN (TRELSTAR DEPOT, TRELSTAR LA)

USES: *Palliation of advanced prostate cancer*

ACTION: LHRH analog; LHRH w/continuous dosing; transient in LH, FSH, testosterone, and estradiol 7–10 day after 1st dose; w/chronic/continuous use (usually 2–4 wk), sustained LH and FSH w/ testicular and ovarian steroidogenesis similar to surgical castration

DOSE: 3.75 mg IM monthly or 11.25 mg IM q3mo

CAUTION: [X, N/A]

CI: Not indicated in females

DISP: Injectable Depot 3.75 mg; LA 11.25 mg

SE: Dizziness, emotional lability, fatigue, headache, insomnia, hypertension, diarrhea, vomiting, erectile dysfunction, retention, UTI, pruritus, anemia, injection site pain, musculoskeletal pain, osteoporosis, allergic reactions

TROSPIUM (SANCTURA, SANCTURA XR)

USES: *Overactive bladder with symptoms of urge incontinence, urgency, frequency*

ACTION: Muscarinic antagonist, bladder smooth muscle tone

DOSE: 20 mg tablet PO b.i.d.; 60 mg ER capsules PO every AM, 1 hr a.c. or on empty stomach. w/CrCl <30 mL/min and elderly

CAUTION: [C, ±]; w/EtOH use, in hot environments, ulcerative colitis, myasthenia gravis, renal/hepatic impairment

CI: Urinary/gastric retention, narrow-angle glaucoma

DISP: Tablet 20 mg; capsules ER 60 mg

SE: Dry mouth, constipation, headache, rash

UROKINASE (ABBOKINASE)

USES: *PE, DVT, restore patency to IV catheters*

ACTION: Converts plasminogen to plasmin; causes clot lysis

DOSE:

Adults and Peds Systemic effect: 4,400 U/kg IV over 10 min, then 4,400–6,000 U/kg/hr for 12 hr. Restore catheter patency: Inject 5,000 U into catheter and aspirate up to 2 doses

CAUTION: [B, +]

CI: Do not use within 10 day of surgery, delivery, or organ biopsy; bleeding, CVA, vascular malformation

DISP: Powder for injection 250,000–U vial

SE: Bleeding, BP, dyspnea, bronchospasm, anaphylaxis, cholesterol embolism

NOTES: aPTT should be <2× normal before use and before starting anticoagulants after

VALACYCLOVIR (VALTREX)

USES: *Herpes zoster; genital herpes; herpes labialis*

ACTION: Prodrug of acyclovir; viral DNA replication. Spectrum: Herpes simplex I and II

DOSE: Zoster: 1 g PO t.i.d. × 7 days. Herpes genitalis CDC-recommended regimens: 1 g PO b.i.d. × 7–10 days. Recurrence: 500 mg/d PO OR 1 g/d PO. Episodic within 1 day of lesion: 500 mg PO b.i.d. × 3 days OR 1 g/d PO × 5 days. Herpes labialis: 2 g PO q12h × 1 day; w/renal failure

CAUTION: [B, +]

DISP: Caplets 500, 1,000 mg

SE: Headache, GI upset, dizziness, pruritus, photophobia

VALSARTAN (DIOVAN)

WARNING: Use during 2nd/3rd trimester of pregnancy can cause fetal harm.

USES: *Hypertension, CHF,* prevent diabetic nephropathy

ACTION: Angiotensin II receptor antagonist

DOSE: 80–160 mg/d, max 320 mg/d

CAUTION: [D, ?/–]; w/K+-sparing diuretics or K+ supplements

CI: Severe hepatic impairment, biliary cirrhosis/obstruction, primary hyperaldosteronism, bilateral renal artery stenosis

DISP: Tablets 40, 80, 160, 320 mg

SE: BP, dizziness, headache, viral infection, fatigue, abdominal pain, diarrhea, arthralgia, fatigue, back pain, hyperkalemia, cough, Cr

VANCOMYCIN (VANCOCIN, VANCOLED)

USES: *Serious MRSA infections; enterococcal infections; PO treatment of S. aureus and C. difficile pseudomembranous colitis*

ACTION: Cell wall synthesis. Spectrum: Gram(+) bacteria and some anaerobes (includes MRSA, Staphylococcus, Enterococcus, Streptococcus sp, C. difficile)

DOSE:

Adults: 1 g IV q12h or 15–20 mg/kg/dose; C. difficile: 125–500 mg PO q6h × 7–10 days.

Peds: 40–60 mg/kg/d IV in divided doses q6–12h; C. difficile: 40–60 mg/kg/d PO × 7–10 day. Neonates. 10–15 mg/kg/dose q12h; w/renal insufficiency

CAUTION: [C, M]

CI: Component allergy; avoid in history hearing loss

DISP: Capsules 125, 250 mg; powder 250 mg/5 mL, 500 mg/6 mL for PO solution; powder for injectable 500 mg, 1,000 mg, 10 g/vial

SE: Oto-/nephrotoxic, GI upset (PO), WBC

NOTES: Not absorbed PO, effect in gut only; give IV slowly (over 1–3 hr) to prevent red-man syndrome (flushing of head/neck/upper torso); IV product PO for colitis. Levels: Peak: 1 hr after infusion; Trough: <0.5 hr before next dose; Therapeutic: Peak: 20–40 g/mL; Trough: 10–20 g/mL; Toxic Peak: >50 g/mL; Trough: >20 g/mL. Half-life: 6–8 hr

VARDENAFIL (LEVITRA)

USES: *ED*

ACTION: PDE5 inhibitor, increases cGMP and NO levels; relaxes smooth muscles, dilates cavernosal arteries

DOSE: 10 mg PO 60 min before sexual activity; titrate; max × 1 = 20 mg; 2.5 mg w/CYP3A4 inhibitors

CAUTION: [Not indicated in women B, –]; w/cardiovascular, hepatic, or renal disease or if sexual activity is not advisable; should not be taken with type 1A or type 3 antiarrhythmics or w/long QT syndrome

CI: W/nitrates, w/use of -adrenergic antagonist

DISP: Tablets 2.5, 5, 10, 20 mg tablets

SE: QT interval BP, headache, dyspepsia, priapism, flushing, rhinitis, sinusitis, flu syndrome, sudden /loss of hearing, tinnitus, nonarteritic anterior ischemic optic neuropathy (NAION)

NOTES: Concomitant -blockers may cause BP; transient global amnesia reports; onset 15 min–1 hr, duration of action 2–8 hr

VERAPAMIL (CALAN, ISOPTIN, VERELAN)

USES: *Angina, hypertension, paroxysmal supraventricular tachycardia, atrial flutter,* migraine prophylaxis, Peyronie disease

ACTION: Calcium channel blocker

DOSE:

Adults: Hypertension: 80–180 mg PO t.i.d. or SR tablets 120–240 mg PO daily to 240 mg b.i.d.; 2.5–5.0 mg IV over 1–2 min; repeat 5–10 mg, in 5–30 min PRN. Peyronie: 10 mg/10

mL intralesionally q2wk, 12 injections total.

Peds: <1 yr: 0.1–0.2 mg/kg IV over 2 min (may repeat in 30 min). 1–16 yr: 0.1–0.3 mg/kg IV over 2 min (may repeat in 30 min); 5 mg max. PO: 1–5 yr: 4–8 mg/kg/d in 3 divided doses. >5 yr: 80 mg q6–8h; in renal/hepatic impairment

CAUTION: [C, +]; amiodarone/-blockers/flecainide can cause bradycardia; statins, midazolam, tacrolimus, theophylline levels may be ; w/elderly patients

CI: Conduction disorders, cardiogenic shock; -blocker/thiazide combo, dofetilide, pimozide, ranolazine

DISP: Tablets 40, 80, 120 mg; tablets ER 120, 180, 240 mg; tablets ER 24–h 180, 240, mg; capsules SR 120, 180, 240, 360 mg; capsules ER 100, 200, 300 mg; injectable 5 mg/2 mL

SE: Gingival hyperplasia, constipation, BP, bronchospasm, HR or conduction disturbances

NOTES: Topical gel (15%) use reported in Peyronie disease

VINBLASTINE (VELBAN, VELBE)

WARNING: Chemotherapeutic agent; handle w/caution

USES: *Hodgkin disease/NHLs, mycosis fungoides, cancer (testis, renal cell, breast, NSCLC), AIDS-related Kaposi sarcoma,* choriocarcinoma, histiocytosis

ACTION: Microtubule assembly

DOSE: 0.1–0.5 mg/kg/wk (4–20 mg/m2); in hepatic failure

CAUTION: [D, ?]

CI: Intrathecal use

DISP: Injectable 1 mg/mL in 10 mg vial

SE: Bone marrow (especially leukopenia), N/V, constipation, neurotoxicity, alopecia, rash, myalgia, tumor pain

VINCRISTINE (ONCOVIN, VINCASAR PFS)

WARNING: Chemotherapeutic agent; handle w/caution; fatal if administered intrathecally

USES: *ALL, breast cancer, SCLC, sarcoma (eg, Ewing tumor, rhabdomyosarcoma), Wilms tumor, Hodgkin disease/NHLs, neuroblastoma, multiple myeloma*

ACTION: Promotes disassembly of mitotic spindle, causing metaphase arrest

DOSE: 0.4–1.4 mg/m2 (single doses 2 mg/max); in hepatic failure

CAUTION: [D, ?]

CI: Intrathecal use

DISP: Injectable 1 mg/mL, 5 mg vial

SE: Neurotoxicity commonly dose-limiting, jaw pain (trigeminal neuralgia), fever, fatigue, anorexia, constipation and paralytic ileus, bladder atony; no significant bone marrow

w/standard doses; tissue necrosis w/extravasation

VITAMIN B6

See “Pyridoxine.”

VITAMIN B12

See “Cyanocobalamin.”

VITAMIN E (-TOCOPHEROL, MANY OTC FORMS)

USES: *Dietary supplement,* Peyronie disease plaque

ACTION: Antioxidant, protects against free radicals, protects RBC from hemolysis

DOSE: Peyronie: 400–1,000 IU/d PO

CAUTION: [A/C if exceeds RDA/+]; may hemorrhagic stroke risk

CI: Hypersensitivity

DISP: Multiple oral, topical forms; capsules 200, 400, 600, 1,000 IU typical

SE: D, cramps, nausea

NOTES: In SELECT prostate chemoprevention trial, did not reduce prostate cancer risk alone or with selenium

VORICONAZOLE (VFEND)

USES: *Invasive aspergillosis, candidemia, serious fungal infections*

ACTION: Ergosterol synthesis. Spectrum: Candida, Aspergillus, Scedosporium, Fusarium sp

DOSE:

Adults and Peds: >12 yr: IV: 6 mg/kg q12h × 2, then 4 mg/kg b.i.d.; may to 3 mg/kg/dose. PO: <40 kg: 100 mg q12h, up to 150 mg; >40 kg: 200 mg q12h, up to 300 mg; w/mild–mod hepatic impairment; IV w/renal impairment × 1 dose; PO w/o food

CAUTION: [D, ?/–]

CI: Severe hepatic impairment, w/CYP3A4 substrates

DISP: Tablets 50, 200 mg; suspension 200 mg/5 mL; 200 mg injectable

SE: Visual changes, fever, rash, GI upset, LFTs

NOTES: Check for multiple drug interactions (eg, dose w/phenytoin)

WARFARIN (COUMADIN)

WARNING: Can cause major or fatal bleeding

USES: *Prophylaxis/treatment of PE, DVT, AF w/embolization,* other postop indications

ACTION: Vitamin K-dependent clotting factors in order: VII-IX-X-II

DOSE:

Adults: Titrate, INR 2.0–3.0 for most; mechanical valves INR is 2.5–3.5. American College of Chest Physicians Guidelines: 5 mg initial, may use 7.5–10 mg; if elderly or w/other bleeding risk factors; maintenance 2–10 mg/d PO, follow daily INR initially to adjust dosage.

Peds: 0.05–0.34 mg/kg/24 hr PO or IV; follow PT/INR to adjust dosage; monitor vitamin K intake; w/hepatic impairment/elderly

CAUTION: [X, +]

CI: Severe hepatic/renal disease, bleeding, peptic ulcer, pregnancy

DISP: Tablets 1, 2, 2.5, 3, 4, 5, 6, 7.5, 10 mg; injectable

SE: Bleeding due to over-anticoagulation or injury and therapeutic INR; bleeding, alopecia, skin necrosis, purple-toe syndrome

NOTES: Monitor vitamin K intake (effect); INR preferred test; to rapidly correct over-anticoagulation: Vitamin K, fresh-frozen plasma, or both; highly teratogenic. Caution patient on taking w/other meds, especially ASA. Common warfarin interactions: Potentiated by: Acetaminophen, EtOH (w/liver disease), amiodarone, cimetidine, ciprofloxacin, cotrimoxazole, erythromycin, fluconazole, flu vaccine, isoniazid, itraconazole, metronidazole, omeprazole, phenytoin, propranolol, quinidine, tetracycline. Inhibited by: Barbiturates, carbamazepine, chlordiazepoxide, cholestyramine, dicloxacillin, nafcillin, rifampin, sucralfate, high-vitamin K foods. Consider genotyping for VKORC1 and CYP2C9.

WITCH HAZEL (TUCKS PADS, OTHERS [OTC])

USES: After bowel movement, in cleansing to decrease local irritation or relieve hemorrhoids; after anorectal surgery, episiotomy, vaginal hygiene

ACTIONS

Astringent

DOSE: Apply PRN

CAUTION: [?, ?]; external use only

CI: None

DISP: Presoaked pads 50% witch hazel

SE: Mild itching or burning

ZOLEDRONIC ACID (ZOMETA, RECLAST)

USES: *Hypercalcemia of malignancy (HCM), skeletal-related events in prostate cancer, multiple myeloma, and metastatic bone lesions (Zometa)*; *postmenopausal osteoporosis, Paget disease (Reclast)*

ACTION: Bisphosphonate; osteoclastic bone resorption

DOSE: Zometa HCM: 4 mg IV over 15 min; may re-treat in 7 day w/adequate renal function. Zometa bone lesions/myeloma: 4 mg IV over >15 min, repeat q3–4wk PRN; extend w/ Cr. Reclast: 5 mg IV annually

CAUTION: [C, ?/–]; diuretics, aminoglycosides; ASA-sensitive asthmatics; avoid invasive dental procedures

CI: Bisphosphonate allergy; urticaria, angioedema, w/dental procedures

DISP: Vial 4 mg, 5 mg

SE: All w/renal dysfunction; fever, flu-like syndrome, GI upset, insomnia, anemia; electrolyte abnormalities, bone, joint, muscle pain, osteonecrosis of jaw

NOTES: Requires vigorous prehydration; do not exceed recommended doses/infusion duration to renal dysfunction; follow Cr; effect prolonged w/Cr ; avoid oral surgery; dental exam recommended prior to therapy; dose w/renal dysfunction; give CA2+ and vitamin D supplements; under study to prevent development of bone mets in Abnormal uterine bleeding, diabetes insipidus, familial adenomatous polyposis.

* This chapter is based on data in and modified from Gomella LG, Haist S, Adams A, eds. Clinicians' Pocket Drug Reference, 2010 Edition. New York: McGraw Hill, 2010.

SECTION VII Appendix

Reproduced with permission from Moore C, Huebler D, Zimmermann T, et al. The Aging Males Symptom Scale (AMS) as outcome measure for treatment of androgen deficiency. Eur Urol 2004;46:80–87.

Reproduced with permission from the American Urologic Association. Based on data from Wolf JS Jr, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol. 2008;179(4):1379–1390.

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(With permission from Cook Urological, Inc., “French Catheter Scale”)

Based on data from Rosen A, et al. The international index of erectile dysfunction (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822–830, with permission.

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Litwin M, et al. The National Institutes of Health Chronic Prostatitis Symptom Index: Development and Validation of a New Outcome Measure. J Urol 1999;162(2):369–375, with permission.

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Kattan MW, Potters L, Blasko JC, et al. Pretreatment nomogram for predicting freedom from recurrence after permanent prostate brachytherapy in prostate cancer. Urology 2001;58(3):393–399, with permission.

Zelefsky MJ, Kattan MW, Fearn P, et al. Pretreatment nomogram predicting ten-year biochemical outcome of three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for prostate cancer. Urology 2007;70(2):283–287, with permission.

**Values are percent probability.

From Rosen RC, et al. 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(6):319–326, with permission.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:410.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:262.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:280.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:310.

Note: Ta (noninvasive verrucous carcinoma) and Tis (carcinoma in situ) are Stage Grouping 0.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:348.

Note: There is no pathologic stage T1. For pT3a, R1 descriptor indicates positive surgical margin (residual disease). Gleason score (Gl) is only used for stage grouping and not clinical staging.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:338.

Note: Ta (noninvasive papillary carcinoma) and Tis (carcinoma in situ) are Stage Grouping 0.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:320.

S = serum markers.

Note: Tis (carcinoma in situ) is Grouping Stage 0.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:354.

Note: Ta (noninvasive papillary, polypoid, or verrucous carcinoma) and Tis (carcinoma in situ) are Stage Grouping 0.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:362.

Note: Ta (noninvasive papillary carcinoma) and Tis (carcinoma in situ) are Stage Grouping 0.

From Rubin P, Hansen JT, eds. TNM Staging Atlas. Philadelphia: Lippincott Williams & Wilkins; 2007:328.

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