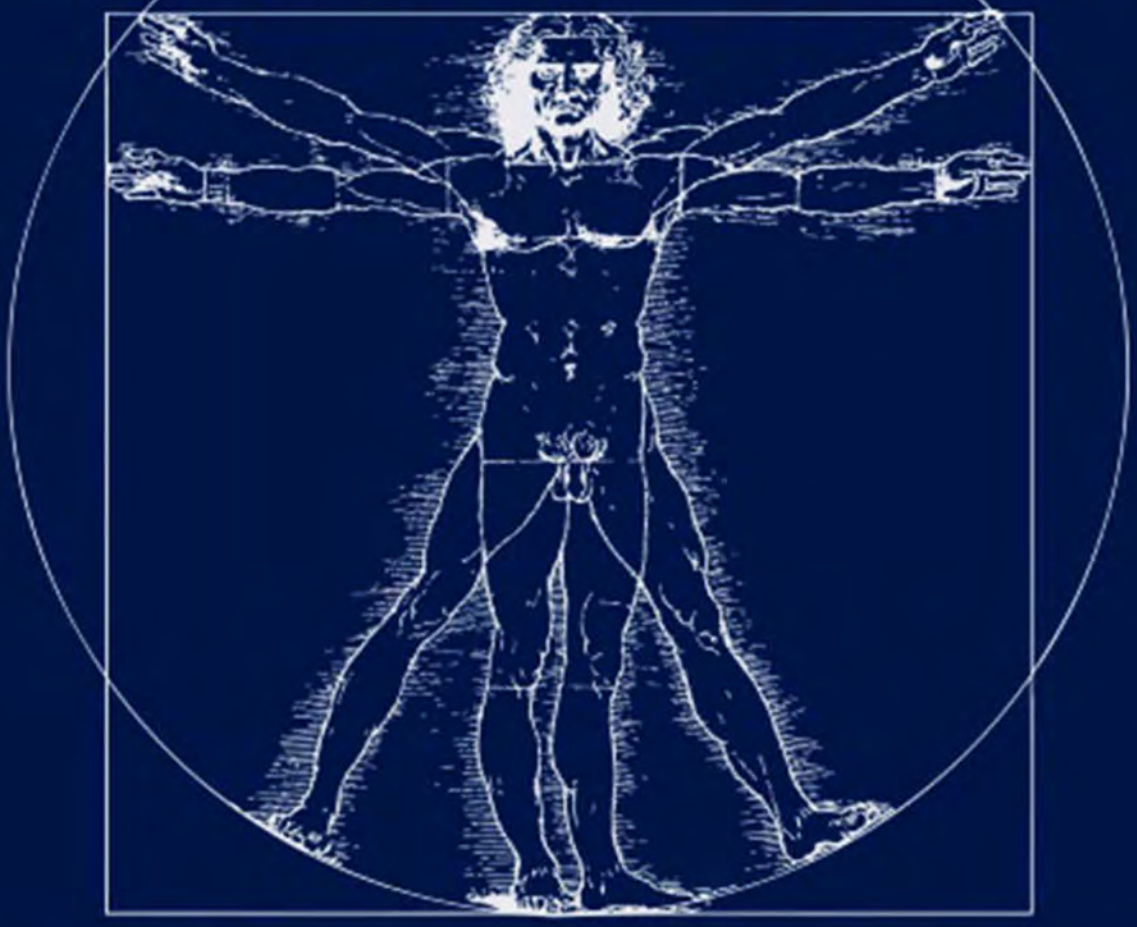
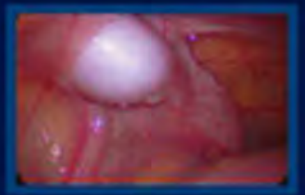
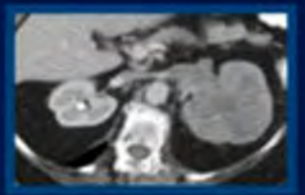
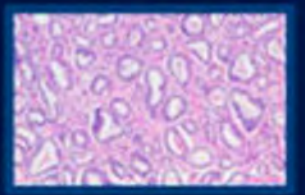
Alan W. Partin · Roger R. Dmochowski
Louis R. Kavoussi · Craig A. Peters

Campbell-Walsh-Wein
UROLOGY



TWELFTH EDITION

ELSEVIER

Campbell-Walsh-Wein
UROLOGY

Campbell-Walsh-Wein

UROLOGY

Editor-in-Chief

Alan W. Partin, MD, PhD

The Jakurski Family Director
Urologist-in-Chief
Chairman, Department of Urology
Professor, Departments of Urology, Oncology and Pathology
Johns Hopkins Medical Institutions
Baltimore, Maryland

Editors

Roger R. Dmochowski, MD, MMHC, FACS

Professor, Urologic Surgery, Surgery and Gynecology
Program Director, Female Pelvic Medicine and Reconstructive Surgery
Vice Chair for Faculty Affairs and Professionalism
Section of Surgical Sciences
Associate Surgeon-in-Chief
Vanderbilt University Medical Center
Nashville, Tennessee

Louis R. Kavoussi, MD, MBA

Professor and Chair
Department of Urology
Zucker School of Medicine at Hofstra/Northwell
Hempstead, New York;
Chairman of Urology
The Arthur Smith Institute for Urology
Lake Success, New York

Craig A. Peters, MD

Chief, Pediatric Urology
Children's Health System Texas;
Professor of Urology
University of Texas Southwestern Medical Center
Dallas, Texas

TWELFTH EDITION

ELSEVIER

Elsevier
1600 John F. Kennedy Blvd.
Ste 1600
Philadelphia, PA 19103-2899

CAMPBELL-WALSH-WEIN UROLOGY, TWELFTH EDITION
ISBN: 978-0-323-54642-3
Volume I ISBN: 978-0-323-76066-9
Volume II ISBN: 978-0-323-76067-6
Volume III ISBN: 978-0-323-76068-3

INTERNATIONAL EDITION
ISBN: 978-0-323-67226-9
Volume I ISBN: 978-0-323-76005-8
Volume II ISBN: 978-0-323-76006-5
Volume III ISBN: 978-0-323-76007-2

Notice

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds or experiments described herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made. To the fullest extent of the law, no responsibility is assumed by Elsevier, authors, editors or contributors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Previous editions copyrighted 2016, 2012, 2007, 2002, 1998, 1992, 1986, 1978, 1970, 1963, and 1954.

ISBN: 978-0-323-54642-3

Senior Content Strategist: Belinda Kuhn
Senior Content Development Specialist: Jennifer Ehlers
Publishing Services Manager: Catherine Jackson
Senior Project Manager: Kate Mannix
Design Direction: Amy Buxton

Printed in Canada

Last digit is the print number: 9 8 7 6 5 4 3 2 1

Dedicated to my wife, family, residents, and faculty, all of whom have supported me in this work in various and important ways and helped make this edition of Campbell-Walsh-Wein *possible.*

AP

For this edition of Campbell's *I would like to thank my spouse and my children for their unbelievable support during my career in urology. I would also like to thank my past and present residents and fellows for all that they have taught me about the importance of listening. I would like to recognize a few mentors who have taught me a great deal about the specialty and humanity: Dr. Herb Seybold, Dr. Marty Resnick, Dr. Joe Segura, Dr. Joseph Corriere, Dr. George Benson, Dr. Gerald Jordan, and Dr. Jay Smith.*

RD

To my mentors, whose reassuring voices forever guide me: Bill Catalona, Ralph Clayman, Alan Retik, and Pat Walsh.

LK

The privilege of compiling and editing this book makes us reflect on the vast body of knowledge and experience that makes up the field of urology, and the efforts and dedication of our predecessors and mentors, to whom I dedicate this work. Without the examples, teaching, and inspiration (with not infrequent cajoling and correction), none of us would have been able to grow into who we are or participate in this textbook. For myself, these mentors have been many and varied, guiding me to this day in areas of clinical care, teaching, research, and mentoring. Some are no longer with us but they all continue to inspire.
I also include my wife and children, who inspire, teach, and support me in so many ways. Their commitment has meant the world to me.

CP

PREFACE

Continuing in a great tradition of publishers, editors, and authors, we proudly present to you, our readers, the twelfth edition of the "Bible of Urology"—*Campbell-Walsh-Wein Urology*. Started in 1954 as *Campbell's Urology* and retitled *Campbell-Walsh Urology* in 2012, the present editors felt it was appropriate to honor Alan J. Wein, MD, PhD (Hon) for his many years of dedication to this text by adding his name to the previous chief editors. During his time as chief editor, Dr. Wein was responsible for keeping the textbook in pace with a rapidly growing field in medicine—for this diligence and dedication we are grateful.

As with previous editions, the twelfth edition presents many exciting advances in our use and understanding of technology, physiology, pharmacology, epidemiology, and pathophysiology while maintaining our basic classical urological knowledge.

We are dedicated to keeping the content of this textbook fresh and on the cutting edge of care. *CWW-12* adds 10 novel chapters and more than 150 first-time authors, including several new authors from international sites. *CWW-12* has 3 volumes, 162 chapters, 3706 pages, and more than 3000 illustrations.

The format continues to include color images, Key Points, Suggested Readings, boldfaced important text, and online linkable references to streamline the access and usefulness of the material. Additionally, as in previous editions, a companion Review book with questions and answers for each chapter is available separately under the leadership of Drs. Alan Wein and Thomas F. Kolon.

Volume I (54 chapters) covers basic urological evaluation, imaging and principles and fundamentals of surgery, endourology, and laparoscopy. Also in Volume I is a completely revamped and updated evaluation, the exstrophy-epispadias complex, pediatric stone disease, hypospadias, disorders of sexual development, and many more topics.

Volume II (50 chapters) covers infections within the urinary tract, sexually transmitted diseases, male reproduction, male infertility, erectile dysfunction, neoplasms/management of the testes and penis, medical/surgical management of urological stone disease, and many more topics.

Volume III (58 chapters) covers anatomy, physiology, pharmacology, pathophysiology, oncology, and surgery of the adrenal glands; all chapters covering diagnosis, physiology, and pathophysiology of female and male lower urinary tract disorders; all oncologic aspects (imaging, diagnosis, staging, treatment, and outcomes) of the bladder and prostate; urinary diversion; and physiology, diagnosis, and medical and surgical treatment of benign prostatic hyperplasia.

We all remain extremely proud once again to present you with this textbook and are especially thankful for our spouses and families who have put up with us during the months of review, editing, and proofing. We also give special thanks to the hundreds of authors whose time, expertise, and effort have made all of this possible. We would also like to thank our editorial support staff from Elsevier: Jennifer S. Ehlers (Senior Content Development Specialist) and Belinda Kuhn (Senior Content Strategist), who helped us to coordinate *CWW-12*.

We truly hope you will enjoy reading this textbook.

From the Editors
Alan W. Partin
Roger R. Dmochowski
Louis R. Kavoussi
Craig A. Peters

CONTRIBUTORS

Robert Abouassaly, MD, MS
Assistant Professor, Urology
University Hospitals Case Medical Center
Cleveland, Ohio

Ömer Acar, MD
Department of Urology
College of Medicine
University of Illinois at Chicago
Chicago, Illinois

Mark C. Adams, MD, FAAP
Professor of Urology and Pediatrics
Vanderbilt University
Nashville, Tennessee

Riyad Taher Al-Mousa, MBBS, SSCU, FEBU, MSHA
Consultant Urologist/Neuro-urologist
Urology Department
King Fahad Specialist Hospital–Dammam
Dammam, Saudi Arabia

Mohamad E. Allaf, MD
Vice Chairman and Professor of Urology, Oncology, and Biomedical Engineering
Director of Minimally Invasive and Robotic Surgery
Department of Urology
Brady Urological Institute
Johns Hopkins University School of Medicine
Baltimore, Maryland

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

Christopher B. Anderson, MD, MPH
Assistant Professor, Urology
Columbia University Medical Center
New York, New York

Karl-Erik Andersson, MD, PhD
Professor
Aarhus Institute for Advanced Studies
Aarhus University
Aarhus, Jutland, Denmark;
Professor
Wake Forest Institute for Regenerative Medicine
Wake Forest University School of Medicine
Winston-Salem, North Carolina

Sero Andonian, MD, MSc, FRCS(C), FACS
Associate Professor
Department of Urology
McGill University
Montreal, Canada

Emmanuel S. Antonarakis, MD
Professor of Oncology and Urology
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Jodi A. Antonelli, MD
Assistant Professor
Department of Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Joshua Augustine, MD
Associate Professor of Medicine
Cleveland Clinic Lerner College of Medicine
Cleveland Clinic
Cleveland, Ohio

Paul F. Austin, MD
Professor
Division of Urologic Surgery
Washington University School of Medicine
St. Louis, Missouri

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

Gina M. Badalato, MD
Assistant Professor, Urology
Columbia University Medical Center
New York, New York

Daniel A. Barocas, MD, MPH, FACS
Associate Professor, Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee

Julia Spencer Barthold, MD
Principal Research Scientist
Nemours Biomedical Research/Division of Urology
Alfred I. duPont Hospital for Children
Wilmington, Delaware;
Professor
Urology and Pediatrics
Thomas Jefferson University
Philadelphia, Pennsylvania

Laurence S. Baskin, MD
Chief of Pediatric Urology
University of California–San Francisco Benioff Children's Hospital
San Francisco, California

Stuart B. Bauer, MD
Professor of Surgery (Urology)
Harvard Medical School;
Senior Associate in Urology
Department of Urology
Boston Children's Hospital
Boston, Massachusetts

Mitchell C. Benson, MD
Herbert and Florence Irving Professor and Chairman Emeritus
Department of Urology
Columbia University;
Attending Physician
Department of Urology
New York Presbyterian Hospital–Columbia
New York, New York

Sara L. Best, MD
Associate Professor
Department of Urology
University of Wisconsin School of Medicine and Public Health
Madison, Wisconsin

Lori A. Birder, PhD
Professor of Medicine and Pharmacology
Medicine–Renal Electrolyte Division
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

Jay T. Bishoff, MD
Director, Intermountain Urological Institute
Intermountain Health Care
Salt Lake City, Utah

Trinity J. Bivalacqua, MD, PhD
R. Christian Evenson Professor of Urology
Johns Hopkins University
Baltimore, Maryland

Marc A. Bjurlin, DO, MSc
Assistant Professor, Urology
New York University
New York, New York

Brian G. Blackburn, MD
Clinical Associate Professor
Internal Medicine/Infectious Diseases and Geographic Medicine
Stanford University School of Medicine
Stanford, California

Bertil Blok, MD, PhD
Department of Urology
Erasmus Medical Center
Rotterdam, Netherlands

Michael L. Blute, MD
Chief, Department of Urology
Walter S. Kerr, Jr., Professor of Urology
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Timothy B. Boone, MD, PhD
Chairman, Urology
Houston Methodist Hospital;
Professor and Associate Dean
Weill Cornell Medical College
Houston, Texas

Stephen A. Boorjian, MD, FACS
Carl Rosen Professor of Urology
Mayo Clinic
Rochester, Minnesota

Kristy McKiernan Borawski, MD
Clinical Assistant Professor of Urology
Department of Urology
University of North Carolina–Chapel Hill
Chapel Hill, North Carolina

Michael S. Borofsky, MD
Assistant Professor, Urology
University of Minnesota
Minneapolis, Minnesota

Steven B. Brandes, MD
Department of Urology
Columbia University Medical Center
New York, New York

Michael C. Braun, MD
Chief of Renal Service
Texas Children's Hospital;
Professor
Renal Section Chief
Department of Pediatrics
Program Director, Pediatric Nephrology Fellowship Program
Baylor College of Medicine
Houston, Texas

Gregory A. Broderick, MD
Professor of Urology
Department of Urology
Mayo Clinic College of Medicine;
Program Director
Urology Residency Program
Mayo Clinic
Jacksonville, Florida

Elizabeth Timbrook Brown, MD, MPH
Assistant Professor, Urology
MedStar Georgetown University Hospital
Washington, DC

Benjamin M. Brucker, MD
Assistant Professor, Urology
New York University
New York, New York

Kathryn L. Burgio, PhD
Professor of Medicine
Department of Medicine
Division of Gerontology, Geriatrics, and Palliative Care
University of Alabama at Birmingham;
Associate Director for Research
Birmingham/Atlanta Geriatric Research, Education, and Clinical Center
Birmingham VA Medical Center
Birmingham, Alabama

Arthur L. Burnett II, MD, MBA
Patrick C. Walsh Distinguished Professor of Urology
Department of Urology
Johns Hopkins School of Medicine
Baltimore, Maryland

Jeffrey A. Cadeddu, MD
Professor of Urology and Radiology
University of Texas Southwestern Medical Center
Dallas, Texas

Anne P. Cameron, MD, FRCSC, FPMRS
Associate Professor, Urology
University of Michigan
Ann Arbor, Michigan

Steven C. Campbell, MD, PhD
Professor of Surgery
Department of Urology
Cleveland Clinic
Cleveland, Ohio

Douglas A. Canning, MD
Professor of Surgery (Urology)
Perelman School of Medicine
University of Pennsylvania;
Chief, Division of Urology
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Paolo Capogrosso, MD
Department of Urology
Vita-Salute San Raffaele University
Milan, Italy

Michael A. Carducci, MD
AEGON Professor in Prostate Cancer Research
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Johns Hopkins University School of Medicine
Baltimore, Maryland

Maude Carmel, MD
Assistant Professor
Department of Urology at University of Texas Southwestern Medical Center
Dallas, Texas

Peter R. Carroll, MD, MPH
Professor and Chair, Urology
University of California, San Francisco
San Francisco, California

K. Clint Cary, MD, MPH
Assistant Professor
Department of Urology
Indiana University
Indianapolis, Indiana

Erik P. Castle, MD
Professor of Urology
Mayo Clinic Arizona
Phoenix, Arizona

Toby C. Chai, MD
Professor and Chair, Department of Urology
Boston University School of Medicine;
Chief of Urology
Boston Medical Center
Boston, Massachusetts

Charbel Chalouhy, MD
Assistant Professor of Urology
Campus des Sciences Médicales
St. Joseph University
Beirut, Lebanon

Alicia H. Chang, MD, MS
Instructor
Department of Internal Medicine/ Infectious Diseases and Geographic Medicine
Stanford University School of Medicine
Stanford, California;
Medical Consultant
Los Angeles County Tuberculosis Control Program
Los Angeles County Department of Public Health
Los Angeles, California

Christopher R. Chapple, MD, FRCS (Urol)
Professor and Consultant Urologist
Department of Urology
The Royal Hallamshire Hospital, Sheffield Teaching Hospitals
Sheffield, South Yorkshire, United Kingdom

Thomas Chi, MD
Associate Professor
Associate Chair for Clinical Affairs
Department of Urology
University of California–San Francisco
San Francisco, California

John P. Christodouleas, MD, MPH
Professor of Radiation Oncology
Urologic Cancer Program
Penn Medicine
Philadelphia, Pennsylvania

Peter E. Clark, MD
Professor and Chairman, Urology
Atrium Health;
Chair, Urologic Oncology
Levine Cancer Institute
Charlotte, North Carolina

Douglass B. Clayton, MD, FAAP
Assistant Professor
Urologic Surgery
Vanderbilt University
Nashville, Tennessee

Joshua A. Cohn, MD
Assistant Professor of Urology
Department of Urology
Einstein Healthcare Network;
Assistant Professor of Urology
Department of Surgery, Division of Urologic Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Michael Joseph Conlin, MD, MCR
Professor, Urology
Portland VA Medical Center;
Professor, Urology
Oregon Health & Sciences University
Portland, Oregon

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

Kimberly L. Cooper, MD
Associate Professor of Urology
Columbia University Medical Center
New York, New York

Lawrence A. Copelovitch, MD
Assistant Professor of Pediatrics
Department of Nephrology
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Hillary L. Copp, MD
Associate Professor, Pediatric Urology
University of California–San Francisco
San Francisco, California

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

Anthony J. Costello, FRACS, MD
Professor, Urology
Royal Melbourne Hospital, Parkville Victoria
Victoria, Australia

Lindsey Cox, MD
Assistant Professor of Urology
Medical University of South Carolina
Charleston, South Carolina

Paul L. Crispen, MD
Associate Professor
Department of Urology
University of Florida
Gainesville, Florida

Juanita M. Crook, MD, FRCPC
Professor, Radiation Oncology
University of British Columbia;
Radiation Oncologist
Center for the Southern Interior
British Columbia Cancer Agency
Kelowna, British Columbia, Canada

Gerald Cunha, PhD
Professor Emeritus, Urology
School of Medicine
University of California, San Francisco
San Francisco, California

Douglas M. Dahl, MD, FACS
Associate Professor of Surgery
Harvard Medical School;
Chief, Division of Urologic Oncology
Department of Urology
Massachusetts General Hospital
Boston, Massachusetts

Siamak Daneshmand, MD
Associate Professor of Urology (Clinical Scholar)
Institute of Urology
University of Southern California, Los Angeles
Los Angeles, California

Casey A. Dauw, MD
Assistant Professor, Urology
University of Michigan
Ann Arbor, Michigan

Shubha K. De, MD, FRCSC
Assistant Professor
Department of Surgery
Division of Urology
University of Alberta
Edmonton, Alberta, Canada

Guarionex Joel DeCastro, MD, MPH
Assistant Professor, Urology
Columbia University Medical Center;
Department of Urology
New York Presbyterian Hospital/Columbia University
New York, New York

Jean J.M.C.H. de la Rosette, MD, PhD
Professor, Urology
AMC University Hospital
Amsterdam, Netherlands

Francisco T. Dénes, MD, PhD
Associate Professor, Division of Urology
Chief, Pediatric Urology
University of São Paulo Medical School;
Hospital das Clínicas
São Paulo, Brazil

Dirk J.M.K. De Ridder, MD, PhD, FEBU
Professor, Urology
University Hospitals KU Leuven
Leuven, Belgium

Mahesh R. Desai, MS, FRCS
Chief Urologist and Managing Trustee
Department of Urology
Muljibhai Patel Urological Hospital, Nadiad
Gujarat, India

David Andrew Diamond, MD
Urologist-in-Chief
Department of Urology
Boston Children's Hospital;
Professor of Surgery (Urology)
Harvard Medical School
Boston, Massachusetts

Heather N. Di Carlo, MD
Director, Pediatric Urology Research
Assistant Professor of Urology
Johns Hopkins Medicine
Baltimore, Maryland

Colin P.N. Dinney, MD
Chairman and Professor
Department of Urology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Roger R. Dmochowski, MD, MMHC, FACS
Professor, Urologic Surgery, Surgery and Gynecology
Program Director, Female Pelvic Medicine and Reconstructive Surgery
Vice Chair for Faculty Affairs and Professionalism
Section of Surgical Sciences
Associate Surgeon-in-Chief
Vanderbilt University Medical Center
Nashville, Tennessee

Charles G. Drake, MD, PhD
Associate Professor of Oncology, Immunology, and Urology
James Buchanan Brady Urological Institute
Johns Hopkins University;
Attending Physician
Department of Oncology
Johns Hopkins Kimmel Cancer Center
Baltimore, Maryland

Brian Duty, MD
Associate Professor, Urology
Oregon Health & Science University
Portland, Oregon

James A. Eastham, MD
Chief, Urology Service
Department of Surgery
Memorial Sloan-Kettering Cancer Center;
Professor, Urology
Weill Cornell Medical Center
New York, New York

Scott Eggener, MD
Professor, Surgery
University of Chicago
Chicago, Illinois

Mohamed Aly Elkoushy, MD, MSc, PhD
Professor, Urology
Faculty of Medicine
Suez Canal University
Ismailia, Egypt

Jonathan Scott Ellison, MD
Assistant Professor of Urology
Medical College of Wisconsin
Children's Hospital of Wisconsin
Milwaukee, Wisconsin

Sammy E. Elsamra, MD
Assistant Professor of Surgery (Urology)
Department of Urology
Rutgers Robert Wood Johnson Medical School;
Director of Robotic Surgical Services
Robert Wood Johnson University Hospital
RWJ-Barnabas Health
New Brunswick, New Jersey

Jonathan I. Epstein, MD
Professor of Pathology, Urology, Oncology
The Reinhard Professor of Urological Pathology
Director of Surgical Pathology
The Johns Hopkins Medical Institutions
Baltimore, Maryland

Carlos R. Estrada, MD, MBA
Associate Professor, Surgery
Harvard Medical School;
Associate in Urology
Boston Children's Hospital
Boston, Massachusetts

Jairam R. Eswara, MD
Assistant Surgeon
Division of Urology
Brigham and Women's Hospital
Boston, Massachusetts

Fernando A. Ferrer, MD, FACS, FAAP
Professor of Urology
Department of Urology
Mount Sinai School of Medicine
New York, New York

Neil Fleshner, MD, MPH, FRCSC
Professor of Surgery and Martin Barkin Chair
Department of Urology
University of Toronto;
Surgeon, Uro-Oncology
University Health Network
Toronto, Ontario, Canada

Bryan Foster, MD
Associate Professor
Department of Radiology
Oregon Health & Science University
Portland, Oregon

Richard S. Foster, MD
Professor, Department of Urology
Indiana University
Indianapolis, Indiana

Pat F. Fulgham, MD
Director of Surgical Oncology
Department of Urology
Texas Health Presbyterian Dallas
Dallas, Texas

Arvind P. Ganpule, MS, DNB
Department of Urology
Muljibhai Patel Urological Hospital
Nadiad, Gujarat, India

Kris Gaston, MD
Carolinas Medical Center
Charlotte, North Carolina

John P. Gearhart, MD
The James Buchanan Brady Urological Institute
Johns Hopkins Medical Institutions
Baltimore, Maryland

Matthew T. Gettman, MD
Professor and Vice-Chair, Urology
Mayo Clinic
Rochester, Minnesota

Reza Ghavamian, MD
Eastern Regional Director of Urology
Department of Urology
Northwell Health
Greenlawn, New York;
Professor of Urology
Zucker School of Medicine at Hofstra Northwell
New Hyde Park, New York

Bruce R. Gilbert, MD, PhD
Professor of Urology
The Smith Institute for Urology
Zucker School of Medicine of Hofstra/Northwell
New Hyde Park, New York

Timothy D. Gilligan, MD, MS, FASCO
Associate Professor of Medicine
Solid Tumor Oncology
Cleveland Clinic Lerner College of Medicine;
Program Director, Hematology/Oncology Fellowship
Taussig Cancer Institute
Cleveland Clinic
Cleveland, Ohio

David A. Goldfarb, MD
Professor of Surgery, CCLCM
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio

Marc Goldstein, MD, DSc (hon), FACS
Matthew P. Hardy Distinguished Professor of Urology and Male Reproductive Medicine
Department of Urology and Institute for Reproductive Medicine
Weill Medical College of Cornell University;
Surgeon-in-Chief, Male Reproductive Medicine, and Surgery
Department of Urology and Institute for Reproductive Medicine
New York Presbyterian Hospital–Weill Cornell Medical Center
New York, New York

Leonard G. Gomella, MD, FACS
Professor and Chair
Department of Urology
Thomas Jefferson University
Philadelphia, Pennsylvania

Alex Gomelsky, MD
B.E. Trichel Professor and Chairman
Department of Urology
Louisiana State University Health–Shreveport
Shreveport, Louisiana

Mark L. Gonzalgo, MD, PhD
Professor and Vice Chairman, Urology
University of Miami Miller School of Medicine
Miami, Florida

Michael A. Gorin, MD
Assistant Professor
Department of Urology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Tamsin Greenwell, MD, PhD
Consultant Urological Surgeon
University College London Hospitals
London, United Kingdom

Tomas L. Griebling, MD, MPH
John P. Wolf 33-Degree Masonic Distinguished Professor of Urology
Department of Urology
The Landon Center on Aging
The University of Kansas
Kansas City, Kansas

Khurshid A. Guru, MD
Chair, Department of Urology
Director of Robotic Surgery
Robert P. Huben Endowed Professor of Urologic Oncology
Roswell Park Comprehensive Cancer Center
Buffalo, New York

Thomas J. Guzzo, MD, MPH
Assistant Professor of Urology
The Hospital of the University of Pennsylvania
University of Pennsylvania
Philadelphia, Pennsylvania

Jennifer A. Hagerty, DO
Attending Physician
Departments of Surgery/Urology
Nemours/Alfred I. duPont Hospital for Children
Wilmington, Delaware;
Assistant Professor
Departments of Urology and Pediatrics
Sidney Kimmel Medical College of Thomas Jefferson University
Philadelphia, Pennsylvania

Simon J. Hall, MD
Professor
Smith Institute for Urology
Hofstra Northwell School of Medicine
Lake Success, New York

Barry Hallner, MD
Associate Program Director, Female Pelvic Medicine & Reconstructive Surgery
Assistant Professor
Departments of OB/GYN and Urology
Louisiana State University Health
New Orleans School of Medicine
New Orleans, Louisiana

Ethan J. Halpern, MD, MSCE
Professor of Radiology and Urology
Department of Radiology
Thomas Jefferson University
Philadelphia, Pennsylvania

Misop Han, MD, MS
Professor, Urology and Oncology
Johns Hopkins Medicine
Baltimore, Maryland

Philip M. Hanno, MD, MPH
Clinical Professor, Urology
Stanford University School of Medicine
Palo Alto, California

Siobhan M. Hartigan, MD
Female Pelvic Medicine and Reconstructive Surgery Fellow
Department of Urology
Vanderbilt University Medical Center
Nashville, Tennessee

Christopher J. Hartman, MD
Assistant Professor of Urology
The Smith Institute for Urology
Northwell Health System
Long Island City, New York

Hashim Hashim, MBBS, MRCS (Eng), MD, FEBU, FRCS (Urol)
Consultant Urological Surgeon
Honorary Professor
Director of the Urodynamics Unit
Bristol Urological Institute
Southmead Hospital
Bristol, United Kingdom

Dorota J. Hawksworth, MD, MBA
Director of Andrology and Male Sexual Health
Department of Urology
Walter Reed National Military Medical Center
Bethesda, Maryland

Sarah Hazell, MD
Radiation Oncology Resident
Department of Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University School of Medicine
Baltimore, Maryland

John P.F.A. Heesakkers, MD, PhD
Urologist
Radboudumc
Nijmegen, Netherlands

Sevann Helo, MD
Southern Illinois University School of Medicine
Division of Urology
Springfield, Illinois

Amin S. Herati, MD
Assistant Professor of Urology
Department of Urology
The James Buchanan Brady Urological Institute
Johns Hopkins University School of Medicine;
Assistant Professor
Gynecology and Obstetrics
Johns Hopkins University School of Medicine
Baltimore, Maryland

C.D. Anthony Herndon, MD, FAAP, FACS
Professor of Surgery
Director of Pediatric Urology
Surgeon-in-Chief, Children's Hospital of Richmond
Department of Urology
Virginia Commonwealth University
Richmond, Virginia

Piet Hoebeke, MD, PhD
Professor, Urology
Dean, Faculty of Medicine and Health Sciences
Ghent University
Ghent, Belgium

David M. Hoenig, MD
Professor and Chief
North Shore University Hospital
Smith Institute for Urology
North Shore-LIJ-Hofstra University
Lake Success, New York

Michael Hsieh, MD, PhD
Stirewalt Endowed Director
Biomedical Research Institute
Rockville, Maryland;
Associate Professor, Urology
George Washington University
Washington, DC

Valerio Iacovelli, MD
Urology Unit
University of Rome Tor Vergata
San Carlo di Nancy General Hospital
GVM Care and Research
Rome, Italy

Stephen V. Jackman, MD
Professor, Urology
University of Pittsburgh
Pittsburgh, Pennsylvania

Joseph M. Jacob, MD, MCR
Assistant Professor, Urology
SUNY Upstate Medical Center
Syracuse, New York

Micah A. Jacobs, MD, MPH
Department of Urology
University of Texas Southwestern Medical School
Dallas, Texas

Thomas W. Jarrett, MD
Professor and Chairman, Urology
George Washington University
Washington, DC

Gerald H. Jordan, MD, FACS, FAAP (Hon), FRCS (Hon)
Associate Professor, Urology
Eastern Virginia Medical School
Norfolk, Virginia

Martin Kaefer, MD
Professor, Urology
Indiana University School of Medicine
Indianapolis, Indiana

Kamaljot S. Kaler, MD
Clinical Assistant Professor
Section of Urology
Department of Surgery
University of Calgary
Calgary, Alberta, Canada

Panagiotis Kallidonis, MD, MSc, PhD, FEBU
Consultant Urological Surgeon
Department of Urology
University of Patras
Patras, Greece

Steven Kaplan, MD
Professor and Director
The Men's Health Program
Department of Urology
Icahn School of Medicine at Mount Sinai
New York, New York

Max Kates, MD
Assistant Professor, Urology
Johns Hopkins Medical Institutions
Baltimore, Maryland

Melissa R. Kaufman, MD, PhD
Associate Professor, Urologic Surgery
Vanderbilt University
Nashville, Tennessee

Louis R. Kavoussi, MD, MBA
Professor and Chair
Department of Urology
Zucker School of Medicine at Hofstra/Northwell
Hempstead, New York;
Chairman of Urology
The Arthur Smith Institute for Urology
Lake Success, New York

Parviz K. Kavoussi, MD, FACS
Reproductive Urologist
Department of Urology
Austin Fertility and Reproductive Medicine;
Adjunct Assistant Professor
Psychology: Neuroendocrinology and Motivation
University of Texas at Austin
Austin, Texas

Miran Kenk, PhD
University Health Network
Toronto, Canada

Mohit Khera, MD, MBA, MPH
Professor of Urology
Scott Department of Urology
Baylor College of Medicine
Houston, Texas

Antoine E. Khoury, MD, FRCSC, FAAP
Walter R. Schmid Professor of Pediatric Urology
Head of Pediatric Urology
Children's Hospital of Orange County
Orange, California

Eric A. Klein, MD
Chairman, Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio

Laurence Klotz, MD, FRCSC
Professor, Surgery
University of Toronto;
Urologist
Sunnybrook Health Sciences Centre
Toronto, Ontario, Canada

Bodo Egon Knudsen, MD, FRCSC
Associate Professor
Vice Chair Clinical Operations
Department of Urology
Wexner Medical Center
The Ohio State University
Columbus, Ohio

Kathleen C. Kobashi, MD
Section Head, Urology and Renal Transplantation
Virginia Mason Medical Center
Seattle, Washington

Chester J. Koh, MD
Associate Professor of Urology (Pediatric)
TCH Department of Surgery
Scott Department of Urology
Baylor College of Medicine
Texas Children's Hospital
Houston, Texas

Ervin Kocjancic, MD
Professor of Urology
Department of Urology
University of Illinois Health and Science
Chicago, Illinois

Badrinath R. Konety, MD, MBA
Professor and Chair, Dougherty Family Chair in UroOncology
Associate Director for Clinical Affairs and Clinical Research
Masonic Cancer Center;
Department of Urology
University of Minnesota
Minneapolis, Minnesota

Casey E. Kowalik, MD
Department of Urologic Surgery
Vanderbilt University
Nashville, Tennessee

Martin A. Koyle, MD, FAAP, FACS, FRCSC, FRCS (Eng)
Division Head, Pediatric Urology
Women's Auxiliary Chair in Urology and Regenerative Medicine
Hospital for Sick Children;
Professor of Surgery
University of Toronto
Toronto, Ontario, Canada

Amy E. Krambeck, MD
Michael O. Koch Professor of Urology
Indiana University
Indianapolis, Indiana

Jessica E. Kreshover, MD, MS
Assistant Professor
Arthur Smith Institute for Urology
Donald and Barbara Zucker School of Medicine at Hofstra-Northwell
Lake Success, New York

Venkatesh Krishnamurthi, MD
Director, Kidney/Pancreas Transplant Program
Glickman Urological and Kidney Institute, Transplant Center
Cleveland Clinic Foundation
Cleveland, Ohio

Ryan M. Krlin, MD
Assistant Professor of Urology
Department of Urology
Louisiana State University
New Orleans, Louisiana

Alexander Kutikov, MD, FACS
Professor and Chief, Urologic Oncology
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Jaime Landman, MD
Professor of Urology and Radiology
Chairman, Department of Urology
University of California Irvine
Orange, California

Brian R. Lane, MD, PhD
Chief, Urology
Spectrum Health;
Associate Professor
Michigan State University College of Human Medicine
Grand Rapids, Michigan

David A. Leavitt, MD
Assistant Professor, Urology
Vattikuti Urology Institute
Henry Ford Health System
Detroit, Michigan

Eugene K. Lee, MD
Assistant Professor, Urology
University of Kansas Medical Center
Kansas City, Kansas

Gary E. Lemack, MD
Professor of Urology and Neurology
University of Texas Southwestern Medical Center
Dallas, Texas

Thomas Sean Lendvay, MD, FACS
Professor, Urology
University of Washington;
Professor, Pediatric Urology
Seattle Children's Hospital
Seattle, Washington

Herbert Lepor, MD
Professor and Martin Spatz Chairman
Department of Urology
NYU School of Medicine;
Chief, Urology
NYU Langine Health System
New York, New York

Evangelos Liatsikos, MD, PhD
Professor, Urology
University of Patras
Patras, Greece

Sey Kiat Lim, MBBS, MRCS (Edinburgh), MMed (Surgery), FAMS (Urology)
Associate Consultant, Urology
Changi General Hospital
Singapore

W. Marston Linehan, MD
Chief, Urologic Oncology Branch
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Richard Edward Link, MD, PhD
Carlton-Smith Chair in Urologic Education
Associate Professor of Urology
Director, Division of Endourology and Minimally Invasive Surgery
Scott Department of Urology
Baylor College of Medicine
Houston, Texas

Jen-Jane Liu, MD
Director of Urologic Oncology
Assistant Professor
Department of Urology
Oregon Health & Science University
Portland, Oregon

Stacy Loeb, MD, MSc
Assistant Professor, Urology and Population Health
New York University and Manhattan Veterans Affairs
New York, New York

Christopher J. Long, MD
Assistant Professor of Urology
Department of Surgery
Division of Urology
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Roberto Iglesias Lopes, MD, PhD
Assistant Professor
Division of Urology
Department of Surgery
University of São Paulo Medical School
São Paulo, Brazil

Armando J. Lorenzo, MD, MSc, FRCSC, FAAP, FACS
Staff Paediatric Urologist
Department of Surgery
Division of Urology
Hospital for Sick Children;
Associate Professor
Department of Surgery
Division of Urology
University of Toronto
Toronto, Ontario, Canada

Yair Lotan, MD
Professor
Department of Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Alvaro Lucioni, MD
Department of Urology
Virginia Mason Medical Center
Seattle, Washington

Tom F. Lue, MD, ScD (Hon), FACS
Professor of Urology
University of California–San Francisco
San Francisco, California

Nicolas Lumen, MD, PhD
Professor, Urology
Ghent University Hospital
Ghent, Belgium

Marcos Tobias Machado, MD, PhD
Head, Urologic Oncology Section
Department of Urology
Faculdade de Medicina do ABC, Santo André
São Paulo, Brazil

Stephen D. Marshall, MD
Attending Physician
Laconia Clinic Department of Urology
Lakes Region General Hospital
Laconia, New Hampshire

Aaron D. Martin, MD, MPH
Associate Professor
Department of Urology
Louisiana State University Health Sciences Center;
Pediatric Urology
Children's Hospital New Orleans
New Orleans, Louisiana

Laura M. Martinez, MD
Instructor in Clinical Urology
Houston Methodist
Houston, Texas

Timothy A. Masterson, MD
Associate Professor, Urology
Indiana University Medical Center
Indianapolis, Indiana

Surena F. Matin, MD
Professor
Department of Urology
The University of Texas M.D. Anderson Cancer Center;
Medical Director
Minimally Invasive New Technology in Oncologic Surgery (MINTOS)
The University of Texas M.D. Anderson Cancer Center
Houston, Texas

Brian R. Matlaga, MD, MPH
Professor
James Buchanan Brady Urological Institute
Johns Hopkins Medical Institutions
Baltimore, Maryland

Kurt A. McCammon, MD, FACS
Devine Chair in Genitourinary Reconstructive Surgery
Chairman and Program Director
Professor
Department of Urology
Eastern Virginia Medical School
Norfolk, Virginia

James M. McKiernan, MD
Chairman and Professor, Urology
Columbia University Medical Center/NYPH
New York, New York

Chris G. McMahon, MBBS, FAChSHP
Director
Australian Centre for Sexual Health
Sydney, New South Wales, Australia

Kevin T. McVary, MD, FACS
Professor and Chairman
Division of Urology
Department ofSurgery
Southern Illinois University School of Medicine
Springfield, Illinois

Luis G. Medina, MD
Medical Doctor and Researcher
Department of Urology
University of Southern California
Los Angeles, California

Kirstan K. Meldrum, MD
Professor
Department of Surgery
Central Michigan University
Saginaw, Michigan

Matthew J. Mellon, MD, FACS
Associate Professor, Urology
Indiana University
Indianapolis, Indiana

Maxwell V. Meng, MD
Professor, Urology
Chief, Urologic Oncology
University of California–San Francisco
San Francisco, California

David Mikhail, MD, FRCSC
Endourology Fellow
Department of Urology
Arthur Smith Institute for Urology/Northwell Health
New Hyde Park, New York

Nicole L. Miller, MD
Associate Professor
Department of Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee

Alireza Moinzadeh, MD
Director of Robotic Surgery
Institute of Urology
Lahey Hospital & Medical Center
Burlington, Massachusetts;
Assistant Professor, Urology
Tufts University School of Medicine
Boston, Massachusetts

Robert M. Moldwin, MD
Professor of Urology
The Arthur Smith Institute for Urology
Hofstra Northwell School of Medicine
Lake Success, New York

Manoj Monga, MD, FACS
Director, Stevan Streem Center for Endourology & Stone Disease
Department of Urology
Cleveland Clinic
Cleveland, Ohio

Francesco Montorsi, MD, FRCS (Hon)
Professor and Chairman, Urology
Vita-Salute San Raffaele University
Milan, Italy

Daniel M. Moreira, MD, MHS
Assistant Professor, Urology
University of Illinois at Chicago
Chicago, Illinois

Allen F. Morey, MD, FACS
Professor, Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Todd M. Morgan, MD
Associate Professor
Department of Urology
University of Michigan
Ann Arbor, Michigan

John J. Mulcahy, MD, PhD, FACS
Clinical Professor, Urology
University of Alabama
Birmingham, Alabama

Ravi Munver, MD, FACS
Vice Chairman
Department of Urology
Hackensack University Medical Center;
Professor of Surgery (Urology)
Department of Urology
Seton Hall-Hackensack Meridian School of Medicine
Hackensack, New Jersey

Stephen Y. Nakada, MD, FACS, FRCS (Glasg.)
Professor and Chairman, The David T. Uehling Chair of Urology
Department of Urology
University of Wisconsin School of Medicine and Public Health;
Professor and Chairman
Department of Urology
University of Wisconsin Hospital and Clinics
Madison, Wisconsin

Neema Navai, MD
Assistant Professor, Urology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Diane K. Newman, DNP, ANP-BC, FAAN
Adjunct Professor of Urology in Surgery
Division of Urology
Perelman School of Medicine;
Research Investigator Senior
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

Craig Stuart Niederberger, MD, FACS
Clarence C. Saelhof Professor and Head
Department of Urology
University of Illinois at Chicago College of Medicine;
Professor, Bioengineering
University of Illinois at Chicago College of Engineering
Chicago, Illinois

Victor W. Nitti, MD
Professor of Urology and Obstetrics & Gynecology
Shlomo Raz Chair in Urology
Chief, Division of Female Pelvic Medicine and Reconstructive Surgery
David Geffen School of Medicine at UCLA
Los Angeles, California

Samuel John Ohlander, MD
Assistant Professor, Urology
University of Illinois at Chicago
Chicago, Illinois

L. Henning Olsen, MD, DMSc
Professor, Urology
Section of Pediatric Urology
Aarhus University Hospital
Skejby, Denmark;
Professor
Institute of Clinical Medicine
Aarhus University
Aarhus, Denmark

Aria F. Olumi, MD
Professor of Surgery/Urology
Department of Urologic Surgery
Beth Israel Deaconess Medical Center
Harvard Medical School
Boston, Massachusetts

Nadir I. Osman, MBChB (Hons), MRCS
Department of Urology
Royal Hallmashire Hospital
Sheffield, South Yorkshire, United Kingdom

Brandon J. Otto, MD
Assistant Professor, Urology
University of Florida
Gainesville, Florida

Priya Padmanabhan, MD, MPH
Assistant Professor, Pelvic Reconstruction and Voiding Dysfunction
The University of Kansas
Kansas City, Kansas

Rodrigo Lessi Pagani, MD
Assistant Professor, Urology
University of Illinois at Chicago
Chicago, Illinois

Lance C. Pagliaro, MD
Professor
Department of Genitourinary Medical Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Ganesh S. Palapattu, MD
Chief of Urologic Oncology
Associate Professor, Urology
University of Michigan
Ann Arbor, Michigan

Drew A. Palmer, MD
Endourology Fellow
Department of Urology
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

Jeffrey S. Palmer, MD, FACS, FAAP
Director, Pediatric and Adolescent Urology Institute
Cleveland, Ohio

Lane S. Palmer, MD, FACS
Professor and Chief, Pediatric Urology
Cohen Children's Medical Center of New York
Zucker School of Medicine of Hofstra/Northwell
Long Island, New York

Meyeon Park, MD, MAS
Assistant Professor in Residence, Medicine
University of California–San Francisco
San Francisco, California

William P. Parker, MD
Department of Urology
University of Kansas Health System
Kansas City, Kansas

Alan W. Partin, MD, PhD
The Jakurski Family Director
Urologist-in-Chief
Chairman, Department of Urology
Professor, Departments of Urology, Oncology and Pathology
Johns Hopkins Medical Institutions
Baltimore, Maryland

Roshan M. Patel, MD
Clinical Instructor
Department of Urology
University of California–Irvine
Orange, California

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

David F. Penson, MD, MPH
Professor and Chair, Urologic Surgery
Vanderbilt University;
Director
Center for Surgical Quality and Outcomes Research
Vanderbilt Institute for Medicine and Public Health
Nashville, Tennessee

Craig A. Peters, MD
Chief, Pediatric Urology
Children's Health System Texas;
Professor of Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Curtis A. Pettaway, Sr., MD
Professor
Department of Urology
University of Texas M.D. Anderson Cancer Center
Houston, Texas

Janey R. Phelps, MD
Department of Anesthesia
University of North Carolina School of Medicine
Chapel Hill, North Carolina

Ryan Phillips, MD, PhD
Resident Physician
Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University School of Medicine
Baltimore, Maryland

Phillip M. Pierorazio, MD
Associate Professor
Urology and Oncology
Brady Urological Institute and Department of Urology
Johns Hopkins University
Baltimore, Maryland

Hans G. Pohl, MD, FAAP
Associate Professor, Urology and Pediatrics
Children's National Medical Center
Washington, DC

Thomas J. Polascik, MD
Professor, Urologic Surgery
Duke Comprehensive Cancer Center
Duke Cancer Institute
Durham, North Carolina

Michel Pontari, MD
Professor and Vice-Chair, Urology
Lewis Katz School of Medicine at Temple University
Philadelphia, Pennsylvania

John C. Pope IV, MD
Professor, Urologic Surgery and Pediatrics
Vanderbilt University Medical Center
Nashville, Tennessee

Jay D. Raman, MD, FACS
Professor and Chief, Urology
Penn State Health Milton S. Hershey Medical Center
Hershey, Pennsylvania

Ranjith Ramasamy, MD
Director, Reproductive Urology
Department of Urology
University of Miami
Miami, Florida

Ardeshir R. Rastinehad, DO, FACOS
Director, Focal Therapy and Interventional Urology
Associate Professor of Radiology and Urology
Icahn School of Medicine at Mount Sinai
New York, New York

Yazan F.H. Rawashdeh, MD, PhD
Consultant Pediatric Urologist
Section of Pediatric Urology
Aarhus University Hospital
Aarhus, Denmark

Pramod P. Reddy, MD
The Curtis Sheldon and Jeffrey Wacksman Chair of Pediatric Urology
Division of Pediatric Urology
Cincinnati Children's Hospital Medical Center;
Professor of Surgery
Division of Urology
University of Cincinnati College of Medicine
Cincinnati, Ohio

W. Stuart Reynolds, MD, MPH
Assistant Professor, Urologic Surgery
Vanderbilt University
Nashville, Tennessee

Koon Ho Rha, MD, PhD, FACS
Professor
Department of Urology
Urological Science Institute
Yonsei University College of Medicine
Seoul, Republic of Korea

Lee Richstone, MD
Chief, Urology
Long Island Jewish Medical Center
Lake Success, New York;
System Vice Chairman, Urology
Northwell Health
New York, New York

Stephen Riggs, MD
Urologic Oncology
Levine Cancer Institute
Charlotte, North Carolina

Richard C. Rink, MD, FAAP, FACS
Emeritus Professor, Pediatric Urology
Riley Hospital for Children Indiana University School of Medicine;
Faculty, Pediatric Urology
Peyton Manning Children's Hospital St. Vincent
Indianapolis, Indiana

Michael L. Ritchey, MD
Professor, Urology
Mayo Clinic College of Medicine
Phoenix, Arizona

Claus G. Roehrborn, MD
Professor and Chairman, Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Ashley Evan Ross, MD, PhD
Assistant Professor, Urology
Johns Hopkins Brady Urological Institute
Baltimore, Maryland

Sherry S. Ross, MD
Department of Anesthesia
The University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

Christopher C. Roth, MD
Associate Professor of Urology
Louisiana State University Health Sciences Center;
Pediatric Urology
Childrens Hospital New Orleans
New Orleans, Louisiana

Kyle O. Rove, MD
Urologist
St. Louis Children's Hospital
Washington University
St. Louis, Missouri

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

Steven P. Rowe, MD
Assistant Professor
Department of Radiology
Johns Hopkins University
Baltimore, Maryland

Matthew P. Rutman, MD
Associate Professor, Urology
Columbia University College of Physicians and Surgeons
New York, New York

Simpa S. Salami, MD, MPH
Assistant Professor
Department of Urology
University of Michigan
Ann Arbor, Michigan

Andrea Salonia, MD, PhD
Director, Urological Research Institute
Milan, Italy

Edward M. Schaeffer, MD, PhD
Professor and Chair, Urology
Northwestern University
Chicago, Illinois

Bruce J. Schlomer, MD
Assistant Professor, Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Michael J. Schwartz, MD, FACS
Associate Professor of Urology
The Smith Institute for Urology
Hofstra Northwell School of Medicine
New Hyde Park, New York

Allen D. Seftel, MD
Professor of Urology
Department of Surgery
Cooper Medical School of Rowan University;
Chief, Division of Urology
Cooper University Health Care
Camden, New Jersey

Rachel Selekman, MD, MAS
Instructor, Surgery
Division of Pediatric Urology
Children's National Medical Center
Washington, DC

Abhishek Seth, MD
Assistant Professor, Urology
Baylor College of Medicine
Houston, Texas

Karen S. Sfanos, PhD
Assistant Professor, Pathology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Paras H. Shah, MD
Urologic Oncology
Department of Urology
Mayo Clinic
Rochester, Minnesota

Mohammed Shahait, MBBS
Clinical Instructor of Urology
University of Pittsburgh Medical Center
Pittsburgh, Pennsylvania

Robert C. Shamberger, MD
Chief of Surgery
Boston Children's Hospital;
Robert E. Gross Professor of Surgery
Harvard Medical School
Boston, Massachusetts

Alan W. Shindel, MD, MAS
Associate Professor, Urology
University of California, San Francisco
San Francisco, California

Aseem Ravindra Shukla, MD
Director of Minimally Invasive Surgery
Department of Pediatric Urology
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Jay Simhan, MD, FACS
Vice Chairman, Department of Urology
Einstein Healthcare Network;
Associate Professor of Urology
Temple Health/Fox Chase Cancer Center
Philadelphia, Pennsylvania

Brian Wesley Simons, DVM, PhD
Assistant Professor, Urology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Eila C. Skinner, MD
Professor and Chair, Urology
Stanford University
Stanford, California

Armine K. Smith, MD
Assistant Professor
Brady Urological Institute
Johns Hopkins University;
Assistant Professor, Urology
George Washington University
Washington, DC

Daniel Y. Song, MD
Associate Professor, Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University School of Medicine
Baltimore, Maryland

Rene Sotelo, MD
Physician, Surgeon, Urologist
Minimally Invasive and Robotic Surgery Center
Instituto Medico La Floresta, Caracas
Miranda, Venezuela

Michael W. Sourial, MD, FRCSC
Assistant Professor, Urology
Wexner Medical Center
The Ohio State University
Columbus, Ohio

Anne-Françoise Spinoit, MD, PhD
Pediatric and Reconstructive Urologist
Department of Urology
Ghent University Hospital
Ghent, Belgium

Arun K. Srinivasan, MD
Pediatric Urologist
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Ramaprasad Srinivasan, MD, PhD
Head, Molecular Cancer Section
Urologic Oncology Branch
Center for Cancer Research
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Irina Stanasel, MD
Assistant Professor, Urology
University of Texas Southwestern Medical Center/Children's Health
Dallas, Texas

Andrew J. Stephenson, MD, MBA, FRCSC, FACS
Associate Professor of Surgery
Department of Urology
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University;
Director, Urologic Oncology
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio

Julie N. Stewart, MD
Assistant Professor
Department of Urology
Houston Methodist Hospital
Houston, Texas

John Stites, MD
Minimally Invasive and Robotic Urologic Surgery
Hackensack University Medical Center
Hackensack, New Jersey

Douglas W. Storm, MD, FAAP
Assistant Professor
Department of Urology
University of Iowa Hospitals and Clinics
Iowa City, Iowa

Douglas William Strand, PhD
Assistant Professor, Urology
University of Texas Southwestern Medical Center
Dallas, Texas

Li-Ming Su, MD
David A. Cofrin Professor of Urologic Oncology
Chairman, Department of Urology
University of Florida College of Medicine
Gainesville, Florida

Chandru P. Sundaram, MD, FACS, FRCS (Eng)
Professor, Urology
Indiana University School of Medicine;
Program Director and Director of Minimally Invasive Surgery
Department of Urology
Indiana University School of Medicine
Indianapolis, Indiana

Samir S. Taneja, MD
James M. and Janet Riha Neissa Professor of Urologic Oncology
Departments of Urology and Radiology
NYU Langone Medical Center
New York, New York

Nikki Tang, MD
Assistant Professor, Dermatology
Johns Hopkins University
Baltimore, Maryland

Gregory E. Tasian, MD, MSc, MSCE
Assistant Professor, Urology and Epidemiology
University of Pennsylvania–Perelman School of Medicine;
Attending Physician, Urology
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Kae Jack Tay, MBBS, MRCS (Ed), MMed (Surgery), MCI, FAMS (Urology)
Consultant
Department of Urology
Singapore General Hospital
SingHealth Duke-NUS Academic Medical Center
Singapore

John C. Thomas, MD, FAAP, FACS
Associate Professor of Urologic Surgery
Division of Pediatric Urology
Monroe Carell Jr. Children's Hospital at Vanderbilt
Nashville, Tennessee

J. Brantley Thrasher, MD, FACS
William L Valk Distinguished Professor
Department of Urology
University of Kansas Medical Center
Kansas City, Kansas

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

Chad R. Tracy, MD
Assistant Professor, Urology
University of Iowa
Iowa City, Iowa

Paul J. Turek, MD, FACS, FRSM
Director
The Turek Clinic
San Francisco, California

Mark D. Tyson, MD, MPH
Department of Urology
Mayo Clinic College of Medicine and Science
Phoenix, Arizona

Robert G. Uzzo, MD, FACS
Professor and Chairman
Department of Surgery
The G. Willing "Wing" Pepper Professor in Cancer Research
Adjunct Professor of Bioengineering
Temple University College of Engineering
Fox Chase Cancer Center–Temple University Health System
Lewis Katz School of Medicine
Philadelphia, Pennsylvania

Brian A. VanderBrink, MD
Urologist
Division of Urology
Cincinnati Children's Hospital
Cincinnati, Ohio

Alex J. Vanni, MD, FACS
Associate Professor
Department of Urology
Lahey Hospital and Medical Center
Burlington, Massachusetts

David J. Vaughn, MD
Professor of Medicine
Division of Hematology/Oncology
Department of Medicine
Abramsom Cancer Center at the University of Pennsylvania
Philadelphia, Pennsylvania

Vijaya M. Vemulakonda, MD, JD
Associate Professor of Pediatric Urology
Division of Urology
Department of Surgery
University of Colorado School of Medicine
Aurora, Colorado

Manish A. Vira, MD
Vice Chair of Urologic Research
Smith Institute for Urology
Northwell Health
Lake Success, New York;
Associate Professor of Urology
Zucker School of Medicine of Hofstra/Northwell
Hempstead, New York

Ramón Virasoro, MD
Associate Professor, Urology
Eastern Virginia Medical School
Norfolk, Virginia;
Fellowship Director, Urology
Universidad Autonoma de Santo Domingo
Santo Domingo, Dominican Republic

Alvin C. Wee, MD
Surgical Director, Kidney Transplantation
Glickman Urological and Kidney Institute
Cleveland Clinic
Cleveland, Ohio

Elias Wehbi, MD, FRCSC
Assistant Professor
Department of Urology–Division of Pediatric Urology
University of California Irvine
Orange, California

Alan J. Wein, MD, PhD (Hon), FACS
Founders Professor and Emeritus Chief of Urology
Co-Director, Urologic Oncology Program
Co-Director, Voiding Function and Dysfunction Program
Division of Urology
Penn Medicine, Perelman School of Medicine
Philadelphia, Pennsylvania

Dana A. Weiss, MD
Assistant Professor, Urology
University of Pennsylvania;
Attending Physician, Urology
The Childrens Hospital of Philadelphia
Philadelphia, Pennsylvania

Jeffrey P. Weiss, MD, FACS
Professor and Chair
Department of Urology
SUNY Downstate College of Medicine
Brooklyn, New York

Robert M. Weiss, MD
Donald Guthrie Professor of Surgery/Urology
Yale University School of Medicine
New Haven, Connecticut

Charles Welliver, Jr., MD
Assistant Professor
Division of Urology
Albany Medical College
Albany, New York

Hunter Wessells, MD, FACS
Professor and Nelson Chair
Department of Urology
Affiliate Member
Harborview Injury Prevention and Research Center
University of Washington
Seattle, Washington

Duncan T. Wilcox, MD, MBBS
Surgeon-in-Chief
Ponzio Family Chair of Pediatric Urology
Department of Pediatric Urology
Children's Hospital Colorado
Aurora, Colorado

Jack Christian Winters, MD, FACS
Professor and Chairman, Urology
Louisiana State University Health Sciences Center
New Orleans, Louisiana

Anton Wintner, MD
Instructor in Surgery
Harvard Medical School;
Assistant in Urology
Massachusetts General Hospital
Boston, Massachusetts

J. Stuart Wolf, Jr., MD, FACS
Professor and Associate Chair for Clinical Integration and Operations
Departments of Surgery and Perioperative Care
Dell Medical School
The University of Texas at Austin
Austin, Texas

Christopher E. Wolter, MD
Assistant Professor, Urology
Mayo Clinic Arizona
Phoenix, Arizona

Dan Wood, PhD
Consultant Urologist in Adolescent and Reconstructive Surgery
The University College Hospitals
London, United Kingdom

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

Hailiu Yang, MD
Department of Urology
Cooper Health
New York, New York

Richard Nithiphaisal Yu, MD, PhD
Pediatric Urology Attending
Department of Urology
Boston Children's Hospital
Boston, Massachusetts

Joseph Zabell, MD
Assistant Professor
Department of Urology
University of Minnesota
Minneapolis, Minnesota

Mark R. Zaontz, MD
Professor of Clinical Urology in Surgery
Perelman School of Medicine
University of Pennsylvania;
Attending Physician, Urology
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Rebecca S. Zee, MD, PhD
Chief Resident of Urology
University of Virginia School of Medicine
Charlottesville, Virginia

VIDEO CONTENTS

PART I

Clinical Decision Making

1 Evaluation of the Urologic Patient: History and Physical Examination

Sammy E. Elsamra, MD

The evaluation of a patient must always begin with a thorough and appropriate history and physical examination. By using an organized system of information accrual, the urologist can gather information pertinent to the cause (or contributing factors) of a disease and obtain information salient to its treatment. To do so reliably for every patient, a reproducible system of history and physical examination has been developed and is taught routinely at all medical schools, usually in the preclinical years. Laboratory and radiologic examinations should be performed based on the findings of history and physical examination to narrow the differential diagnosis and arrive at an accurate diagnosis. A proper history and physical examination also allow for the development of rapport and trust between physician and patient, which can prove invaluable in counseling patients on subsequent diagnostic and treatment decisions.

Often health care providers are tempted to solicit information from the medical record or previously obtained labs and images. Although reviewing such data is critical, the urologist must be careful not to fall into the trap of relying too heavily on this data without input from the patient; chart lore, aberrant labs, and "incidentalomas" encountered may steer subsequent diagnostic evaluations and treatment away from the true illness. In our practice we have encountered patients with hematuria whose penile tumor is identified on physical examination.

This chapter provides a concise yet comprehensive discussion pertinent to the urologist of taking a history and performing a physical exam.

HISTORY

Overview

The medical history is the foundation for the evaluation and management of urologic patients. Often a well-obtained history provides the diagnosis or at least properly directs the health care provider to arrive at the correct diagnosis. Establishing several parameters helps to optimize the encounter. First, the environment should be warm, comforting, and nonthreatening for the patient. If the provider has any control over the waiting room or intake process, these should be made as easy as possible for the patient to navigate; this avoids agitating the patient before beginning the provider-patient encounter. Difficulties with parking or with front office staff may upset a patient before meeting the provider. The patient is directed to the examination room; ideally the physician reviews the patient's vitals and prior records before entering this room. A physician's knock before entering the room and an introduction upon entering help to put the patient at ease. If possible, the room should be properly set up for ideal provider-patient positioning, face to face, without any barriers (especially a computer). If a computer is used during the session, the provider ideally should still face the patient and place the computer off to the side so that the patient does not feel secondary to the computer. Although such factors may seem insignificant, it is clear that nonverbal communication is most responsible for communicating emotions, attitudes, and affect (Silverman and Kinnersley, 2010). In fact, studies have shown that patients may reveal more or less information based on level of eye contact and physician posture during the encounter (Byrne and Heath, 1980).

In addition to establishing an optimal setup, the physician must appreciate the patients' level of comprehension. Whether this entails assessing their ability to communicate in interview language or their ability to comprehend complex matters, the physician must assess level of comprehension by reading nonverbal cues or asking patients to summarize the discussion. Further, the patient encounter may be enhanced by the presence of a family member or friend. Often patients may not be as aware of pertinent historical details that family members may be able to supply. Further, when patients are given difficult news (e.g., cancer diagnosis, recommendation to remove an organ), they often cease to listen effectively (Kessels, 2003). The family member or friend may be able to focus, take notes, and relay the information provided by the physician to the patient at a time when the shock of the unfortunate news has passed. Even without shocking news, some instructions or discussions regarding risks, benefits, and alternative treatments may be lengthy and complex, and a second person in audience helps reinforce that information.

A complete history includes the chief complaint, history of present illness (HPI), past medical and surgical history, history of allergic reactions, social and family history, and a review of systems. The surgeon should obtain this information in a direct fashion. Patients should be given the opportunity to express any concerns or pertinent history, but often the physician must focus the conversation to obtain the information necessary to make a diagnosis and avoid pitfalls in treatment.

Chief Complaint

Often patients can identify an issue as urologic. Therefore they may present directly to the urologist with a particular problem or chief complaint. The chief complaint is the reason why the patient is seeking urologic care; this should be the urologist's focus. Although other urologic issues may be identified, the urologist's goal should be to target the chief complaint to allay the patient's immediate concerns. For example, the patient presents with urinary frequency is identified to have a renal mass; addressing the renal mass but not addressing the urinary frequency may be seen as ineffective care by the patient. With a clear chief complaint, the urologist should begin to think of a differential diagnosis and then narrow the possibilities with the HPI.

History of Present Illness

The HPI incorporates questions to identify the timing, severity, nature, and factors that may exacerbate or relieve the issue identified in the chief complaint. For an efficient HPI, the urologist creates a differential diagnosis based on the chief complaint and then asks questions to help support or oppose a diagnosis on the differential list.

The following sections review a variety of typical chief complaints to highlight considerations for the HPI.

Pain

Pain can often be a chief complaint or a factor elicited while obtaining the HPI. The astute clinician must be able to identify the location of pain and characterize its nature; this information will help pinpoint the cause or, at a minimum, direct further examination and testing. It is prudent to assess the onset and duration and to ascertain if this pain episode has occurred previously. In our practice, we have encountered patients with initial obstructive ureteral stones with renal colic (and little experience with kidney stones) who often inappropriately attribute the pain to some gastrointestinal or musculoskeletal cause. However, the same patient will then become very familiar with the nature of this obstructing stone pain and associated symptoms and readily identify the presence of an obstructing stone upon recurrence of such pain.

Often patients can localize pain. While gathering the HPI, the physician should direct patients to point to the site of maximal pain with one finger. An important distinction is made between pain and tenderness. Later in the physical examination, the physician must assess if there is tenderness (pain with palpation) in that location or elsewhere. Although pain and tenderness often overlap in location, a site of pain without tenderness may be the result of referred pain. An example is testicular pain without testicular tenderness; the pain in the testicle can often be referred pain from an obstructing ipsilateral ureteral stone.

The severity of the pain should be assessed and documented. Pain severity can be characterized as mild, moderate, or severe or based on a 1-to-10 scale. This commonly used scale as described by Wong and Baker in 1988 uses face illustrations with increasing appearance of distress/discomfort along a 10-point scale (Wong and Baker, 1988). This scale helps document the severity of pain before and after intervention.

Pain can be due to distention from obstruction or inflammation within the parenchyma of a genitourinary (GU) organ. Obstructive pain results in distention of a hollow organ (or hollow portion) of the organ resulting from some obstruction (e.g., ureteral stone for renal pelvis or ureter and bladder outlet obstruction for bladder). In the kidney, for example, this can result in colicky-type pain, typified by a patient with intermittent pain for which the patient is always moving to seek a position of comfort. This contrasts with parenchymal pain, such as pyelonephritis, which is typified by constant pain and is the result of inflammation, infection, or subcapsular bleeding causing distention within the parenchyma of the GU organ. This pain is typified by a patient who lays still, seeking not to exacerbate the pain with motion.

An understanding of nervous system anatomy can facilitate comprehension of some of the associated signs or symptoms seen with GU pain. For example, the celiac plexus is responsible for the visceral innervation of the foregut and the kidneys. Therefore irritation of the kidneys can result in paroxysmal nausea and vomiting. In addition, irritation of the ureter may result in referred pain to the ipsilateral testicle in men or labium in women because of the common nerve supply to these areas. Rarely pain can be due to tumor infiltration of the periparenchymal nerves. However, often this is a late sign and a manifestation of advanced disease.

Pain of an acute nature often is due to a clear cause. Obstruction or inflammation of an organ causes the release of prostaglandins or chemokines that result in noxious stimulation of nerves. These signals are transmitted from the peripheral nervous system to the central nervous system and perceived as pain. This mechanism is complex, and signals can be amplified or diminished en route to the central nervous system (Urban and Gebhart, 1999). Medications and techniques used to treat pain either target the noxious chemoneural agent (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs] inhibit the production of prostaglandins) or interfere with opioid or other receptors in the brain. Chronic pain can be much more complex with possible signal imprinting within the pain, resulting in the sensation of pain without noxious stimuli, such as in chronic pelvic pain disorder or fibromyalgia (Woolf, 2011). When no clear urologic cause is identified after an appropriately thorough evaluation, referral to a pain specialist should be considered.

Renal Pain. Renal pain is typified by location in the ipsilateral costovertebral angle just lateral to the vertebral spine and inferior to the 12th rib. It can be due to obstruction of the ipsilateral collecting system (causing colicky-type pain) or inflammation or infection of the renal parenchyma (causing flank pain and costovertebral angle tenderness). The pain may radiate anteriorly across the flank and toward the abdominal midline or down toward the ipsilateral scrotum or labium. Pain in this location also can be from gastrointestinal or musculoskeletal sources. Intraperitoneal causes of pain often are typified by a relationship to food ingestion or irregularity with bowel function. Further, peritoneal irritation causes peritoneal signs on abdominal exam (exquisite tenderness to any abdominal motion). Further tenderness would be most pronounced anteriorly (such as the Murphy sign for acute cholecystitis) as opposed to costovertebral angle tenderness (CVAT). Intraperitoneal pathology may cause ipsilateral shoulder pain from diaphragmatic irritation via the phrenic nerve; renal pain typically does not.

Ureteral Pain. Ureteral pain typically is due to ureteral obstruction, is acute in onset, and is located to the ipsilateral lower quadrant. The acute distention of the ureter and hyperperistalsis result in pain as prostaglandins accumulate, causing ureteral spasm, which in turn causes increased lactic acid production, which in turn irritates type A and C nerve fibers in the ureteral wall. These nerve fibers conduct signal toward T11-L1 dorsal root ganglia, and this irritation is perceived as pain. Ureteral obstruction of a gradual or partial nature may not cause pain. The point of ureteral obstruction may result in referred pain to the ipsilateral scrotum or penis. Obstruction at the ureterovesical junction also may result in irritative voiding symptoms (with noncommiserate urinary volume).

Vesicle Pain. If the bladder is inflamed (as in cystitis) or distended because of obstruction (as in acute urinary retention), suprapubic pain may be present. Inflammation of the bladder caused by infection or interstitial cystitis is worst when the bladder is distended, so patients may report improvement in suprapubic pain with voiding. Patients also may describe strangury, a sharp and stabbing pain at the end of urination (presumably resulting from final contraction of the inflamed detrusor). In sensate bladders, acute urinary retention can be easily identified from the history: profound desire to urinate without ability to do so. However, in patients with flaccid atonic bladders, large volumes of urine can be retained without any symptoms.

Prostatic Pain. Inflammation of the prostate, prostatitis, can result in pain that is located deep within the pelvis. It can be difficult to localize and sometimes is confused with rectal pain. Irritative voiding symptoms (urinary frequency, urgency, and dysuria) are often associated with irritation of the prostate.

Penile Pain. The differential for penile pain includes paraphimosis, ulcerative penile lesions (e.g., cancer or herpes), or referred pain from cystitis/prostatitis in the flaccid penis. In the rigid penis, Peyronie disease or priapism may be the cause.

Scrotal Pain. Pain within the scrotum may be due to irritation of the scrotal skin, such as an inflamed pustule from an ingrown hair or from the testicles and cord within. Epididymitis and orchitis are typified by testicular pain that may be relieved by maneuvers that elevate or support the testis. Torsion of the testicle or its appendages result in acute vascular congestion and pain (and in the case of testicular torsion is a surgical emergency). Varicoceles may result in a dull ache particularly toward the end of the day from accumulated vascular congestion. Again, because of common embryologic origins and therefore neurologic pathways, pain within the kidney or ureter may be referred to the ipsilateral scrotum.

Narcotic Considerations. Currently, the United States is dealing with an alarmingly high rate of opioid abuse. On October 6, 2017, the president of the United States declared a national public health emergency to help curtail opioid abuse and diversion (https://cnn.com, 2018). Diversion, or the exchange of prescription controlled substances for money or illicit substances, has placed physicians in a precarious position. Physicians and pharmaceutical companies

have been implicated in contributing to this epidemic by falsely promoting synthetic narcotics as "safer" than natural narcotics or by being complacent in prescribing narcotic pain medication. To this end, many recent studies have sought to identify and quantify the severity of pain of certain urologic diseases and surgery and to assess the utility of nonopioid analgesics for patients. In general, urologic conditions causing pain should be addressed promptly to minimize the need for narcotic use. Non-narcotic analgesia (NSAIDs, physical therapy, neuromodulation, acupuncture) should be used whenever possible to minimize narcotic use. Patients with pain with no identifiable urologic cause should not be offered narcotics and rather should be referred to their primary care physician and/or pain management specialists.

Urologists also should be cognizant of signs for narcotic-seeking behavior and narcotic abuse. All medical students are taught the side effects of narcotics. Besides euphoria, patients often are afflicted with constipation/ileus, dizziness, nausea, vomiting, tolerance, physical dependence, and respiratory depression (Benyamin et al., 2008). Patients seeking narcotics may come from unusual locations, exhibit inconsistent behavior (facile walking in hallway but difficulty walking in examination room), demonstrate noncompliant follow-up, demonstrate disinterest in non-narcotic analgesia, or request specific narcotics by brand name (Pretorius and Zurick, 2008). Clearly, it is important to obtain a thorough HPI seeking any discrepancies and/or rehearsed answers to avoid contributing to this epidemic.

Hematuria

Hematuria, or the presence of blood in the urine, is a concerning urologic sign in adults and must be evaluated because it may signal the presence of a urologic cancer in up to 25% of patients with this complaint. Hematuria comes in two varieties: gross and microscopic. Gross hematuria is often alarming to the patient, whereas microscopic hematuria is unnoticed by the patient until it is detected by a urinalysis. Critical to the HPI for hematuria are the age, presence of irritative voiding symptoms, smoking history, and industrial chemical exposure history because these are risk factors for detecting cancer. Further, exposure to alkylating chemotherapy, analgesic abuse history, or chronic foreign objects in the urinary tract should increase suspicion for GU malignancy.

After excluding urinary tract infection (particularly in young women), history of nephrologic pathology, trauma, or recent urologic manipulation, the physician should give the patient a full urologic evaluation for hematuria according to American Urological Association (AUA) guidelines. Interestingly, several studies demonstrate age as a risk factor for GU malignancy detection on evaluation for hematuria; however, children with GU malignancies have been described (Commander et al., 2017). In fact, the most common cause of gross hematuria in a patient older than 50 years of age is bladder cancer.

Hematuria must be differentiated from pseudohematuria, whereby the urine may appear red because of dehydration or certain medicines or foods (Hubbard and Amin, 1977). The way to differentiate hematuria from pseudohematuria is to obtain a clean midstream urine sample and assess for red blood cells (RBCs) on the microscopic analysis. The urine dipstick alone is not sufficient for determining the presence of true hematuria because it may signal the presence of "hematuria" when no RBCs are present but rather other solutes that discolor the urine. In fact, proceeding with a full hematuria evaluation for dipstick pseudohematuria is associated with unnecessary cost and low yield for detecting malignancy (Rao et al., 2010).

When encountering a patient with hematuria, the physician must ascertain duration of onset and several associated factors. Patients should be queried as to which portion of the urinary stream contains urine: the initial part of the stream, the entire stream, or the terminal portion of the urinary stream. Initial stream hematuria often signifies mild bleeding from a prostatic or urethral source, and terminal hematuria often signifies bladder neck irritation that expresses hematuria upon contraction of the bladder neck at the end of urination. Other helpful clues include any associated pain and clots associated with the hematuria.

Hematuria usually is painless, but pain can occur when clots obstruct the upper urinary tract (see Renal Pain earlier) or cause urinary retention. The shape of clots can help elucidate their origin: clots formed in the upper tract often have a vermiform shape, whereas cuboid clots are likely produced in the bladder.

Lower Urinary Tract Symptoms

Patients often come to the urologist with lower urinary tract symptoms (LUTS). LUTS are symptoms associated with the urinary bladder and its outlet. Such symptoms can be due to any combination of obstructive or irritative causes. Causes of lower urinary tract obstruction include benign prostatic hyperplasia (BPH), obstructive prostate cancer, urethral stricture disease, dysfunctional voiding, detrusor-external sphincter dyssynergia, severe phimosis, and severe meatal stenosis. In short, anything that can obstruct or narrow the caliber of the urethra can cause obstructive LUTS. Although a complete obstruction results in urinary retention, a partial obstruction results in obstructive LUTS (oLUTS); namely sensation of incomplete urinary emptying, urinary frequency (more frequently than every 2 hours), intermittency (intermittent flow of urinary steam), weak urinary stream, and urinary straining (requiring Valsalva maneuver to aid in voiding). In patients with weak detrusor muscle activity, even a minimally obstructive outlet can result in oLUTS or even urinary retention. Therefore it is important to consider causes for hypocontractile or acontractile bladders when evaluating a patient with oLUTS. It is also important to remark that bladder outlet obstruction may result in varying levels of urinary retention. Some patients may urinate their bladder volume incompletely and therefore have an elevated residual volume, whereas other patients may not be able to urinate at all and be in outright urinary retention. Often the progression of obstruction, for instance in BPH, is slow, and therefore changes in urinary stream may not be easily acknowledged by the patient. Further, because of such acclimation and possibly peripheral neuropathy, many patients may not appreciate the level of obstruction they have (which would be evidenced by objective measures of weak urinary stream and elevated residual stream). Oddly enough, chronic bladder outlet obstruction can result in detrusor irritability with irritative voiding symptoms.

Irritative LUTS (iLUTS) include urinary frequency, urgency, and dysuria. Causes of irritative voiding symptoms, other than chronic bladder outlet obstruction, include overactive bladder, cystitis, prostatitis, bladder stones, or bladder cancer. Urinary frequency entails urinary voiding of more than five or six times per day. It is normal to void up to twice per night, but nocturia of more than twice per night merits urologic evaluation. A bladder diary is helpful in determining if the urinary frequency may be due to incomplete bladder emptying, overactive bladder, or polyuria (increased urinary output). Polyuria may be due to polydipsia (behavioral or otherwise), diabetes mellitus, diabetes insipidus, or other reasons.

The rationale for the use of a bladder diary is located elsewhere in the text. A bladder diary, briefly, is a tabulation of all fluid ingested and all urine produced by a patient with associated times and volumes. Preferably patients note sensations of urgency or urinary incontinence on this tabulation. Typically a bladder diary is kept for 48 hours. The bladder diary can help provide insight into the functional capacity of a bladder, which should be around 300 to 400 mL in a normal adult and can help quantify the severity of nocturia. Daytime frequency without nocturia may be due to psychogenic reasons (e.g., anxiety). Nocturia without daytime frequency can be due to increased nighttime polyuria. This can be due to excessive fluid intake before bed (which can be easily elucidated from the bladder diary) or increased intravascular volume resulting from the return of fluid from lower extremity peripheral edema upon elevation of legs for recumbency of sleep. Further, as patients age, renal concentrating ability diminishes, which may result in increased urine production at night when renal blood flow is increased (Weiss and Blaivas, 2000).

Urinary urgency indicates difficulty in postponing urination. Although this sensation may be normal if a patient has held his or her urine for a prolonged period, it should not occur otherwise. Dysuria is painful urination and is typically due to inflammation

within the bladder. The pain is often felt along the urethra or referred to the urethral meatus. It is important to highlight that irritative voiding symptoms, particularly in patients older than 50 years and with smoking history, can be the only sign of an occult bladder cancer, particularly carcinoma in situ; therefore a low threshold for cystoscopy should exist for patients presenting with iLUTS.

Urinary hesitancy refers to delay in the start of urination. Typically, micturition occurs a second after the urinary sphincter relaxes. However, in men with bladder outlet obstruction, there may a prolongation of this delay. Postvoid dribbling refers to the loss of a few drops of urine at the end of urination. This is often an early symptom of urethral obstruction related to BPH and is due to the escape of urine into the urethra that is not "milked back" into the bladder at the end of urination (Stephenson and Farrar, 1977). Men may describe shaking the penis to evacuate such residual urine and prevent wetting their clothes. Straining refers to the use of Valsalva maneuver or manual abdominal pressure (i.e., Crede voiding) to help push the urine out and can be easily performed by the patient.

The AUA symptom score was introduced in 1992 and quantifies the presence of many of the symptoms mentioned above onto a scale. The questionnaire assesses whether incomplete emptying, urinary frequency, intermittency, urgency, weak stream, straining, and nocturia were present over the prior month. Answer choices range from 0 to 5 for each question depending on prevalence (not at all, less than 1 time in 5, less than half the time, about half the time, more than half the time, and almost always). Nocturia, however, is not a prevalence over the prior month but rather the typical number of times the patient arises from sleep to urinate (0 to 5; 5 representing 5 times or more per night). The sum of the values indicates the severity of symptoms (0 to 7 is mild, 8 to 19 is moderate, 20 to 35 is severe). The International Prostate Symptom Score (IPSS) is the AUA symptom score with the addition of a quality-of-life score (Barry et al., 1992) (Table 1.1). Although this tool has many limitations (nonspecific, requires sixth-grade reading level, may not be answered by those with neurologic conditions) is very useful in quantifying and standardizing urinary symptoms to help compare patient encounters after intervention (MacDiarmid et al., 1998).

Urinary Incontinence. Urinary incontinence is the involuntary passage of urine. The reasons for urinary incontinence are many and can be due to several pathologies. In general when the pressure within the bladder is greater than the resistance provided by the urethra, or when it is bypassed, urinary incontinence may occur. A thorough differential diagnosis can help the urologist direct the questioning to arrive at the likely diagnosis. It is helpful to understand the eight categories of urinary incontinence.

Stress Incontinence. Stress urinary incontinence refers to the involuntary passage of urine with any activity that increases intra-abdominal pressure. This is typically indicative of weakness in the urinary sphincter and can be seen in multiparous women, postmenopausal women, and men who have had radical prostatectomy or another procedure affecting the outlet (aggressive transurethral resection of the prostate [TURP]). Patients complain of such loss of urine with Valsalva maneuvers, typically coughing, sneezing, laughing, or heavy lifting. Generally, the treatment for stress urinary incontinence involves exercises or surgeries that increase the resistance of the urinary outlet (e.g., Kegel exercises, urethral sling, artificial urinary sphincters, urethral bulking).

Urge Incontinence. Urinary urgency, described previously, may be due to a myriad of reasons. This occurs when a patient experiences involuntary passage of urine coincident with sensation of urinary urgency. This is often a symptom of severe overactive bladder, cystitis, or neurogenic bladder or may occur in patients with poorly compliant bladders. Just as with urinary urgency, urge incontinence may be a

TABLE 1.1 International Prostate Symptom Score

SYMPTOM	NOT AT ALL	<1 TIME IN 5	LESS THAN HALF THE TIME	ABOUT HALF THE TIME	MORE THAN HALF THE TIME	ALMOST ALWAYS	YOUR SCORE
1. INCOMPLETE EMPTYING							
Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. FREQUENCY							
Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5	
3. INTERMITTENCY							
Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. URGENCY							
Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	

TABLE 1.1 International Prostate Symptom Score—cont'd

SYMPTOM	NOT AT ALL	<1 TIME IN 5	LESS THAN HALF THE TIME	ABOUT HALF THE TIME	MORE THAN HALF THE TIME	ALMOST ALWAYS	YOUR SCORE
5. WEAK STREAM Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. STRAINING Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	NONE	**1 TIME**	**2 TIMES**	**3 TIMES**	**4 TIMES**	**≥5 TIMES**	
7. NOCTURIA Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
TOTAL INTERNATIONAL PROSTATE SYMPTOM SCORE							

QUALITY OF LIFE DUE TO URINARY SYMPTOMS	DELIGHTED	PLEASED	MOSTLY SATISFIED	MIXED—ABOUT EQUALLY SATISFIED AND DISSATISFIED	MOSTLY DISSATISFIED	UNHAPPY	TERRIBLE
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

From Cockett A, Aso Y, Denis L: Prostate symptom score and quality of life assessment. In Cockett ATK, Khoury S, Aso Y, et al., eds: *Proceedings of the Second International Consultation on Benign Prostatic Hyperplasia (BPH); 27-30 June 1993,* Paris, Channel Island, 1994, Jersey: Scientific Communication International, pp 553–555.

sign of occult bladder cancer, and this diagnosis must be considered. Treatment for urge incontinence is distinct from that of stress urinary incontinence in that treatment focuses on measures to relax the bladder (e.g., anticholinergic medical therapy, intravesical Botox, neuromodulation).

Mixed Urinary Incontinence. Patients often may have urinary urgency with loss of urine and loss of urine with Valsalva maneuvers. These patients should be characterized as having mixed incontinence, and their treatments should reflect both processes; the treatment of one cause of incontinence but not the other may result in exacerbation of symptoms.

Continuous Incontinence. Patients with continuous urinary incontinence complain of constant wetness in the perineum that is independent of the urge to urinate or maneuvers associated with increased intra-abdominal pressure. Typical of continuous incontinence are processes that bypass the bladder outlet; mainly urinary fistulas. In women, a urinary fistula between the urinary bladder or ureter and the vaginal vault may result in continuous incontinence. Patients complaining of continuous incontinence should be asked about a history of gynecologic surgery, radiation, or traumatic childbirth. Continuous incontinence can be congenital. Such is the case with an ectopic ureter, in which the typically dysplastic upper pole moiety of a duplicated kidney drains into the vaginal or perineum, bypassing the external urinary sphincter. The parents of juvenile patients with ectopic ureters may report unsuccessful toilet training. As adults such patients may complain of urinary incontinence continuously during the day, which may be less severe at night. The absence of urinary incontinence at night may reflect the collection of urine in the saccular upper pole moiety, which is more dependent when the patient is in the recumbent position.

Pseudoincontinence. Some female patients may experience symptoms similar to continuous urinary incontinence but fail to demonstrate true urinary incontinence. Patients with chronic vaginal discharge may complain of continuous perineal wetness, which may be confused with continuous urinary incontinence. Also, severe labial fusions may result in retention of urine within the vaginal vault and mimic continuous incontinence (Palla et al., 2010). Clearly, a thorough pelvic examination may help identify such causes.

Overflow Incontinence. Often referred to as paradoxic incontinence, overflow incontinence occurs when the urinary volume within the bladder approaches and exceeds bladder capacity, resulting in an increase in intravesicle pressure greater than urethral outlet resistance.

The pressure is released by the decrease in urinary bladder volume associated with incontinence. This is likely to occur at night when the patient is less likely to guard against this incontinence. Guarding is voluntary contraction of the pelvic floor muscles in an attempt to prevent urinary incontinence and can occur with any cause of urinary incontinence. Overflow incontinence can be resolved by treating the outflow obstruction, hence the paradoxic nature of this incontinence. Overflow incontinence is usually present in male patients with prolonged history of bladder outlet obstruction. Because of the gradual progression of symptoms, such patients may not be aware of their obstructive symptoms (as noted earlier).

Functional Incontinence. Patients with limited mobility or limited access to a toilet or urinal may experience urinary incontinence. Such patients may have intact bladder-outlet anatomy and physiology but may simply be unable to move in time to void in a urinal or toilet. Therefore the urologist must assess mobility in the elderly patient with urinary incontinence.

Elderly patients also may have diminishment of their cognitive abilities and awareness and may lose the social inhibition to soil oneself. Therefore an assessment of cognitive ability should be considered in elderly patients with what ultimately may be volitional urination.

Enuresis. Urinary incontinence during sleep, known as enuresis, is normal in children up to 3 years of age. It persists in about 15% of children up to 5 years of age and in up to 1% of adolescents up to 15 years of age (Forsythe and Redmond, 1974). Primary enuresis (enuresis that has always been present) persistent beyond 6 years of age should be evaluated by a urologist as ectopic ureter in the female patient. Secondary enuresis (enuresis with onset after child has ceased bedwetting) may be associated with child abuse and bullying (Zhao et al., 2015).

Sexual Dysfunction

Patients with sexual dysfunction often are referred to the urologist. Although sexual dysfunction often is encountered in women with LUTS (Elsamra et al., 2010), the urologist also must be familiar with the different components of sexual dysfunction in men. Men may complain of erectile dysfunction or impotence, when this is merely a symptom of another problem.

Erectile Dysfunction. The AUA and National Institutes of Health (NIH) Consensus Conference on Impotence in 1993 have defined erectile dysfunction (ED) as the inability to attain and/or maintain penile erection sufficient for satisfactory intercourse. Incidence of ED is significant and can affect more than 50% of men over the age of 40 years. The basic causes of ED (vasculogenic, neurogenic, psychogenic, endocrinologic, and medication side effect) help direct the medical interview. For instance, poorly controlled diabetes mellitus (DM) may result in peripheral neuropathy or vasculopathy, which can affect erectile quality. Antihypertensives, antidepressants, antipsychotic medications, and medications that directly or indirectly affect testosterone levels may all potentially contribute to ED. Therefore a thorough history should explore whether the patient is taking such medications or is afflicted with such ailments that are known to cause ED. Understanding the timing and situational nature of erections in the patient complaining of ED may help identify the cause. For instance, patients who experience situational ED (can have erections with one partner but not another or can attain sufficient erection with visual or manual stimulation) or those who have adequate nocturnal tumescence may have a psychogenic cause. Further, ED can be a harbinger of occult coronary artery disease and should merit consultation to a cardiologist (Nehra, 2012).

Because much of the assessment of ED is subjective, a questionnaire may be a useful tool to quantify and monitor the level of ED. The International Index of Erectile Function (IIEF) and the abbreviated IIEF-6 (also known as the Sexual Health Index for Men [SHIM]) are validated questionnaires often used to quantify and monitor erectile function, orgasmic function, sexual desire, intercourse, and overall satisfaction (Kriston et al., 2008).

Loss of Libido. ED can be the result of hypogonadism. Hypogonadism can be primary or secondary, and if a low serum testosterone is identified, evaluation of serum prolactin and gonadotropins should be performed. Symptoms of hypogonadism include change in sleep patterns, emotional changes, decreased strength, weight gain, infertility, and ED. The amount of testosterone necessary to maintain libido is usually less than that required for full stimulation of the prostate and seminal vesicles. Therefore patients with adequate ejaculatory volume are unlikely to have hypogonadism severe enough to cause loss of libido. Depression, several medications, or severe medical illnesses (e.g., cancer) can result in loss of libido.

Because libido is a subjective measure, clinical questionnaires may be the best tool to quantify and monitor a patient's sexual desire. Several validated questionnaires have been produced to aid in the evaluation for hypogonadism: the Androgen Deficiency in Aging Questionnaire (ADAM), the Aging Male Survey, and the Massachusetts Male Aging Study Questionnaire (Wiltink, 2009). Although these surveys may not correlate with serologic hypogonadism, the Hypogonadism Related Symptom Scale may offer greater sensitivity and specificity based on serum testosterone levels (Wiltink, 2009).

Premature Ejaculation. According to the International Society of Sexual Medicine Guidelines, premature ejaculation is either less than 1 minute (if lifelong) or 3 minutes (if acquired) and must be associated with inability to delay ejaculation and with negative personal consequence (Althof et al., 2014). Unfortunately, many patients presenting with the complaint of premature ejaculation often have unrealistic expectations for intravaginal ejaculatory latency time. Intravaginal ejaculatory latency time (IELT) was evaluated in five countries, and median time to ejaculation was 5.4 minutes in one study published in 2005. Further, a survey of sexual therapists supported IEJT of 1 to 2 minutes as too short but 3 to 7 minutes as adequate and 7 to 12 minutes as desirable (Corty and Guardiani, 2008). In patients with true premature ejaculation, vaginal quieting or sexual counseling should be offered. Although possibly helpful, treatment with a serotonin reuptake inhibitor should be offered infrequently (Montague et al., 2010). Because of latency to erectile function postejaculation, some patients with erectile dysfunction actually may have normal latency in attaining erections postejaculation.

Failure to Ejaculate. Several causes exist for anejaculation. Androgen deficiency, sympathetic denervation, use of pharmacologic agents, and a history of bladder neck/prostate surgery can result in decreased volume of ejaculation or anejaculation. Therefore the patient should be assessed for hypogonadism. Systemic hypogonadism (see earlier) or local decreased stimulation of prostate and seminal vesicles as seen with 5-alpha-reductase inhibitor administration often used for alopecia or enlarged prostate can result in lower volume ejaculate. A history of retroperitoneal surgery, especially retroperitoneal lymphadenectomy, as is done for testicular cancer, should be established because transection of the sympathetic nerve fibers results in anejaculation. Alpha-adrenergic antagonists (e.g., tamsulosin) and surgeries that affect the bladder neck (e.g., TURP) may result in retrograde ejaculation. Patients with advanced diabetes also may experience anejaculation.

Anorgasmia. Orgasm is the euphoria associated with a series of muscular contractions in the genital region and the release of endorphins. It usually is associated with ejaculation in men. Orgasm can occur without erection or ejaculation in men (e.g., postprostatectomy). Absence of orgasm can be due to psychogenic causes and several medications used to treat psychiatric ailments. In cases of impaired pudendal nerve function (e.g., diabetic peripheral neuropathy) anorgasmia can occur as well. Such patients may benefit from neurologic evaluation (e.g., vibratory testing to assess penile sensation) or referral to a sexual counselor.

Hematospermia

Hematospermia is the presence of blood in the ejaculate. With rare exception it is due to nonspecific inflammation of the prostate or seminal vesicles and usually resolves spontaneously. This can be associated with ejaculation after a long duration of sexual abstinence. If blood is persistent beyond several weeks, the urologist should consider an evaluation including a genital examination, digital rectal

examination, prostate specific antigen, cystoscopy, and urine cytology to exclude GU tuberculosis or cancer.

Pneumaturia

Pneumaturia is the passage of gas within the urine. This can sometimes be an alarming finding for the patient because this may interrupt the urinary flow and sound like flatus from the urethra. Pneumaturia is most commonly due to a fistula between the gastrointestinal system and the bladder. Therefore such patients should be screened for Crohn disease, enteritis, or history of recent intra-abdominal surgery or radiation. Rarely, pneumaturia may be due to gas-forming bacteria within the urinary tract. Therefore patients also should be screened for history of severe urinary tract infections or immunocompromised states.

Urethral Discharge

This is the most common symptom of sexually transmitted infection (STI). Patients should be screened for high-risk sexual behavior. Bloody discharge may be concerning for urethral carcinoma.

Fevers and Chills

It should be determined, in a patient who reports fevers, if the fevers are subjective or if they were measured objectively with a thermometer. The method by which the temperature was obtained (thermometer used orally vs. rectally vs. auricular or temporal scanner) can affect the accuracy of the measured temperature compared with the core temperature and may be important to note in pediatric patients. Rigors (or chills) may or may not be associated with fevers but can be independently concerning for bacteremia or other severe infection. The severity and site of infection may affect whether a patient will have fevers or chills. For example, cystitis rarely causes fever, but the diagnosis of pyelonephritis often requires presence of a fever. A patient with fevers and chills may signal a systemic response to an infectious process or sepsis and merit further evaluation or even possibly hospitalization. Fevers and chills in the elderly or immunocompromised should be especially concerning.

Constitutional Symptoms

Constitutional symptoms are fevers, chills, night sweats, anorexia, weight loss, fatigue, or lethargy. Sometimes these are referred to as B symptoms, borrowed from non-Hodgkin lymphoma staging. Such symptoms can signal the presence of advanced inflammatory, infectious, or malignant processes such as GU tuberculosis or advanced bladder cancer.

Medical History

It is incumbent upon the urologist to obtain an accurate medical history because many of the patients' medical problems may have urologic implications. Moreover, it is important to understand the severity of the medical illness and the compliance with treatment. For instance, knowing that patients are afflicted with DM is important, but so is knowing if their glucose is well controlled with or without insulin and if they have peripheral neuropathy associated with their diabetes. (A good question to ask is, "Is a recent HgbA1C available?")

Patients often may not be aware of all their medical conditions. Soliciting input from a family member or reviewing a recent note from the primary care provider also may help. A good place to start is to assess the patient's medication list and determine medical illnesses based on that. However, this can be misleading because several medications may be administered for different reasons (e.g., hydrochlorothiazide for hypercalciuria vs. hypertension) and patients may not be compliant with all their medications.

Even though the patient, family member, or recent medical documentation may not mention a medical illness, the urologist must remain vigilant to ensure there are no undiagnosed medical conditions that can adversely affect the patient or any subsequent urologic treatment. The classic example of this is occult coronary artery disease in the urologic patient who may require surgery soon. Although patients may have never had a "heart attack," they may, if prompted, report shortness of breath or chest pain with activity, and this may be a signal of undiagnosed coronary artery disease. Another example is a large patient with a large collar size who does not provide a medical history of obstructive sleep apnea, but, if prompted, his spouse may report nighttime snoring and irregular breathing or daytime fatigue in the patient. Clearly, the diagnosis of coronary artery disease and obstructive sleep apnea, among others, can have implications for treatment.

Performance Status

The functional ability of patients is a testament to their overall health and their ability to withstand challenging treatments such as invasive surgery or chemotherapy. At the most basic level, the activities of daily living (ADLs), which include dressing, eating, ambulating, toileting, and hygiene, and the instrumental ADLs, which include cleaning and maintaining a house, managing money, preparing meals, shopping, and community participation, can be easily assessed during the perioperative setting to help determine risk for surgery. Levitt et al. evaluated nearly 200 patients who underwent percutaneous nephrolithotomy, identified deficiency in ADLs in 16% of patients, and identified deficit in ADLs as an independent predictor of complications better than Charlson Comorbidity Index or the American Society of Anesthesiology Score (Leavitt et al., 2014).

Several performance status scales have been developed and are used mostly for oncologic purposes. These scales include the Eastern Cooperative Oncology Group score and Karnofsky performance status grade, which classify patients according to their ability to perform physical activity of a strenuous or nonstrenuous nature, ability to self-care, ability to stay out of bed, or moribund status. Using such scales may be beneficial particularly in transmitting an impression of overall health to another provider; they are a clear factor in health assessment.

Past Surgical History

Prior surgery in a patient may have clear impact on the patient's assessment and subsequent treatment options. Prior surgeries, related to GU anatomy of interest or not, may indicate additional adhesions or obliteration of surgical planes, which can render subsequent surgery difficult. For example, a patient with extensive intra-abdominal surgery undergoing subsequent laparoscopic surgery may benefit from Hasson technique or visual port access as opposed to Veress needle access (Gaunay, 2016). Further, abstracting surgical anatomic details in a prior operative report may help the surgeon ascertain the utility of a subsequent procedure. For instance, a patient who underwent a prior TURP may have an operative report that includes TURP, but the operative details may reveal that only a channel TURP was performed, therefore opening the possibility that a subsequent TURP may be beneficial. Further, a prior operative report may provide vital information regarding anatomy or other difficulties encountered.

Medications

A thorough knowledge of medications can provide information regarding the presence and severity of a medical illness, possible cause for urologic complaints from medication side effects, and a target for cessation or adjustment in the perioperative period. Several examples to highlight these principles are as follows:

1. A patient with diabetes on several medications and large doses of insulin may have severe diabetes and be more likely to have peripheral neuropathy, even if he or she is not on a medication for peripheral neuropathy.
2. A patient on tamsulosin may complain of anejaculation or lightheadedness, not knowing the side effect profile of this medication.
3. A patient with hematuria on anticoagulation or antiplatelet therapy may benefit from temporary cessation (in addition to a full evaluation).

This last example can be used to highlight several pitfalls with poor medical history taking and its impact. For example, a patient on baby aspirin may be taking this for primary coonary artery disease prophylaxis or for prevention of coronary artery stent thrombosis.

TABLE 1.2 Drugs Associated With Urologic Side Effects

UROLOGIC SIDE EFFECTS	CLASS OF DRUGS	SPECIFIC EXAMPLES
Decreased libido	Antihypertensives	Hydrochlorothiazide
Erectile dysfunction	Psychotropic drugs	Propranolol Benzodiazepines
Ejaculatory dysfunction	α-Adrenergic antagonists	Prazosin Tamsulosin α-Methyldopa
	Psychotropic drugs	Phenothiazines Antidepressants
Priapism	Antipsychotics Antidepressants Antihypertensives	Phenothiazines Trazodone Hydralazine Prazosin
Decreased spermatogenesis	Chemotherapeutic agents Drugs with abuse potential Drugs affecting endocrine function	Alkylating agents Marijuana Alcohol Nicotine Antiandrogens Prostaglandins
Incontinence or impaired voiding	Direct smooth muscle stimulants Others Smooth muscle relaxants Striated muscle relaxants	Histamine Vasopressin Furosemide Valproic acid Diazepam Baclofen
Urinary retention or obstructive voiding symptoms	Anticholinergic agents or musculotropic relaxants Calcium channel blockers Antiparkinsonian drugs α-Adrenergic agonists Antihistamines	Oxybutynin Diazepam Flavoxate Nifedipine Carbidopa Levodopa Pseudoephedrine Phenylephrine Loratadine Diphenhydramine
Acute renal failure	Antimicrobials Chemotherapeutic drugs Others	Aminoglycosides Penicillins Cephalosporins Amphotericin Cisplatin Nonsteroidal anti-inflammatory drugs Phenytoin
Gynecomastia	Antihypertensives Cardiac drugs Gastrointestinal drugs Psychotropic drugs Tricyclic antidepressants	Verapamil Digoxin Cimetidine Metoclopramide Phenothiazines Amitriptyline Imipramine

Clearly this would have consequence regarding when and if such medications should be ceased. See Table 1.2 for a list of drugs associated with urologic side effects.

Allergies

Patients must be asked about allergies during the initial encounter, and allergy lists should be verified for accuracy on subsequent encounters. The inciting medication and the reaction should be written because many patients confuse allergy with side effect (e.g., red-man syndrome for vancomycin or upset stomach with antibiotics). Such medical allergies should be highlighted in the electronic medical record (EMR) to prevent inadvertent prescription or administration of such medication.

Social History

The social history includes an evaluation of tobacco, alcohol, and illicit drug consumption. The agent and the method of use have medical implications. Tobacco can be chewed, smoked, or vaped.

A patient who chews tobacco may still benefit from a nicotine patch during a hospitalization but may not necessarily have the urothelial cancer risk associated with smoking. Vaping, which may not have many of the carcinogens associated with combustion, may still provide derivatives of nicotine that promote malignant changes in urothelial and lung cell lines (Lee et al., 2018), although the long-term effect is still unknown.

Alcohol use should be evaluated because it may increase oncologic risk and risk for liver disease, which have clear implications for patient care. Alcohol use also can affect LUTS and sexual function. More acutely, a patient who ingests significant amounts of alcohol and is hospitalized may suffer from life-threatening withdrawal if a prophylactic measure such as Clinical Institute Withdrawal Assessment for Alcohol (CIWA) or alcohol replacement is not ordered. Patients with heavy alcohol ingestion often understate the amount of alcohol consumed. Anticipating this can allow for the provider to better order prophylactic measures.

Illicit Drug Use

There are many classes of illicit drugs (e.g., cocaine, narcotics, methamphetamines), all of which can be consumed via a myriad of modes. Knowing the agent used and the mode can prepare the provider for anticipating challenges in subsequent care in addition to the risk for communicable diseases if the intravenous mode is used. Because of the illicit nature and social stigma of such drugs, many patients may not be forthright about use; therefore the provider may need to establish high levels of trust to encourage the patient to divulge such information. Alternatively, review of prior medical records can help ascertain these risky habits.

Sexual Relations

Patients may engage in sexual behavior with a single person or multiple people of the same or different gender. The physician should not presume a monogamous, heterosexual relationship. Nonaccusatory questions such as, "Do you partake in sexual relations with men, women, or both? A single partner or many?" may allow the patient to provide an accurate answer without being defensive regarding alternative lifestyle. Clearly such information is important to assess for risk for STI and to assess social support structure.

Domestic Station

Typically patients are asked if they are married or single and who lives in the home with them. It is also beneficial to understand if the patient has family or friends who live nearby. Assessing where the patient lives and with whom is important for planning subsequent care. A patient with little or no social support may not fare well after a complex, life-altering surgery. Further, this information may provide insight regarding what treatment options a patient may find unacceptable (e.g., an elderly man who is the sole caretaker of an elderly handicapped woman may not be willing to undergo major surgery with long convalescence). Screening for domestic violence or other unsafe domestic situation should be completed at this time as well.

Occupation

Understanding the patient's current or prior occupations provides the urologist with greater insight into the patient's world-view and socioeconomic status as well as possible industrial exposure to possible carcinogenic agents.

Family History

Many diseases with urologic manifestations have a clear genetic component, and their mode of transmission (e.g., autosomal dominant) is well defined. Examples include adult polycystic kidney disease, tuberous sclerosis, von Hippel-Lindau disease, renal tubular acidosis, and cystinuria. Other diseases, such as prostate cancer or urolithiasis, have a well appreciated familial component, although the precise pattern of inheritance is not understood. Often the age at diagnosis of the family member can direct screening age. A recent study by Bratt et al. evaluated nearly 52,000 Swedish men with fathers or brothers with prostate cancer and identified an increased risk of prostate cancer incidence with a brother diagnosed (30% vs. 13% in the general population) and a father and a brother diagnosed (48% vs. 13% in the general population) (Bratt et al., 2016; Nordström, 2016). Therefore identifying not only the presence of disease in the family but also the frequency within the family may be important in screening such patients for disease.

Review of Systems

A review of systems is a comprehensive system-based checklist to determine if there are any other complaints or ailments that the patient may have. This may be a valuable opportunity to identify important issues that may not be related to the chief complaint.

PHYSICAL EXAMINATION

A complete and thorough physical examination is essential for any patient encounter. It often allows the urologist to select the most appropriate next step.

Vital Signs

Physical examination should start with a general set of vital signs. The objectively measured temperature, heart rate, blood pressure, respiratory rate, and pain rating can identify immediately the critically ill patient who may not necessarily be best served by waiting for an appointment. In the office setting, a defined normal range should be established, with patients beyond this acceptable range referred to the physician immediately to triage. All office staff should be assigned a role in assessing patients for critical illness or severe distress. In my clinical practice, we have encountered such patients who are profoundly hypotensive or tachycardic who benefited from rapid transportation to the emergency room.

Some have advocated for a rapid screening tool used to assess distress and measures set in place to provide such patients with prompt attention from social worker, mental health professional, or pastoral care (JNCCN, 2003). Such a tool can be considered a sixth vital sign and can help decrease the anxiety and distress within an already stressful waiting room.

General Appearance

Every medical student is instructed regarding the four modes of physical examination: inspection, auscultation, percussion, and palpation. Inspection is the first mode and can be applied to the entire patient at the onset of the encounter. Several general observations should be made, including level of pain or emotional distress, nutritional status, socioeconomic status and appropriateness in dress, overall strength or mobility of patient, appearance of skin quality, and quality of dentition. Often patients' appearance is compared with the stated age and noted accordingly (e.g., an ill patient or one with poor self-care may appear much older than stated age). Several diseases may have stigmata, such as jaundice with advanced liver disease, buffalo hump or skin striae with Cushing disease, exophthalmos with Graves disease, fibrofolliculomas in patients with Birt-Hogg-Dube syndrome, cogwheel rigidity in Parkinson disease, and apparent erection with priapism.

A preliminary assessment of frailty and nutritional status can be made upon general inspection. Frailty has been defined as the "excess vulnerability to stressors, with a reduced ability to maintain or regain homeostasis after a destabilizing event" by the American Geriatric Society (Xue, 2011). Several simple tools have been established and validated as markers for frailty. The gait speed (Dudzińska-Griszek et al., 2017) and get-up-and-go test (Pamoukdjian et al., 2015) as well as grip strength can be obtained easily as part of the standard encounter. Calf circumference (Landi et al., 2014) also has been assessed with an inverse relationship with frailty.

Many other clues can be obtained from the general physical examination. The quality of the dentition or moist mucous membranes can be a sign of health and hydration, respectively. For morbidly obese patients or patients with skeletal deformities, I have found that positioning the patient in the anticipated operative position while in the office prevents any surprises in the operating room.

Kidneys

The kidneys are located in the retroperitoneum and surrounded by the psoas muscle, diaphragm, oblique muscles, and the peritoneum with its contents. Aside from very large renal masses in small children or very thin adults, the kidneys should not be visible. In fact, the kidneys may be difficult to palpate under normal conditions. Because of the location of the liver, the right kidney may be inferior to the level of the left kidney, and palpation of the lower pole can be appreciated on deep inspiration.

The overlying skin in the upper quadrant and the costovertebral angle should be inspected, however, for any superficial lesions that may be causing "flank pain." Assessment of the skin sensation for pain, temperature, and light touch can be performed with a spoke-wheel or pin, cool object, and fine brush, respectively. Patients with herpes zoster may experience prodromal hyperesthesia before eruption of vesicles.

Bimanual examination, or renal ballottement, can be performed by placing the nonexamining hand posteriorly at the costophrenic angle and palpating for the kidney with the examining hand through the anterior abdominal wall (Fig. 1.1). Deep inspiration can help inferiorly displace the kidney to aid in exposure. In neonates and infants, ballottement can be performed between the thumb, placed anteriorly on the abdomen, and remaining four fingers, placed posteriorly at the costovertebral angle. Often large flank masses originate from the kidney in neonates, and transillumination may be feasible. If such a mass is fluid filled (cyst or hydronephrosis), then a dull reddish glow can be appreciated. However, if the flank mass is from a solid process (tumor or polycystic kidney), then no glow will be appreciated.

Turbulent vascular flow within the renal artery, suggestive of renal artery stenosis or large renal arteriovenous fistula, theoretically can be observed with auscultation. However, if such a bruit is appreciated, it is nonspecific for renal artery source and should be evaluated further with appropriate imaging (ultrasound with Doppler or angiography). Percussion of the kidneys often refers to the assessment of pain when the base of a closed hand of the examiner contacts the costovertebral angle. The examiner should approach this examination technique gently and avoid using excessive force because a simple tap may elicit the positive sign.

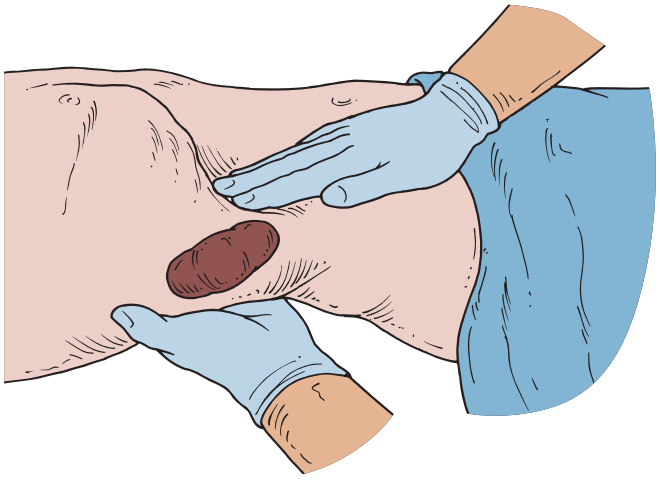


Fig. 1.1. Bimanual examination of the kidney.

Bladder

The bladder is located within the pelvis and can be palpable only as the bladder distends to a level above the pubis, typically greater than 150 mL. At a volume of approximately 500 mL, the bladder may be visible as a lower midline abdominal mass in thin patients. Percussion starting at the level of the pubic symphysis and ascending toward the umbilicus can help determine the level of distention because the pitch may change from dull to resonant beyond the bladder. Ballottement also can aid in palpation of the bladder.

A bimanual examination (Figs. 1.2 and 1.3) is performed to assess the mobility of the bladder and is the standard of care for examination of patients with large bladder tumors postresection (Chang et al., 2016). Even in the era of CT and MRI, a bimanual examination can improve upon the performance of these images for the prediction of pT3 disease (Rozanski et al., 2015) and was found to be an independent predictor of pT3 disease on multivariate analysis.

Penis

The phallus should be inspected for hair distribution, lesions on the skin, and the presence or absence of a foreskin. In the pediatric population, Tanner stage should be noted. Lesions on the penile skin can include superficial vesicles suggestive of herpes simplex or ulcerative lesions concerning for other sexually transmitted diseases or squamous cell carcinoma of the penis or venereal warts (condyloma acuminata) concerning for human papillomavirus (HPV) infection. Often patients may inquire about prominent vasculature on the phallus, particularly in children, and this is often normal.

The foreskin, if present, should be retracted to ensure that there are no penile tumors; most penile tumors involve the prepuce or

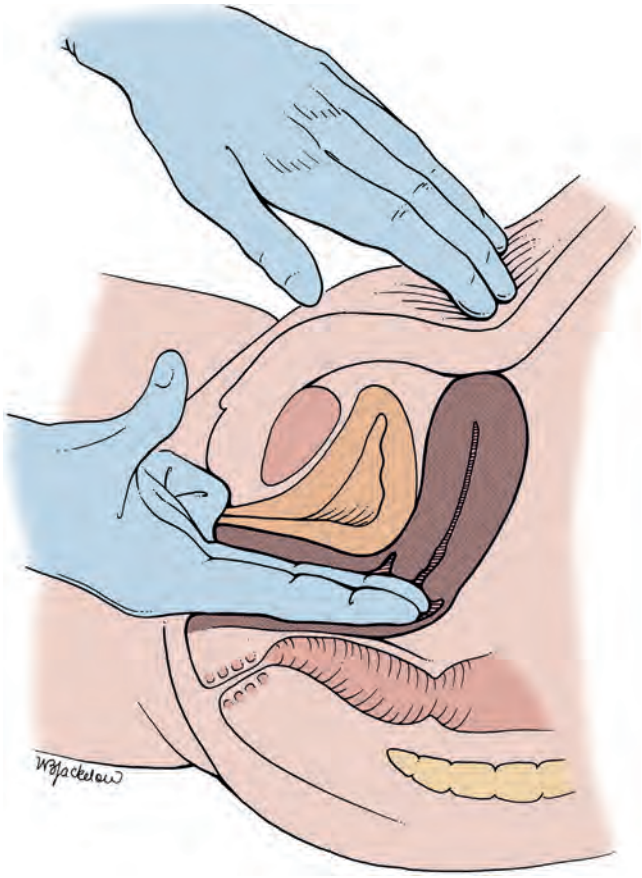


Fig. 1.2. Bimanual examination of the bladder in the female. (From Swartz MH: *Textbook of physical diagnosis*, Philadelphia, 1989, Saunders, p 405.)

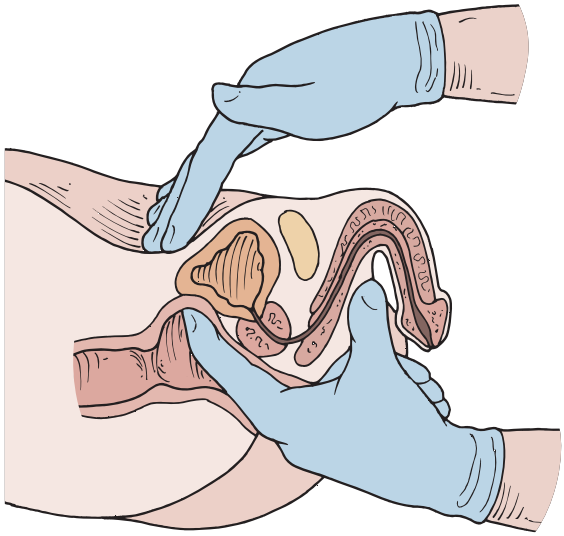


Fig. 1.3. Bimanual examination of the bladder in the male.

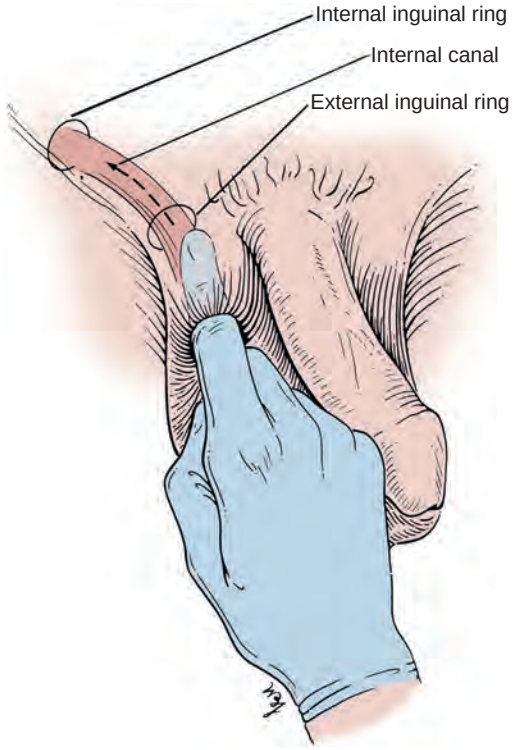


Fig. 1.4. Examination of the inguinal canal. (From Swartz MH: *Textbook of physical diagnosis*, Philadelphia, 1989, Saunders, p 376.)

the glans penis. The urethra should be inspected for location and absence of stenosis and presence of urethral discharge. Discharge, if present, should be characterized, and ideally a sample should be obtained if there is concern for STI. If hypospadias (ectopic location of urethral meatus on ventral aspect of penis) is identified, location and caliber of urethral meatus are noted (e.g., mega-meatus). A rare finding would be epispadias, in which the meatus is located on the dorsal aspect of the penis, although this is often seen with other profound GU anomalies such as bladder exstrophy. Palpation of the phallus can reveal dense subcutaneous plaques on the underlying fascia, which is concerning for Peyronie disease, which may also be demonstrated as curvature in the erect penis. Palpation of the urethra, if tender, is suggestive of periurethritis. Spongiofibrosis, which has implications for urethral reconstruction, can be palpated along the corpora spongiosum only if it is severe.

Scrotum and Contents

The scrotum contains the testicles and spermatic cord structures. The scrotal skin, which has hair and sebaceous glands, should be assessed for infectious processes (e.g., tinea cruris, cellulitis, pustules), which are more common, and malignant processes (squamous cell carcinoma typical of chimney sweeps), which are rare. Often such infectious processes are of minimal clinical consequence. Tinea cruris and cellulitis may be manifested by erythema and tenderness, whereas an abscess may demonstrate an area of fluctuance or purulent drainage. In the immunocompromised patient or in patients with limited capacity for self care, such infections can progress to Fournier gangrene, which is typified by necrotic "black" skin, foul odor, dishwater discharge, and crepitus.

The impression of the testicles should be assessed for their size and orientation. Although one testicle may be slightly inferior to the other, they should be of similar size and in the vertical orientation. However, in a patient with unilateral testicular pain, the testicle with a foreshortened cord and a horizontal lie can be concerning for testicular torsion. The absence of a cremasteric reflex (light touch to inner thigh resulting in cremasteric muscle contraction and ascension of the ipsilateral testicle) is a very specific sign for testicular torsion in pediatric patients.

Palpation of the testicles, epididymi, and spermatic cords should begin with the normal testicle. The testicles have a firm, rubbery consistency with a smooth ovoid surface. Typical size is 6 cm in length and 4 cm in width with variation seen among different races. Testicular size can be better assessed with an orchiometer (goniometer). Gliding the testicles between the examiner's fingers of both hands allows for palpation of the contour of the surface. A testicle that is small can be suggestive of prior infarct, surgery, hypogonadism, or endocrinopathy such as Klinefelter disease. Tenderness of the testis or the epididymis may indicate orchitis or epididymitis, respectively. Masses in the testes are hard and obliterate the smooth contour of the testis and should be considered testicular cancer till proven otherwise. Epididymal masses, on the other hand, which obliterate the distinct ridge of tissue posterior to the testis, are almost always benign. The vas deferens should be palpable bilaterally on each cord, high in the scrotum, and feel like a thick al dente linguini. Transillumination can be performed in the scrotal mass to assess for fluid content (e.g., hydrocele). To accentuate a varicocele, typically described as a "bag of worms," inspection and palpation of the scrotum should be performed with the patient supine, standing, and standing with Valsalva.

Examination for hernia can be performed by placing the examiner's index finger over the testis and invaginating the scrotum up toward the external ring (Fig. 1.4). The other hand is used to palpate over the internal ring and Hesselbach triangle (bordered by the inferior epigastric artery, the inguinal ligament, and the midline). The patient is instructed to perform Valsalva maneuver at that point, and the examiner assesses for a hernia as a distinct bulge that descends against the tip of the index finger. In children, the presence of a hernia can be appreciated by assessing for the "silk glove" sign. The potential space within the hernia sac allows for the hernia sac to roll over itself, resembling the sensation of rolling over the finger of a silk glove.

Digital Rectal Examination

The digital rectal examination (DRE) can be performed for assessment of prostate size, detection or provocation of prostatitis, and screening for prostate cancer. A DRE with a concurrent lower abdominal exam (bimanual examination) typically is performed in a patient who has undergone a transurethral resection of bladder tumor while still anesthetized. A gentle DRE also can be performed in neonates with disorders of sexual differentiation to evaluate for internal müllerian

structures (e.g., uterus). Although prior recommendations included DRE for men ages 40 and older, current AUA guidelines state that prostate cancer screening should be offered in men of average risk from the age of 55 to 69 at an interval of every 2 years.

To have a DRE, the patient should be standing with feet shoulder width apart and bent nearly 90 degrees at the waist. The patient can benefit from using the table to support this position by placing his hand or elbows on the table. Alternatively, the patient may be in a lateral decubitus position, flexed at the hips and knees, on the examining table. The patient is to be reassured throughout this part of the examination. The examiner's nondominant hand is used to spread the gluteal folds and expose the anus, which should be inspected for hemorrhoids or other lesions. The examiner's gloved finger with adequate lubrication then is advanced gently through the anus with the nondominant hand placed on the patient's anterior thigh or lower abdomen to provide gentle counter-traction. The finger is advanced until the prostate is palpable. The normal prostate is the size of a chestnut and should feel soft, similar to that of the contracted thenar eminence. Nodular firmness (which feels like a flexed knuckle) is concerning for prostate cancer and should merit biopsy. Adequate supplies to allow for the patient to cleanse himself and privacy should be provided before concluding the encounter.

Pelvic Examination in the Female

The female pelvic exam is performed by the urologist to evaluate for pelvic organ prolapse, urinary incontinence, dyspareunia, blood per urethra or vagina, and anterior vaginal masses. The patient should be instructed to disrobe from the waist down and wear an examining gown and then is placed on the examining table. Footrests (stirrups) are used to flex and abduct the thighs and flex the knees. If a male urologist is to perform a pelvic examination, this must be done with the presence of a female chaperone (nurse or medical assistant).

Visual inspection of the external genitalia and introitus should evaluate for atrophic changes, erosions, ulcers, discharge, or genital warts. The labia should be separated, and the urethra inspected for prolapse, caruncle, hyperplasia, or cysts. Ideally with a full bladder, the patients should be instructed to perform Valsalva maneuver to elicit stress urinary incontinence. The insertion of a half of a speculum may allow for appropriate visualization of one wall of the vagina. With Valsalva, the examiner can evaluate for prolapse from the bladder, apex, or rectum. Palpation of the urethra can reveal a mass or promote a discharge, which may raise suspicion for urethral diverticulum. Bimanual examination should be performed by placing two of the examiner's fingers of the dominant hand into the vaginal vault (one finger if the introitus is small) and placing the nondominant hand over the lower abdomen and palpating for pelvic mass or tenderness. The female pelvic exam is intrusive and should be performed based on clinical suspicion and not for screening. For screening examinations the patient should be referred to the gynecologist. Children, adolescents, and young women should rarely need a pelvic examination from the urologist.

Neurologic Examination

A sensory dermatome map can help localize the location of a neurologic deficit (Fig. 1.5). Most sensory deficits of the genitalia and perianal area indicate a lesion in the sacral nerves or their root. Evaluation of bulbocavernosal reflex can indicate whether this reflex arc is intact. This reflex tests the integrity of the spinal cord–mediated reflex arc involving S2-S4. Squeezing the glans penis or clitoris should result in immediate contraction of the anal sphincter muscles, which can be appreciated during a DRE. Alternatively, in patients with a Foley catheter indwelling, tugging on the Foley catheter can elicit this response.

SPECIAL POPULATIONS

Children

Although pediatric urology practice includes the care of infants, toddlers, children, adolescents, and young adults (sometimes up to age 26 years), the needs of each of these subgroups of pediatrics may be very different. Infants and toddlers may not be able to provide

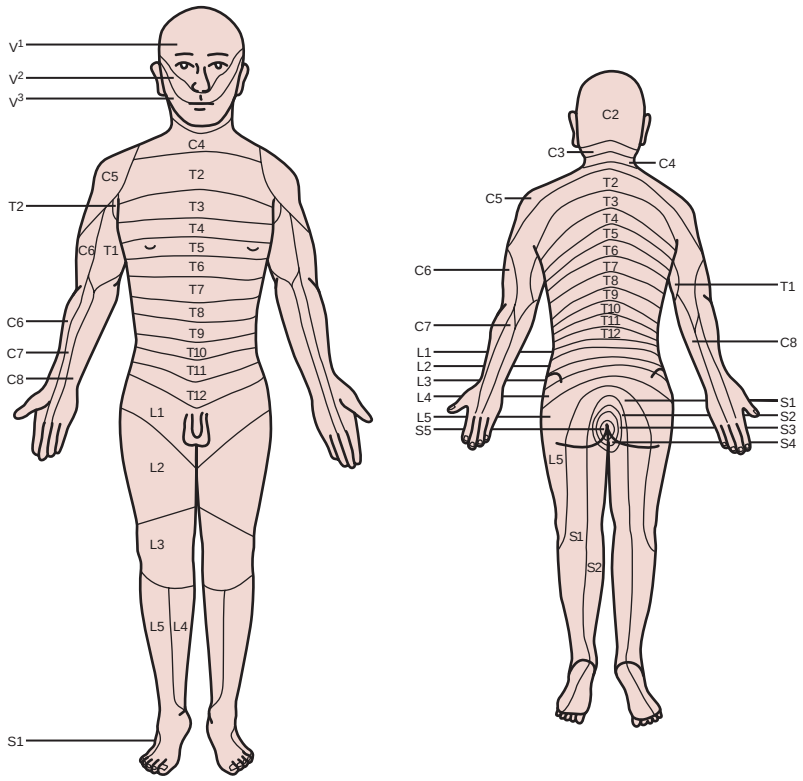


Fig. 1.5. Sensory dermatome maps used to help localize the level of neurologic deficit.

an HPI; therefore any clinical questions are directed toward the parents or guardians. Adolescents and young adults likely require some input from the parent or guardian but will also require some privacy. Questions pertinent to social history (alcohol, smoking, drugs, sexual activity) should be directed to the patient in private. The examination of infants, toddlers, and children should include a comfortable, nonthreatening environment. Often pediatric urologists do not wear a white coat because of the association of white coats with painful doctor's visits and immunizations. The examination ideally should be performed with the help of the family member to decrease the child's distress with the exam. Children are particularly sensitive to the cold and pain, and maneuvers resulting in this should be reserved for the end of the visit.

Elderly

Geriatric patients require much care and attention because they may not have the same physical and cognitive ability as younger patients. Again, a comfortable, nonthreatening environment should be provided. As with pediatric patients, input from the family member or caretaker may be invaluable; however, privacy should not be compromised. Elderly patients may have decreased mobility, and the examination room should be set up for this: lower examination tables, possibly Hoyer lifts for those who are wheelchair bound, blankets and pillows to facilitate comfortable position. Elderly patients can have pseudodementia, which is depression of cognitive affect and ability related to an illness. Therefore it is very important that baseline physical and cognitive abilities be assessed and occult illness be considered.

Transgender and Gender Nonbinary People

It is estimated that 5 in 1000 persons in the United States are transgender or gender nonbinary. These people may have reluctance to seek medical care because of the social stigma associated with their lifestyle. Regardless of the caretaker's belief system, such people should still be offered compassionate medical care as would be afforded to any other person. Caretakers should demonstrate cultural humility and meet their patients without preconceptions.

A few definitions are beneficial to help standardize documentation and communication. Sex often refers to chromosomal or gonadal sex, which is assigned from birth, whereas gender (or gender identity) is a person's perceived internal self. A transgender person's gender is different from the sex attributed at birth. A transgender woman is a male at birth but has a female gender identity. A transgender man is a female at birth but has a male gender identity. Transgender masculine or feminine connotates a directionality and not a full conversion, towards the gender identity. Patients who do not identify with a single gender are referred to as nonbinary. The patient's name, the term "the patient," or neutral pronouns (*they, them*, or *their* instead of *he/she* or *his/hers*) are used in such patients. Cross-dressing refers to patients who wear clothing of the opposite sex assigned to them at birth for entertainment, self-expression, or sexual pleasure. Sexual orientation is independent of all these prior definitions and is not related to gender identity.

Currently many offices may not be set up ideally to treat transgender patients in a culturally neutral way. Office staff should be educated regarding proper terminology and refrain from expressing judgment. The electronic medical record ideally should have gender identity as a two-step question: gender identity and assigned sex at birth. Further, the presence of gender-neutral bathrooms can decrease some of the tensions associated with caring for transgender and non-transgender patients.

Secondary sexual characteristics should be identified and noted. Patients should be asked what steps they have taken toward their gender, restricted to cross-dressing, hormonal therapy, or gender-affirming surgery (and its extent). Examination of gender-sensitive areas (breasts and genitalia) should be reserved for purpose, as they should in non-transgender patients. Explaining the anatomy and the steps for each exam may help decrease the anxiety associated with a pelvic exam. Establishing a trusting physician-patient relationship before delving into a pelvic exam also may prove beneficial. Pharmaceutical adjuncts include the administration of a benzodiazepine before exam to help decrease anxiety associated with the exam or administration of topical estrogen creams for 1 to 2 weeks before the exam to help counter the effect of exogenous androgens.

CONCLUSION

The history and physical examination are the foundation of any urologic encounter. Obtaining a thorough history and performing a proper physical examination can help detect urologic issues that are not detectable by other means (laboratory or radiology). Having a broad differential diagnosis can help direct the HPI. Understanding nuances associated with elderly, pediatric, and transgender patients can help the practitioner offer urologic care to a wider population.

KEY POINTS

- The urologist should perform a history and physical examination in a systematic approach, such that pertinent information can be obtained in a reliable fashion to help ascertain diagnosis or at least direct subsequent laboratory and/or radiographic evaluations.
- A broad differential diagnosis is beneficial and can help direct the history of present illness.
- Several disease states and medications have urologic side effects and can have implications for subsequent urologic surgery.
- Physical examination should be thorough but not unnecessarily invasive.
- Special considerations must be made for children, the elderly, and transgender patients.

REFERENCES

The complete reference list is available online at ExpertConsult.com.

REFERENCES

Althof S, McMahon C, Waldinger M, et al: An update of the International Society of Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE), *J Sex Med* 11(6):1392–1422, 2014.

Barry MJ, Fowler FJ Jr, O'Leary MP, et al: The American urological association symptom index for benign prostatic hyperplasia, *J Urol* 148:1549, 1992.

Benyamin R, Trescot A, Datta S, et al: Opioid complications and side effects, *Pain Physician* 11:S105–S120, 2008.

Byrne P, Heath C: Practitioners' use of non-verbal behaviour in real consultations, *J R Coll Gen Pract* 30:327–331, 1980.

Chang SS, Boorjian SA, Chou R, et al: Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline, *American Urological Association Education and Research, Inc.* 2016.

Commander C, Johnson D, Raynor M, et al: Detection of upper tract urothelial malignancies by computed tomography urography in patients referred for hematuria at a large tertiary referral center, *Urology* 102:31–37, 2017.

Corty E, Guardiani JM: Canadian and American sex therapists' perceptions of normal and abnormal ejaculatory latencies: how long should intercourse last?, *J Sex Med* 5:1251, 2008.

Dudzińska-Griszek J, Szuster K, Szewieczek J: Grip strength as a frailty diagnostic component in geriatric inpatients, *Clin Interv Aging* 12:1151–1157, 2017.

Elsamra S, Nazmy M, Shin D, et al: Female sexual dysfunction in urological patients: findings from a major metropolitan area in the USA, *BJU Int* 106(4):524–526, 2010.

Forsythe WI, Redmond A: Enuresis and spontaneous cure rate: study of 1129 enuretics, *Arch Dis Child* 49:259, 1974.

Gaunay GS, Elsamra SE, Richstone L: Trocars: site selection, instrumentation, and overcoming complications, *J Endourol* 30(8):833–843, 2016.

Hubbard J, Amin M: Pseudohematuria, *Urology* 10(3):190, 1977.

Kessels RP: Patients' memory for medical information, *J R Soc Med* 96:219–222, 2003.

Kriston L, Gunzler C, Harms A, et al: Confirmatory factor analysis of the German version of the international index of erectile function (IIEF): A comparison of four models, *J Sex Med* 5:92, 2008.

Landi F, Onder G, Russo A, et al: Calf circumference, frailty and physical performance among older adults living in the community, *Clin Nutr* 33:539–544, 2014.

Leavitt DA, Theckumparampil N, Moreira DM, et al: Continuing aspirin therapy during percutaneous nephrolithotomy: unsafe or underutilized? *J Endourol* 28(12):1399–1403, 2014.

Lee H, Parka S, Wenga M, et al: E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells, *Proc Natl Acad Sci U S A* 115(7):E1560–E1569, 2018.

MacDiarmid S, Goodson T, Holmes T, et al: An assessment of the comprehension of the American urological association symptom index, *J Urol* 159:873, 1998.

Montague D, Jarow J, Broderick G, et al: Pharmacologic management of premature ejaculation, *AUA Guidelines* 2010.

National Comprehensive Cancer Network: Distress management. Clinical practice guidelines, *J Natl Compr Canc Netw* 1(3):344–374, 2003.

Nehra A, Jackson G, Miner M, et al: The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease, *Mayo Clin Proc* 87(8):766–778, 2012.

Nordström T, Bratt O, Örtegren J, et al: A population-based study on the association between educational length, prostate-specific antigen testing, and use of prostate biopsies, *Scand J Urol* 50(2):104–109, 2016.

Opioid crisis fast facts. (2018). https://www.cnn.com/2017/09/18/health/opioid-crisis-fast-facts/index.html.

Palla L, De Angelis B, Lucarini L, et al: A case of labial fusion and urinary pseudo-incontinence in an elderly woman. A surgical treatment and a review, *Eur Rev Med Pharmacol Sci* 14(5):491–493, 2010.

Pamoukdjian F, Paillaud E, Zelek L, et al: Measurement of gait speed in older adults to identify complications associated with frailty: a systematic review, *J Geriatr Oncol* 6:484–496, 2015.

Pretorius R, Zurick G: A systematic approach to identifying drug-seeking patients, *Fam Pract Manag* 15:A3–A5, 2008.

Rao PK, Gao T, Phol M, et al: Dipstick pseudohematuria: unnecessary consultation and evaluation, *J Urol* 183:560–565, 2010.

Rozanski A, Benson C, McCoy JA, et al: Is exam under anesthesia still necessary for the staging of bladder cancer in the era of modern imaging?, *Bladder Cancer* 1:91–96, 2015.

Silverman J, Kinnersley P: Doctors' non-verbal behaviour in consultations: look at the patient before you look at the computer, *Br J Gen Pract* 76–78, 2010.

Stephenson TP, Farrar DJ: Urodynamic study of 15 patients with postmicturition dribble, *Urology* 9:404, 1977.

Urban M, Gebhart G: Supraspinal contributions to hyperalgesia, *Proc Natl Acad Sci U S A* 96(14):7687–7692, 1999.

Weiss J, Blaivas J: Nocturia, *J Urol* 163:5, 2000.

Wiltink J, Beutel ME, Brahler E, et al: Hypogonadism-related symptoms: development and evaluation of an empirically-derived self-rating instrument (HRS 'Hypogonadism Related Symptom Scale'), *Andrologia* 41:297–304, 2009.

Wong D, Baker CM: Pain in children: comparison of assessment scales, *Pediatr Nurs* 14:9–17, 1988.

Woolf CJ: Central sensitization: implications for the diagnosis and treatment of pain, *Pain* 152(Suppl 3):S2–S15, 2011.

Xue Q-L: The frailty syndrome: definiton and natural history, *Clin Geriatr Med* 27(2):1–15, 2011.

Zhao P, Velez D, Faiena I, et al: Bullying has a potential role in pediatric lower urinary tract symptoms, *J Urol* 193:1743–1748, 2015.

2 Evaluation of the Urologic Patient: Testing and Imaging

Erik P. Castle, MD, Christopher E. Wolter, MD, and Michael E. Woods, MD

The urologist has various serum, urinary, and radiologic studies available to complement the physical examination and perform a thorough and comprehensive evaluation of the urologic patient. Knowing when to order these studies based on the history and physical findings is crucial to identifying underlying pathology. Urinalysis is one of the more commonly performed laboratory studies, and in some cases the urologist will perform the urinary dipstick and microscopy analysis in the office during the evaluation. Furthermore, many office procedures such as uroflowmetry and cystourethroscopy may be incorporated into the evaluation. It is these laboratory and office studies that may be combined with radiologic testing during the evaluation of the urologic patient.

URINALYSIS

The urinalysis is a fundamental test that should be performed in all urologic patients presenting with urinary symptoms and complaints. **Evaluation of voided urine includes gross examination, dipstick chemical analysis, and microscopic analyses.**

Collection of Urinary Specimens

Males

To avoid contamination in the male patient, **a midstream urine sample is obtained.** Retraction of the foreskin and cleansing of the glans and urethral meatus is performed. The male patient begins urinating into the toilet and then places a wide-mouth sterile container under his penis to collect a midstream sample.

A variety of methods are available to identify a potential source of infection if not clearly from the bladder. One traditional test is the use of four aliquots to differentiate bacteria from the bladder, urethra, and prostate. **These aliquots can be designated Voided Bladder 1, Voided Bladder 2, Expressed Prostatic Secretions, and Voided Bladder 3 (VB1, VB2, EPS, and VB3).** The VB1 specimen is the initial 5 to 10 mL of urine voided, whereas the VB2 specimen is the midstream urine. The EPS is the secretions obtained after gentle prostatic massage, and the VB3 specimen is the initial 2 to 3 mL of urine obtained after prostatic massage. The value of these cultures for localization of urinary tract infections (UTIs) is that the VB1 sample represents urethral flora, the VB2 sample represents bladder flora, and the EPS and VB3 samples represent prostatic flora. The VB3 sample is particularly helpful when little or no prostatic fluid is obtained by massage. The four-part urine sample is particularly useful in evaluating men with suspected bacterial prostatitis (Meares and Stamey, 1968). An alternative is to obtain two aliquots of urine, one before prostatic massage and one following prostatic massage (Nickel et al., 2006). The two-aliquot technique may be easier in some cases and has been demonstrated in one study to show concordance with the four-aliquot test described by Meares and Stamey.

Females

Obtaining a sterile voided urine collection can be a challenge in the female patient. The standard midstream urinalysis in the female patient should be obtained after separating the labia and cleansing the vaginal introitus and external urethral meatus. This is an appropriate method for the routine collection. However, **in the female patient with suspected recurrent UTIs or a history of antibiotic-resistant infections, a catheterized urine sample should always be obtained.**

Neonates and Infants

The usual way to obtain a urine sample in a neonate or infant is to place a sterile plastic bag with an adhesive collar over the infant's genitalia. However, these devices may not be able to distinguish contamination from true UTI. Whenever possible, **all urine samples should be examined within 1 hour of collection and plated for culture and sensitivity if indicated.** If urine is allowed to stand at room temperature for longer periods, bacterial overgrowth may occur, the pH may change, and red and white blood cell casts may disintegrate. If it is not possible to examine the urine promptly, it should be refrigerated at 5°C. When appropriate, a collection of urine via suprapubic aspiration may be obtained.

Physical and Gross Examination of Urine

The visual and physical examination of the urine includes an evaluation of color and turbidity.

Color

Typical, normal urine color is pale yellow as a result of the presence of the pigment urochrome. **Urine color varies most commonly because of concentration, but many foods, medications, metabolic products, and infections may produce abnormal urine color.** It is important for the urologist to be aware of the common causes of abnormal urine color, and these are listed in Table 2.1. For example, bright red color or pink suggests blood that may be active bleeding, and purple or brown urine may indicate an old hemorrhage or a retained clot in the bladder. Brown or cola-colored urine can be a sign of glomerular bleeding and disease. Often, the urine color is an important adjunct to the workup and management of the urologic patient.

Turbidity

Cloudy urine is commonly caused by phosphaturia, a benign process in which excess phosphate crystals precipitate in alkaline urine. Phosphaturia is often intermittent and may occur after meals, and many patients are otherwise asymptomatic. The diagnosis of phosphaturia can be accomplished either by acidifying the urine with acetic acid, which will result in immediate clearing, or by performing a microscopic analysis, which will reveal large amounts of amorphous phosphate crystals.

Pyuria is another common cause of cloudy urine. The large numbers of white blood cells cause the urine to become turbid. Pyuria is readily distinguished from phosphaturia either by smelling the urine (infected urine has a characteristic pungent odor) or by **urine dipstick or microscopic examination.** The presence of leukocyte esterase or identification of leukocytes on microscopic analysis is diagnostic of pyuria. In patients with indwelling tubes such as catheters or percutaneous nephrostomy tubes, the smell and turbidity of the urine may often be a contributing deciding factor in determining treatment. For example, in a patient with a **long-term indwelling nephrostomy tube and worsening cloudy, smelly urine, the urologist may choose to give both an antibiotic and an antifungal before any manipulation or procedures** while awaiting the results of a urinalysis and culture.

Rare causes of cloudy urine include chyluria (in which there is an abnormal communication between the lymphatic system and the urinary tract resulting in lymph fluid being mixed with urine), lipiduria, hyperoxaluria, and hyperuricosuria.

TABLE 2.1 Common Causes of Abnormal Urine Color

COLOR	CAUSE
Colorless	Very dilute urine Overhydration
Cloudy/milky	Phosphaturia Pyuria Chyluria
Red	Hematuria Hemoglobinuria/myoglobinuria Anthocyanin in beets and blackberries Chronic lead and mercury poisoning Phenolphthalein (in bowel evacuants) Phenothiazines (e.g., Compazine) Rifampin
Orange	Dehydration Phenazopyridine (Pyridium) Sulfasalazine (Azulfidine)
Yellow	Normal Phenacetin Riboflavin
Green-blue	Biliverdin Indicanuria (tryptophan indole metabolites) Amitriptyline (Elavil) Indigo carmine Methylene blue Phenols (e.g., IV cimetidine [Tagamet], IV promethazine [Phenergan]) Resorcinol Triamterene (Dyrenium)
Brown	Urobilinogen Porphyria Aloe, fava beans, and rhubarb Chloroquine and primaquine Furazolidone (Furoxone) Metronidazole (Flagyl) Nitrofurantoin (Furadantin)
Brown-black	Alcaptonuria (homogentisic acid) Hemorrhage Melanin Tyrosinosis (hydroxyphenylpyruvic acid) Cascara, senna (laxatives) Methocarbamol (Robaxin) Methyldopa (Aldomet) Sorbitol

IV, Intravenous.
From Hanno PM, Wein AJ. *A clinical manual of urology*. Norwalk, CT: Appleton-Century-Crofts; 1987:67.

CHEMICAL EXAMINATION OF URINE

The chemical examination of the urine involves the assessment of various characteristics of the urine via a urine dipstick. Urine dipsticks provide a quick and inexpensive method for detecting abnormal substances within the urine. Dipsticks are short, plastic strips with small marker pads that are impregnated with different chemical reagents that react with abnormal substances in the urine to produce a colorimetric change. **Dipstick tests include those for specific gravity, pH, blood, protein, glucose, ketones, urobilinogen, leukocyte esterase, and nitrites.**

Substances listed in Table 2.1 that produce an abnormal urine color may interfere with appropriate color development on the dipstick. A common medication that may interfere with the dipstick analysis is phenazopyridine (Pyridium). Phenazopyridine turns the urine bright orange and makes dipstick evaluation of the urine unreliable.

The technique of obtaining an accurate dipstick determination includes completely immersing it in a fresh uncentrifuged urine specimen and then withdrawing it quickly while drawing the edge along the rim of the container to remove excess urine. The dipstick should be held horizontally until the appropriate time for reading and then compared with the color chart. **Excess urine on the dipstick or holding the dipstick in a vertical position will allow mixing of chemicals from adjacent reagent pads on the dipstick, resulting in a faulty diagnosis.** False-negative results for glucose and bilirubin may be seen in the presence of elevated ascorbic acid concentrations in the urine. However, increased levels of ascorbic acid in the urine do not interfere with dipstick testing for hematuria. Highly buffered alkaline urine may cause falsely low readings for specific gravity and may lead to false-negative results for urinary protein. **Other common causes of false results with dipstick testing are outdated test strips and exposure of the sticks**, leading to damage to the reagents. Alterations in the color of the pads before immersing the sticks should be a sign of an outdated or exposed stick.

Specific Gravity and Osmolality

Specific gravity of urine is easily determined from a urinary dipstick and usually varies from 1.001 to 1.035. Specific gravity usually reflects the patient's state of hydration but may also be affected by abnormal renal function, the amount of material dissolved in the urine. A specific gravity less than 1.008 is regarded as dilute, and a specific gravity greater than 1.020 is considered concentrated. Acute or chronic renal insufficiency can be associated with a specific gravity of 1.010.

In general, specific gravity reflects the state of hydration but also affords some idea of renal concentrating ability. Conditions that decrease specific gravity include diuretics, increased fluid intake, diabetes insipidus, and other causes of decreased renal concentrating ability. Conversely, specific gravity can be increased with uncontrolled diabetes mellitus caused by glycosuria, inappropriate secretion of antidiuretic hormone, and any condition causing dehydration. It should be noted that intravenous injection of some iodinated contrasts and administration of dextran can cause a rise in specific gravity above 1.035.

Osmolality is a measure of the amount of material dissolved in the urine and usually varies between 50 and 1200 mOsm/L. Urine osmolality most commonly varies with hydration, and the same factors that affect specific gravity will also affect osmolality. Urine osmolality can be an indicator of renal function, and any abnormal value should be further investigated with additional testing for renal compromise. Furthermore, with alterations in urine osmolality such as very dilute urine (below 308 mOsm), reliable assessment of red blood cells in urine can be compromised due to lysis (Vaughan and Wyker, 1971).

pH

The dipstick test strip incorporates two colorimetric indicators, methyl red and bromothymol blue, which yield clearly distinguishable colors over the pH range from 5 to 9. Urinary pH may vary from 4.5 to 8; the average pH varies between 5.5 and 6.5. A urinary pH between 4.5 and 5.5 is considered acidic, whereas a pH between 6.5 and 8 is considered alkaline.

In general, the urinary pH reflects the pH in the serum. In patients with metabolic or respiratory acidosis, the urine is usually acidic; conversely, in patients with metabolic or respiratory alkalosis, the urine is alkaline. Renal tubular acidosis (RTA) presents an exception to this rule. In patients with both type I and II RTA, the serum is acidemic, but the urine is alkalotic because of continued loss of bicarbonate in the urine. In severe metabolic acidosis in type II RTA,

the urine may become acidic, but in type I RTA, the urine is always alkaline, even with severe metabolic acidosis (Morris and Ives, 1991). Urinary pH determination is used to establish the diagnosis of RTA; **inability to acidify the urine below a pH of 5.5 after administration of an acid load is diagnostic of RTA**.

Urine pH determinations are also useful in the diagnosis and treatment of UTIs and urinary calculus disease. **In patients with a presumed UTI, an alkaline urine with a pH greater than 7.5 suggests infection with a urea-splitting organism, most commonly *Proteus*.** Urease-producing bacteria convert ammonia to ammonium ions, markedly elevating the urinary pH and causing precipitation of calcium magnesium ammonium phosphate crystals. Crystallization may result in staghorn calculi.

Urinary pH is usually acidic in patients with uric acid and cystine lithiasis. Alkalinization of the urine is an important feature of therapy in both conditions, and frequent monitoring of urinary pH is necessary to ascertain adequacy of therapy.

Blood/Hematuria

Normal urine should contain less than 3 erythrocytes per HPF. A positive dipstick for blood in the urine indicates either hematuria, hemoglobinuria, or myoglobinuria. **The chemical detection of blood in the urine is based on the peroxidase-like activity of hemoglobin.** When in contact with an organic peroxidase substrate, hemoglobin catalyzes the reaction and causes subsequent oxidation of a chromogen indicator, which changes color according to the degree and amount of oxidation. The degree of color change is directly related to the amount of hemoglobin present in the urine specimen. Dipsticks frequently demonstrate both colored dots and field color change. If present, free hemoglobin and myoglobin in the urine are absorbed into the reagent pad and catalyze the reaction within the test paper, thereby producing a field change effect in color. Intact erythrocytes in the urine undergo hemolysis when they come in contact with the reagent test pad, and the localized free hemoglobin on the pad produces a corresponding dot of color change. The greater the number of intact erythrocytes in the urine specimen, the greater the number of dots that will appear on the test paper, and a coalescence of the dots occurs when there are more than 250 erythrocytes/mL.

Hematuria can be distinguished from hemoglobinuria and myoglobinuria by microscopic examination of the centrifuged urine; the presence of a large number of erythrocytes establishes the diagnosis of hematuria. If erythrocytes are absent, examination of the serum will distinguish hemoglobinuria and myoglobinuria. A sample of blood is obtained and centrifuged. In hemoglobinuria, the supernatant will be pink. This is because free hemoglobin in the serum binds to haptoglobin, which is water insoluble and has a high molecular weight. This complex remains in the serum, causing a pink color. Free hemoglobin will appear in the urine only when all of the haptoglobin-binding sites have been saturated. In myoglobinuria, the myoglobin released from muscle is of low molecular weight and water soluble. It does not bind to haptoglobin and is therefore excreted immediately into the urine. Therefore in myoglobinuria the serum remains clear.

The sensitivity of urinary dipsticks in identifying microscopic hematuria, defined as greater than or equal to 3 erythrocytes per HPF of centrifuged sediment examined microscopically, is higher than 90%. Conversely, the specificity of the dipstick for hematuria compared with microscopy is somewhat lower, reflecting a higher false-positive rate with the dipstick (Shaw et al., 1985). Things to consider when considering the possibility of a false positive include: contamination of the urine in females when they may be menstruating; significant dehydration, which can result in a higher concentration of erythrocytes; and vigorous exercise, which has been reported to result in clinically significant hematuria (Akiboye and Sharma, 2018). The normal individual excretes about 1000 erythrocytes/mL of urine, with the upper limits of normal varying from 5000 to 8000 erythrocytes/mL (Kincaid-Smith, 1982). Therefore, examining urine of high specific gravity such as the first-void specimen increases the likelihood of a false-positive result.

The efficacy of hematuria screening using the dipstick to identify patients with significant urologic disease is somewhat controversial. Because of the risk for false positives that may lead one to order additional costly and invasive testing, **the dipstick result should be confirmed with a microscopic examination of the centrifuged urinary sediment**. Several societies including the American Urological Association (AUA) have released guidelines (https://www.auanet.org/guidelines/asymptomatic-microhematuria-(2012-reviewed-for-currency-2016) or consensus statements and agree that a urinary dipstick alone is inadequate to confirm the diagnosis of hematuria.

Differential Diagnosis and Evaluation of Hematuria

One of the early signs and symptoms of nephrologic or urologic disease is microscopic or gross hematuria. Interpreting the microscopic findings of the urinalysis can be helpful in working through the differential diagnosis. Differentiating between nephrologic and urologic causes is critical when deciding what additional tests may need to be ordered. **Identifying the hematuria as nephrologic versus urologic and glomerular versus nonglomerular is one of the first steps in the analysis.**

Hematuria of nephrologic origin is frequently associated with casts in the urine and almost always associated with significant proteinuria. Significant gross hematuria of urologic origin is unlikely to elevate the protein concentration in the urine into the 100 to 300 mg/dL or 2+ to 3+ range on dipstick, and proteinuria of this magnitude almost always indicates glomerular or tubulointerstitial renal disease prompting a consultation with nephrology. Morphologic evaluation of erythrocytes in the centrifuged urinary sediment also helps localize their site of origin. **Erythrocytes arising from glomerular disease are typically dysmorphic and show a wide range of morphologic alterations. Conversely, erythrocytes arising from tubulointerstitial renal disease and of urologic origin have a uniformly round shape;** these erythrocytes may or may not retain their hemoglobin ("ghost cells"), but the individual cell shape is consistently round.

Glomerular Hematuria

Glomerular hematuria is suggested by the presence of dysmorphic erythrocytes, RBC casts, proteinuria, and brown or cola-colored urine. Of those patients with glomerulonephritis proven by renal biopsy, however, about 20% will have hematuria alone without RBC casts or proteinuria (Fassett et al., 1982).

The glomerular disorders associated with hematuria are listed in Table 2.2. Further evaluation of patients with glomerular hematuria

TABLE 2.2 Glomerular Disorders in Patients With Glomerular Hematuria

DISORDER	PATIENTS
IgA nephropathy (Berger disease)	30
Mesangioproliferative GN	14
Focal segmental proliferative GN	13
Familial nephritis (e.g., Alport syndrome)	11
Membranous GN	7
Mesangiocapillary GN	6
Focal segmental sclerosis	4
Unclassifiable	4
Systemic lupus erythematosus	3
Postinfectious GN	2
Subacute bacterial endocarditis	2
Others	4
Total	100

GN, Glomerulonephritis; *IgA*, immunoglobulin A.
Modified from Fassett RG, Horgan BA, Mathew TH. Detection of glomerular bleeding by phase-contrast microscopy. *Lancet.* 1982;1(8287):1432–1434.

should begin with a thorough history and possibly a consultation with nephrology. Hematuria in children and young adults, usually males, associated with low-grade fever and an erythematous rash suggests a diagnosis of immunoglobulin A (IgA) nephropathy (Berger disease). A family history of renal disease and deafness suggests familial nephritis or Alport syndrome. Hemoptysis and abnormal bleeding associated with microcytic anemia are characteristic of Goodpasture syndrome, and the presence of a rash and arthritis suggest systemic lupus erythematosus. Finally, poststreptococcal glomerulonephritis should be suspected in a child with a recent streptococcal upper respiratory tract or skin infection.

Further laboratory evaluation often includes measurement of serum creatinine, creatinine clearance, and a 24-hour urine protein determination. Although these tests will quantitate the specific degree of renal dysfunction, further tests are usually required to establish the specific diagnosis and particularly to determine whether the disease is caused by an immune or a nonimmune etiology. **Frequently, a renal biopsy is necessary to establish the precise diagnosis, and biopsies are particularly important if the result will influence subsequent treatment of the patient.** Renal biopsies are extremely informative when examined by an experienced pathologist using light, immunofluorescence, and electron microscopy.

An algorithm for the evaluation of glomerular hematuria is shown in Fig. 2.1.

IgA Nephropathy (Berger Disease)

IgA nephropathy, or Berger disease, is the most common cause of glomerular hematuria, accounting for about 30% of cases (Fassett et al., 1982). Therefore it is described in greater detail in this section. IgA nephropathy occurs most commonly in children and young adults, with a male predominance (Berger and Hinglais, 1968). Patients typically present with hematuria after an upper respiratory tract infection or exercise. Hematuria may be associated with a low-grade fever or rash, but most patients have no associated systemic symptoms. Gross hematuria occurs intermittently, but microscopic hematuria is a constant finding in some patients. The disease is chronic, but the prognosis in most patients is excellent. Renal function remains normal in the majority, but about 25% will subsequently develop renal insufficiency. Older age at onset, initial abnormal renal function, consistent proteinuria, and hypertension are indicators of a poor prognosis (D'Amico, 1988).

The pathologic findings in Berger disease are limited to either focal glomeruli or lobular segments of a glomerulus. The changes are proliferative and usually confined to mesangial cells (Berger and Hinglais, 1968). Renal biopsy reveals deposits of IgA, IgG, and β_{1c}-globulin, although IgA and IgG mesangial deposits are found in other forms of glomerulonephritis as well. The role of IgA in the disease remains uncertain, although the deposits may trigger an inflammatory reaction within the glomerulus (van den Wall Bake et al, 1989). Because gross hematuria frequently follows an upper respiratory tract infection, a viral etiology has been suspected but not established. The frequent association between hematuria and exercise in this condition remains unexplained.

The clinical presentation of IgA glomerulonephritis is alarming and similar to certain systemic diseases, including Schönlein-Henoch purpura, systemic lupus erythematosus, bacterial endocarditis, and Goodpasture syndrome. Therefore a careful clinical and laboratory evaluation is indicated to establish the correct diagnosis. The presence of RBC casts establishes the glomerular origin of the hematuria. In the absence of casts, a urologic evaluation is indicated to exclude the urinary tract as a source of bleeding and to confirm that the hematuria is arising from both kidneys. The diagnosis of IgA nephropathy is confirmed by renal biopsy demonstrating the classic deposits of immunoglobulins in mesangial cells, as described earlier in this chapter. Once the diagnosis has been established, repeat evaluations for hematuria are generally not indicated. Although there is no effective treatment for this condition, renal function remains stable in most patients, and there are no other known long-term complications.

Nonglomerular Hematuria

Medical/Nonsurgical

Medical causes of nonglomerular hematuria of renal origin are secondary to either tubulointerstitial, renovascular, or systemic disorders. **The urinalysis in nonglomerular hematuria is distinguished from that of glomerular hematuria by the presence of circular erythrocytes**

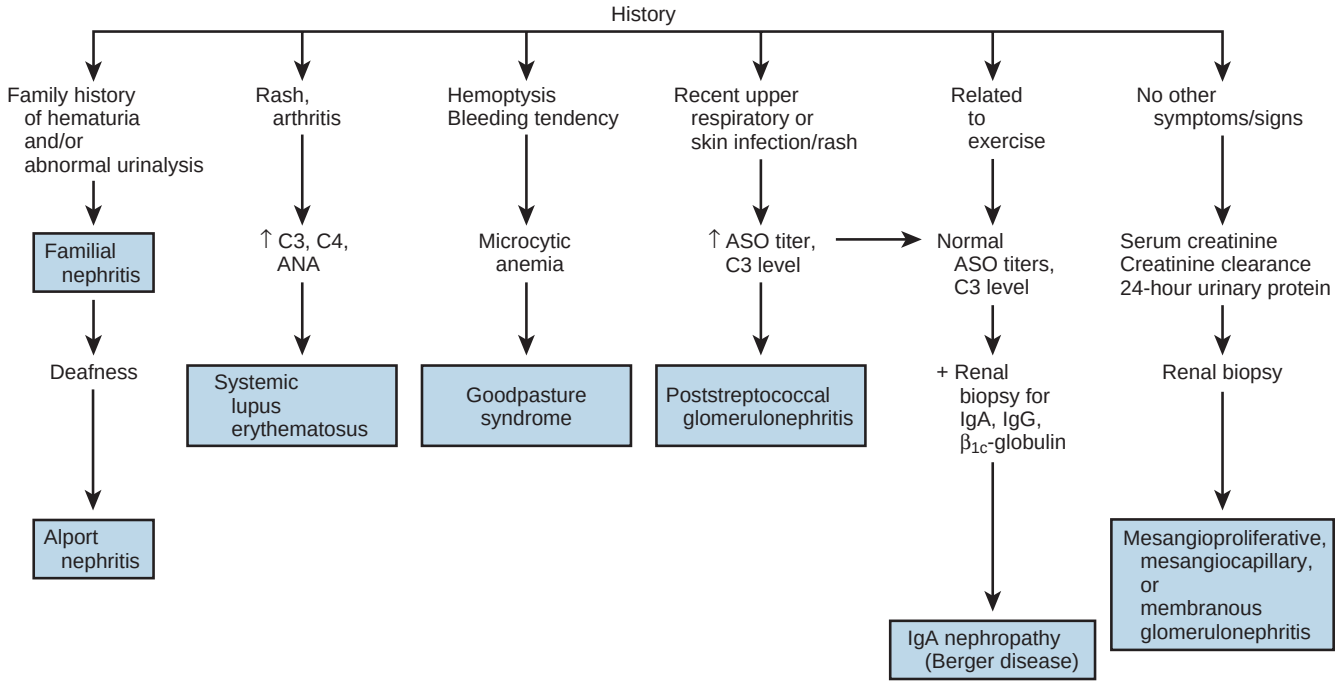


Fig. 2.1. Evaluation of glomerular hematuria (dysmorphic erythrocytes, erythrocyte casts, and proteinuria). *ANA*, Antinuclear antibody; *ASO*, antistreptolysin O; *Ig*, immunoglobulin.

and the absence of erythrocyte casts. It is frequently associated with significant proteinuria, which distinguishes these nephrologic diseases from urologic diseases in which the degree of proteinuria is usually minimal, even with heavy bleeding.

As with glomerular hematuria, a careful history frequently helps establish the diagnosis. A family history of hematuria or bleeding tendency suggests the diagnosis of a blood dyscrasia, which should be investigated further. A family history of urolithiasis associated with intermittent hematuria may indicate inherited stone disease, which should be investigated with serum and urine measurements of calcium and uric acid. A family history of renal cystic disease should prompt further radiologic evaluation for medullary sponge kidney and adult polycystic kidney disease. **Papillary necrosis as a cause of hematuria should be considered in diabetics, African-Americans (secondary to sickle cell disease or trait), and suspected analgesic abusers.**

Medications may induce hematuria, particularly anticoagulants. **Anticoagulation at normal therapeutic levels, however, does not predispose patients to hematuria.** In one study, the prevalence of hematuria was 3.2% in anticoagulated patients versus 4.8% in a control group. Urologic disease was identified in 81% of patients with more than one episode of microscopic hematuria, and the cause of hematuria did not vary between groups (Culclasure et al., 1994). Thus anticoagulant therapy per se does not appear to increase the risk for hematuria unless the patient is excessively anticoagulated. Therefore, in patients on anticoagulation, hematuria should not be attributed to the medication, and a proper thorough workup should be performed as it would in any other patient that is not anticoagulated.

Exercise-induced hematuria can be observed in patients with a recent history of vigorous exercise such as extreme or long-distance running (Akiboye and Sharma, 2018). In long-distance runners (>10 km), it is usually noted at the conclusion of the run, and rapidly disappears with rest. The hematuria may be of renal or bladder origin. An increased number of dysmorphic erythrocytes have been noted in some patients, suggesting a glomerular origin. Exercise-induced hematuria may be the first sign of underlying glomerular disease such as IgA nephropathy. Conversely, cystoscopy in patients with exercise-induced hematuria frequently reveals punctate hemorrhagic lesions in the bladder, suggesting that the hematuria is of bladder origin.

Vascular disease may also result in nonglomerular hematuria. Renal artery embolism and thrombosis, arteriovenous fistulae, and renal vein thrombosis may all result in hematuria. Physical examination may reveal severe hypertension, a flank or abdominal bruit, or atrial fibrillation. In such patients, further evaluation for renal vascular disease should be undertaken. Microscopic hematuria has also been reported in Nutcracker syndrome associated with pelvic congestion (Chau et al., 2018; Gulleroglu et al., 2014).

Surgical

Nonglomerular hematuria caused by surgical and urologic causes includes pathology of the collecting system of the urinary tract. Common causes include urologic tumors, stones, benign prostatic hyperplasia, and urinary tract infections.

The urinalysis in both nonglomerular medical and surgical hematuria is similar in that both are characterized by circular erythrocytes and the absence of erythrocyte casts. Essential hematuria is suggested, however, by the absence of significant proteinuria usually found in nonglomerular hematuria of renal parenchymal origin. It should be remembered, however, that proteinuria is not always present in glomerular or nonglomerular renal disease.

Asymptomatic microscopic hematuria (AMH) "is defined as three or greater RBC/HPF on a properly collected urinary specimen in the absence of an obvious benign cause" (Davis et al., 2012, reviewed and validated 2016). The AUA guideline on the diagnosis, evaluation, and follow-up of AMH in adults provides 19 guideline statements and an algorithm for AMH (https://www.auanet.org/guidelines/asymptomatic-microhematuria-(2012-reviewed-for-currency-2016)).

Proteinuria

Healthy adults excrete 80 to 150 mg of protein in the urine daily. The qualitative detection of proteinuria in the urinalysis should raise the suspicion of underlying renal disease. **Proteinuria may be the first indication of renovascular, glomerular, or tubulointerstitial renal disease, or it may represent the overflow of abnormal proteins into the urine in conditions such as multiple myeloma.** Proteinuria can also occur secondary to nonrenal disorders and in response to various physiologic conditions such as strenuous exercise.

The protein concentration in the urine depends on the state of hydration, but it seldom exceeds 20 mg/dL. In patients with dilute urine, however, significant proteinuria may be present at concentrations less than 20 mg/dL. **Normally, urine protein is about 30% albumin, 30% serum globulins, and 40% tissue proteins, of which the major component is Tamm-Horsfall protein.** This profile may be altered by conditions that affect glomerular filtration, tubular reabsorption, or excretion of urine protein. Determination of the urine protein profile by such techniques as protein electrophoresis may help determine the etiology of proteinuria.

Pathophysiology

Most causes of proteinuria can be categorized into one of three categories: glomerular, tubular, or overflow. Glomerular proteinuria is the most common type of proteinuria and results from increased glomerular capillary permeability to protein, especially albumin. Glomerular proteinuria occurs in any of the primary glomerular diseases such as IgA nephropathy or in glomerulopathy associated with systemic illness such as diabetes mellitus. Glomerular disease should be suspected when the 24-hour urine protein excretion exceeds 1 g and is almost certain to exist when the total protein excretion exceeds 3 g.

Tubular proteinuria results from failure to reabsorb normally filtered proteins of low molecular weight such as immunoglobulins. In tubular proteinuria, the 24-hour urine protein loss seldom exceeds 2 to 3 g, and the excreted proteins are of low molecular weight rather than albumin. Disorders that lead to tubular proteinuria are commonly associated with other defects of proximal tubular function such as glycosuria, aminoaciduria, phosphaturia, and uricosuria (Fanconi syndrome).

Overflow proteinuria occurs in the absence of any underlying renal disease and is caused by an increased plasma concentration of abnormal immunoglobulins and other low–molecular-weight proteins. The increased serum levels of abnormal proteins result in excess glomerular filtration that exceeds tubular reabsorptive capacity. The most common cause of overflow proteinuria is multiple myeloma, in which large amounts of immunoglobulin light chains are produced and appear in the urine (Bence Jones protein).

Detection

Qualitative detection of abnormal proteinuria is most easily accomplished with a dipstick impregnated with tetrabromophenol blue dye. The color of the dye changes in response to a pH shift related to the protein content of the urine, mainly albumin, leading to the development of a blue color. Because the background of the dipstick is yellow, various shades of green will develop, and the darker the green, the greater the concentration of protein in the urine. The minimal detectable protein concentration by this method is 20 to 30 mg/dL. **False-negative results can occur in alkaline urine, dilute urine, or when the primary protein present is not albumin.** Nephrotic range proteinuria in excess of 1 g/24 h, however, is seldom missed on qualitative screening. Precipitation of urinary proteins with strong acids such as 3% sulfosalicylic acid will detect proteinuria at concentrations as low as 15 mg/dL and is more sensitive at detecting other proteins and albumin. Patients whose urine is negative on dipstick but strongly positive with sulfosalicylic acid should be suspected of having multiple myeloma, and the urine should be tested further for Bence Jones protein.

If qualitative testing reveals proteinuria, this should be quantitated with a 24-hour urinary collection. Further qualitative assessment of

abnormal urinary proteins can be accomplished by either protein electrophoresis or immunoassay for specific proteins. **Protein electrophoresis is particularly helpful in distinguishing glomerular from tubular proteinuria. In glomerular proteinuria, albumin makes up about 70% of the total protein excreted, whereas in tubular proteinuria, the major proteins excreted are immunoglobulins, with albumin making up only 10% to 20%. Immunoassay is the method of choice for detecting specific proteins such as Bence Jones protein in multiple myeloma.**

Evaluation

Proteinuria should first be classified by its timing into transient, intermittent, or persistent. Transient proteinuria occurs commonly, especially in the pediatric population, and usually resolves spontaneously within a few days (Wagner et al., 1968). It may result from fever, exercise, or emotional stress. In older patients, transient proteinuria may be caused by congestive heart failure. If a nonrenal cause is identified and a subsequent urinalysis is negative, no further evaluation is necessary. If proteinuria persists, it should be evaluated further.

Proteinuria may also occur intermittently, and this is frequently related to postural change (Robinson, 1985). Proteinuria that occurs only in the upright position is a frequent cause of mild, intermittent proteinuria in young males. Total daily protein excretion seldom exceeds 1 g, and urinary protein excretion returns to normal when the patient is recumbent. Orthostatic proteinuria is thought to be secondary to increased pressure on the renal vein while standing. It resolves spontaneously in about 50% of patients and is not associated with morbidity. Therefore if renal function is normal in patients with orthostatic proteinuria, no further evaluation is indicated.

Persistent proteinuria requires further evaluation, and most cases have a glomerular etiology. A quantitative measurement of urinary protein should be obtained through a 24-hour urine collection, and a qualitative evaluation should be obtained to determine the major proteins excreted. The findings of greater than 2 g of protein excreted per 24 hours, of which the major components are high-molecular-weight proteins such as albumin, establish the diagnosis of glomerular proteinuria. Glomerular proteinuria is the most common cause of abnormal proteinuria, especially in patients presenting with persistent proteinuria. If glomerular proteinuria is associated with hematuria characterized by dysmorphic erythrocytes and erythrocyte casts, the patient should be evaluated as outlined earlier for glomerular hematuria (see Fig. 2.1). Patients with glomerular proteinuria who have no or little associated hematuria should be evaluated for other conditions, of which the most common is diabetes mellitus. Other possibilities include amyloidosis and arteriolar nephrosclerosis.

In patients in whom total protein excretion is 300 to 2000 mg/day, of which the major components are low–molecular-weight globulins, further qualitative evaluation with immunoelectrophoresis is indicated. This will determine whether the excess proteins are normal or abnormal. Identification of normal proteins establishes a diagnosis of tubular proteinuria, and further evaluation for a specific cause of tubular dysfunction is indicated.

If qualitative evaluation reveals abnormal proteins in the urine, this establishes a diagnosis of overflow proteinuria. Further evaluation should be directed to identify the specific protein abnormality. The finding of large quantities of light-chain immunoglobulins or Bence Jones protein establishes a diagnosis of multiple myeloma. Similarly, the finding of large amounts of hemoglobin or myoglobin establishes the diagnosis of hemoglobinuria or myoglobinuria. An algorithm for the evaluation of proteinuria is shown in Fig. 2.2.

Glucose and Ketones

Urine testing for glucose and ketones is useful in screening patients for diabetes mellitus. Normally, almost all of the glucose filtered by the glomeruli is reabsorbed in the proximal tubules. Although small amounts of glucose may normally be excreted in the urine, these amounts are not clinically significant and are below the level of detectability with the dipstick. If, however, the amount of glucose

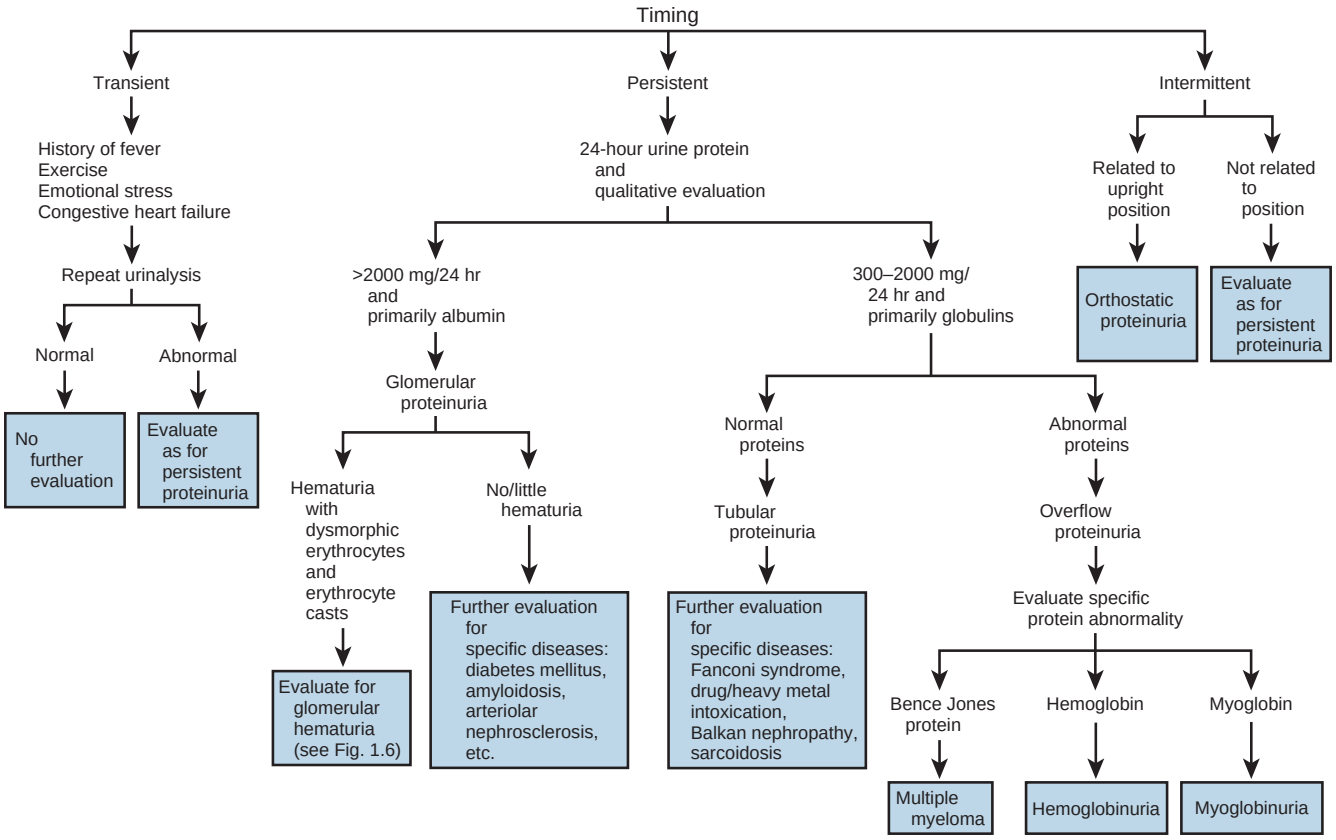


Fig. 2.2. Evaluation of proteinuria.

filtered exceeds the capacity of tubular reabsorption, glucose will be excreted in the urine and detected on the dipstick. **This so-called *renal threshold* corresponds to serum glucose of about 180 mg/dL; above this level, glucose will be detected in the urine.**

Glucose detection with the urinary dipstick is based on a double sequential enzymatic reaction yielding a colorimetric change. In the first reaction, glucose in the urine reacts with glucose oxidase on the dipstick to form gluconic acid and hydrogen peroxide. In the second reaction, hydrogen peroxide reacts with peroxidase, causing oxidation of the chromogen on the dipstick, producing a color change. **This double-oxidative reaction is specific for glucose, and there is no cross-reactivity with other sugars.** The dipstick test becomes less sensitive as the urine increases in specific gravity and temperature.

Ketones are not normally found in the urine but will appear when the carbohydrate supplies in the body are depleted and body fat breakdown occurs. This happens most commonly in diabetic ketoacidosis but may also occur during pregnancy and after periods of starvation or rapid weight reduction. **Ketones excreted include acetoacetic acid, acetone, and β-hydroxybutyric acid. With abnormal fat breakdown, ketones will appear in the urine before the serum.**

Dipstick testing for ketones involves a colorimetric reaction: Sodium nitroprusside on the dipstick reacts with acetoacetic acid to produce a purple color. **Dipstick testing will identify acetoacetic acid at concentrations of 5 to 10 mg/dL but will not detect acetone or β-hydroxybutyric acid.** A dipstick that tests positive for glucose should also be tested for ketones, and diabetes mellitus is suggested. False-positive results, however, can occur in acidic urine of high specific gravity, in abnormally colored urine, and in urine containing levodopa metabolites, 2-mercaptoethane sulfonate sodium, and other sulfhydryl-containing compounds (Csako, 1987).

Bilirubin and Urobilinogen

Normal urine contains no bilirubin and only small amounts of urobilinogen. There are two types of bilirubin: direct (conjugated) and indirect. Direct bilirubin is made in the hepatocyte, where bilirubin is conjugated with glucuronic acid. **Conjugated bilirubin has a low molecular weight, is water soluble, and normally passes from the liver to the small intestine through the bile ducts, where it is converted to urobilinogen. Therefore conjugated bilirubin does not appear in the urine except in pathologic conditions in which there is intrinsic hepatic disease or obstruction of the bile ducts.**

Indirect bilirubin is of high molecular weight and bound in the serum to albumin. It is water insoluble and therefore does not appear in the urine, even in pathologic conditions.

Urobilinogen is the end product of conjugated bilirubin metabolism. Conjugated bilirubin passes through the bile ducts, where it is metabolized by normal intestinal bacteria to urobilinogen. Normally, about 50% of the urobilinogen is excreted in the stool, and 50% is reabsorbed into the enterohepatic circulation. A small amount of absorbed urobilinogen, about 1 to 4 mg/day, will escape hepatic uptake and be excreted in the urine. Hemolysis and hepatocellular diseases that lead to increased bile pigments can result in increased urinary urobilinogen. Conversely, obstruction of the bile duct or antibiotic usage that alters intestinal flora, thereby interfering with the conversion of conjugated bilirubin to urobilinogen, will decrease urobilinogen levels in the urine. In these conditions, serum levels of conjugated bilirubin rise.

There are different dipstick reagents and methods to test for both bilirubin and urobilinogen, but the basic physiologic principle involves the binding of bilirubin or urobilinogen to a diazonium salt to produce a colorimetric reaction. False-negative results can occur in the presence of ascorbic acid, which decreases the sensitivity for detection of bilirubin. False-positive results can occur in the presence of phenazopyridine because it colors the urine orange and, similar to the colorimetric reaction for bilirubin, turns red in an acid medium.

Leukocyte Esterase and Nitrite Tests

Leukocyte esterase activity indicates the presence of white blood cells in the urine. The presence of nitrites in the urine is strongly suggestive of bacteriuria. Thus both tests have been used to screen patients for UTIs. The most accurate method to diagnose infection is by microscopic examination of the urinary sediment to identify pyuria and subsequent urine culture. **If the dipstick is positive for leukocyte esterase but negative for nitrites, noninfectious causes of inflammation should be considered and a microscopic analysis and urine culture should be obtained before any empirical antibiotic therapy should be prescribed.**

Leukocyte esterase is produced by neutrophils and catalyzes the hydrolysis of an indoxyl carbonic acid ester to indoxyl (Gillenwater, 1981). The indoxyl formed oxidizes a diazonium salt chromogen on the dipstick to produce a color change. It is recommended that leukocyte esterase testing be done 5 minutes after the dipstick is immersed in the urine to allow adequate incubation (Shaw et al., 1985). The sensitivity of this test subsequently decreases with time because of lysis of the leukocytes. Leukocyte esterase testing may also be negative in the presence of infection because not all patients with bacteriuria will have significant pyuria. Therefore if one uses leukocyte esterase testing to screen patients for UTI, it should always be done in conjunction with nitrite testing for bacteriuria (Pels et al, 1989).

Other causes of false-negative results with leukocyte esterase testing include increased urinary specific gravity, glycosuria, presence of urobilinogen, medications that alter urine color, and ingestion of large amounts of ascorbic acid. **The major cause of false-positive leukocyte esterase tests is specimen contamination.**

Nitrites are not normally found in the urine, but many species of gram-negative bacteria can convert nitrates to nitrites. Nitrites are readily detected in the urine because they react with the reagents on the dipstick and undergo diazotization to form a red azo dye. The specificity of the nitrite dipstick for detecting bacteriuria is higher than 90% (Pels et al., 1989). The sensitivity of the test, however, is considerably less, varying from 35% to 85%. The nitrite test is less accurate in urine specimens containing fewer than 10^5 organisms/mL (Kellogg et al., 1987). As with leukocyte esterase testing, the major cause of false-positive nitrite testing is contamination.

A protocol combining the visual appearance of the urine with leukocyte esterase and nitrite testing has been proposed when in-office microscopy is not available (Fig. 2.3). It reportedly detects 95% of infected urine specimens and decreases the need for microscopy by as much as 30% (Flanagan et al., 1989). Other studies, however, have shown that dipstick testing is not an adequate replacement for microscopy (Propp et al., 1989). As stated earlier, any

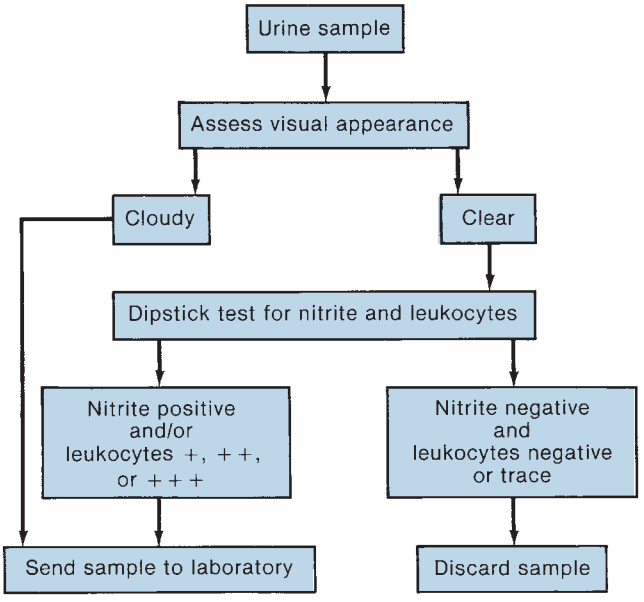


Fig. 2.3. Protocol for determining the need for urine sediment microscopy in an asymptomatic population. (From Flanagan PG, Rooney PG, Davies EA, et al. Evaluation of four screening tests for bacteriuria in elderly people. *Lancet.* 1989;1(8647):1117–1119. © by The Lancet Ltd., 1989.)

dipstick test that is positive for only one without the other should be confirmed with microscopy and culture before prescribing any treatment. In summary, it has not been demonstrated conclusively that dipstick testing for UTI can replace microscopic examination of the urinary sediment.

Urinary Sediment

Obtaining and Preparing the Specimen

A clean-catch midstream urine specimen should be obtained. As described earlier, uncircumcised men should retract the prepuce and cleanse the glans penis before voiding. It is more difficult to obtain a reliable clean-catch specimen in females because of contamination with introital leukocytes and bacteria. **If there is any suspicion of a UTI in a female, a catheterized urine sample should be obtained for culture and sensitivity**.

If possible, **the first-void urine specimen is the specimen of choice and should be examined within 1 hour.** A standard procedure for preparation of the urine for microscopic examination has been described (Cushner and Copley, 1989). Ten to 15 milliliters of urine should be centrifuged for 5 minutes at 3000 rpm. The supernatant is then poured off, and the sediment is resuspended with 0.3 mL of saline in the centrifuge tube by gently tapping the bottom of the tube. Although the remaining small amount of fluid can be poured onto a microscope slide, this usually results in excess fluid on the slide. It is better to use a small pipette to withdraw the residual fluid from the centrifuge tube and to place it directly on the microscope slide. This usually results in an ideal volume of between 0.01 and 0.02 mL of fluid deposited on the slide. The slide is then covered with a coverslip. The edge of the coverslip should be placed on the slide first to allow the drop of fluid to ascend onto the coverslip by capillary action. The coverslip is then gently placed over the drop of fluid, and this technique allows for most of the air between the drop of fluid and the coverslip to be expelled. If one simply drops the coverslip over the urine, the urine will disperse over the slide and there will be a considerable number of air bubbles that may distort the subsequent microscopic examination.

Microscopy Technique

Microscopic analysis of urinary sediment should be performed with both low-power (×100 magnification) and high-power (×400 magnification) lenses. At least 10 to 20 microscopic fields should be analyzed. The use of an oil immersion lens for higher magnification is seldom, if ever, necessary. Under low power, the entire area under the coverslip should be scanned. **Particular attention should be given to the edges of the coverslip, where casts and other elements tend to be concentrated.** Low-power magnification is sufficient to identify erythrocytes, leukocytes, casts, cystine crystals, oval fat macrophages, and parasites such as *Trichomonas vaginalis* and *Schistosoma hematobium*.

High-power magnification is necessary to distinguish circular from dysmorphic erythrocytes, to identify other types of crystals, and, particularly, to identify bacteria and yeast. In summary, **the urinary sediment should be examined microscopically for (1) cells, (2) casts, (3) crystals, (4) bacteria, (5) yeast, and (6) parasites.**

Cells

Erythrocyte morphology may be determined under high-power magnification. Although phase contrast microscopy has been used for this purpose, circular (nonglomerular) erythrocytes can generally be distinguished from dysmorphic (glomerular) erythrocytes under routine brightfield high-power magnification (Figs. 2.4 to 2.8). **This is assisted by adjusting the microscope condenser to its lowest aperture, thus reducing the intensity of background light. This allows one to see fine detail not evident otherwise and also creates the effect of phase microscopy because cell membranes and other sedimentary components stand out against the darkened background.**

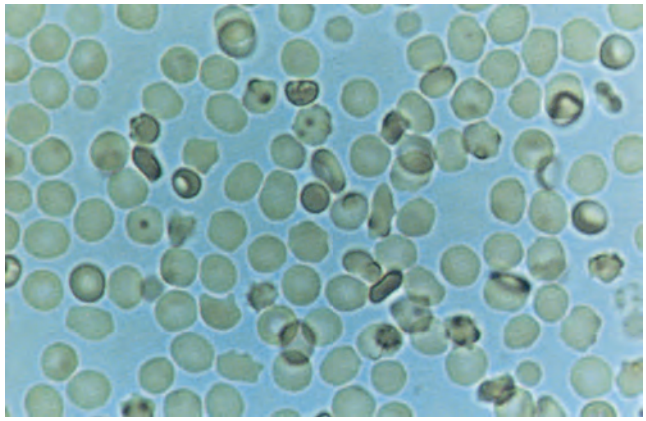


Fig. 2.4. Red blood cells, both smoothly rounded and mildly crenated, typical of epithelial erythrocytes.

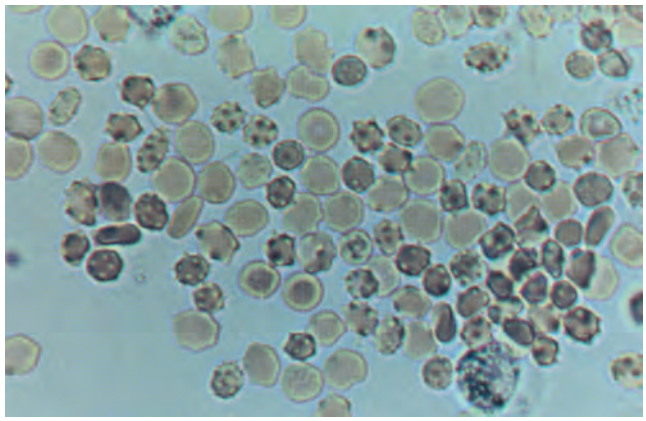


Fig. 2.5. Red blood cells from a patient with a bladder tumor.

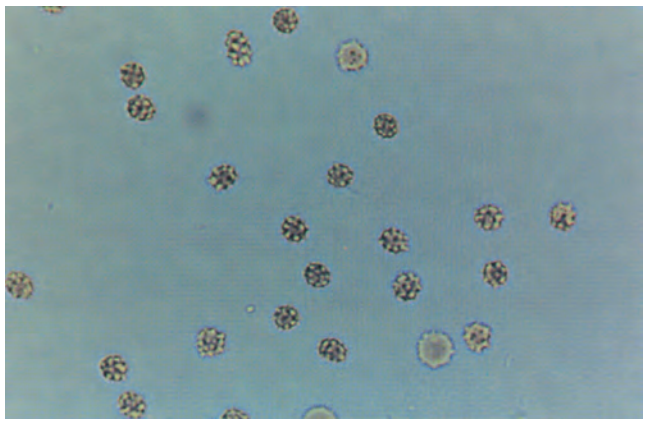


Fig. 2.6. Red blood cells from a patient with interstitial cystitis. Cells were collected at cystoscopy.

Circular erythrocytes generally have an even distribution of hemoglobin with either a round or crenated contour, whereas dysmorphic erythrocytes are irregularly shaped with minimal hemoglobin and irregular distribution of cytoplasm. Automated techniques for performing microscopic analysis to distinguish the two types of erythrocytes have been investigated but have not yet been accepted into general urologic practice and are probably unnecessary. In one study using a standard Coulter counter, microscopic analysis was found to be 97% accurate in differentiating between the two types of erythrocytes

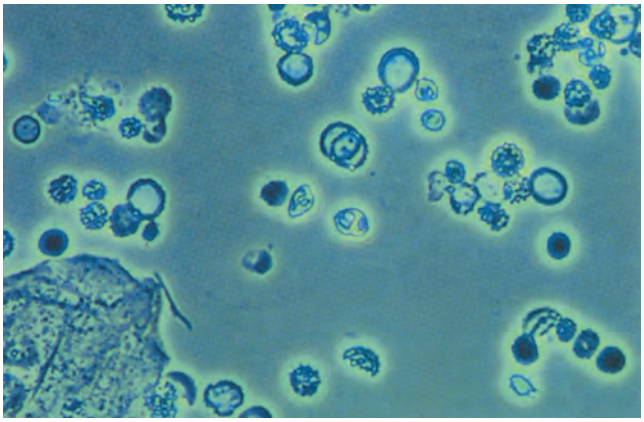


Fig. 2.7. Red blood cells from a patient with Berger disease. Note variations in membranes characteristic of dysmorphic red blood cells.

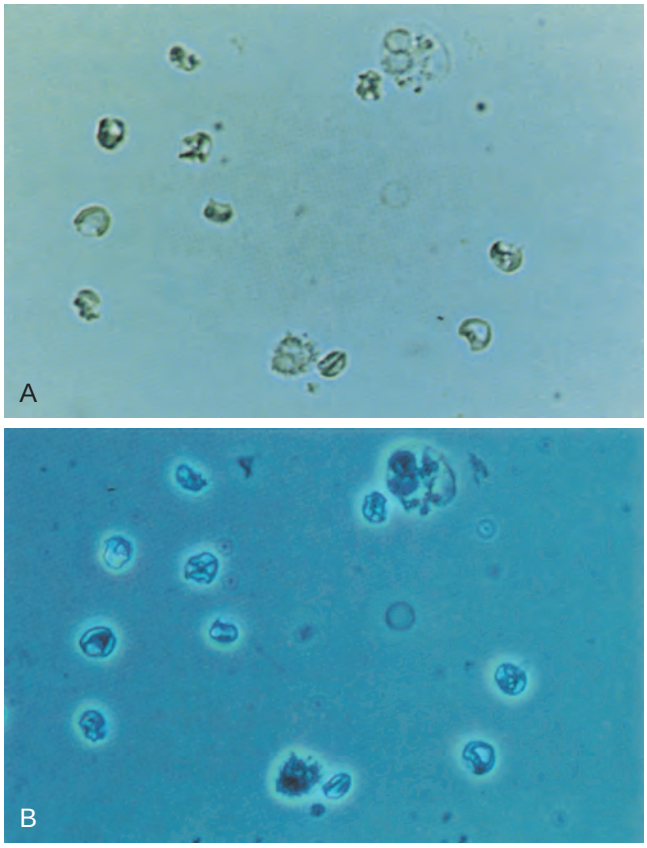


Fig. 2.8. Dysmorphic red blood cells from a patient with Wegener granulomatosis. (A) Brightfield illumination. (B) Phase illumination. Note irregular deposits of dense cytoplasmic material around the cell membrane.

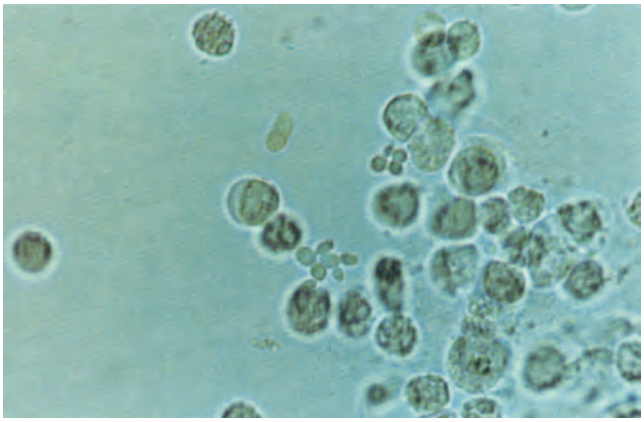


Fig. 2.9. *Candida albicans.* Budding forms surrounded by leukocytes.

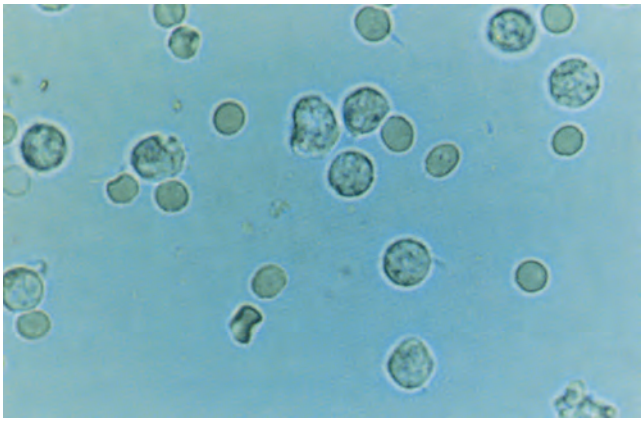


Fig. 2.10. Old leukocytes. Staghorn calculi with Proteus infection.

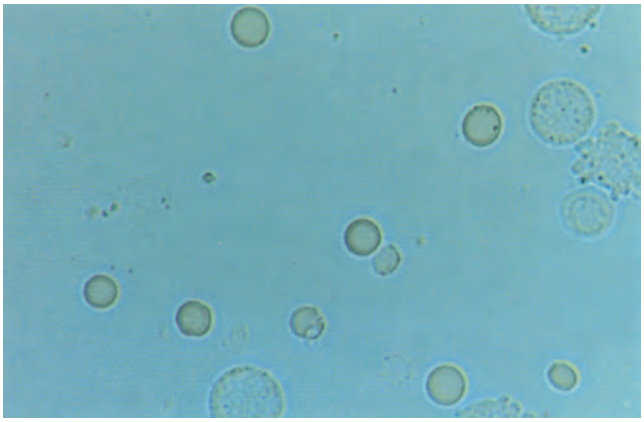


Fig. 2.11. Fresh "glitter cells" with erythrocytes in background.

(Sayer et al., 1990). **Erythrocytes may be confused with yeast or fat droplets** (Fig. 2.9). Erythrocytes can be distinguished, however, because yeast will show budding, and oil droplets are highly refractile.

Leukocytes can generally be identified under low-power magnification and definitively diagnosed under high-power magnification (Figs. 2.10 and 2.11; see Fig. 2.9). It is normal to find 1 or 2 leukocytes per HPF in men and up to 5 per HPF in women in whom the urine sample may be contaminated with vaginal secretions. A greater number of leukocytes generally indicates infection or inflammation in the urinary tract. It may be possible to distinguish **old leukocytes, which have a characteristic small and wrinkled appearance** and which are commonly found in the vaginal secretions of normal women, from fresh leukocytes, which are generally indicative of urinary tract pathology. Fresh leukocytes are generally larger and rounder, and, when the specific gravity is less than 1.019, the granules in the cytoplasm demonstrate glitterlike movement, so-called *glitter cells.*

Epithelial cells are commonly observed in the urinary sediment. Squamous cells are frequently detected in female urine specimens and are derived from the lower portion of the urethra, the trigone of postpubertal females, and the vagina. **Squamous epithelial cells are large, have a central small nucleus about the size of an erythrocyte, and have an irregular cytoplasm with fine granularity.** Transitional epithelial cells may arise from the remainder of the urinary tract (Fig. 2.12). Transitional cells are smaller than squamous cells, have a larger nucleus, and demonstrate prominent cytoplasmic granules near the nucleus. Malignant transitional cells have altered

nuclear size and morphology and can be identified with either routine Papanicolaou staining or automated flow cytometry.

Renal tubular cells are the least commonly observed epithelial cells in the urine but are most significant because their presence in the urine is always indicative of renal pathology. Renal tubular cells may be difficult to distinguish from leukocytes, but they are slightly larger.

Casts

A cast is a protein coagulum that is formed in the renal tubule and traps any tubular luminal contents within the matrix. **Tamm-Horsfall mucoprotein is the basic matrix of all renal casts; it originates from tubular epithelial cells and is always present in the urine.** When the casts contain only mucoproteins, they are called *hyaline casts* and may not have any pathologic significance. Hyaline casts may be seen in the urine after exercise or heat exposure but may also be observed in pyelonephritis or chronic renal disease.

RBC casts contain entrapped erythrocytes and are diagnostic of glomerular bleeding, most likely secondary to glomerulonephritis (Figs. 2.13 and 2.14). White blood cell casts are observed in acute glomerulonephritis, acute pyelonephritis, and acute tubulointerstitial nephritis. Casts with other cellular elements, usually sloughed renal tubular epithelial cells, are indicative of nonspecific renal damage (Fig. 2.15). Granular and waxy casts result from further degeneration of cellular elements. Fatty casts are seen in nephrotic syndrome, lipiduria, and hypothyroidism.

Crystals

Identification of crystals in the urine is particularly important in patients with stone disease because it may help determine the etiology (Fig. 2.16). Although other types of crystals may be seen in normal patients, **the identification of cystine crystals establishes the diagnosis of cystinuria.** Crystals precipitated in acidic urine include calcium oxalate, uric acid, and cystine. Crystals precipitated in an alkaline urine include calcium phosphate and triple-phosphate (struvite) crystals. Cholesterol crystals are rarely seen in the urine and are not related to urinary pH. They occur in lipiduria and remain in droplet form.

Bacteria

Normal urine should not contain bacteria; in a fresh uncontaminated specimen, the finding of bacteria is indicative of a UTI. Because each HPF views between 1/20,000 and 1/50,000 mL, each bacterium seen per HPF signifies a bacterial count of more than 30,000/mL. Therefore, **5 bacteria per HPF reflects colony counts of about 100,000/mL.** This is the standard concentration used to establish the diagnosis of a UTI in a clean-catch specimen. This level should apply only to women, however, in whom a clean-catch specimen is frequently contaminated. The finding of any bacteria in a properly collected midstream specimen from a male patient should be further evaluated with a urine culture.

Under high power, it is possible to distinguish various bacteria. Gram-negative rods have a characteristic bacillary shape (Fig. 2.17), whereas streptococci can be identified by their characteristic beaded chains (Figs. 2.18 and 2.19) and staphylococci can be identified when the organisms are found in clumps (Fig. 2.20).

Yeast

The most common yeast cells found in urine are *Candida albicans*. The biconcave oval shape of yeast can be confused with erythrocytes and calcium oxalate crystals, but **yeasts can be distinguished by their characteristic budding and hyphae** (see Fig. 2.9). Yeasts are most commonly seen in the urine of patients with diabetes mellitus or as contaminants in women with vaginal candidiasis.

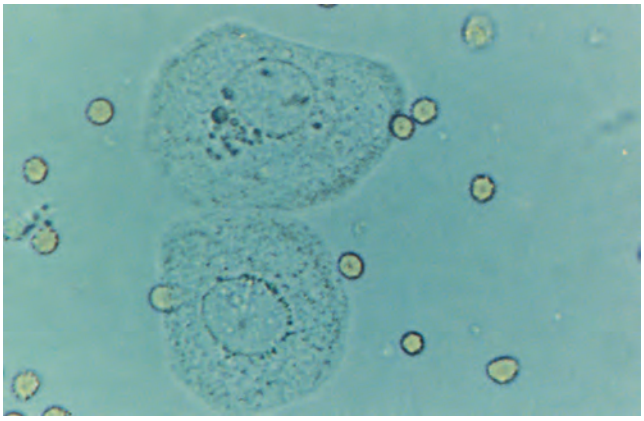


Fig. 2.12. Transitional epithelial cells from bladder lavage.

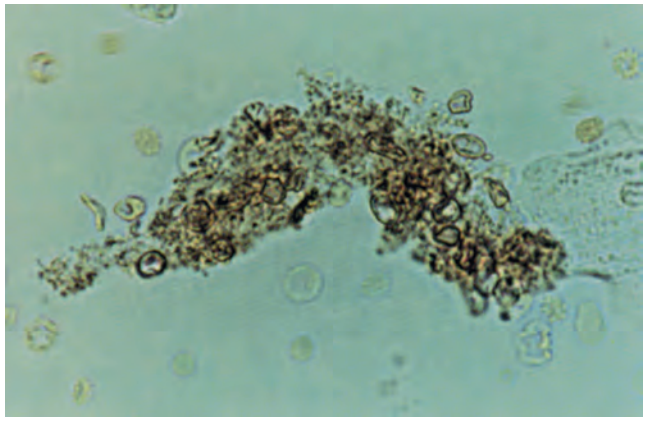


Fig. 2.14. Red blood cell cast.

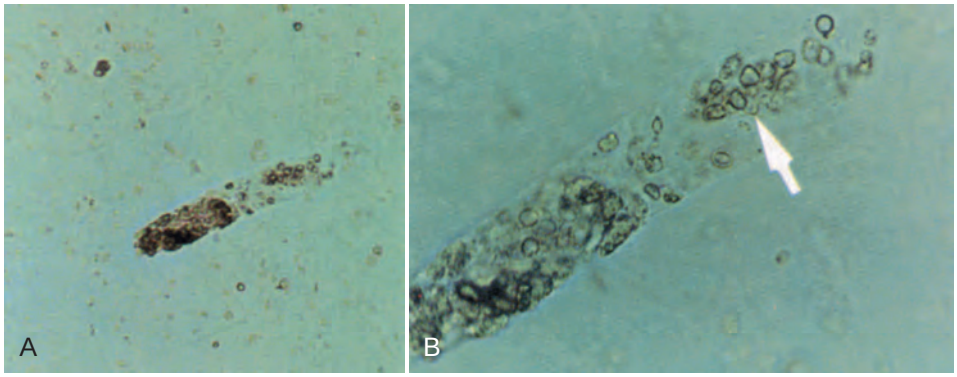


Fig. 2.13. Red blood cell cast. (A) Low-power view demonstrates distinct border of hyaline matrix. (B) High-power view demonstrates the sharply defined red blood cell membranes *(arrow)*.

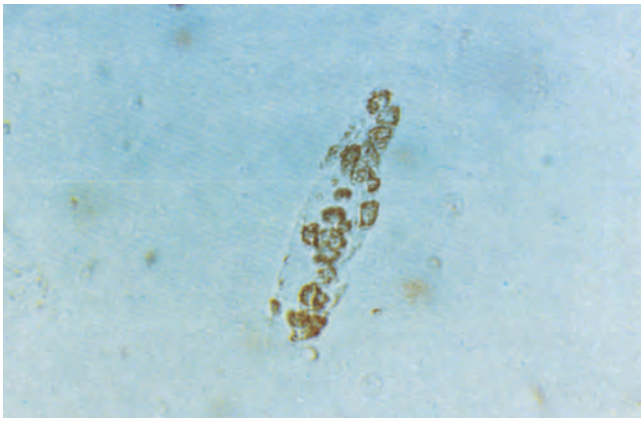


Fig. 2.15. Cellular cast. Cells entrapped in a hyaline matrix.

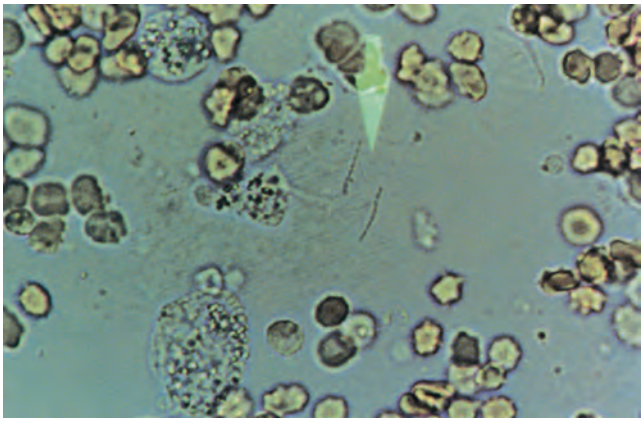


Fig. 2.18. Streptococcal urinary tract infection with typical chain formation *(arrow).*

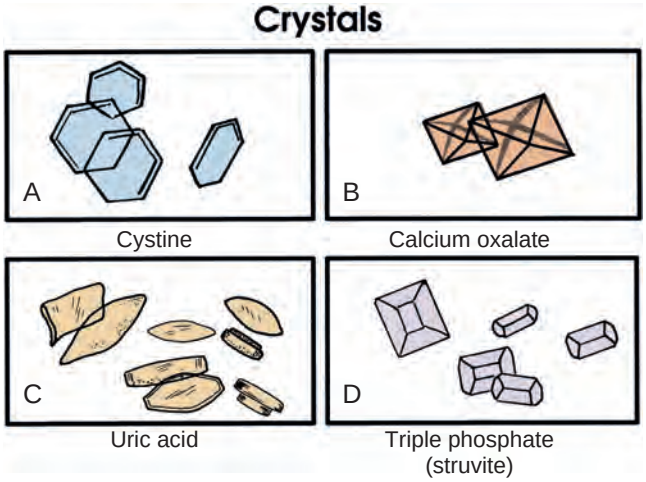


Fig. 2.16. Urinary crystals. (A) Cystine. (B) Calcium oxalate. (C) Uric acid. (D) Triple phosphate (struvite).

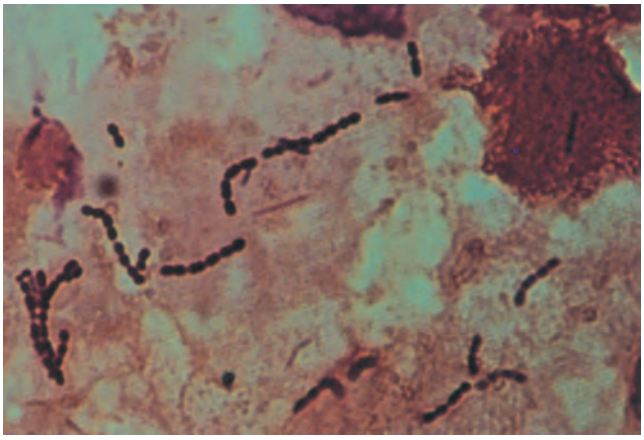


Fig. 2.19. Streptococcal urinary tract infection (Gram stain).

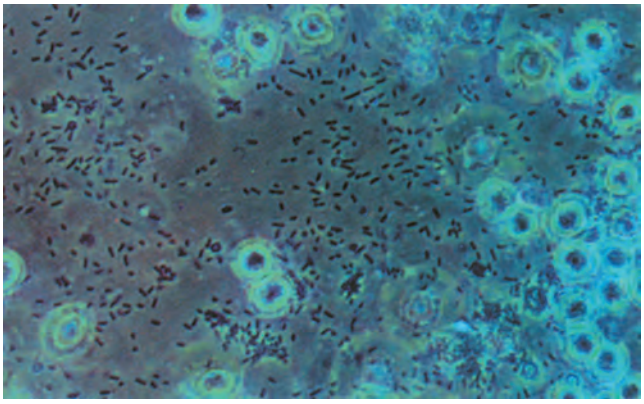


Fig. 2.17. Gram-negative bacilli. Phase microscopy of *Escherichia coli.*

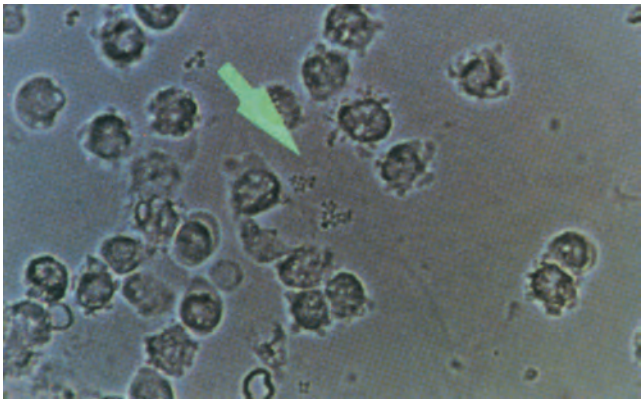


Fig. 2.20. *Staphylococcus aureus* in typical clumps *(arrow).*

Parasites

***Trichomonas vaginalis* is a frequent cause of vaginitis in women and occasionally of urethritis in men.** Trichomonads can be readily identified in a clean-catch specimen under low power (Fig. 2.21). Trichomonads are large cells with rapidly moving flagella that quickly propel the organism across the microscopic field.

***Schistosoma hematobium* is a urinary tract pathogen that is not found in the United States but is extremely common in countries of the Middle East and North Africa. Examination of the urine shows the characteristic parasitic ova with a terminal spike.**

Expressed Prostatic Secretions

Although not strictly a component of the urinary sediment, the expressed prostatic secretions should be examined in any male patient suspected of having prostatitis. Normal prostatic fluid should contain few, if any, leukocytes, and the presence of a larger number or clumps of leukocytes is indicative of prostatitis. **Oval fat macrophages are found in postinfection prostatic fluid** (Figs. 2.22 and 2.23). Normal prostatic fluid contains numerous secretory granules that resemble but can be distinguished from leukocytes under high power because they do not have nuclei.

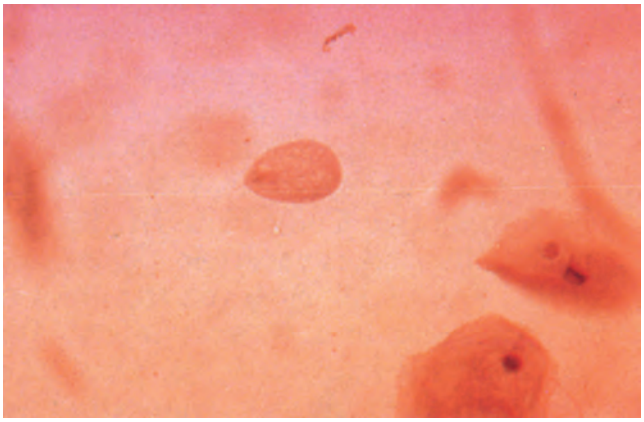


Fig. 2.21. Trichomonad with ovoid shape and motile flagella.

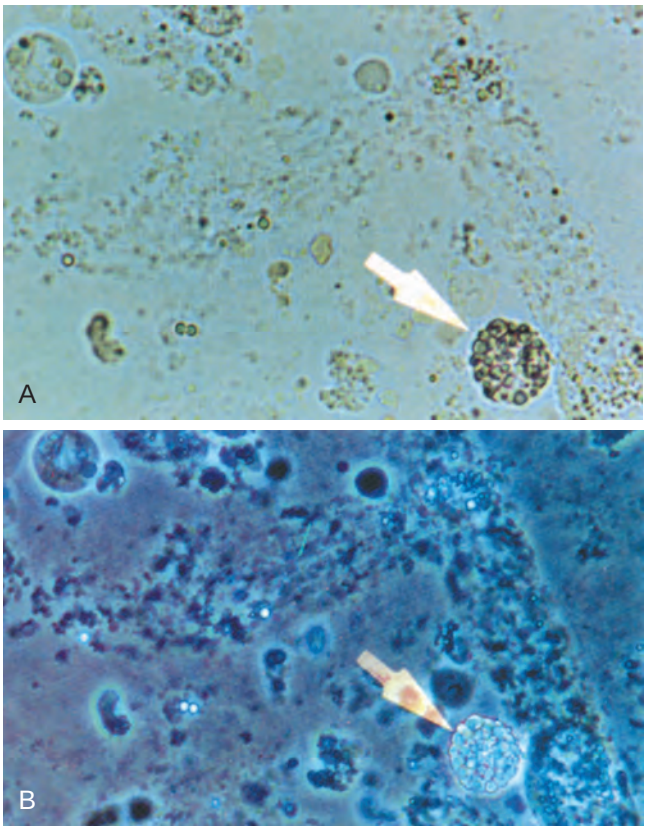


Fig. 2.22. Oval fat macrophage. (A) High-power view showing doubly refractile fat particles *(arrow).* (B) Phase microscopy of the same specimen *(arrow).*

KEY POINTS

- A catheterized urine specimen should be obtained in the female patient with a history of recurrent UTIs or suspected contaminated specimen.
- Hematuria should be stratified into glomerular, nonglomerular, medical, and surgical causes.
- A dipstick alone is inadequate for the diagnosis of microscopic hematuria.
- AMH is defined as greater than or equal to 3 erythrocytes per HPF on a properly collected urinary specimen in the absence of an obvious benign cause.
- A urine dipstick that is positive for only leukocyte esterase or nitrites but not both should be confirmed with microscopic analysis and urine culture.

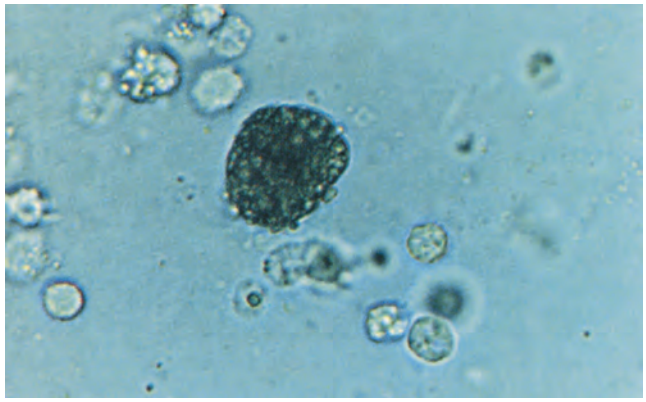


Fig. 2.23. Oval fat macrophage, high-power view. Note the fine secretory granules in the prostatic fluid.

Serum Laboratory Studies

In some cases, assessing for metabolic function is incorporated in the evaluation of the urologic patient. A serum creatinine and calculated glomerular filtration rate (GFR) is often used to assess baseline or current renal function. Identifying any compromise of renal function may be useful when investigating lower or upper tract obstruction or any contributing medical renal disease. **Urgency of intervention and treatment of obstruction will be influenced by renal function.** Furthermore, the presence or history of renal disease is also used in the evaluation of conditions such as hematuria, proteinuria, and anatomic pathology as described earlier. In some cases, additional laboratory values such as serum potassium, CO_2, and liver transaminases are part of the diagnostic evaluation of malignancy or metabolic derangement seen with conditions affecting multiple organ systems including the urinary tract. A complete blood count (CBC) includes a white blood cell count, hemoglobin, hematocrit, and platelet count and may be ordered with or without a differential. This test may be ordered for perioperative purposes, during routine follow-up of patients with malignancy, and in the workup for an infectious process. A CBC may provide useful information to the urologist during evaluation of the urologic patient and help guide additional testing and workup when findings on history and physical examination suggest significant pathology within the urinary tract.

Prostate-Specific Antigen

One of the most important and controversial tumor markers identified is prostate-specific antigen (PSA). It is used by the urologist in the diagnostic evaluation of prostate pathology including cancer, benign prostatic hyperplasia (BPH), and inflammatory conditions of the prostate (prostatitis). **PSA, also known as *human kallikrein peptidase 3(hK3)*, is a serine protease and a member of the kallikrein gene family. It is produced by prostatic luminal epithelial cells.** Although there is significant disagreement across disciplines regarding its use for the detection of prostate cancer, it is a particularly useful tool for the assessment of BPH and prostatitis because of its sensitivity for the detection of prostatic pathology. The PSA level often directly correlates to prostate volume and any significant inflammatory process within the prostate gland. It is also one of the most reliable laboratory tests used when following patients with prostate cancer, particularly following treatment including radiation, radical prostatectomy, and hormonal therapy. **This test may be ordered when evaluating the male patient for prostatic diseases including prostate cancer, urinary obstruction, and symptoms caused by BPH and prostatitis.** Indications, algorithms, and implications for ordering PSA for specific pathology are covered in depth later in this text.

Urinary Markers

Urinary cytology is ordered when urothelial malignancy is suspected. Although in the past it was considered a standard part of the screening

for urothelial cell carcinoma (UCC), deciding to order it in the initial evaluation is tailored to other aspects of the patient's history. Routine use as a screening tool or in the initial evaluation of AMH is not recommended and is more often used to follow patients with a known history of UCC (Davis et al., 2012, reviewed and validated 2016). However, it may be useful in patients with suspicious radiologic abnormalities or in cases in which a high-grade malignancy is suspected. **Urine cytology is highly specific for high-grade UCC, but sensitivity decreases for low-grade UCC ranging from 15.8% to 54.5%** (Steiner et al., 2008). Additional urinary markers including NMP22, BTA stat, and UroVysion FISH are available but are not recommended for routine use or for routine screening for bladder cancer (Davis et al., 2012, reviewed and validated 2016). In select cases and patients, the urologist may order one or more these tests but generally not during the initial evaluation of the urologic patient.

Additional Serum Studies

Some additional serum testing that may be ordered during the initial evaluation of the urologic patient includes serum markers for other urologic malignancies and endocrinologic studies. Examples include the standard markers for testicular cancers: alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), and lactate dehydrogenase (LDH). These are ordered during the initial evaluation of the scrotal mass or tumor that has been diagnosed on imaging such as testicular ultrasonography. Endocrinologic studies including total testosterone, free testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), and thyroxine T4 may be ordered in the workup of the male patient with suspected hypogonadism. Additional serum endocrinologic studies may be ordered in the patient suspected of having endocrine disorders such as Cushing's syndrome or parathyroid disorders, and during the workup of adrenal pathology.

KEY POINTS

- Serum creatinine and glomerular filtration rate should be ordered when renal obstruction of nephrologic disease is suspected.
- Prostate-specific antigen is a very sensitive test for prostate conditions such as BPH and prostatitis and correlates most often with prostate volume.
- Urine cytology is not recommended during the initial evaluation and screening for AMH.
- Urine cytology is very specific for high-grade urothelial carcinoma.

Office Diagnostic Procedures

Uroflowmetry and Ultrasound for Postvoid Residual

Two very common noninvasive tests performed in the urologist's office are uroflowmetry and assessment of postvoid residual (PVR). These are useful tests to obtain some basic information of the voiding status of the patient. Uroflowmetry is performed in the office with the patient voiding either in a standing or seated position. A multiple array of uroflowmeters are available on the market. In general, a peak or maximum flow rate (Qmax), mean flow rate, voided volume is obtained along with a voiding curve/pattern. This information is used to assess the patient for bladder outlet obstruction (BOO) and provide some insight as to the degree of obstruction in the male patient with suspected BPH. **If the Qmax is greater than 20 mL/s, there is a low probability of BOO. Rates between 15 mL/s and 20 mL/s indicate a low probability of BOO, but patients with significant symptomatic complaints may warrant further workup. Rates between 10 mL/s and 15 mL/s are equivocal, and rates less than 10 mL/s are often the result of BOO, urethral stricture, or detrusor impairment (Kelly, 2004).** It is recommended to interpret abnormally low flow rates with caution if the voided volume is less than 100 mL.

A PVR can be obtained as well to assess residual urine in the bladder and can complement the findings of the flow study to provide basic information about voiding. Modern office PVR is determined with a handheld bladder scanner, but if not available, a sterile catheter can be inserted. Using a sterile catheter has the disadvantage of being somewhat invasive and can cause discomfort, trauma, or infection. Threshold values of PVR are not well defined, but volumes less than 100 mL are generally considered within the acceptable range, especially in the older male patient. Conditions that can result in high PVRs include BOO, BPH, detrusor hypocontractility, neurogenic bladder, bladder diverticula, and urethral stricture disease. Further studies and testing based on results of uroflowmetry and PVR should be ordered based on the complete examination of the patient.

Cystometrography and Multichannel Urodynamic Studies

Urodynamic testing is the study of the transport, storage, and evacuation of urine. Testing is performed when a patient is in need of a more comprehensive workup of storage and voiding dysfunction that is not sufficiently diagnosed with history and physical examination. These studies are performed in the office setting, and ambulatory urodynamic studies can be obtained in select cases. **Components of more complex urodynamic studies include cystometrography, electromyography, urethral pressure profile, and pressure flow studies.** Voiding and storage disorders and its workup are covered thoroughly later in this text.

Cystourethoscopy

Office cystourethroscopy is ordered when direct visualization and evaluation of the lower urinary tract is required. It can be performed in the office with modern flexible cystoscopic equipment. Rigid cystoscopy may be performed at the discretion of the urologist in female patients, but most often flexible cystoscopy is better tolerated. Direct examination of the urethra, bladder, and prostatic urethra in male patients can be performed for diagnostic and screening purposes, and in some cases treatments can be administered. The most common reasons office cystourethroscopy is performed is for diagnosis of lower urinary tract malignancy, urinary obstruction, or in some cases to assist with insertion of a urethral catheter. For patients with a urinary diversion such as an ileal conduit, office looposcopy can be performed to assess for pathology within the ilial conduit. This is performed with a flexible cystoscope and is generally well tolerated with only a mild amount of patient discomfort if there is significant pressure and reflux into the upper tracts. **It should be noted that use of antimicrobial prophylaxis during simple diagnostic cystourethroscopy without manipulation is not recommended as per the AUA best practice statement on urologic surgery antimicrobial prophylaxis and should only be used in patients with the risk factors listed in Table 2.3** (Wolf et al, 2008).

TABLE 2.3 Risk Factors Associated With Increased Risk for Infection Following Urologic Procedure

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
Prolonged hospitalization

KEY POINTS

- Uroflowmetry and assessment of PVR should be ordered when lower urinary tract obstruction is suspected.
- Urodynamic studies provide information on disorders of storage and voiding.
- Routine use of antimicrobial prophylaxis is not recommended for office cystourethroscopy, urodynamics, or cystography in the patient without risk factors.

Radiologic Imaging

During the evaluation of the urologic patient, information obtained with the history and findings on physical examination may prompt the need for radiologic testing. Although the details on the principles of imaging studies are covered in depth in later chapters, basic imaging that may be ordered for specific findings are briefly reviewed in the following section. Some imaging studies may be obtained in urology offices equipped to perform the studies, but more complex imaging such as computed tomography (CT), magnetic resonance imaging (MRI), and nuclear imaging is most often obtained at a formal radiologic facility.

Ultrasonography

Most urologists should be familiar with the indications for ordering ultrasonography of the kidneys, bladder, and prostate. In fact, more and more urologists are performing basic renal ultrasonography in the office setting. **Renal ultrasonography is ordered to obtain information on the size and shape of the kidneys, the presence or absence of hydronephrosis, anatomic abnormalities such as cysts and masses, echogenicity, and vasculature**. Medical renal disease should be suspected if there is increased cortical echogenicity relative to the liver or spleen (O'Neill, 2014). Patients with a history of stones or symptoms of flank pain may benefit from renal ultrasonography to assess for possible obstruction. However, the need for more detailed information from other studies such as CT should be weighed against the ease and convenience of performing an office ultrasonography of the kidneys. **Renal ultrasonography is not sufficient as a stand-alone imaging study for the workup of hematuria, and other cross-sectional abdominal imaging should be considered for this diagnosis.** Urologists rarely order ultrasonography of the bladder as a diagnostic study, but the bladder is often assessed during abdominal and renal ultrasonography. Large masses, large stones, and volume can be assessed by basic ultrasonography of the bladder, but limited information is provided by formal ultrasonography of the bladder. It should be noted that ultrasonography of the ureters is very difficult and should not be used as a method to diagnose conditions of the ureter such as stones or malignancy, although routine ultrasonography may be used to detect severe hydroureter.

Ultrasonography of the prostate is ordered and obtained most often in conjunction with prostate biopsy. More recently, prostate ultrasonography is being used along with MRI for the detection and diagnosis of prostate cancer (Moore and Taneja, 2016). Technology to fuse images from the MRI can be used in real-time during ultrasound-guided biopsy to target lesions within the prostate, or cognitive fusion may be used. More detailed analysis on the technology and indications for its use in the diagnosis of prostate cancer will be covered later in this text. A urologist may also order ultrasonography of the prostate without biopsy when assessing volume during the workup of BPH and/or obstruction. Information on the seminal vesicles and ejaculatory duct patency may be acquired for the assessment of ejaculatory and fertility disorders. The presence of full seminal vesicles along with a dilated ejaculatory duct may help the urologist to decide of additional testing or treatment is indicated.

Computed Tomography and Magnetic Resonance Imaging

Cross-sectional abdominal and pelvic imaging may be obtained either with CT or MRI. Both studies can be obtained with or without contrast. The principles on these more complex imaging studies will be covered later in this text, but the basic indications for ordering them in patients are when conditions of the upper tracts and bladder are suspected. The workup of microscopic and gross hematuria includes CT with contrast or MRI if there is a significant contraindication to iodinated contrast. Noncontrast CT is the most sensitive test and the gold standard for the detection of urinary stones. A history of nephrolithiasis with the onset of flank pain should prompt the ordering of a noncontrast CT of the abdomen and pelvis to assess for the presence of urinary stones. **MRI is not useful in the diagnosis and follow-up of urinary stones.** MRI is more useful in the diagnosis and evaluation of soft tissue abnormalities such as renal malignancies, tumor thrombus within the vasculature, pathology of the adrenal glands, cystic structures within the kidneys and urinary tract, and other soft tissue disorders of the abdomen, pelvis, and retroperitoneum.

Intravenous Pyelogram and Plain Radiographs

Intravenous pyelogram (IVP) and standard plain radiographs such as nephrograms have been largely eclipsed by CT and MRI. Nevertheless, there are select indications for these radiographic studies. Although IVP has been replaced by CT for the workup of urinary stones and upper tract abnormalities, especially with low-dose CT protocols that result in lower radiation exposure, one may order an IVP when dynamic imaging of upper tract excretion and obstruction is required and CT with contrast is not available. The urologist should not underestimate the usefulness of a plain radiography of the kidneys, ureters, and bladder (KUB). **A KUB may be ordered in the initial evaluation and follow-up of the nonemergent patient with a urinary stone in the ureter and/or kidneys**. As more than 70% of urinary stones are generally radio-opaque, a KUB can be useful when conservative management of urolithiasis is being pursued. For example, if a patient presents with a ureteral stone that is nonemergent and subsequent imaging may be needed for follow-up, an initial KUB may be obtained, and if the stone is visible then follow-up imaging may consist of a simple KUB rather than CT. Furthermore, patients with nonobstructing kidney stones may be successfully followed with KUB imaging if surveillance is the primary management strategy. Ultimately, patient symptoms may be used to decide if more complex imaging is warranted.

KEY POINTS

- Renal ultrasonography can provide basic screening information on the presence of hydronephrosis and medical renal disease but is not an adequate stand-alone study for the workup of hematuria.
- CT without contrast of the abdomen and pelvis is the gold standard for detecting urinary stones.
- A KUB is a useful and easy test for the follow-up of existing nonemergent radio-opaque urinary stones.

SUMMARY

This chapter provides an overview of the standard testing and imaging that may be part of the initial evaluation of the urologic patient. There are numerous diagnostic modalities within the urologic armamentarium, and a fundamental understanding of when to order these tests is critical when evaluating the urologic patient. The history and physical examination along with a properly collected urinalysis will help develop a differential diagnosis and direct which additional laboratory testing, office procedures, and imaging should be ordered.

REFERENCES

The complete reference list is available online at ExpertConsult.com.

REFERENCES

Akiboye RD, Sharma DM: Haematuria in sport, *Eur Urol Focus* 2018. S2405–S4569(18)30070-1.

Berger J, Hinglais N: Les depots intercapillaires d'IgA-IgG, *J Urol Nephrol (Paris)* 74(9):694–695, 1968.

Chau AH, Abdul-Muhsin H, Peng X, et al: Robotic-assisted left renal vein transposition as a novel surgical technique for the treatment of renal nutcracker syndrome, *J Vasc Surg Cases Innov Tech* 4(1):31–34, 2018.

Culclasure TF, Bray VJ, Hasbargen JA: The significance of hematuria in the anticoagulated patient, *Arch Intern Med* 154(6):649–652, 1994.

Csako G: False-positive results for ketone with the drug mesna and other free-sulfhydryl compounds, *Clin Chem* 33(2 Pt 1):289–292, 1987.

Cushner HM, Copley JB: Back to basics: the urinalysis: a selected national survey and review, *Am J Med Sci* 297(3):193–196, 1989.

D'Amico G: Clinical features and natural history in adults with IgA nephropathy, *Am J Kidney Dis* 12(5):353–357, 1988.

Davis R, Jones JS, Barocas DA, et al: Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline, *J Urol* 188(6 Suppl):2473–2481, 2012.

Fassett RG, Horgan BA, Mathew TH: Detection of glomerular bleeding by phase-contrast microscopy, *Lancet* 1(8287):1432–1434, 1982.

Flanagan PG, Rooney PG, Davies EA, et al: Evaluation of four screening tests for bacteriuria in elderly people, *Lancet* 1(8647):1117–1119, 1989.

Gillenwater JY: Detection of urinary leukocytes by chemstrip-l, *J Urol* 125(3):383–384, 1981.

Gulleroglu K, Gulleroglu B, Baskin E: Nutcracker syndrome, *World J Nephrol* 3(4):277–281, 2014.

Kellogg JA, Manzella JP, Shaffer SN, et al: Clinical relevance of culture versus screens for the detection of microbial pathogens in urine specimens, *Am J Med* 83(4):739–745, 1987.

Kelly CE: Evaluation of voiding dysfunction and measurement of bladder volume, *Rev Urol* 6(Suppl 1):S32–S37, 2004.

Kincaid-Smith P: Haematuria and exercise-related haematuria, *Br Med J* 285(4):1595–1597, 1982.

Meares EM, Stamey TA: Bacteriologic localization patterns in bacterial prostatitis and urethritis, *Invest Urol* 5(5):492–518, 1968.

Moore CM, Taneja SS: Integrating MRI for the diagnosis of prostate cancer, *Curr Opin Urol* 26(5):466–471, 2016.

Morris RC, Ives HE: *Inherited disorders of the renal tubule*, ed 4, Philadelphia, PA, 1991, Saunders, p 1596.

Nickel JC, Shoskes D, Wang Y, 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* 176(1):119–124, 2006.

O'Neill CW: Renal relevant radiology: use of ultrasound in kidney disease and nephrology procedures, *Clin J Am Soc Nephrol* 9(2):373–381, 2014.

Pels RJ, Bor DH, Woolhandler S, et al: Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. II: bacteriuria, *JAMA* 262(9):1221–1224, 1989.

Propp DA, Weber D, Ciesla ML: Reliability of a urine dipstick in emergency department patients, *Ann Emerg Med* 18(5):560–563, 1989.

Robinson RR: Clinical significance of isolated proteinuria. In Avram MM, editor: *Proteinuria*, New York, NY, 1985, Plenum Medical Book, pp 67–82.

Sayer J, McCarthy MP, Schmidt JD: Identification and significance of dysmorphic versus isomorphic hematuria, *J Urol* 143(3):545–548, 1990.

Shaw ST, Poon SY, Wong ET: Routine urinalysis: is the dipstick enough?, *JAMA* 253(11):1596–1600, 1985.

Steiner H, Bergmeister M, Verdorfer I, et al: Early results of bladder-cancer screening in a high-risk population of heavy smokers, *Brit J Urol* 102(3): 291–296, 2008.

van den Wall Bake AW, Daha MR, van Es LA: Immunopathogenetic aspects of IgA nephropathy, *Nephrologie* 10(3):141–145, 1989.

Vaughan ED Jr, Wyker AW Jr: Effect of osmolality on the evaluation of microscopic hematuria, *J Urol* 105(5):709–711, 1971.

Wagner MG, Smith FG Jr, Tinglof BO Jr, et al: Epidemiology of proteinuria: a study of 4807 school children, *J Pediatr* 73(6):825–832, 1968.

Wolf JS, Bennett CJ, Dmochowski RR, et al: *Urologic Surgery Antimicrobial Prophylaxis*. AUA Best Practice: Reviewed and Validity Confirmed 2011; Amended 2012.

3 Urinary Tract Imaging: Basic Principles of CT, MRI, and Plain Film Imaging

Jay T. Bishoff, MD, and Ardeshir R. Rastinehad, DO, FACOS

With advances in all of the imaging modalities, imaging continues to play an indispensable role in the diagnosis and management of urologic diseases. Because many urologic conditions cannot be assessed by physical examination, conventional radiography has long been critical to the diagnosis of conditions of the adrenals, kidneys, ureters, and bladder. The development of new computed tomography (CT) imaging techniques, three-dimensional (3D) reconstruction, improved ultrasound modalities, advances in magnetic resonance imaging (MRI), new radiotracers for positron emission tomography (PET), and the use of intravenous contrast agents provide detailed anatomic, functional, and physiologic information about urologic conditions and are required for accurate and appropriate urologic care. With so many different imaging options available, it is important for the urologist to be familiar with different options and their correct implementation. In this chapter we discuss the indications for imaging in urology, with an emphasis on the underlying physical principles of the imaging modalities. The strengths and limitations of each modality and the techniques necessary to maximize image quality and minimize the risks and harms to urologic patients are discussed.

CONVENTIONAL RADIOGRAPHY

Conventional radiography has largely been replaced by CT and MRI for many evaluations but remains useful for preoperative diagnosis and postoperative evaluation in a variety of different urologic conditions. Conventional radiography includes abdominal plain radiography, intravenous excretory urography, retrograde pyelography, loopography, retrograde urethrography, and cystography. Urologists frequently perform and interpret conventional radiography examinations, including fluoroscopic examinations, in the office and operating room environments.

Physics

Urologists should be familiar with the physics of conventional radiography and fluoroscopy, as well as the implications and dangers of radiation exposure to the patient and the operator. The underlying physical principles of conventional radiography involve emitting a stream of photons from an x-ray source. These photons travel through the air and strike tissue, imparting energy to that tissue. Some of the photons emerge from the patient with varying amounts of energy attenuation and strike an image recorder such as a film cassette or the input phosphor of an image-intensifier tube, thus producing an image (Fig. 3.1).

RADIATION MANAGEMENT IN URORADIOLOGY

When diagnostic radiation passes through tissue, it creates ion pairs. The resultant charge per unit mass of air is referred to as the **radiation exposure**. The current unit of radiation exposure is measured in coulombs (C)/kg. **Absorbed dose** is the energy absorbed from the radiation exposure and is measured in units called gray (Gy). The older unit of absorbed dose was called the rad (1 rad = 100 Gy).

Because different types of radiation have different types of interaction with tissue, a conversion factor is applied to better express the amount of energy absorbed by a given tissue. The application of this conversion factor to the **absorbed dose** yields the **equivalent dose** measured in sieverts (Sv). For diagnostic x-rays the conversion factor is 1, so the absorbed dose is the same as the equivalent dose. When the amount of radiation energy absorbed by patients during therapeutic radiation is discussed, the dose is given in gray. When exposure to patients or medical personnel resulting from diagnostic ionizing radiation procedures is discussed, the dose is given in sieverts.

The distribution of energy absorption in the human body is different based on the body part being imaged and a variety of other factors. The most important risk of radiation exposure from diagnostic imaging is the development of cancer. The **effective dose** is a quantity used to denote the radiation risk (expressed in **sieverts**) to a population of patients from an imaging study. See Table 3.1 for a description of the relationship between these measures of radiation exposure.

The average person living in the United States is exposed to 6.2 mSv of radiation per year from ambient sources, such as radon and cosmic rays, and medical procedures, which account for 36% of the annual radiation exposure (National Council on Radiation Protection and Measurements [NCRP], 2012). The recommended occupational exposure limit to medical personnel is 50 mSv per year (NCRP, 2012). Exposure to the eyes and gonads has a more significant biologic impact than exposure to the extremities, so recommended exposure limits vary according to the body part. The linear no-threshold model (LNT) used in radiation protection to quantify exposition and to set regulatory limits assumes that the long-term biologic damage caused by ionizing radiation is directly proportional to the dose. **Based upon the LNT there is no safe dose of radiation.** An effective radiation dose of as little as 10 mSv may result in the development of a malignancy in 1 of 1000 individuals exposed (National Research Council of the National Academies, 2006).

Relative Radiation Levels

The assessment of biologic risk from radiation exposure is complex. Estimating the range of effective doses for various imaging modalities allows assignment of a **relative radiation level (RRL)** (Table 3.2). The effective dose from a three-phase CT of the abdomen and pelvis without and with contrast may be as high as 25 to 40 mSv. Another often-overlooked source of significant radiation exposure is seen in the use of fluoroscopy. Fluoroscopy for 1 minute results in a radiation dose to the skin equivalent to 10 times that of a single radiograph of the same anatomic area (Geise and Morin, 2000).

Radiation Protection

The cumulative dose of radiation to patients increases relatively rapidly with repeated CT imaging studies or procedures guided by fluoroscopy. Certain patient populations such as those with recurrent renal calculus disease or those with a urologic malignancy may be at increased risk of developing cancer because of repeated exposures to ionizing radiation. Attempts should be made to limit axial imaging studies to the anatomic area of interest and to substitute imaging studies not requiring ionizing radiation when feasible. The cumulative dose of radiation to medical personnel (including physicians) may increase relatively rapidly in circumstances in which fluoroscopy is used.

Reduction in radiation exposure to medical personnel is achieved by three major mechanisms: (1) limiting the time of exposure; (2) maximizing distance from the radiation source; and (3) shielding.

TABLE 3.1 Units of Radiation Exposure and the Clinical Relevance of the Measures

RADIATION QUANTITY	TRADITIONAL UNIT	SI UNIT	CONVERSION	CLINICAL RELEVANCE
Exposure	roentgen (R)	coulomb (C)/kg	1 C/kg = 3876 R	Charge per unit mass
Absorbed dose	rad	gray (Gy)	1 Gy = 100 rad	Energy absorbed by tissue
Equivalent dose	rem	sievert (Sv)	1 Sv = 100 rem	Absorbed energy based on tissue type
Effective dose	rem	sievert (Sv)		Biologic risk associated with absorbed energy

Modified from Geise RA, Morin RL: Radiation management in uroradiology. In Pollack HM, McClennan BL, ed: *Clinical urography,* ed 2, Philadelphia, 2000, Saunders, p 13.

TABLE 3.2 Radiation Exposure From Common Urologic Imaging Procedures

RELATIVE RADIATION LEVEL (RRL)	EFFECTIVE DOSE ESTIMATED RANGE	EXAMPLE EXAMINATIONS
None	0	Ultrasound, MRI
Minimal	<0.1 mSv	Chest radiographs
Low	0.1–1.0 mSv	Lumbar spine radiographs, pelvic radiographs
Medium	1–10 mSv	Abdomen CT without contrast, nuclear medicine, bone scan, ^{99m}Tc-DMSA renal scan, IVP, retrograde pyelograms, KUB, chest CT with contrast
High	10–100 mSv	Abdomen CT without and with contrast, whole-body PET

Modified from American College of Radiology: *ACR Appropriateness Criteria Radiation Dose Assessment Introduction*. http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/RRLInformation.aspx, 2008.

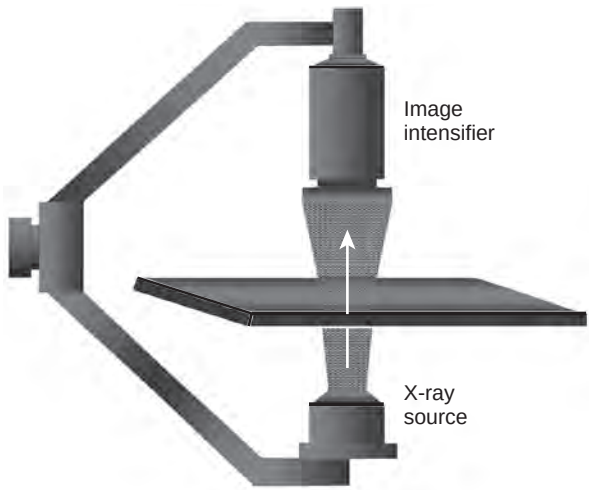


Fig. 3.1. Recommended equipment setup for fluoroscopy. The x-ray source located beneath the table reduces the radiation exposure to the urologist. Locating the image intensifier as close to the patient as feasible reduces scatter radiation. Equipment setup will vary based on application.

Radiation dose during fluoroscopy is directly proportional to the **time of exposure** and to the **number of exposures**. The exposure time during fluoroscopy should be minimized by using short bursts of fluoroscopy and using the "last image hold" feature of the fluoroscopy unit. Radiation beams diverge with distance, and therefore radiation exposure diminishes as the square of the distance from the radiation source. Maintaining the maximum practical distance from an active radiation source significantly decreases exposure to medical personnel. Positioning the image intensifier as close to the patient as feasible substantially reduces scatter radiation. Standard aprons, thyroid shields, radiation-resistant eye protection, and leaded gloves provide significant shielding for medical personnel and should be worn by all personnel involved in the use of fluoroscopy. **A practice of routinely collimating to the minimum required visual fluoroscopy field results in significant reductions in radiation exposure when compared with a usual approach to collimation. This may have important implications for decreasing the risk of malignancy in patients and operators.**

KEY POINTS: CONVENTIONAL RADIOGRAPHY/ RADIATION MANAGEMENT IN URORADIOLOGY

- The effective radiation dose describes the potential for adverse health effects from ionizing radiation.
- The effective dose is a quantity used to denote the radiation risk (expressed in sieverts) to a population of patients from an imaging study. See Table 3.1 for a description of the relationship between these measures of radiation exposure.
- Based upon the LNT model, there is no safe dose of radiation.
- RRLs categorize diagnostic imaging studies by their estimated effective dose of radiation.
- Radiation protection for medical personnel includes (1) limiting time of exposure, (2) maximizing distance from radiation source, and (3) shielding.
- Collimating to the minimum required visual fluoroscopy field reduces exposure to the patient and operator.

CONTRAST MEDIA

The urologist ordering a radiographic evaluation on a patient must consider the risks and benefits associated with a contrast-enhanced imaging study as well as alternative imaging modality that could provide the same information without the need for contrast exposure.

Many different types of contrast media have been used to enhance medical imaging and thus improve diagnostic and therapeutic decisions made by urologists. These agents are used daily throughout the world with great safety and efficacy. However, like all other pharmaceuticals, there are inherent risks associated with the use of contrast media. Adverse side effects and adverse reactions (ARs) can be a direct result from the use of contrast media and vary from minor disturbances to severe, life-threatening situations. Imaging centers must be prepared with trained personnel, readily available medications, equipment, and an ongoing system to educate clinic personnel on the recognition and treatment of ARs associated with contrast media.

Adverse Reactions to Intravascular Contrast Media

The urologists ordering a radiographic study of a patient first must consider the risks and benefits associated with a contrast-enhanced

imaging study as well as alternative imaging modalities that could provide the same information without the need for radiation or contrast exposure.

ARs associated with current intravenous contrast media are uncommon: iodinated: 0.6% aggregate and 0.04% severe (Wang et al., 2008); gadolinium (Gd) based: 0.01% to 0.22% aggregate and 0.008% severe.

Low-osmolality contrast media (LOCM) are associated with low incidence of ARs, and most are not life threatening. Reports of the overall acute AR rates for allergic-like and physiologic reactions (PRs) for nonionic LOCM is 0.2% to 0.7% (Cochran et al., 2001; Mortele et al., 2005; Wang et al., 2008). Serious acute reactions have an incidence of 0.04% (4/10,000) (Katayama et al., 1990). The mortality associated with LOCM injections was reported by the USFDA and drug manufacturers' data from 1990 to 1994 to be 2.1 fatalities per 1 million contrast-enhanced studies using LOCM (Lasser et al., 1987).

The American College of Radiology has divided AR contrast agents into two categories: allergic-like reactions (ALRs) or PRs, and each is subdivided into three categories: mild, moderate, or severe (Table 3.3) (ACR Manual on Contrast Media, 2017).

Allergic-Like Reactions

ALRs manifest in a similar manner to allergic reactions and are now termed "allergic-like" because they are usually idiosyncratic and usually differ immunologically from true ARs. Given that an antigen-antibody response is rarely identified, allergic-like contrast medium reactions are classified as "anaphylactoid," "allergic-like," or "idiosyncratic" (Brockow, 2005; Bush and Swanson, 1991; Cohan and Dunnick, 1987; Dunnick and Cohan, 1994).

The exact mechanism of ALRs is not known but is thought to be a combination of systemic effects (Lasser et al., 1987, 2000)**. ALRs have not been shown to result from a true IgE antibody immunologic reaction to the contrast media** (Dawson et al.,1999). At least four mechanisms may play a role in ALRs: (1) release of vasoactive substances including histamine; (2) activation of physiologic cascades, including complement, kinin, coagulation, and fibrinolytic systems; (3) inhibition of enzymes including cholinesterase, which may cause prolonged vagal stimulation; and (4) the patient's own anxiety and fear of the actual procedure. **ALRs are not dose dependent. Severe reactions have been reported after only 1 cc was injected at the beginning of the procedure and have also occurred after completion of a full dose despite no reaction to the initial test dose** (ACR, 2017; Nelson et al., 1988; Thomsen et al., 1999).

The PRs are not allergic like and represent a physiologic response to the contrast medium molecular properties creating chemotoxicity, effects resulting from hyperosmolality, or binding of specific contrast molecules to activators. Their reactions are often dose and concentration dependent (Bush and Swanson, 1991; Cohan and Dunnick, 1987; Dunnick and Cohan, 1994; Lieberman and Seigle, 1999).

Vasovagal reactions are common PRs, characterized by hypotension and bradycardia and usually self-limiting. These reactions can be related to anxiety and have been known to occur when obtaining consent for the imaging procedure, during venous cannulation, or during administration of contrast medium.

Treatment of Contrast Reactions

Severe contrast reactions are rare but may require immediate treatment. In the case of severe reactions the patient will need emergency care and attention to respiratory and cardiovascular systems. A moderately severe reaction may progress to be severe and life threatening. To reduce the chance of significant morbidity and mortality, a plan and protocol must be in place with trained staff who are trained to recognize, assess, and treat contrast reactions. The evaluation of a patient experiencing a possible reaction includes the following:

- General appearance
- Ability to speak and characterization of the voice
- Respiratory status and oxygen saturation
- Pulse rate and characterization
- Blood pressure

TABLE 3.3 Types of Acute Reactions to Contrast Medium

MILD REACTIONS	
Self-limiting signs or symptoms	
Allergic-Like	**Physiologic**
Limited urticaria/pruritus	Limited nausea/emesis
Limited edema	Transient flushing/warm/chills
Limited throat irritation	Headache/dizziness/anxiety/altered taste
Nasal congestion	Mild hypertension
Sneezing, eye irritation, rhinorrhea	Vasovagal but resolves spontaneously
MODERATE REACTIONS	
Commonly require medical management and may become severe if not treated	
Allergic-Like	**Physiologic**
Diffuse urticaria/pruritus	Protracted nausea/emesis
Diffuse erythema	Hypertension
Facial edema	Chest pain
Throat tightness	Vasovagal responds to treatment
Wheezing/bronchospasm mild	
SEVERE REACTIONS	
Life-threatening, may result in morbidity or mortality if not treated. Cardiac arrest may occur from allergic-like as well as physiologic adverse reactions	
Allergic-Like	**Physiologic**
Diffuse edema/facial edema/shortness of breath	Vasovagal reaction resists treatment
Diffuse erythema and hypotension	Arrhythmia
Laryngeal edema with hypoxia	Seizures
Wheezing/bronchospasm with hypoxia	Hypertensive emergency
Anaphylactic shock/hypotension/tachycardia	

Data from *ACR Manual on Contrast Media*, Version 10.3, 2017.

Treatment: Mild Allergic-Like and Physiologic Reactions. Observation and reassurance are often all that is needed. Usually, no intervention or medication is required. If needed, an H1-receptor blocker such as diphenhydramine (Benadryl) PO/IM/IV 1 to 2 mg/kg up to 50 mg may be helpful in this patient population. Caution is advised: these reactions may progress into a more severe category. Consequently these patients should be observed for 20 to 30 minutes. If necessary, administer chlorpheniramine 4 to 10 mg orally, intravenously, or intramuscularly and diazepam 5 mg for anxiety. For bronchospasm, oxygen 6 to 10 L/min should be administered and a β-agonist inhaler used at 2 puffs (90 mcg/puff) for a total of 180 mcg; this can be repeated up to three times.

Treatment: Moderate Allergic-Like and Physiologic Reactions. Moderate ARs occur in 0.5% to 2% of patients and require treatment but are not immediately life threatening. These reactions are usually transient and require treatment with close observation, using hydrocortisone 100 to 500 mg IM or IV, or β-agonist inhalation

for bronchospasm bronchiolar dilators (metaproterenol [Alupent], terbutaline [Brethaire], or albuterol [Proventil or Ventolin]) 2 to 3 puffs; repeat as necessary. For bronchospasm, oxygen 6 to 10 L/min should be administered and a β-agonist inhaler used at 2 puffs (90 mcg/puff) for a total of 180 mcg; this can be repeated up to three times. Epinephrine can be added to moderate or severe bronchospasm (see the following for epinephrine dosing).

Treatment: Severe Allergic-Like and Physiologic Reactions. Life-threatening reactions occur in approximately 1/1000 uses for high osmolar agents and are far less frequent for LOCM, with both types of agents resulting in mortality rates of 1/170,000 uses (Spring et al., 1997). Immediate treatment is required. The patient usually requires emergency care, involving particular attention to the respiratory and cardiovascular systems. If bronchospasm is severe and not responsive to inhalers, or if an upper airway edema (including laryngospasm) is present, epinephrine should be used promptly. **Rapid administration of epinephrine is the treatment of choice for severe contrast reactions. Epinephrine can be administered IV in the dose of 0.1 mL/kg of 1:10,000 dilution or (0.01 mg/kg) slowly into a running IV infusion of saline and can be repeated every 5 to 15 minutes as needed. The maximum single dose is 1.0 mL (0.1 mg) and can be repeated as needed to a total dose of 1 mg.**

If no IV access is available, the recommended intramuscular dose of epinephrine is 0.01 mg/kg of 1:1000 dilution (0.01 mL/kg) to a maximum of 0.15 mg of 1:1000 if less than 30 kg (0.3 mg if weight is >30 kg) is injected intramuscularly in the lateral thigh. This can be repeated every 5 to 15 minutes up to 1 mL (1 mg) total dose. Subcutaneous injection is much less effective (ACR Manual, 2017; Lightfoot et al., 2009). Epinephrine must be administered with care to patients who have cardiac disease or those who are taking beta-blockers because the unopposed alpha effects of epinephrine in these patients may cause severe hypertension or angina.

Antihistamines do not have a major role in the treatment of severe reactions. Careful monitoring of patient vital signs is paramount; the presence of both hypotension and tachycardia indicates a higher likelihood of anaphylactic reaction. Bradycardia is a sign of vasovagal reaction and therefore the use of beta-blockers is to be avoided. Hypotension resulting from an anaphylactic reaction can be treated with intravenous iso-osmolar fluids (e.g., 0.9% normal saline or Ringer's lactate solution): several liters of fluid may be needed before obtaining a significant hemodynamic response. If fluid and oxygen are unsuccessful in reversing the patient's hypotension, the use of vasopressors is indicated. The most effective vasopressor is dopamine. Dopamine should be used at infusion rates between 2 and 10 mcg/kg/min.

Premedication

There is no known premedication strategy that will eliminate the risk of a severe adverse reaction to contrast media. The regimens suggested in the literature include the use of corticosteroids, antihistamines, H_1 and H_2 antagonists, and ephedrine. Patients at high risk should be premedicated with corticosteroids and possibly with antihistamines 12 to 24 hours before and after use of intravenous radiographic contrast media (IRCM). LOCM should be used in these patients. Several premedication regimens have been proposed to reduce the frequency and/or severity of reactions to contrast media. Two frequently used regimens are outlined in Box 3.1.

Corticosteroid Premedication. Corticosteroid administered before contrast imaging is used to lower the likelihood of an ALR in patients thought to be at risk for a reaction. It has been demonstrated that the use of nonionic contrast media combined with a premedication strategy including corticosteroids results in a reduction in reaction rates compared to other protocols for patients who have experienced a prior contrast media–induced reaction. A randomized trial of premedication for average-risk patients before high-osmolality iodinated contrast medium showed a reduction in mild, intermediate, and severe reactions (Lasser et al., 1987). However, high-osmolality agents are no longer used for intravascular purposes. Another small, randomized trial reported decreased reactions in premedicated patients receiving low-osmolality iodinated contrast medium (O'Malley et al., 2011).

BOX 3.1 Premedication Strategies to Reduce Severity of Reactions to Contrast Media

1. Prednisone: 50 mg by mouth at 13 hours, 7 hours, and 1 hour before contrast media injection
   Plus diphenhydramine (Benadryl) 50 mg intravenously, intramuscularly, or by mouth 1 hour before contrast medium injection
2. Methylprednisolone (Medrol): 32 mg by mouth 12 hours and 2 hours before contrast media injection
   Plus diphenhydramine (Benadryl): 50 mg intravenously, intramuscularly, or by mouth 1 hour before contrast medium injection

From *American College of Radiology Manual on Contrast Media*, version 9, 2013. http://www.acr.org/SecondaryMainMenuCategories/quality_safety/contrast_manual.aspx.

Because severe reactions are rare events, it is difficult to design a study that would be adequately powered to measure a difference. It is estimated that the number of patients needed to premedicate to prevent one reaction in high-risk patients was 69 for avoidance of any reaction, and 569 patients to prevent a severe reaction (Mervak et al., 2015). It is estimated that the number needed to treat to prevent a lethal reaction in high-risk patients would be approximately 50,000 patients (Davenport et al., 2016).

There are no published studies addressing the use of premedication strategies before oral contrast or gadolinium-based intravenous contrast medium in high-risk patients. The current premedication recommendations in these patients are extrapolated from patients receiving intravascular iodinated contrast media.

The risks to patients for premedication with corticosteroids are small and include leukocytosis, asymptomatic hyperglycemia, and possible infection risk (Davenport et al., 2011; Davenport et al., 2016; Lasser, 1988). Diphenhydramine may result in drowsiness.

Premedication Strategies. Oral administration of steroids seems preferable to intravascular administration, with prednisone and methylprednisolone being equally effective. If the patient is unable to take oral medication, 200 mg of hydrocortisone intravenously may be substituted for oral prednisone. **One consistent finding is that steroids should be given at least 6 hours before the injection of contrast media regardless of the route of steroid administration. It is clear that administration for 3 hours or less before contrast does not decrease the incidence of ARs** (Greenberger et al., 1984; Greenberger et al., 1985; Lasser, 1988; Lasser et al., 1987; O'Malley et al., 2011). The minimum duration of premedication is not known. Most studies show that 32 mg of oral methylprednisolone 2 hours before IV use of high-osmolality iodinated contrast in average-risk patients was not effective at prevention of AR, whereas two doses of 32 mg of oral methylprednisolone, one taken 12 hours before contrast and the second taken 2 hours before contrast, was effective (O'Malley et al., 2011).

Supplemental administration of an H_1 antihistamine (e.g., diphenhydramine), orally or intravenously, may reduce the frequency of urticaria, angioedema, and respiratory symptoms.

In emergency situations, intravenous corticosteroid (e.g., 200 mg hydrocortisone) every 4 hours plus an H_1 antihistamine (e.g., 50 mg diphenhydramine) 1 hour before the procedure has been used. In patients who have a prior documented contrast reaction, the use of a different contrast agent has been advocated and may be protective. Switching to a different agent should be in combination with a premedication regimen.

Although rare, ARs have been reported after extravascular instillation of contrast agents (e.g., retrograde pyelography). **In patients with a positive history of previous severe reactions to contrast agents undergoing a nonvascular study, premedication with corticosteroids should be considered.**

Premedication Regimens. Elective premedication with 12 to 13 hours before administration of contrast medium is as follows:

Prednisone: 50 mg oral prednisone at 13 hours, 7 hours, and 1 hour before contrast medium administration, plus 50 mg diphenhydramine IV, IM, or PO 1 hour before contrast administration

or

Methylprednisolone: 32 mg orally 12 hours and again 2 hours before contrast medium administration, plus 50 mg diphenhydramine IV, IM, or PO 1 hour before contrast administration

For patients unable to take oral medication, substitute 200 mg IV hydrocortisone for each does of the or prednisone may be used (Lasser et al., 1987; Mervak et al., 2017).

Accelerated IV Premedication. Premedication regimens less than 4 to 5 hours before administration of contrast medium, with oral or IV medications, have not been shown to be effective. The accelerated 4- to 5-hour regimen is supported by a case series and a retrospective cohort study of 828 patients (Mervak et al., 2017).

1. Methylprednisolone sodium succinate (e.g., Solu-Medrol) 40 mg IV or hydrocortisone sodium succinate (e.g., Solu-Cortef) 200 mg IV immediately and then every 4 hours until contrast medium administration, plus diphenhydramine 50 mg IV 1 hour before contrast medium administration. This regimen usually lasts 4 to 5 hours.
2. Dexamethasone sodium sulfate (e.g., Decadron) 7.5 mg IV immediately and then every 4 hours until contrast medium administration, plus diphenhydramine 50 mg IV 1 hour before contrast medium administration. This regimen may be useful in patients with an allergy to methylprednisolone and usually lasts 4 to 5 hours.
3. Methylprednisolone sodium succinate (e.g., Solu-Medrol) 40 mg IV or hydrocortisone sodium succinate (e.g., Solu-Cortef) 200 mg IV, plus diphenhydramine 50 mg IV, each 1 hour before contrast medium administration. This regimen, and all other regimens with a duration less than 4 to 5 hours, has no evidence of efficacy. It may be considered in emergent situations when there are no alternatives (ACR, 2017).

Delayed Contrast Reactions

Delayed contrast reactions can occur from 3 hours to 7 days after the administration of contrast. These reactions are identified in as many as 14% to 30% of patients after the injection of ionic monomers and in 8% to 10% of patients after the injection of nonionic monomers. The most common of delayed reactions are allergic-like and cutaneous reactions with reported incidence of 0.5% to 9%. The most common reactions include a cutaneous xanthem or pruritis without urticaria. Nausea, vomiting, drowsiness, headache, and flulike symptoms also may occur. These signs and symptoms typically resolve spontaneously (Loh et al., 2010).

Specific Contrast Considerations

Allergy. Patients who have had a prior ALR to contrast medium have a fivefold increased risk for developing a future ALR if exposed to the same class of contrast agent (Jung et al., 2012; Katayama et al., 1990). Patients who have allergies unrelated to contrast are at a two to three times increased risk for an ALR to contrast. Patients with shellfish or iodine allergies are at no greater risk from iodinated contrast medium than are patients with other allergies (Beaty et al., 2008; Boehm, 2008). Patients who have had a reaction to one class of contrast medium are not at higher risk or chance of having a reaction to another type of contrast medium.

Anxiety. Contrast reactions are more common in patients with anxiety and may need reassurance but do not require premedication (Lalli, 1974).

Asthma. A history of asthma increases the chance of an ALR and bronchospasm. Notwithstanding, premedicating based on the history of asthma alone is not recommended (Shehadi, 1975).

Beta-Blockers. It has been suggested that the use of beta-blockers can lower the threshold for contrast reactions, reduce the response to treatment, and increase the risk of more severe contrast reactions (Lane et al., 1993). This risk is modest and consequently premedication and cessation of beta-blockers are not recommended before use of contrast medium.

Cardiac Abnormalities. Patients with underlying severe cardiac disease, including chest pain and cardiac arrest, have an increased incidence and/or severity of cardiovascular side effects. Pulmonary angiography and intracardiac and coronary artery injections carry the highest degree of risk. Possible reactions include hypotension, tachycardia, and arrhythmias. More severe, but uncommon, reactions include congestive heart failure, pulmonary edema, and cardiac arrest. Premedication is not recommended based solely upon cardiac status.

Hyperthyroidism. Iodinated contrast media does not affect thyroid function in patients with a normal functioning thyroid. Patients with hyperthyroidism may develop thyrotoxicosis after exposure to an iodinated contrast medium, but this is a rare event (van der Molen et al., 2004). During acute thyroid storm, iodinated contrast can potentiate thyrotoxicosis and should be avoided in these patients. Iodinated contrast medium can interfere with patients undergoing radioactive iodine therapy or radioactive iodine imaging of the thyroid, and a washout period is recommended after imaging with iodinated contrast medium of 3 to 6 weeks (ACR, 2017; Silberstein et al., 2012).

Myasthenia Gravis. The use of intravenous iodinated contrast medium causing an exacerbation of symptoms in patients with myasthenia gravis (MG) is controversial. Myasthenic exacerbation occurs in approximately 6% of patients with MG exposed to iodinated contrast compared with 1% of patients with MG undergoing contrast CT imaging. Premedication is not recommended solely based on the history of MG (Mehrizi and Pascuzzi, 2014; Somashekar et al., 2013).

Pheochromocytoma. There is no evidence that the use of currently available iodinated or gadolinium contrast medium will induce a hypertensive crisis in patients with pheochromocytoma (Mukherjee et al., 1997).

Sickle Cell Trait and Disease. It has been suggested that contrast medium in sickle cell disease or trait patients may increase the risk of sickle crisis. This has not been seen with the use of current iodinated or gadolinium contrast medium (Morcos, 2005).

Extravasation of Contrast Material. Large volume extravasation can be seen with power injections not monitored with electrical skin impedance devices that detect extravasation and arrest the injection process. When large volume extravasation of IRCM occurs, the result can be swelling, edema, erythema, pain, and cellulitis. The most severe consequences may not be manifest immediately, and the inflammatory reaction usually reaches a maximum in 24 to 48 hours. The primary underlying mechanism is believed to be the hyperosmolality of the contrast agent. Mechanical compression resulting from a compartment syndrome may also occur, leading to tissue necrosis. Management steps are immediate cessation of injection, notification of responsible and referring physicians, and elevation of the affected extremity above the level of the heart. If large volume of extravasate occurs, it is recommended to manually massage to promote drainage. If the patient becomes symptomatic, plastic surgery consultation may also be needed. Admission to the hospital for observation or frequent follow-up in clinic may be necessary in some cases of large volume extravasation.

Postcontrast Acute Kidney Injury. Postcontrast acute kidney injury (PC-AKI) is a nonspecific term assigned to an acute, sudden deterioration in kidney function within 48 hours after IV administration of contrast medium. Contrast-induced nephropathy (CIN) is specific for a sudden decrease in kidney function caused by IV administration of iodinated contrast medium.

The precise pathophysiology is not entirely understood, and many different factors have been implicated: vasoconstriction, direct tubular toxicity, osmotic mechanisms, and chemotoxic mechanisms (Heinrich et al., 2005; Liu et al., 2012).

When used at FDA-recommended doses, gadolinium-based contrast media either do not cause CIN or the incidence is extremely low. However, if administered at higher than FDA-approved doses, gadolinium-based contrast media (GBCM) are more nephrotoxic

than isoattenuating doses of iodinated contrast media (Briguori et al., 2006).

Although there are no standard criteria for CIN, the diagnosis can be made if one of the following occurs within 48 hours after administration of iodinated contrast medium: increase in serum creatinine of >0.3 mg/dL, >50% increase in serum creatinine from baseline, or urine output reduced to <0.5 mL/kg/h for at least 6 hours (Mehta et al., 2007).

Four large studies of more than 40,000 patients have addressed CIN, and all four studies have shown that CIN is less common than previously reported. For patients with a stable baseline estimated glomerular filtration rate (eGFR) of at least 45 mL/min/1.73 m^2 IV, iodinated contrast media are not an independent risk for CIN, and in patients with a eGFR 30 to 44 mL/min/1.73 m^2, IV iodinated contrast media are either not nephrotoxic or rarely the cause of CIN (Davenport et al., 2013a; Davenport et al., 2013b; McDonald et al., 2013; McDonald et al., 2014). IV iodinated contrast material appears to be an independent risk factor for CIN in patients with stage IV and stage V chronic kidney disease whose eGFR is less than 30 mL/min/1.73 m^2.

High doses of IRCM can impair renal function in some patients for 3 to 5 days, and the creatinine level usually returns to baseline in 10 to 14 days. The incidence of contrast agent–related nephropathy is estimated to be 2% to 5%, and of those with CIN, up to 25% have persistent renal dysfunction. Clinical manifestations are highly variable and may be absent or proceed to oliguria. CIN in patients with normal kidney function is rare (Kelly et al., 2008; Pannu et al., 2006). CIN is the third most common cause of acute kidney failure in hospitalized patients (Nash et al., 2002).

Isolating specific risk factors for CIN have proven to be difficult to determine. There is general consensus that the most important preexisting risk factor for CIN is severe renal insufficiency. Other risk factors that have been suspected to lead to CIN include diabetes mellitus, dehydration, cardiovascular disease, diuretic use, advanced age, multiple myeloma, hypertension, hyperuricemia, and repeated doses of iodinated contrast in a short period of time.

The most common patient-related risk factors for CIN are chronic kidney disease (creatinine clearance <60 mL/min), diabetes mellitus, dehydration, diuretic use, advanced age, congestive heart failure, age, hypertension, low hematocrit, and ventricular ejection fraction less than 40%. The patients at highest risk for developing CIN are those with both diabetes *and* preexisting renal insufficiency. Other risk factors are concomitant exposure to chemotherapy, aminoglycoside or nonsteroidal anti-inflammatory agents, hyperuricemia, and diseases that affect renal hemodynamics, such as end-stage liver disease and nephrotic syndrome. Patients with a diagnosis of a paraproteinemia syndrome/disease (e.g., multiple myeloma) or a history of a kidney transplant, renal tumor, renal surgery, or single kidney may also be at higher risk of CIN.

The most common non–patient-related causes are high osmolar contrast agents, ionic contrast, increased contrast viscosity, and multiple contrast-enhanced studies performed within a short period and large contrast volume infused (Pannu et al., 2006).

Despite significant discussion on the part of radiologists and urologists, the literature does not support an absolute serum creatinine level that prohibits the use of contrast media. Prevention of CIN has been the subject of many research studies, and the results have been summarized by several different meta-analyses. In these meta-analyses the baseline serum creatinine of study participants ranged from 0.9 to 2.5 mg/dL. In one survey the policies regarding the cutoff value for serum creatinine varied widely among radiology practices: 35% of respondents used 1.5 mg/dL, 27% used 1.7 mg/dL, and 31% used 2.0 mg/dL (mean 1.78 mg/dL) as a cutoff value in patients with no risk factors other than elevated creatinine; threshold values were slightly lower in people with diabetes (mean 1.68 mg/dL). Patients in end-stage renal disease who have no remaining natural renal function are no longer at risk for CIN and may receive LOCM or iso-osmolar contrast medium (IOCM) (Elicker et al., 2006).

Some radiologists prefer to stratify patients by eGFR instead of serum creatinine, and several studies support this practice. One report showed no risk of CIN from IV iodinated contrast regardless of baseline eGFR (McDonald et al., 2014). Another report identified patients with an eGFR less than 30 mL/min/1.73 m^2 were at significant risk of CIN, and patients with an eGFR 30 to 44 mL/min/1.73 m^2 were at some risk for CIN but not statistically significant risk (Davenport et al., 2013). One report showed that a higher percentage of patients presenting for contrast-enhanced CT had an eGFR less than 60 mL/min/1.73 m^2 than had a serum creatinine greater than 1.4 mg/dL, favoring the use of eGFR instead of serum creatinine (Herts et al., 2008). Presently, there is minimal evidence to suggest that IV iodinated contrast material acts as an independent risk factor for CIN in patient with an eGFR of more than 30 mL/min/1.73 m^2. Therefore it seems that this threshold is supported by the greatest amount of evidence.

The American College of Radiology recommends a baseline serum creatinine level before receiving IV iodinated contrast medium if one or more of the following risk factors are present (ACR Manual on Contrast Media, 2017):

- Age >60 years
- History of renal disease:
  Dialysis
  Kidney transplant
  Solitary kidney
  Renal cancer
  Renal surgery
  Hypertension requiring medical management
  History of diabetes mellitus
  Metformin drug combinations

Prevention of CIN is of great concern and has been a subject of many different studies. Hydration is the major preventative action against CIN. Periprocedural IV hydration with 0.9% saline at 100 mL/h 12 hours before to 12 hours after has been shown to decrease the incidence of CIN after intravenous contrast use (Solomon et al., 2007). **The use of sodium bicarbonate has not been definitively shown to prevent CIN in patients receiving IV iodinated contrast material. (The use of *N*-acetylcysteine for the prevention of CIN is controversial** [Safirestein et al., 2000].**) Currently there is insufficient evidence to make a definitive recommendation for its use, and therefore it should not be considered a substitute for appropriate screening and hydration** (Newhouse and RoyChoudhury, 2013; Zoungas et al., 2009). Furosemide was found to increase the risk of developing CIN (Kelly et al., 2008; Pannu et al., 2006).

Metformin and Iodinated Contrast. Metformin, an oral antihyperglycemic drug used to treat diabetes, is eliminated unchanged through the kidneys, most likely by glomerular filtration and tubular excretion. As a biguanide, it stimulates intestinal production of lactic acid. Some conditions can reduce metformin excretion or increase serum lactate. Such conditions include renal disease (decreases metformin excretion), liver disease (decreases lactic acid metabolism), and cardiac disease (increases anaerobic metabolism). **Patients with type 2 diabetes mellitus on metformin may have an accumulation of the drug after administering IRCM, resulting in biguanide lactic acidosis; they experience vomiting, diarrhea, and somnolence. This condition is fatal in approximately 50% of cases** (Wiholm and Myrhed, 1993). **Biguanide lactic acidosis is rare in patients with normal renal function. Consequently, in patients with normal renal function and no known comorbidities, there is no need to discontinue metformin before IRCM use, nor is there a need to check creatinine after the imaging study. However, in patients with renal insufficiency, metformin should be discontinued the day of the study and withheld for 48 hours. Postprocedure creatinine should be measured at 48 hours and metformin started once kidney function is normal** (Bailey and Turner, 1996). **It is not necessary to discontinue metformin before gadolinium-enhanced magnetic resonance (MR) studies when the amount of gadolinium administered is in the usual dose range of 0.1 to 0.3 mmol per kg of body weight.**

Metformin is an antihyperglycemic agent used to treat diabetes mellitus and other conditions that is excreted in the kidneys by glomerular filtration and tubular excretion. The most significant adverse effect of metformin therapy is the possibility of developing metformin-associated lactic acidosis, which is rare (0.084 cases per 1000 patient-years) but has a mortality of 50% in susceptible patients.

The management of patients taking metformin should include the following information. Patients taking metformin are not at higher risk for CIN than other patients. Iodinated contrast is a potential concern for furthering renal damage in patients with acute kidney injury and those with chronic (stage IV or stage V) kidney disease. There have been no reports of lactic acidosis after IV iodinated contrast medium in patients properly selected for metformin considerations.

Recommendations[a] for patients taking metformin are classified into two categories:

1. Patients with no evidence of acute kidney injury (AKI) and eGFR ≥ 30 mL/min/1.73 m^2 do not need to discontinue metformin before or after IV administration of iodinated contrast media and do not need assessment of renal function after imaging.
2. Patients with AKI or CKD (stage IV, stage V, eGFR < 30 mL/min/1.73 m^2) or are having arterial catheter studies that may result in emboli of any type to the kidneys should have their metformin temporarily discontinued before the procedure for 48 hours and then restarted only after renal function has been revaluated and found to be normal.

Metformin and Gadolinium. It is not necessary to discontinue metformin before contrast medium administration when the amount of gadolinium contrast material is in the normal and usual dose range of 0.1 to 0.3 mmol/kg body weight.

Magnetic Resonance Imaging Contrast Agents

Because MRI offers previously unseen detailed soft tissue imaging compared with CT, it was initially believed that MRI would not require contrast enhancement. However, by 2005, almost 50% of MRI studies were being performed with contrast media. Extracellular MRI contrast agents contain paramagnetic metal ions. Copper, manganese, and gadolinium were the potential paramagnetic ions for use with MRI. Gadolinium, however, is the most powerful, having seven unpaired electrons, but its toxicity required encapsulation by a chelate. Paramagnetic agents such as gadolinium are positive enhancers, reducing the T1 and T2 relaxation times and increasing tissue signal intensity on T1-weighted images, while having little effect on T2-weighted images.

Gadolinium

Acute adverse reactions are encountered less frequently with GBCM than after administration of iodinated contrast media. The frequency of all acute adverse events after an injection of 0.1 or 0.2 mmol/kg of gadolinium chelate ranges from 0.07% to 2.4%. The vast majority of these reactions are mild, including coldness at the injection site, nausea, emesis, headache, warmth or pain at the injection site, paresthesias, dizziness, and itching. Reactions resembling an ALR occur in 0.004% to 0.7% of cases. Reactions consisting of rash, hives, or urticaria are most frequent; the patient rarely develops bronchospasm. The severe, life-threatening anaphylactoid or nonallergic anaphylactic reactions are exceedingly rare (0.0001% to 0.001%). In a meta-analysis of 687,000 gadolinium doses for MRI, there were only 5 severe reactions. In another survey based on 20 million administered doses there were 55 cases (0.0003%) of severe reactions. Fatal reactions to gadolinium chelate agents have been reported, but they are extremely rare events. There have been no documented vaso-occlusive or hemolytic complications when administering GBCM to patients with sickle cell disease (Dillman et al., 2011; Elicker et al., 2006). Gadolinium agents are considered to have no nephrotoxicity at approved doses for MRI. However, because of the risk of nephrogenic systemic fibrosis (NSF) in patients with severe renal dysfunction, its use in this patient population requires some precaution and a review of the current recommendations.

Extracellular MRI agents are known to interfere with some serum chemistry assays. For example, serum calcium tests often are measured as a false reading of hypocalcemia for 24 hours after MRI with gadolinium enhancement, even though serum calcium is actually in the normal range. Other tests, including iron, magnesium, iron-binding capacity, and zinc, may also have spurious results. Biochemical assessment is more reliable when performed 24 hours after exposure to GBCM.

Nephrogenic Systemic Fibrosis

NSF is a fibrosing disease of the skin, subcutaneous tissues, lungs, esophagus, heart, and skeletal muscles. Initial symptoms typically include skin thickening and/or pruritus. Symptoms and signs may develop and progress rapidly, with some affected patients developing contractures and joint immobility within days of exposure. Death may result in some patients, presumably as a result of visceral organ involvement.

In 1997 NSF was described in dialysis patients who had not been exposed to GBCM. The condition was previously known as nephrogenic fibrosing dermopathy. In 2006 and again in 2007 independent reports surfaced defining a strong association with GBCM in patients with advanced renal disease (Grobner, 2006; Mackerman et al., 2007). **It is now accepted that GBCM exposure is a necessary factor in the development of NSF. Onset of NSF varies between 2 days and 3 months, with rare cases appearing years after exposure** (Shabana et al., 2008). **Early manifestations include subacute swelling of distal extremities, followed by severe skin induration and later even organ involvement.** In a 2007 survey performed by the American College of Radiology, 156 cases of NSF were reported by 27 responding institutions; 140 of these 156 patients were known to have received GBCM. In 78 patients, the specific GBCM was known: 45 of them received gadodiamide, 17 gadopentetate dimeglumine, 13 gadoversetamide, and 3 gadobenate dimeglumine. NSF after gadoteridol administration has also been reported. Many of the cases in which agents other than gadodiamide and gadopentetate dimeglumine were used are confounded by the fact that affected patients were injected with other agents as well (ACR, 2017). Between 12% and 20% of confirmed cases of NSF have occurred in patients with acute kidney injury. Patients with end-stage kidney disease and eGFR less than 15 mL/min/1.73 m^2 and severe CKD and eGFR 15 to 29 mL/min/1.73 m^2 have a 1% to 7% chance of developing NSF after MRI with gadolinium agents (Todd et al., 2007).

Patients with glomerular filtration rate (GFR) less than 30 mL/min/1.73 m^2 not on chronic dialysis are the most difficult patient population in terms of choosing imaging modality. They are at risk for CIN if exposed to iodinated contrast media for CT imaging and are at significant risk of developing NSF if exposed to GBCM during MRI. Recent data suggest that the risk of NSF may be greatest in patients with a GFR of less than 15 mL/min/1.73 m^2 who have a 1% to 7% chance of developing NSF after GBCM MRI, with the incidence being much less in patients with GFRs that are higher (Kanal et al., 2008). There is a single report of NSF in a patient with eGFR greater than 30 mL/min/1.73 m^2. In the chronic kidney disease patient population, it is recommended that contrast media be avoided if possible. If MRI contrast media is absolutely essential, use of the lowest possible doses (needed to obtain a diagnostic study) of selected GBCM is recommended. In this setting, the patient should be informed of the risks of GBCM administration and must give their consent to proceed. There is no proof that any GBCM is completely safe in this patient group; however, some have suggested avoiding gadodiamide and considering use of macrocyclic agents (Kanal et al., 2008). Patients with CKD but GFR exceeding 30 mL/min/1.73 m^2 are considered to be at extremely low or no risk for developing NSF if a dose of GBCM of 0.1 mmol/kg or less is used. Patients with GFR greater than 60 mL/min/1.73 m^2 do not appear to be at increased risk of developing NSF; the current consensus is that all GBCM can be administered safely to these patients.

The exact mechanism causing NSF is not known. It is believed, but not definitely proven, that gadolinium ions dissociate from the chelates in gadolinium-based contrast agent (GBCA) patients with poor renal clearance. The free gadolinium binds with anions such as phosphate, and the result is an insoluble precipitate that becomes

[a]Recommendations from American College of Radiology: *ACR Manual on Contrast Media*, Version 10.3, 2017, p 48.

deposited in different tissues with subsequent fibrotic reaction (Abraham et al., 2008; Collidge et al., 2007).

The ACR Committee on Drugs and Contrast Media (ACR Manual on Contrast Media, 2017) has concluded that patients considered to be at risk for NSF and who should have precontrast renal function testing include patients with a history of the following:

- Renal disease:
  Dialysis
  Severe or end-stage CKD (eGFR <30 mL/min/1.73 m^2) without dialysis
  AKI
  Solitary kidney
  Known kidney cancer
- Hypertension requiring medical therapy
- Diabetes mellitus

KEY POINTS: CONTRAST MEDIA

- People with type II diabetes with renal insufficiency on oral metformin biguanide hyperglycemic therapy are at risk for developing biguanide lactic acidosis after exposure to intravascular radiologic contrast media and should stop metformin the day before the procedure and restart 48 hours after if they have a normal or baseline serum creatinine.
- Patients at risk for adverse reaction to contrast include patients with previous adverse reaction, history of asthma, severe cardiac disease, renal insufficiency, dehydration, sickle cell anemia, anxiety, apprehension, hyperthyroidism, and presence of adrenal pheochromocytoma.
- Epinephrine can be administered IV in the dose of 0.01 mg/kg of 1:10,000 dilution or 0.1 mL/kg slowly into a running IV infusion of saline and can be repeated every 5 to 15 minutes as needed. If no IV access is available, the recommended intramuscular dose of epinephrine is 0.01 mg/kg of 1:1000 dilution (or 0.01 mL/kg to a maximum of 0.15 mg of 1:1000 if <30 kg; 0.3 mg if weight is >30 kg) injected intramuscularly in the lateral thigh.
- Patients at greatest risk for contrast-induced nephropathy are those with diabetes mellitus and dehydration.
- Steroids given to prevent adverse contrast agents should be given at least 6 hours before injection.

INTRAVENOUS UROGRAPHY

Once the mainstay of urologic imaging, the intravenous excretory urographic (IVU) study has almost been replaced by CT and MRI imaging. With the ability of new scanners to perform axial, sagittal, and coronal reconstruction of the upper tract urinary system, practically all of the data and information obtained by traditional IVU can be realized with CT. In addition, some parenchymal defects, cysts, and tumors can be better delineated with CT than IVU.

Technique

Bowel prep may help to visualize the entire ureters and upper collecting systems. Patients with chronic constipation may benefit most from complete bowel prep with clear liquids for 12 to 24 hours and an enema 2 hours before the procedure.

Before injection of contrast, a scout radiograph or KUB (kidneys, ureters, bladder) film is taken demonstrating the top of the kidneys and the entire pelvis to the pubic symphysis. This allows determination of adequate bowel prep, confirms correct positioning, and exposes kidney stones or bladder stones.

Contrast is injected as a bolus of 50 to 100 cc of contrast. The nephrogenic phase is captured with a radiograph immediately after injection. In the past, tomograms were used to look for parenchymal defects, but now CT or MRI imaging is preferred. A film is taken at 5 minutes and then additional films at 5-minute intervals until the question that prompted the IVU is answered. Abdominal compression may be used to better visualize the ureters. Occasionally oblique films are used to better define the course of the ureter in the bony pelvis and to precisely differentiate ureteral stones from pelvic calcifications.

Upright films may be helpful in certain situations. In the rare case of suspected symptomatic renal ptosis, IVU can be particularly helpful (Fig. 3.2). Supine films are compared with upright films to measure the degree of ptosis. Such a comparison cannot be made with MRI or CT imaging. In the case of calyceal stones or milk of calcium stones, layering of the contrast can be helpful to evaluate the anatomy of the calyx harboring the stones.

Postvoid films are obtained to evaluate the presence of outlet obstruction, prostate enlargement, and bladder-filling defects, including stones and urothelial cancers.

Indications

1. Demonstration of the renal collecting systems and ureters
2. Investigation of the level of ureteral obstruction
3. Intraoperative opacification of collecting system during extracorporeal shock wave lithotripsy or percutaneous access to the collecting system
4. Demonstration of renal function during emergent evaluation of unstable patients
5. Demonstration of renal and ureteral anatomy in special circumstances (e.g., ptosis, after transureteroureterostomy, and after urinary diversion)

PLAIN ABDOMINAL RADIOGRAPHY

The plain abdominal radiograph is a conventional radiography study, which is intended to display the KUB. The plain abdominal radiograph may be employed (1) as a primary study or (2) as a scout film in anticipation of contrast media. Plain films are widely used in the management of renal calculus disease. Plain radiography is also useful in evaluation of the trauma patient because it can be performed as a portable study in the trauma unit. Secondary findings on plain radiography such as rib fractures, fractures of the transverse processes of the vertebral bodies, and pelvic fractures may indicate serious associated urologic injuries.

Technique

An abdominal plain radiograph is obtained with the patient in the supine position, using an anterior to posterior exposure. The study typically includes that portion of the anatomy from the level of the diaphragm to the inferior pubic symphysis. It may occasionally be necessary to make two exposures to cover the desired anatomic field. Depending on the indication for the study oblique films are obtained to clarify the position of structures in relation to the urinary tract. If small bowel obstruction or free peritoneal air is suspected, upright films will be obtained.

Indications

1. Preliminary film in anticipation of contrast administration
2. Assessment of the presence of residual contrast from a previous imaging procedure
3. Pre- and post-treatment assessment of renal calculus disease
4. Assessment of the position of drains and stents
5. Adjunct to the investigation of blunt or penetrating trauma to the urinary tract

Limitations

Although plain film radiography is often used in the evaluation of renal colic, it is unreliable in the demonstration of calculus disease for a variety of reasons: (1) overlying stool and bowel gas may

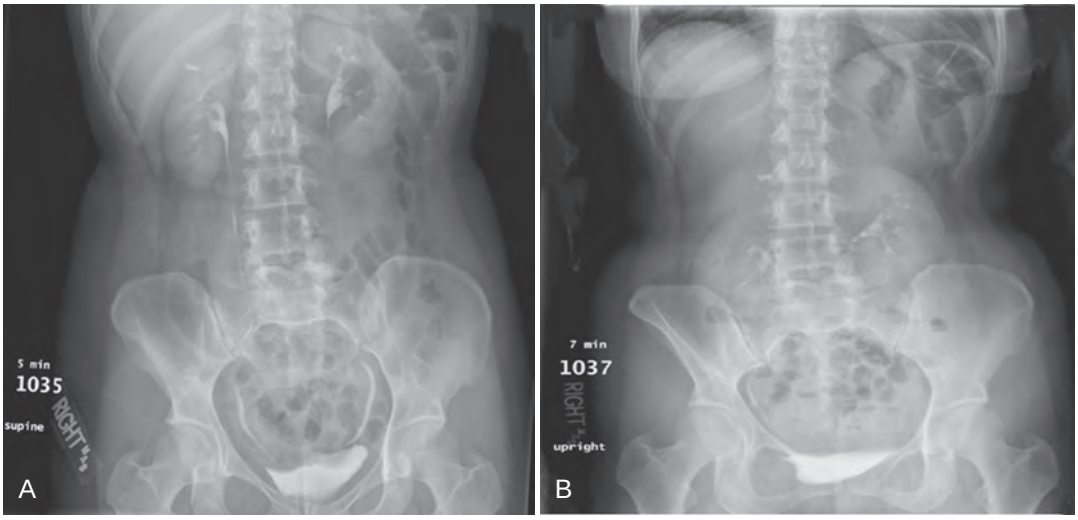


Fig. 3.2. Intravenous excretory urogram (IVU) in a 40-year-old woman with the complaint of a mobile mass in the right lower quadrant with standing associated with bilateral flank and back pain that resolved in the supine position. (A) Supine IVU shows kidneys in the normal position, with normal ureters and proximal collecting systems. (B) Standing film shows significant displacement of both kidneys with the right kidney moving onto the pelvis as described by the patient.

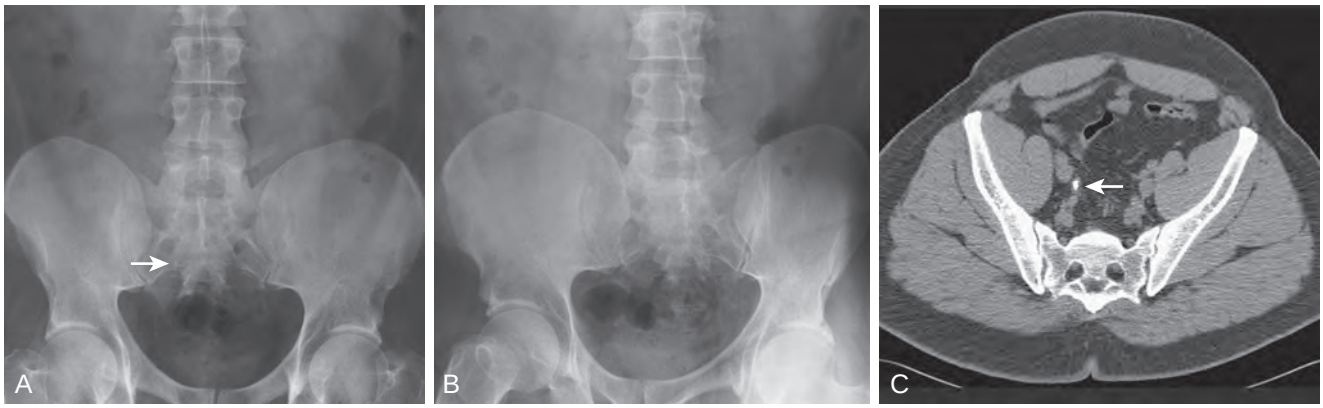


Fig. 3.3. (A) Right ureteral calculus *(arrow)* overlying the sacrum is difficult to visualize on the plain film. (B) The right posterior oblique study fails to confirm the location of the ureteral calculus. (C) CT confirms this 6-mm calculus in the right ureter at the level of the third sacral segment.

obscure small calculi; (2) stones may be obscured by other structures such as bones or ribs (Fig. 3.3); (3) calcifications in pelvic veins or vascular structures may be confused with ureteral calculi; and (4) stones that are poorly calcified or composed of uric acid may be radiolucent. Nevertheless, plain film radiography is valuable in assessing the suitability of a patient for extracorporeal shock wave lithotripsy because the ability to identify the stone on fluoroscopy is critical to targeting. Furthermore, a KUB is very cost effective for monitoring residual stone burden after treatment (Fig. 3.4). For complex pathology of the urinary tract, plain abdominal radiography has been supplanted by axial imaging. Plain radiography has a very limited role in evaluating soft tissue abnormalities of the urinary tract.

RETROGRADE PYELOGRAPHY

Retrograde pyelograms are performed to opacify the ureters and intrarenal collecting system by the retrograde injection of contrast media. Any contrast media that can be used for excretory urography is also acceptable for retrograde pyelography. Attempts should be made to sterilize the urine before retrograde pyelography because there is a risk of introducing bacteria into the upper urinary tracts or into the bloodstream. Although many studies are able to document the presence or absence of dilation of the ureter, retrograde pyelography has the unique ability to document the normalcy of the ureter distal to the level of obstruction and to better define the extent of the ureteral abnormality.

Technique

Retrograde pyelography usually is performed with the patient in the dorsal lithotomy position. An abdominal plain radiograph (scout film) is obtained to ensure that the patient is in the appropriate position to evaluate the entire ureter and intrarenal collecting system. Cystoscopy is performed and the ureteral orifice is identified.

Contrast may be injected through either a nonobstructing catheter or an obstructing catheter. Nonobstructing catheters include whistle-tip, spiral-tip, or open-ended catheters. Use of nonobstructing catheters allows passage of the catheter into the ureter and up to the collecting system, over a guidewire if necessary. Contrast then can be introduced directly into the upper collecting system and the ureters visualized by injection of contrast as the catheter is withdrawn.

The other commonly employed method is the use of an obstructing ureteral catheter such as a bulb-tip, cone-tip, or wedge-tip catheter. These catheters are inserted into the ureteral orifice and then pulled back against the orifice to effectively obstruct the ureter. Contrast is

then injected to opacify the ureter and intrarenal collecting system. Depending on the indication for the study, it is useful to dilute the contrast material (to 50% or less) with sterile fluid. This prevents subtle filling defects in the collecting system or ureter from being obscured. Care should be taken to evacuate air bubbles from the syringe and catheter before injection. Such air bubble artifacts could be mistaken for stones or tumors.

After air is expelled from the catheter into the bladder, the ureteral orifice is intubated. Contrast is injected slowly, usually requiring from 5 to 8 cc to completely opacify the ureter and intrarenal collecting system in adults (Fig. 3.5). More or less contrast may be required depending on the size of the patient and the capaciousness of the collecting system. Limited use of fluoroscopy while injecting helps prevent overdistension of the collecting system and reduces the risk of extravasation of contrast.

Historically, when a retrograde pyelogram consisted of a series of radiographs taken at intervals, it was important to document various stages of filling and emptying of the ureter and collecting systems. Because of peristalsis the entire ureter will often not be seen on any given static exposure or view. With current equipment, including tables that incorporate fluoroscopy, it is possible to evaluate the ureter during peristalsis in real time, thus reducing the need for static image documentation. Documentary still images or "spot films" may be saved for future comparison. Urologists interpret retrograde pyelograms in real time as they are performed.

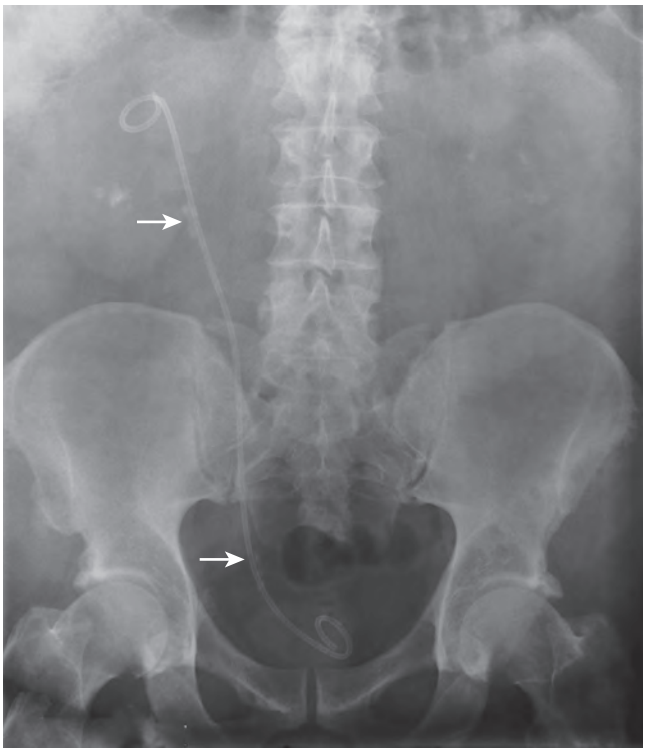


Fig. 3.4. KUB demonstrating residual stone fragments *(arrows)* adjacent to a right ureteral stent 1 week after right extracorporeal shock wave lithotripsy.

Indications

1. Evaluation of congenital ureteral obstruction
2. Evaluation of acquired ureteral obstruction
3. Elucidation of filling defects and deformities of the ureters or intrarenal collecting systems
4. Opacification or distention of collecting system to facilitate percutaneous access
5. In conjunction with ureteroscopy or stent placement
6. Evaluation of hematuria
7. Surveillance of transitional cell carcinoma
8. In the evaluation of traumatic or iatrogenic injury to the ureter or collecting system

Limitations

Retrograde pyelography may be difficult in cases in which the bladder is involved with diffuse inflammation or neoplastic changes, especially when bleeding is present. Identification of the ureteral orifices may be facilitated by the intravenous injection of indigotindisulfonate sodium or methylene blue in such cases. Changes associated with bladder outlet obstruction may result in angulation of the intramural ureters. This may make cannulation with an obstructing catheter difficult. Attempts to cannulate the ureteral orifice may result in trauma to the ureteral orifice and extravasation of contrast material into the bladder wall. The potential for damage to the intramural ureter must be weighed against the potential information to be obtained by the retrograde pyelogram.

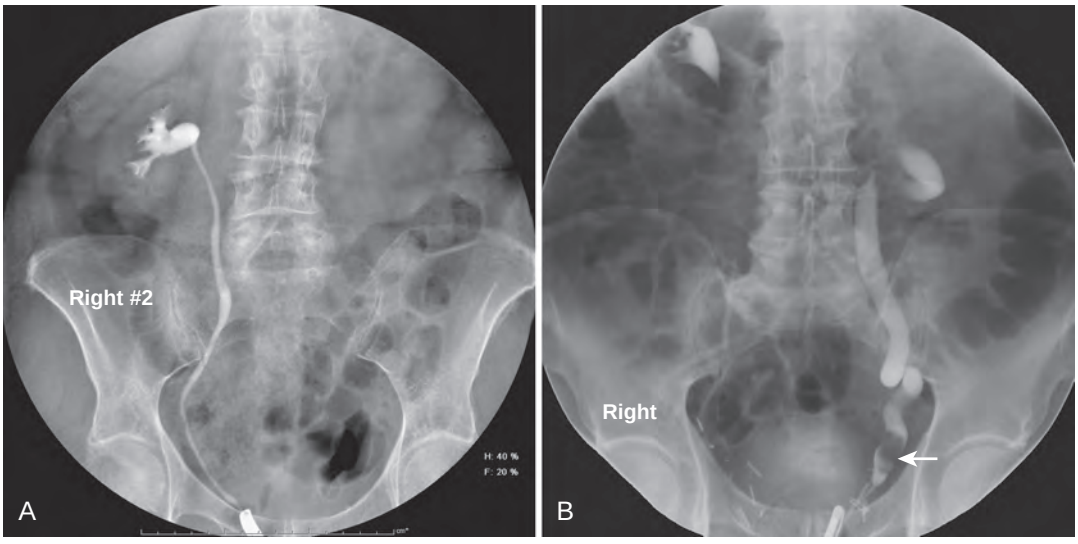


Fig. 3.5. (A) Right retrograde pyelogram performed using an 8-Fr cone-tipped ureteral catheter and dilute contrast material. The ureter and intrarenal collecting system are normal. (B) Left retrograde pyelogram using an 8-Fr cone-tipped ureteral catheter. A filling defect in the left distal ureter *(arrow)* is a low-grade transitional cell carcinoma. The ureter demonstrates dilation, elongation, and tortuosity, the hallmarks of chronic obstruction.

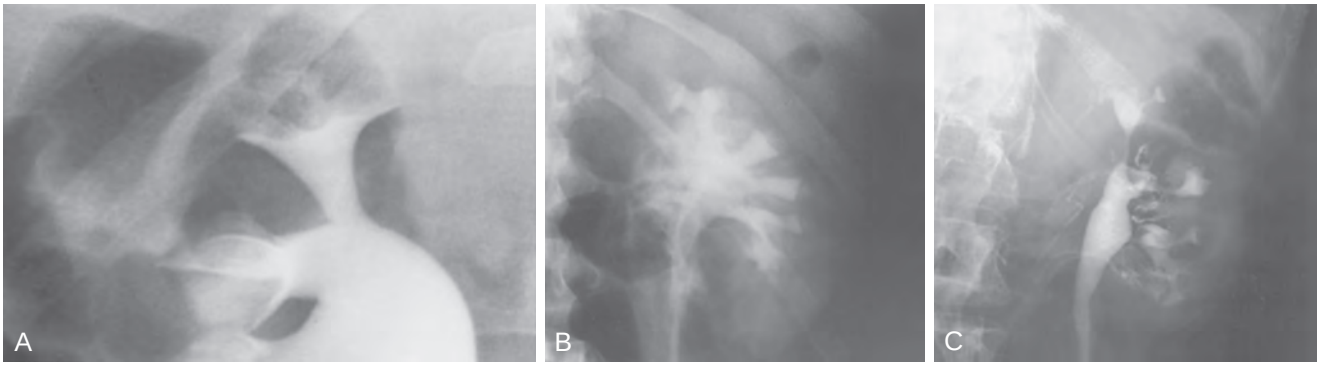


Fig. 3.6. Patterns of backflow during retrograde pyelography. (A) Pyelotubular backflow. (B) Pyelosinus backflow. (C) Pyelolymphatic backflow.

Complications

Backflow occurs during retrograde pyelography when contrast is injected under pressure and escapes the collecting system. Contrast may escape the collecting system by one of four routes: **Pyelotubular backflow** occurs when contrast fills the distal collecting ducts producing opacification of the medullary pyramids (Fig. 3.6A). **Pyelosinus backflow** occurs when a tear in the calyces at the fornix allows contrast to leak into the renal sinus (Fig. 3.6B). **Pyelolymphatic backflow** is characterized by opacification of the renal lymphatic channels (Fig. 3.6C). **Pyelovenous backflow** is seen when contrast enters the venous system, resulting in visualization of the renal vein.

Although backflow does not usually cause measurable clinical harm, the potential implications of backflow include (1) introduction of bacteria from infected urine into the vascular system and (2) the absorption of contrast media, which could result in adverse reactions in susceptible patients. It has been demonstrated that the risk of significant urinary tract infection is only about 10% and the risk of sepsis is low when antibiotic prophylaxis therapy is administered before endoscopic procedures (including retrograde pyelography) (Christiano et al., 2000). Although contrast reactions are rare with retrograde pyelography, they have been reported (Johenning, 1980; Weese et al., 1993). In patients with documented severe contrast allergy, prophylactic pretreatment may be appropriate. In those patients considered at risk, care should be taken to inject under low pressures to minimize the probability of backflow and absorption of the contrast into the vasculature system.

LOOPOGRAPHY

Loopography is a diagnostic procedure performed in patients who have undergone urinary diversion. Historically the term "loopogram" has been associated with ileal conduit diversion but may be used in reference to any bowel segment serving as a urinary conduit. When imaging patients with a continent diversion involving a reservoir or neobladder, "pouch-o-gram" would be more accurately descriptive. Because an ileal conduit urinary diversion usually has freely refluxing ureterointestinal anastomoses, the ureters and upper collecting systems may be visualized. In other forms of diversion, the ureterointestinal anastomoses may be purposely nonrefluxing. In such circumstances, when opacification of the upper urinary tract is desirable, antegrade ureteral imaging such as IVU, CT, or MR urography or antegrade nephrostography may be required. When the patient has compromised renal function or is allergic to iodinated contrast material, loopogram can be performed with a low risk of systemic absorption (Hudson et al., 1981).

Technique

The patient is positioned supine. An abdominal plain radiograph is obtained before the introduction of contrast material (Fig. 3.7A). A commonly employed technique is to insert a small-gauge catheter into the ostomy of the loop, advancing it just proximal to the abdominal wall fascia. The balloon on such a catheter can then be inflated to 5 to 10 cc with sterile water. By gently introducing contrast through the catheter, the loop can be distended, usually producing bilateral reflux into the upper tracts. Oblique films should be obtained to evaluate the entire length of the loop (see Fig. 3.7). Because of the angle at which many loops are constructed, a traditional anteroposterior (AP) view often shows a foreshortened loop and could miss a substantial pathology. A drain film should be obtained (see Fig. 3.7). This may demonstrate whether there is obstruction of the conduit.

Indications

1. Evaluation of infection, hematuria, renal insufficiency, or pain after urinary diversion
2. Surveillance of upper urinary tract for obstruction
3. Surveillance of upper urinary tract for urothelial neoplasia
4. Evaluation of the integrity of the intestinal segment or reservoir

RETROGRADE URETHROGRAPHY

A retrograde urethrogram is a study meant to evaluate the anterior and posterior urethra. Retrograde urethrography may be particularly beneficial in demonstrating the total length of a urethral stricture, which cannot be negotiated by cystoscopy. Retrograde urethrography also demonstrates the anatomy of the urethra distal to a stricture, which may not be assessable by voiding cystourethrography. Retrograde urethrography may be performed in the office or in the operating room before performing visual internal urethrotomy or formal urethroplasty.

Technique

A plain film radiograph is obtained before injection of contrast. The patient usually is positioned slightly obliquely to allow evaluation of the full length of urethra. The penis is placed on slight tension. A small catheter may be inserted into the fossa navicularis with the balloon inflated to 2 cc with sterile water. Contrast then is introduced via a catheter-tipped syringe. Alternatively, a penile clamp (e.g., Brodney clamp) may be used to occlude the urethra around the catheter (Fig. 3.8).

Indications

1. Evaluation of urethral stricture disease
   a. Location of stricture
   b. Length of stricture
2. Assessment for foreign bodies
3. Evaluation of penile or urethral penetrating trauma
4. Evaluation of traumatic gross hematuria

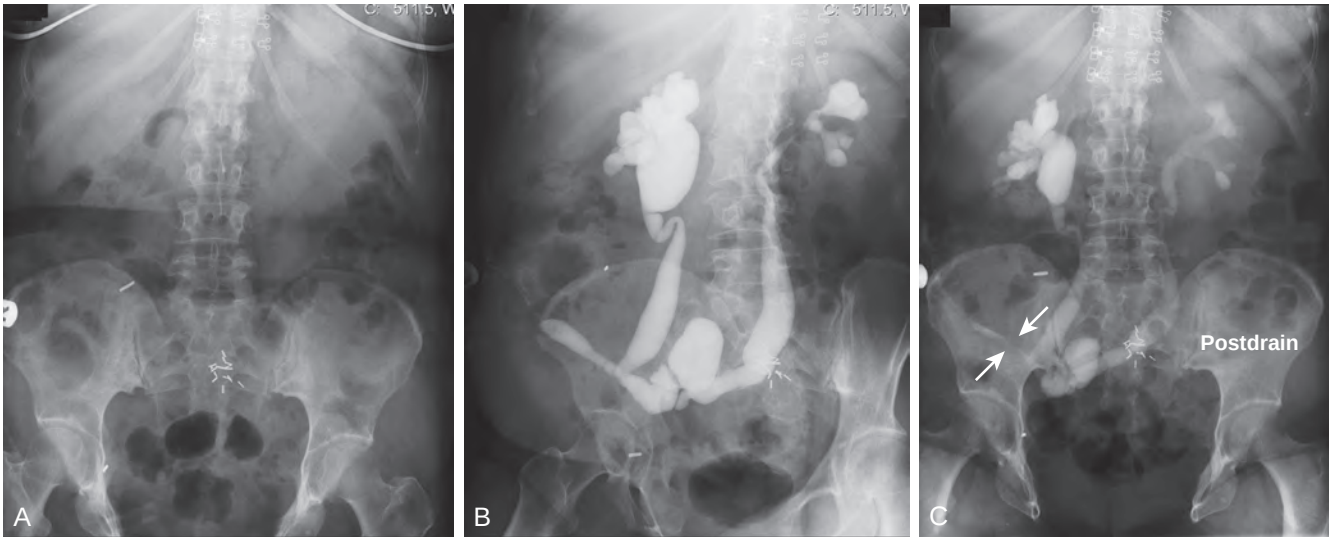


Fig. 3.7. Loopogram in a patient with epispadius/exstrophy and ileal conduit urinary diversion. The plain film (A) shows wide diastasis of the pubic symphysis. After contrast administration via a catheter placed in the ileal conduit, free reflux of both ureterointestinal anastomoses is demonstrated (B). (C) A postdrain radiograph demonstrates persistent dilation of the proximal loop indicating mechanical obstruction of the conduit *(arrows).*

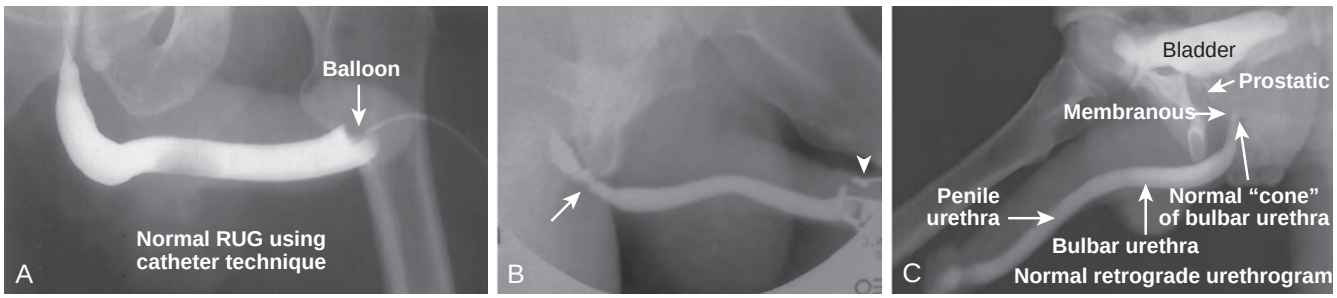


Fig. 3.8. Normal retrograde urethrogram demonstrating (A) the balloon technique for retrograde urethrography, (B) Brodney clamp *(arrowhead)* technique; note the bulbar urethral stricture *(arrow)*, and (C) normal structures of the male urethra.

STATIC CYSTOGRAPHY

Static cystography is employed primarily to evaluate the structural integrity of the bladder. The shape and contour of the bladder may give information about neurogenic dysfunction or bladder outlet obstruction. Filling defects such as tumors and stones may be appreciated.

Technique

The patient is positioned supine. A plain radiograph is performed to evaluate for stones and residual contrast and to confirm position and technique. The bladder is filled under gravity with 200 to 400 cc of contrast depending on bladder size and patient comfort. Adequate filling is important to demonstrate intravesical pathology or bladder rupture. Oblique films should be obtained because posterior diverticula or fistulae may be obscured by the full bladder. A postdrainage film completes the study (Fig. 3.9).

Indications

1. Evaluation of intravesical pathology
2. Evaluation of bladder diverticula
3. Evaluation of inguinal hernia involving the bladder
4. Evaluation of colovesical or vesicovaginal fistulae
5. Evaluation of bladder or anastomotic integrity after surgical procedure
6. Evaluation of blunt or penetrating trauma to the bladder

Limitations

Abdominal and pelvic CT are so commonly used in the evaluation of blunt or penetrating trauma to the abdomen that CT cystography is often performed in conjunction with the trauma evaluation. However, studies have shown that conventional static cystography is as sensitive as CT cystography in detecting bladder rupture (Broghammer and Wessells, 2008; Quagliano et al., 2006).

VOIDING CYSTOURETHROGRAM

A voiding cystourethrogram (VCUG) is performed to evaluate the anatomy and physiology of the bladder and urethra. The study provides valuable information regarding the posterior urethra in pediatric patients. VCUG has long been used to demonstrate vesicoureteral reflux.

Technique

The study may be performed with the patient supine or in a semiupright position using a table capable of bringing the patient into the full upright position. A preliminary pelvic plain radiograph is obtained. In children, a 5- to 8-Fr feeding tube is used to fill the bladder to the appropriate volume. Patient comfort should be taken into account when determining the appropriate volume. In the adult population a standard catheter may be placed and the bladder filled

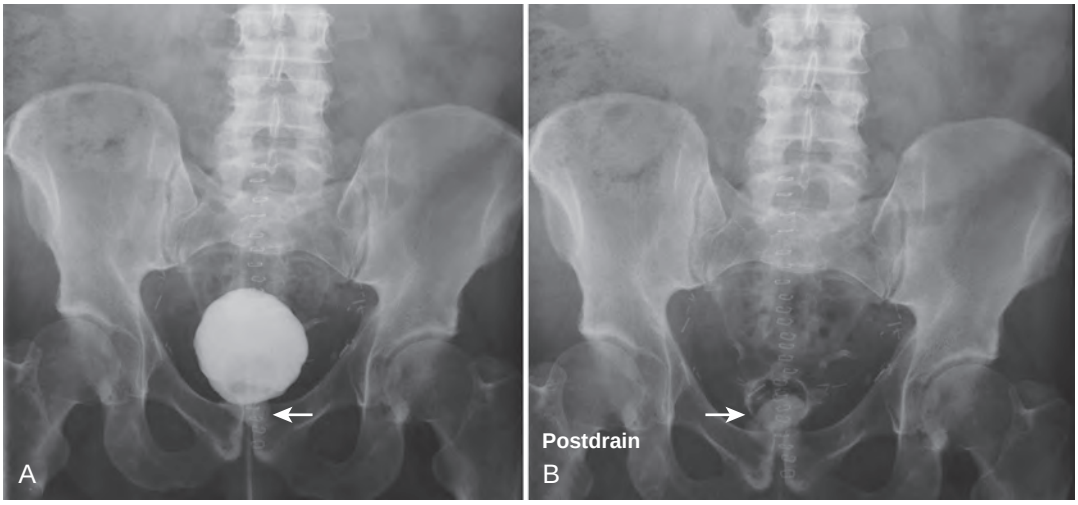


Fig. 3.9. The patient has undergone radical retropubic prostatectomy. (A) During bladder filling, contrast is seen adjacent to the vesicoureteral anastomoses *(arrow).* (B) The postdrain film clearly demonstrates a collection of extravasated contrast *(arrow).*

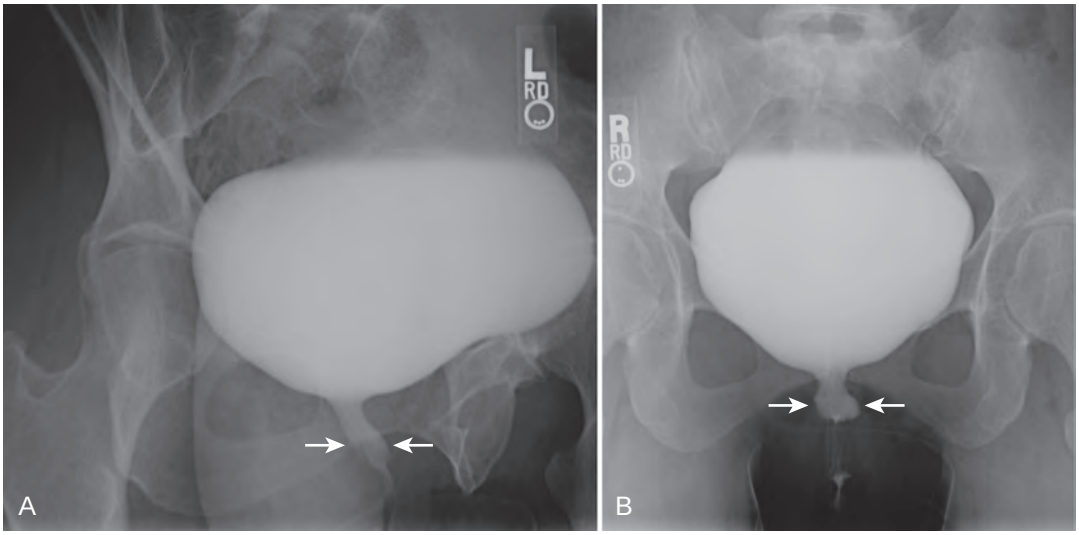


Fig. 3.10. A voiding cystourethrogram performed for the evaluation of recurrent urinary tract infection in this female patient. (A) An oblique film during voiding demonstrates thickening of the midureteral profile *(arrows).* (B) After interruption of voiding a ureteral diverticulum is clearly visible extending posteriorly and to the left of the midline *(arrows).*

to 200 to 400 cc. The catheter is removed and a film is obtained. During voiding, AP and oblique films are obtained. The bladder neck and urethra may be evaluated by fluoroscopy during voiding. Bilateral oblique views may demonstrate low-grade reflux, which cannot be appreciated on the AP film. In addition, oblique films demonstrate bladder or urethral diverticula, which are not always visible in the straight AP projection. Postvoiding films should be performed (Fig. 3.10).

Indications

1. Evaluation of structural and functional bladder outlet obstruction
2. Evaluation of reflux
3. Evaluation of the urethra in males and females

Limitations

This study requires bladder filling using a catheter. This may be traumatic in children and difficult in some patients with anatomic abnormalities of the urethra or bladder neck. Filling of the bladder may stimulate bladder spasms at low volumes, and some patients are unable to hold adequate volumes for investigation. **Bladder filling in patients with spinal cord injuries higher than T6 may precipitate autonomic dysreflexia** (Barbaric, 1976; Fleischman and Shah, 1977; Linsenmeyer et al., 1996).

NUCLEAR SCINTIGRAPHY

Radionuclide imaging is the procedure of choice to evaluate renal obstruction and function. It is very sensitive to changes that induce focal or global changes in kidney function. Because neither gadolinium or iodinated intravenous contrast agents are used, scintigraphy does not damage the kidney, has no lingering toxicity, results in minimal absorbed radiation, and is free from allergic reactions. Compared with other diagnostic imaging studies such as retrograde pyelogram, renal scintigraphy is noninvasive, has minimal risk and minimal discomfort, and allows determination of the function of the kidney.

Once the agent is intravenously injected, gamma scintillation cameras measure radiation emitted from the radioisotope and digital

work stations gather, process, and display the information. There is an extensive list of radiopharmaceuticals used for renal scintigraphy. This section is limited to those agents most commonly used in urologic practice.

Technetium^{99m}–diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) is primarily a glomerular filtration agent (Gates, 2004; Peters, 1998). It is most useful for evaluation of obstruction and renal function. Because it is excreted through the kidney and dependent on GFR, it is less useful in patients with renal failure because impaired GFR may limit adequate evaluation of the collecting system and ureters. It is readily available and relatively inexpensive (Klopper et al., 1972).

Technetium^{99m}-dimercaptosuccinic acid (^{99m}Tc-DMSA) is cleared by filtration and secretion.

^{99m}Tc-DMSA localizes to the renal cortex with very little accumulation in the renal papilla and medulla (Lin et al., 1974). Therefore it is most useful for identifying cortical defects or ectopic or abhorrent kidneys. With these properties, ^{99m}Tc-DMSA can distinguish a benign functioning abnormality in the kidney from a space-occupying malignant lesion, which would not have normal renal function. No valuable information on the ureter or collecting system can be obtained with ^{99m}Tc-DMSA but remains a standard for renal cortical imaging.

Technetium^{99m}-mercaptoacetyltriglycine (^{99m}Tc-MAG3) is an excellent agent for imaging because of its photon emission, 6-hour half-life, and ease of preparation. It is cleared mainly by tubular secretion (Fritzberg et al., 1986). A small amount, approximately 10%, of MAG3 is excreted by extrarenal means, and most of this is hepatobiliary excretion (Eshima et al., 1990; Itoh, 2001). Because it is bound extensively to protein in plasma, it is limited in its ability to measure GFR but is an excellent choice for patients with renal insufficiency and urinary obstruction. The tracer is well suited for evaluation of renal function and diuretic scintigraphy. It is also an excellent tracer to evaluate renal plasma flow.

Diuretic Scintigraphy

Nuclear medicine imaging plays a crucial role unmet by CT, MRI, or ultrasound in the diagnosis of upper tract obstruction, and its unique characteristics provide noninvasive information regarding dynamic renal function. The diuretic renal scan using ^{99m}Tc-MAG3 can provide differential renal function and clearance time comparing right and left kidneys, which is pivotal in patient management. The initial phase is the flow phase, in which 2-second images are gathered for 2 minutes and then 1-second images for 60 seconds. The flow phase shows renal uptake, background clearance, and abnormal vascular lesions, which may indicate arteriovenous malformations, tumors, or active bleeding. In the second phase, the renal phase, time to peak uptake is typically between 2 and 4 minutes. The renal phase is the most sensitive indicator of renal dysfunction; 1-minute images are taken for 30 minutes. In the final phase, the excretory phase, 1-minute images are taken for 30 minutes. **A diuretic (usually furosemide 0.5 mg/kg) is administered when maximum collecting system activity is visualized. The $T_{1/2}$ is the time it takes for collecting system activity to decrease by 50% from that at the time of diuretic administration. This is highly technician dependent because the diuretic must be given when the collecting system is displaying maximum activity. Transit time through the collecting system in less than 10 minutes is consistent with a normal, nonobstructed collecting system. $T_{1/2}$ of 10 to 20 minutes shows mild to moderate delay and may be a mechanical obstruction. The patient's perception of pain after diuretic administration can be helpful for the treating urologist to consider when planning surgery in the patient with middle to moderate obstruction. A $T_{1/2}$ of greater than 20 minutes is consistent with a high-grade obstruction. The level of obstruction usually can be determined as can abnormalities such as ureteral duplication** (Ell and Gambhir, 2004). A normal renal scan is shown in Fig. 3.11.

Hepatobiliary excretion can cause false-positive readings if the area of intestinal activity or gallbladder activity is included in the area of interrogations during the study (Fig. 3.12).

The diuretic renal scan is another imaging study in which communication with the interpreting physician is vital for correct performance of the test as well as appropriate interpretation. For example, there are times when patients with unilateral or bilateral ureteral stents are sent for diuretic scintigraphy to determine differential renal function. If a bladder catheter is not placed and is open to drainage during the diuretic renal scan, the radiopharmaceutical excreted from the healthy kidney may wash up into or back flow via the ureteral stent into the stented kidney, giving the false-positive appearance to have more function than is physiologically present.

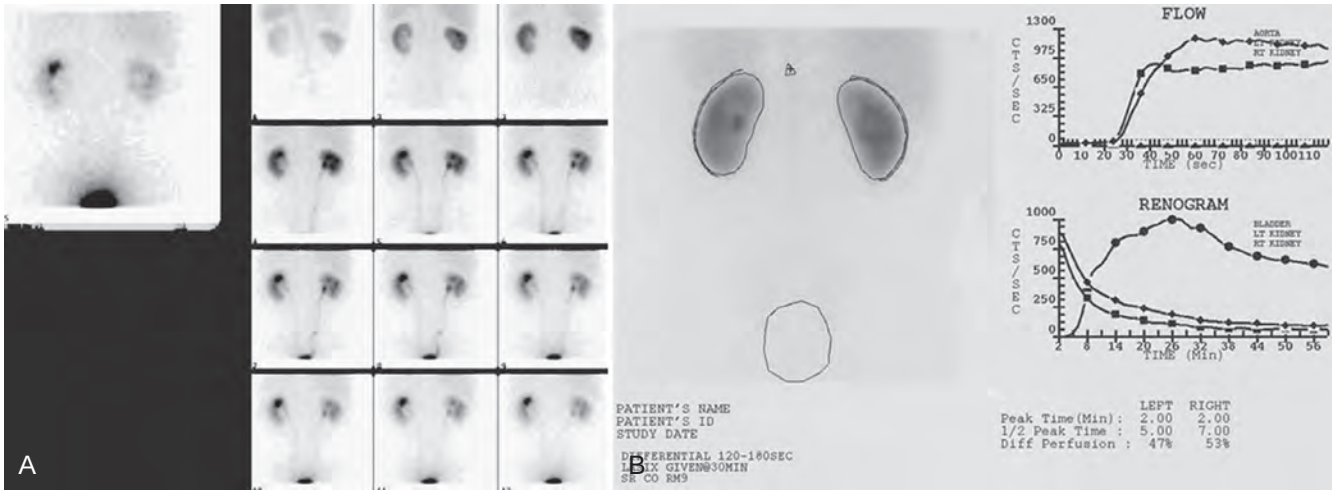


Fig. 3.11. (A) Technetium^{99m}-mercaptoacetyltriglycine (^{99m}Tc-MAG3) perfusion images demonstrate normal, prompt, symmetric blood flow to both kidneys. (B) Perfusion time-activity curves demonstrating essentially symmetric flow to both kidneys. Note the rising curve typical of ^{99m}Tc-MAG3 flow studies. Dynamic function images demonstrate good uptake of tracer by both kidneys and prompt visualization of the collecting systems. This renogram demonstrates prompt peaking of activity in both kidneys. The downslope represents prompt drainage of activity from the kidneys. Printout of quantitative data shows the differential renal function to be 47% on the left, 53% on the right. The normal half-life for drainage is less than 20 minutes when ^{99m}Tc-MAG3 is used. The $T_{1/2}$ is 5 min on the left and 7 min on the right, consistent with both kidneys being unobstructed.

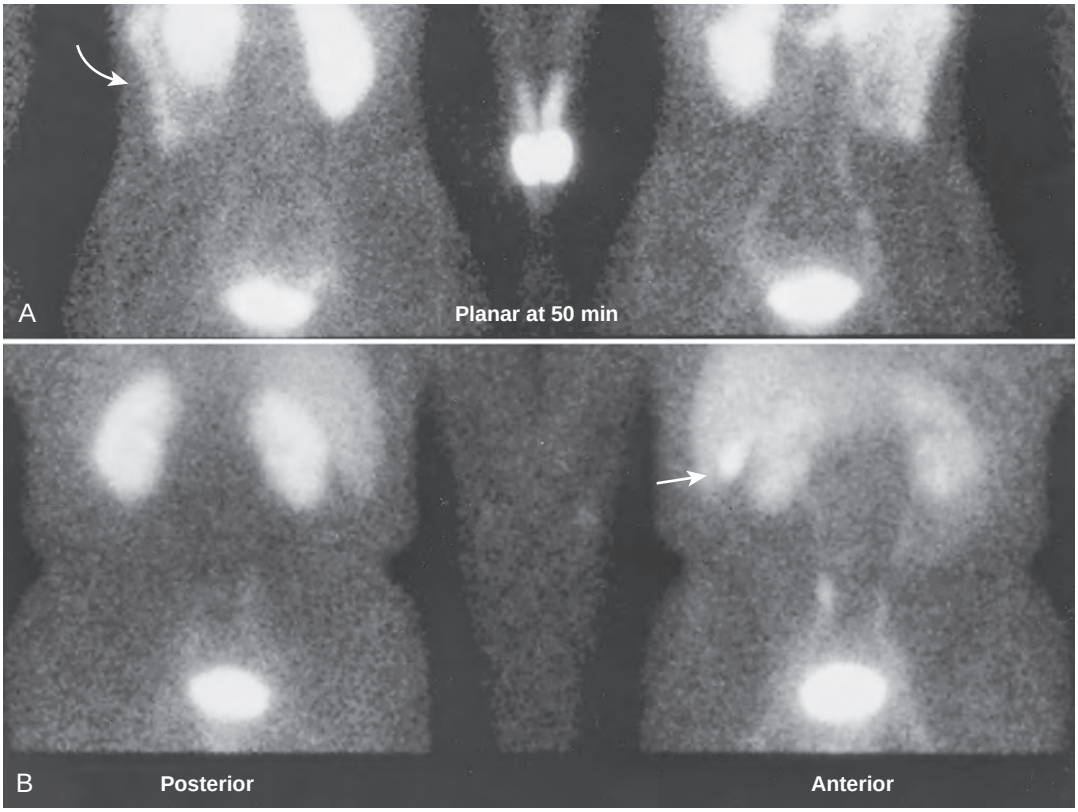


Fig. 3.12. Delayed static images in the posterior and anterior projections demonstrate intestinal activity (*arrow* in A) and gallbladder activity (*arrow* in B), reflecting a normal mode of excretion of ^{99m}Tc-MAG3. Gallbladder activity, in particular, can cause false-positive interpretation when it overlies activity in the renal collecting system or is inappropriately included in the area of interrogation. Liver activity is variable and tends to be more pronounced in children and patients with renal insufficiency.

This false-positive test may lead to inappropriately reconstructing a kidney that has little or insufficient function.

Nuclear Medicine in Urologic Oncology

Whole-Body Bone Scan

Conventional radionuclide imaging in urologic malignancy has long been the standard for detecting bone metastasis. The whole-body bone scan, or skeletal scintigraphy, is the most sensitive method for detecting bone metastasis (Narayan et al., 1988). A "positive" bone scan is not specific for cancer and may require plain film radiography, CT, or MRI to confirm as well as correlation with prior history of bone fractures, trauma, surgery, or arthritis. In patients with diffuse metastatic bone involvement, the bone scan can be mistaken for normal because there is uniformly increased uptake in the bony structures (Kim et al., 1991).

Positron Emission Tomography

One of the most rapidly changing areas of imaging in urologic oncology is in the use of PET/CT and PET/MRI. Depending on the radiotracer used, PET offers diagnostic information based on glucose, choline, or amino acid metabolism and has been applied to imaging tumor cell proliferation and tissue hypoxia in urologic malignancies. PET with 2-[^{18}F]fluoro-2-deoxy-D-glucose (^{18}F-FDG), available since the late 1990s, exploits the increased use and high uptake of glucose by malignant cells and provides new imaging opportunities in urology. The radiopharmaceutical most commonly used for PET in oncology is ^{18}F-FDG, an analog of glucose that is preferentially taken up and trapped inside malignant cells. For more than a decade, integrated PET/CT, in which a full-ring-detector clinical PET scanner and multidetector-row helical CT scanner are combined, has made it possible to acquire metabolic and anatomic imaging data using a single device in a single diagnostic session and provides precise anatomic localization of suspicious areas of increased ^{18}F-FDG uptake.

In urologic oncology, the use of ^{18}F-FDG has been limited by low tumor uptake and physiologic excretion of ^{18}F-FDG through the urinary system masking ^{18}F-FDG uptake by the primary urologic carcinoma. **The diagnostic performance of FDG-PET is hampered by the renal excretion of FDG and by the low metabolic activity often seen in tumors such as prostate cancer. However, new PET tracers, including radiolabeled choline, acetate, and others may offer alternatives with improved diagnostic abilities. There is consistent evidence that FDG-PET provides important diagnostic information in detecting metastatic and recurrent testicular germ cell tumors, and it may offer additional information in the staging and restaging of bladder and renal cancer** (Kitajima et al., 2014, 2016; Powles et al., 2011; Rioja et al., 2010).

Molecular imaging with PET is showing promise to individualize the surgical and medical care of urologic oncology patients. PET provides unique insights into molecular pathways of diseases. PET using [F-18]-fluorodeoxyglucose (FDG) has gained increasing acceptance for the diagnosis, staging, and treatment monitoring of some genitourinary (GU) tumor types.

Kidney Cancer

Contrast-enhanced CT provides accurate information for detection and staging of renal cell carcinoma (RCC). Extrarenal metastatic disease is more easily detected by ^{18}F-FDG PET/CT and is useful for staging, restaging, and treatment of advanced RCC. A meta-analysis of 14 studies included 517 patients, demonstrated a pooled sensitivity of ^{18}F-FDG PET or PET/CT to be 79% for intrarenal tumors and 84%

for extrarenal metastases, and that ^{18}F-FDG PET/CT increased the pooled sensitivity to 91% (Ferda et al., 2013; Wang et al., 2012). Other investigators have evaluated the clinical impact of ^{18}F-FDG PET/CT for restaging renal cancer in 104 patients after surgery and demonstrated that the sensitivity and specificity were 74% and 80%, respectively (Alongi et al., 2016).

Bladder Cancer

For localized bladder cancer, ^{18}F-FDG PET has not been widely used because its physiologic activity excreted through the urinary system interferes with visualization of the primary bladder cancer and locoregional lymph nodes (LNs). A meta-analysis showed that the sensitivity and specificity of ^{18}F-FDG PET/CT for detecting bladder cancer was 80% (95% CI 71%–87%) and 84% (95% CI 69%–93%), respectively (Wang et al., 2014).

In patients with metastatic disease ^{18}F-FDG PET/CT is useful for staging and restaging (detection of metastatic lesions) of bladder cancer. A systematic review and meta-analysis of 6 studies involving 236 patients showed that the pooled sensitivity and specificity for staging and restaging (metastatic lesions) were 82% (95% CI 0.72–0.89) and 89% (95% CI 0.81–0.95), respectively (Lu et al., 2012).

Prostate Cancer

Many different PET tracers are being actively investigated for use in PET/CT imaging for prostate cancer. It is well known that the ability of ^{18}F-FDG PET to detect cancer is based on increased expression of cellular membrane glucose transporter 1 (GLUT1) and enhanced hexokinase II enzyme activity within tumor cells. Preclinical studies have examined the expression of GLUT1 in prostate cancer cell lines and found that it is higher in those that are poorly differentiated in comparison with well-differentiated hormone-sensitive cell lines (Jadvar et al., 2005). This suggests that GLUT1 transporter expression increases with increasing disease grade and may explain the higher ^{18}F-FDG accumulation in castration-resistant than in castration-sensitive tumors and the modulatory effect of androgen on the glucose metabolism of castration-sensitive tumors.

^{18}F-FDG PET/CT is of limited value for detection and localization of primary prostate cancer and initial staging of disease because most primary tumors are slow growing, well differentiated, multiple, and small, with tumor uptake levels that can overlap with those of normal tissue, prostatitis, or benign prostatic hyperplasia (BPH).

^{11}C-choline and ^{18}F-fluorocholine are well-established tracers routinely employed at some PET centers for imaging of prostate cancer. Focal choline uptake in the prostate could arouse suspicion of prostate cancer, but nonmalignant causes, such as high-grade prostatic intraepithelial neoplasia, prostatitis, BPH, and normal tissue, also can be sources of false-positive focal activity (Reske et al., 2006).

In the largest preoperative series (n = 210) of intermediate- and high-risk patients who had undergone radical prostatectomy (RP) with surgical LN dissection, the sensitivity and specificity for detection of pelvic LN metastases were 73% and 88%, with a node-based sensitivity and specificity of 56% and 94%, respectively (Poulsen et al., 2012).

Choline PET/CT is a useful modality for detection of bone metastasis. In a patient-based analysis of patients with prostate-specific antigen (PSA) progression after primary treatment, comparing ^{11}C-choline PET/CT and bone scintigraphy for detection of bone metastasis, ^{11}C-choline PET/CT had better sensitivity and specificity (Picchio et al., 2012). Choline PET/CT can be useful in restaging of biochemically recurrent prostate cancer, particularly when the PSA level becomes significantly elevated. Many reports have discussed the usefulness of choline PET/CT for detecting sites of recurrence in patients with PSA failure, and choline PET/CT is employed routinely for this purpose at a number of PET centers (Picchio et al., 2012).

^{11}C-acetate PET/CT has also been used for identification of recurrent prostate cancer in the setting of PSA failure, with a reported sensitivity of 59% to 83% (Kitajima et al., 2014).

PET with ^{18}F-sodium fluoride (^{18}F-NaF) is a highly sensitive radiotracer for skeletal metastases whose uptake reflects the increased regional blood flow, and bone turnover in malignant bone lesions has been reported to be more sensitive for detection of skeletal metastases than bone scintigraphy (Even-Sapir et al., 2006). The combined administration of ^{18}F-NaF and ^{18}F-FDG in a single PET/CT scan for cancer detection has been advocated for detection of extraskeletal and skeletal lesions. It has been reported that ^{18}F-NaF/FDG PET/CT is superior to whole-body MRI and bone scintigraphy for evaluating the extent of skeletal disease (Minamimoto et al., 2015).

Prostate-specific membrane antigen (PSMA) has been used as a relevant target for imaging of prostate cancer. PSMA is a cell-surface protein expressed at higher levels in prostate carcinoma tissue than in other tissues, and its expression is associated with tumor aggressiveness, androgen independence, metastatic disease, and disease recurrence. Mainly available in Europe, PSMA-targeting ligands have been labeled with ^{68}Ga for PET imaging, and this approach shows some promise for detection of prostate carcinoma recurrence. The use of ^{68}Ga-PSMA PET/CT in 248 patients (PSA 0.2–59.4 ng/mL, median 1.99 ng/mL) treated with RP demonstrated that the patient-based detection rate was 89.5%; the detection rates for PSA levels of ≥2, 1 to <2, 0.5 to <1, and 0.2 to <0.5 ng/mL were 96.8%, 93.0%, 72.7%, and 57.9%, respectively. ^{68}Ga-PSMA PET/CT reveals a high degree of positivity within the clinically important range of low PSA values (<0.5 ng/mL), which in many cases can substantially influence further clinical management (Eiber et al., 2015). It has been demonstrated that ^{68}Ga-PSMA PET/CT may be superior to ^{18}F-choline PET/CT and conventional imaging modalities (bone scintigraphy and contrast-enhanced CT of the chest, abdomen, and pelvis) or identification of disease recurrence in the setting of biochemical failure (Morigi et al., 2015). Fig. 3.13 shows different PET images.

Adrenal Cancer

Malignant adrenal disease tends to have higher ^{18}F-FDG uptake compared with benign adrenal lesions. A meta-analysis, including 21 selected studies with a total of 1391 lesions (824 benign, 567 malignant) in 1217 patients revealed a pooled sensitivity of 97% (95% CI 93%–98%) and specificity of 91% (95% CI 87%–94%) of ^{18}F-FDG PET/CT (SUV_{max} or standard uptake ratio) for differentiating between malignant and benign adrenal disease (Boland et al., 2011). A multicenter study demonstrated that ^{18}F-FDG PET/CT showed the better diagnostic accuracy of diagnosing primary adrenal malignancy (adrenocortical carcinoma, malignant pheochromocytoma, neuroblastoma, and lymphoma) than contrast-enhanced CT (Cistaro et al., 2015). The diagnostic performance of ^{18}F-FDG PET/CT for differentiating metastatic adrenal tumors from adrenal adenoma is high (sensitivity, specificity, and accuracy are 82%, 92%, and 90%) as well as adrenal protocol CT (unenhanced early and delayed contrast-enhanced CT) and, moreover, the combination of ^{18}F-FDG PET/CT and adrenal protocol CT can improve the ^{18}F-FDG PET/CT or adrenal protocol CT diagnostic accuracy for differentiation of metastatic adrenal tumors from adrenal adenoma, reducing false-positive cases (Ardito et al., 2015; Park et al., 2014).

Testis Cancer

^{18}F-FDG PET/CT is useful for initial staging of testicular cancer and determining the viability of residual masses after completion of treatment, especially in patients with seminoma. The clinical impact of ^{18}F-FDG PET/CT for staging and restaging of testicular tumors was evaluated in 51 cases of seminoma and 70 cases of nonseminoma. PET/CT showed good sensitivity and specificity for detection of seminoma lesions (92% and 84%, respectively), but its sensitivity was lower for nonseminoma forms (77% and 95%, respectively); it influenced the clinical management of 47 out of 51 (92%) seminomas and 59 out of 70 (84%) nonseminomas (Ambrosini et al., 2014). A meta-analysis including four selected studies with a total of 130 patients evaluated the diagnostic accuracy of ^{18}F-FDG PET/CT for prediction of viable residual tumors after chemotherapy in patients with metastatic seminoma and demonstrated that it was superior to CT for determining tumor size and predicting tumor viability: sensitivity was 72% versus 63%, specificity was 92% versus 59%, positive predictive value (PPV) was 70% versus 28%, and negative

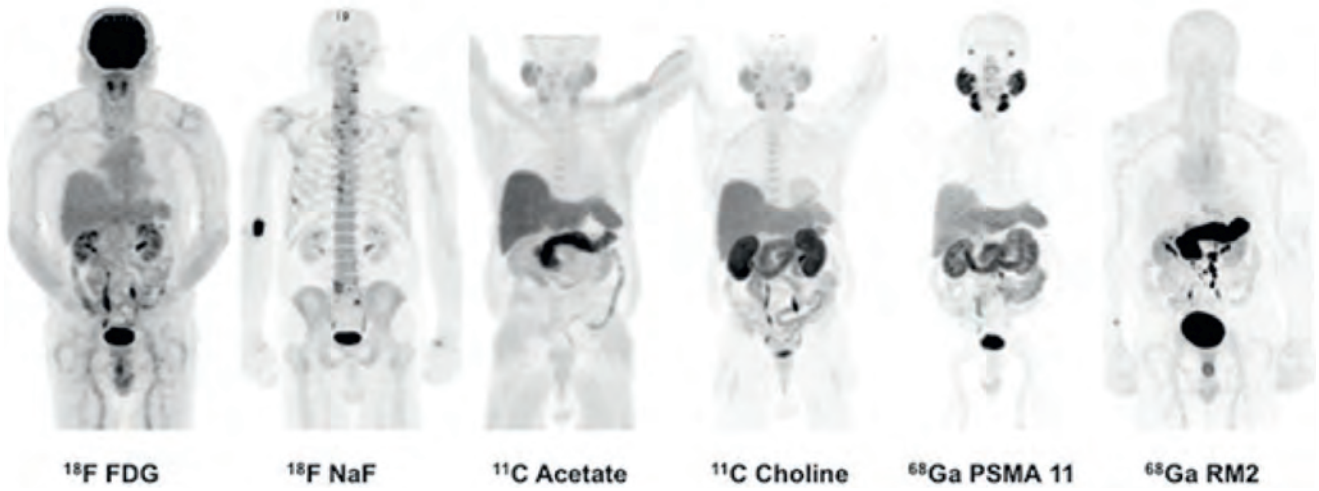


Fig. 3.13. Six different PET tracers used to evaluate an 83-year-old man with a T2b nodule and a prostate-specific antigen (PSA) level of 5.4, confirmed Gleason 5+4 prostate adenocarcinoma, and treated with intensity-modulated pelvic radiotherapy and androgen blockade. After PSA nadir of 0.11, biochemical recurrence occurred with PSA of 1.83 and negative conventional imaging. Patient was followed for 40 months under watch-and-wait strategy due to no identification of sites of recurrent disease despite increasing PSA up to 18.7 at the time of positive Ga-68 PSMA 11 and Ga-68 RM2 (both show retroperitoneal lymph nodes whereas all other studies are negative). (Image courtesy of Andrei Iagaru, MD, Stanford University.)

predictive value (NPV) was 93% versus 86%, respectively (Müller et al., 2011). Another review and meta-analysis including nine selected studies with a total of 375 patients showed that ^{18}F-FDG PET/CT had a pooled sensitivity of 78% (95% CI: 67%–87%), a specificity of 86% (95% CI 81%–89%), a PPV of 58% (95% CI 48%–68%), an NPV of 94% (95% CI 90%–96%), and an accuracy of 84% (95% CI 80%–88%) (Treglia et al., 2014). These results mean that negative ^{18}F-FDG PET/CT findings warrant follow-up if only to avoid inappropriate subsequent treatment (surgery, chemotherapy, or radiotherapy), whereas positive ^{18}F-FDG PET/CT findings suggest a high possibility of residual seminoma, although a false-positive result cannot be excluded in view of the low PPV.

Several limitations of PET imaging for testis cancer should be noted when considering ^{18}F-FDG PET: (1) Lesions of less than 1 cm are often not detected because of the limited spatial resolution of PET. (2) Mature teratoma has variable low ^{18}F-FDG uptake or no uptake and cannot be distinguished from necrosis or fibrosis, and therefore ^{18}F-FDG PET is not recommended for characterization of residual masses after therapy for nonseminomatous germ cell cancers, which frequently harbor residual foci of mature teratoma. (3) There should be a minimum of 6 weeks between the end of chemotherapy and acquisition of an ^{18}F-FDG PET/CT scan to avoid any false-positive findings resulting from chemotherapy-induced inflammatory and granulomatous tissues or false-negative results resulting from temporary suppression of tumor cell activities (Bachner et al., 2012; Kazuhiro et al., 2016; Oechsle et al., 2008). Fig. 3.14 shows testis PET/CT before and after chemotherapy.

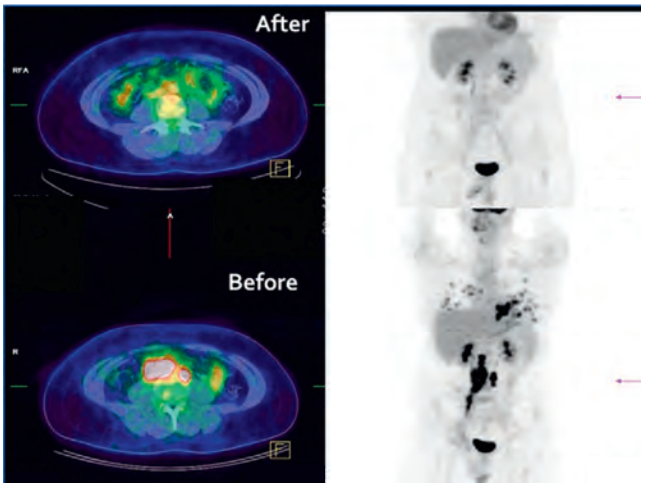


Fig. 3.14. Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) PET/CT is useful for staging and restaging of seminoma in patients treated with chemotherapy. This patient presented with a right-sided seminoma with bulky right-sided retroperitoneal lymph nodes. PET/CT after chemotherapy shows no uptake in the previously positive nodal region.

Positron Emission Tomography Magnetic Resonance Imaging

There is increasing interest in the integration of PET/MRI systems because PET/MRI would have advantages over PET/CT, including improved soft-tissue contrast, the possibility of performing simultaneous instead of sequential acquisitions, and the availability of sophisticated MRI sequences (diffusion and perfusion imaging, functional MRI, and MR spectroscopy) while offering a significant decrease in radiation exposure. Its use had been demonstrated in patients with RCC, bladder cancer, prostate cancer, and pheochromocytoma, which is of foremost importance for serial follow-up and pediatric imaging (Table 3.4).

KEY POINTS: NUCLEAR SCINTIGRAPHY

- During diuretic renal scan, the diuretic must be given when maximum activity is seen in the kidney.
- An elimination $T_{1/2}$ less than 10 minutes is an unobstructed system, and a $T_{1/2}$ greater than 20 minutes is consistent with high-grade obstruction.
- If ureteral stents are in place, patients undergoing diuretic renal scan should have an unclamped bladder catheter in place during the study.
- Technetium^{99m}-mercaptoacetyl triglycerine (MAG3) is the agent of choice for diuretic renal scan to determine differential renal function and obstruction.

TABLE 3.4 PET Tracer in Urologic Oncology

BIOLOGIC ANALOG	PROCESS TARGETED	EFFECT
^{18}F-FDG Glucose	Glucose transporters and hexokinases	Aerobic and anaerobic glycolysis, glucose consumption
^{11}C-choline Choline	Choline kinase	Cell membrane metabolism, tumor proliferation
^{18}F-choline Choline	Choline kinase	Cell membrane metabolism, tumor proliferation
^{11}C-acetate Acetate	Tricarboxylic acid cycle and fatty acid synthase	Lipid synthesis
^{18}F-FDHT Testosterone	Androgen receptor	Measures androgen receptor
^{18}F-NaF Fluoride	Hydroxyl and bicarbonate ions of bone hydroxyapatite	Measures bone status
^{18}F-FMISO NA	Measures hypoxia	Tumor hypoxia
^{18}F-FLT NA	Thymidine kinase	Nucleic acid synthesis, tumor proliferation
^{18}F-FACBC Amino-fluorocyclobutane-carboxylic acid	Neutral A–A type amino acid uptake and protein synthesis	Protein synthesis
^{68}Ga-PSMA Prostate-specific membrane antigen	Prostate cell surface protein	Tumor aggressiveness, androgen independence

Data from Kazuhiro K, Shingo Y, Kazuhito F, et al: Update on advances in molecular PET in urological oncology. *Jpn J Radiol* 34:470–485, 2016.

COMPUTED TOMOGRAPHY

The 1979 Nobel Prize in Medicine and Physiology was awarded to Allan M. Cormack and Sir Godfrey N. Hounsfield for the development of computer-assisted tomography. Although basic principles remain the same, significant advances have resulted in the development of multidetector CT devices, improving soft-tissue detail and allowing the possibility of rapid 3D reconstruction of the entire genitourinary system.

CT has become one of the most integral parts of urologic practice, and the CT urogram (CTU) has replaced IVU as the imaging modality of choice in modern urology for the workup of hematuria, urologic malignancies, detection of kidney stones, and preoperative planning. As in the case of conventional radiographic imaging, the basis for CT imaging is the attenuation of x-ray photons as they pass through the patient. Tomography is an imaging method that produces 3D images of internal structures by recording the passage of x-rays as they pass through different body tissues. In the case of CT, a computer reconstructs cross-sectional images of the body based upon measurements of x-ray transmission through thin slices of the body tissue (Brant, 1999). A collimated x-ray beam is generated on one side of the patient and the amount of transmitted radiation is measured by a detector placed on the opposite side of the x-ray beam. These measurements are then repeated systematically while a series of exposures from different projections is made as the x-ray beam rotates around the patient. The result is production of a 3D image of internal structures in the human body by recording the passage of different energy waves through various internal structures. Data collected by the detectors are reconstructed by computerized algorithms to result in a viewable tomographic display.

There are several different imaging variables that are adjusted to allow adequate, detailed image resolution, while minimizing the time on the scanner and limiting exposure to radiation. The variable application of pitch, beam collimation, detector size, and tube voltage are used by the radiologist and imaging technologist for ideal image requisition. A detailed description of each of these variables is beyond the scope of this chapter.

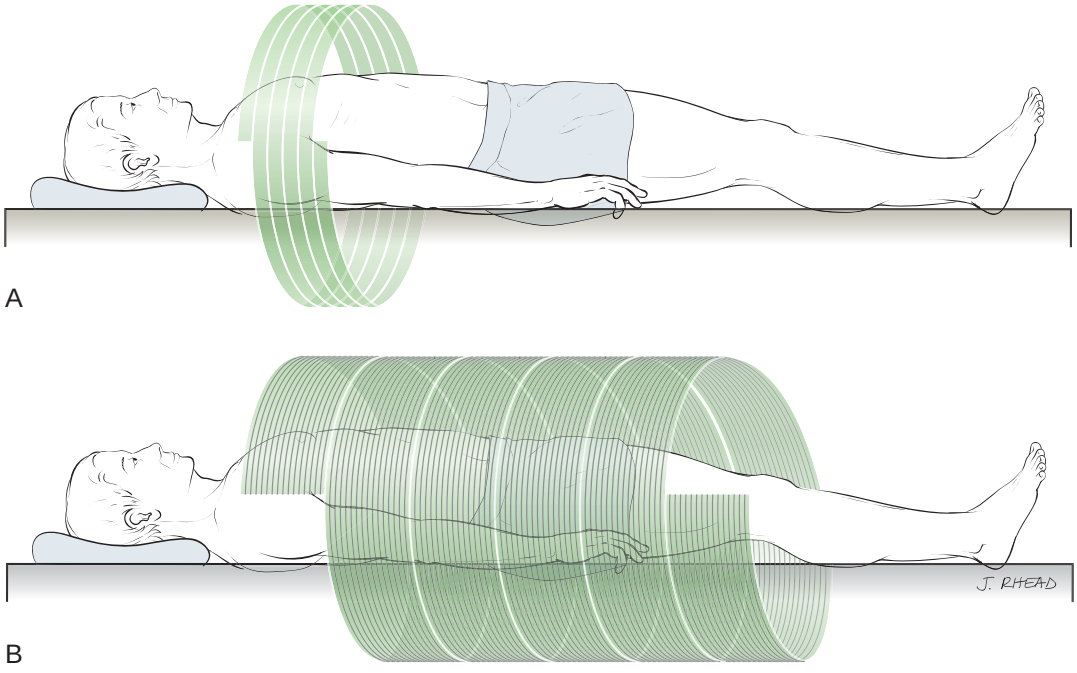
Perhaps the greatest recent advancement in CT is the use of helical image acquisition techniques with multichannel or multidetectors (MDCTs). In a helical CT the patient moves through a continuously rotating gantry. The helical raw images are processed using interpolation algorithms to visualize the internal structures as sagittal, coronal, or axial reconstructed images. The "single-slice spiral CT," introduced in 1988, had a single row of detectors and required multiple passes to visualize a small area of interrogation. The standard scanners in use today have between 64 and 320 rows of detectors, which allow the patient's entire body to be imaged during a single breath hold, with few or no motion artifacts, more precise diagnostic accuracy, increased concentration of contrast material, shorter scanning time, less radiation exposure, and significant increase in anatomic coverage with a single scan. CT scanners with 750 rows of detectors are currently being developed. For example, a 640-slice CT scanner with a gantry rotation of 0.275 seconds can image 16 cm (6.3 inches) in a single rotation with 0.5-mm slices and some scanners can capture 73 cm/s (28 inches/s), capturing all of the body's organs in a single rotation of the central x-ray–emitting gantry (Mahesh, 2002; Wang and Vannier, 1994) (Fig. 3.15).

Readily available software is capable of complex and accurate 3D processing of CT images to recreate the urinary system. These 3D images offer improved preoperative planning, appreciation of proximity to adjacent organs, and the ability to define vasculature and improve communication with patients who can now easily see their particular pathology and better appreciate the challenges faced by their surgeon. These images are often used for printing of 3D organ models. In some complex urology cases, the segmentation and formatting of CT images to create 3D renderings can be more useful during surgery than 3D printed organs (Christiansen et al., 2018) (Fig. 3.16).

Dual-source CT (DSCT) is a relatively new technique used for diagnostic imaging, using two rotating tubes to acquire high- and low-voltage images, allowing tissue differentiation, visualization of tendons and ligaments, improved CT angiography, and differentiation of kidney stones based upon stone composition (Coursey, 2010). Use of DSCT helps make a reliable distinction between uric acid and calcium oxalate and between brushite and uric acid stones (Botsikas, 2013; Ferrandino, 2010).

Real-time CT fluoroscopy is available as an option on new CT imaging equipment. CT fluoroscopy gives a 3D CT image that is much more detailed and offers greater soft-tissue contrast and resolution than conventional CT. The most common use in urology is for biopsy of the kidney. CT fluoroscopy helps to overcome movement of the kidney during respiratory variation. It also has been used for fluid aspiration, drain placement, catheter placement, percutaneous cryoablation, and radiofrequency ablation of renal tumors. **One significant disadvantage of CT fluoroscopy is the increased radiation exposure to the patient and radiologist or surgeon performing the procedure** (Daly et al., 1999; Gupta et al., 2006; Keat, 2001).

The CT urogram (CTU) is an excretory urography in which the MDCT is used for imaging of the urinary tract. It is indicated in the workup of hematuria, kidney stones, renal masses, renal colic, and urothelial tumors. The CT scan examination starts with



Fig, 3.15. (A) CT scanner with a single-row detector requires five circular passes around the patient to image a small area of the patient's body. (B) With a 16-slice, multirow detector, the chest, abdomen, and pelvis can be imaged with five circular passes, easily obtained during a single breath hold. The thin slices offered by the 16-slice detector offer much greater detail of internal structures.

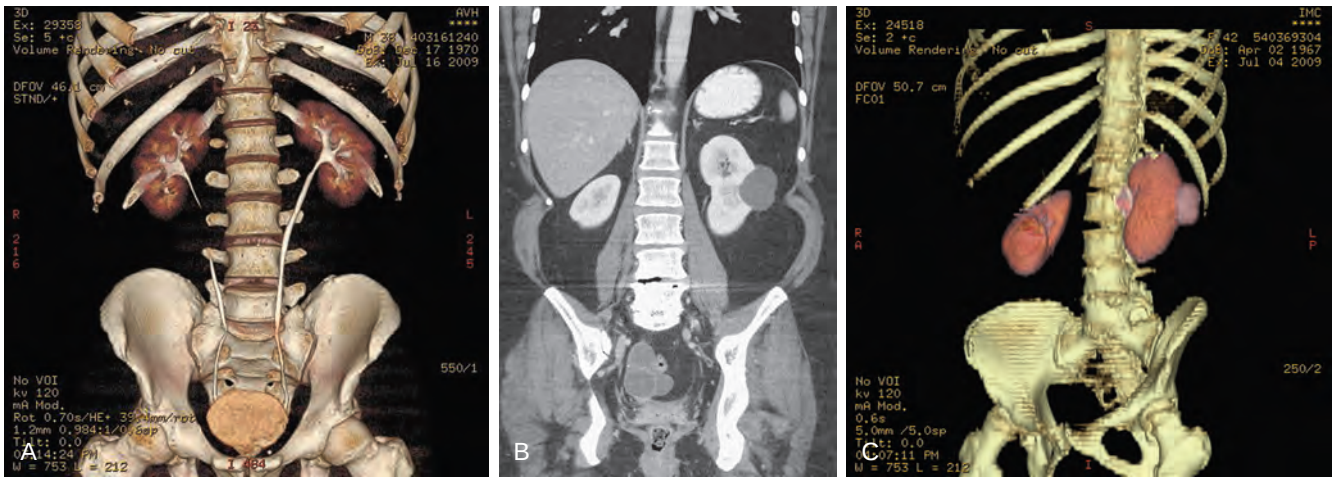


Fig. 3.16. (A) 3D colored reconstruction of the kidneys ureter and bladder from CT urogram. (B) Coronal reconstruction in a patient with a clear cell renal cell carcinoma in a complex renal cystic mass and enhancing mural nodule. (C) 3D reconstruction of the same patient with slight posterior rotation.

the physician's request for imaging. Radiologists around the world appreciate, from the urologist, a brief description of the question to be answered by the CT scan. Equipped with a better understanding of why the CT scan was ordered, the radiologist and the CT technician can adjust different CT variables and choose the appropriate contrast media needed to deliver a valuable report to the ordering urologist.

Urologists often request a CT evaluation of the abdomen and pelvis. An abdominal CT scan starts at the diaphragm and ends at the iliac crest. If the pelvis is to be imaged, a separate request usually is required. The pelvic CT scan begins at the iliac crest and terminates at the pubis symphysis. Intravenous contrast may be required for better delineation of soft tissue. Oral contrast is not commonly used in urology but may be helpful in certain cases to differentiate bowel from lymph nodes, scar, or tumor (Fig. 3.17).

Hounsfield Units

A single CT image generated by the scanner is divided into many tiny blocks of different shades of black and white called pixels. The actual gray scale of each pixel on a CT depends upon the amount of radiation absorbed at that point, which is termed an *attenuation value*. **Attenuation values are expressed in Hounsfield units (HU). The Hounsfield units scale or attenuation value is based upon a reference scale in which air is assigned a value of −1000 HU**

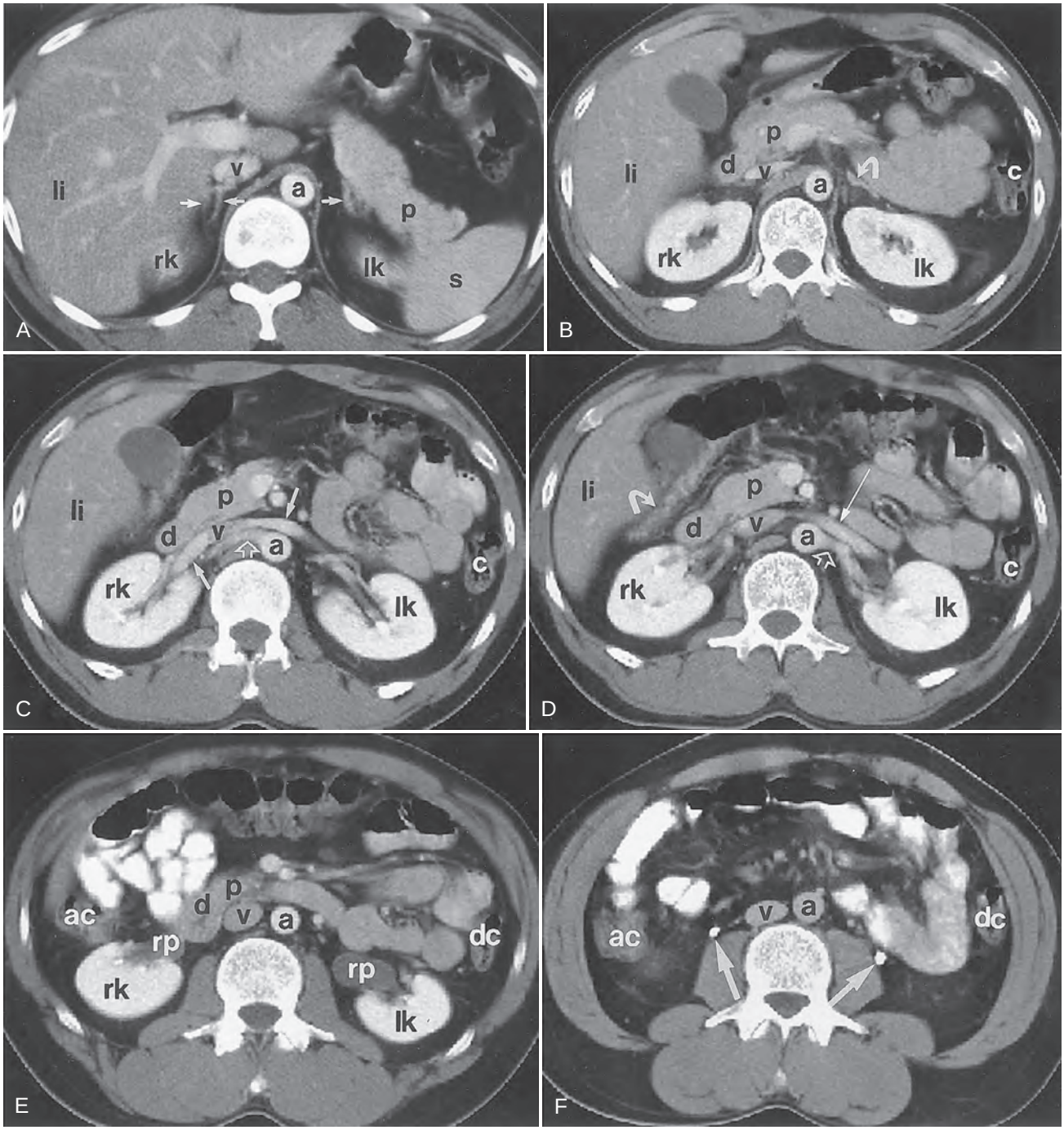


Fig. 3.17. CT of the abdomen and pelvis demonstrating normal genitourinary anatomy. (A) The adrenal glands are indicated with *arrows.* The upper pole of the right and left kidneys is indicated with *rk* and *lk,* respectively. *a,* aorta; *li,* liver; *p,* pancreas; *s,* spleen; *v,* inferior vena cava. (B) Scan through the upper pole of the kidneys. The left adrenal gland is indicated with an *arrow. a,* aorta; *c,* colon; *d,* duodenum; *li,* liver; *lk,* left kidney; *p,* pancreas; *rk,* right kidney; *v,* inferior vena cava. (C) Scan through the hilum of the kidneys. The main renal veins are indicated with *solid arrows,* and the right main renal artery is indicated with an *open arrow. a,* aorta; *c,* colon; *d,* duodenum; *li,* liver; *lk,* left kidney; *p,* pancreas; *rk,* right kidney; *v,* inferior vena cava. (D) Scan through the hilum of the kidneys slightly caudal to C. The left main renal vein is indicated with a *solid straight arrow,* and the left main renal artery is indicated with an *open arrow.* The hepatic flexure of the colon is indicated with a *curved arrow. a,* Aorta; *c,* colon; *d,* duodenum; *li,* liver; *lk,* left kidney; *p,* pancreas; *rk,* right kidney; *v,* inferior vena cava. (E) Scan through the mid to lower polar region of the kidneys. *a,* Aorta; *ac,* ascending colon; *d,* duodenum; *dc,* descending colon; *lk,* left kidney; *p,* pancreas; *rk,* right kidney; *rp,* renal pelvis; *v,* inferior vena cava. (F) CT scan obtained below the kidneys reveals filling of the upper ureters *(arrows).* The wall of the normal ureter is usually paper thin or not visible on CT. *a,* aorta; *ac,* ascending colon; *dc,* descending colon; *v,* inferior vena cava.

Continued

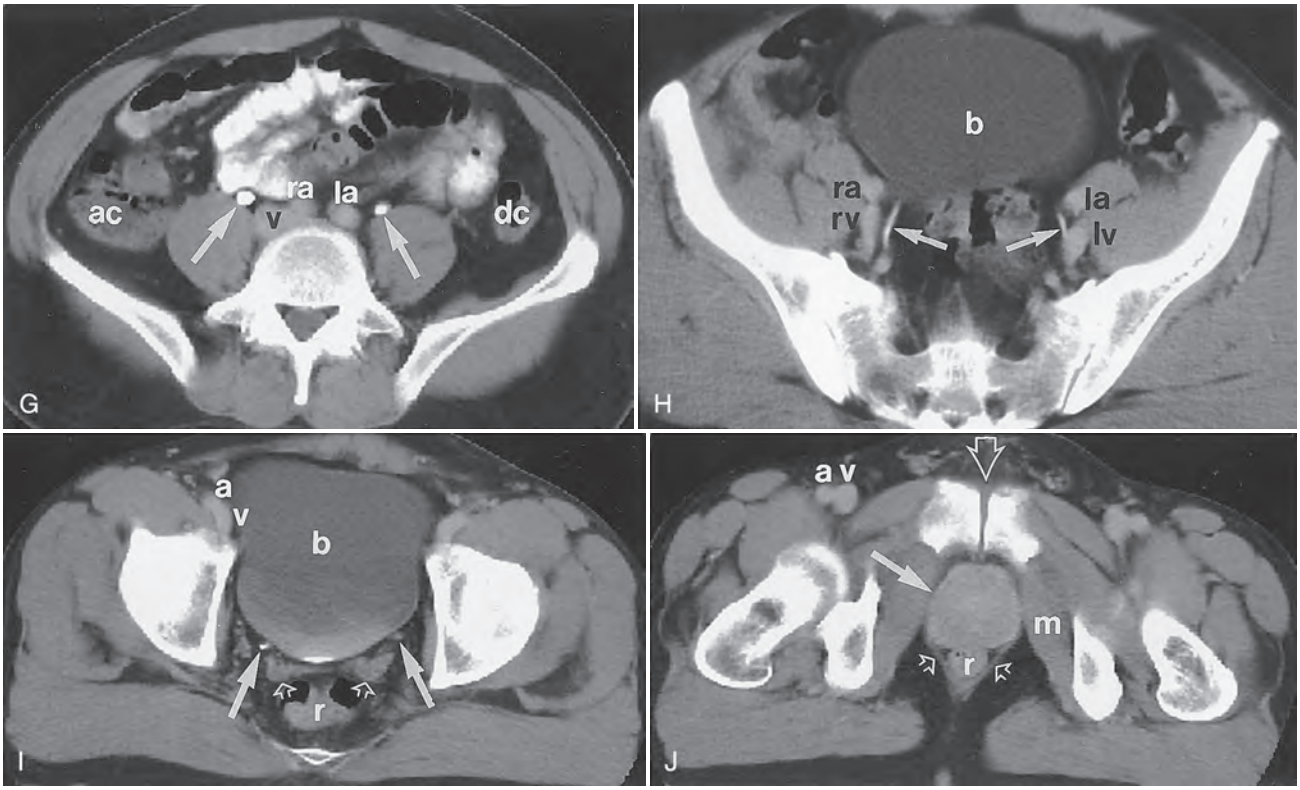


Fig. 3.17., cont'd (G) Contrast filling of the midureters *(arrows)* on a scan obtained at the level of the iliac crest and below the aortic bifurcation. *ac,* Ascending colon; *dc,* descending colon; *la,* left common iliac artery; *ra,* right common iliac artery; *v,* inferior vena cava. (H) The distal ureters *(arrows)* course medial to the iliac vessels on a scan obtained below the promontory of the sacrum. *b,* urinary bladder; *la,* left external iliac artery; *lv,* left external iliac vein; *ra,* right external iliac artery; *rv,* right external iliac vein. (I) Scan through the roof of the acetabulum reveals distal ureters *(solid arrows)* near the ureterovesical junction. The bladder *(b)* is filled with urine and partially opacified with contrast material. The normal seminal vesicle *(open arrows)* usually has a paired bow-tie structure with slightly lobulated contour. *a,* Right external iliac artery; *r,* rectum; *v,* right external iliac vein. (J) Scan at the level of the pubic symphysis *(open arrow)* reveals the prostate gland *(solid arrow). a,* Right external iliac artery; *m,* obturator internus muscle; *r,* rectum; *v,* right external iliac vein.

and dense bone is assigned the value of +1000 HU. Water is assigned 0 HU.

Urolithiasis

Patients in the emergency department with abdominal pain or renal colic are frequently evaluated with CT imaging. The use of nonenhanced CT imaging to identify urolithiasis was first reported in 1995 (Smith et al., 1995) and has become the standard diagnostic tool to evaluate renal colic. It offers the advantage over IVU of avoiding contrast and has the ability to diagnose other abdominal abnormalities that can also cause abdominal pain. MDCT can readily diagnose radiolucent stones that may not have been seen on IVU, as well as small stones even in the distal ureter (Federle et al., 1981). **With the exception of some indinavir stones, all renal and ureteral stones can be detected on helical CT scan** (Schwartz et al., 1999). In the workup of urolithiasis, the unenhanced CT has a sensitivity ranging between 96% and 100% and specificity ranging between 92% and 100% (Memarsadeghi et al., 2005). **Stones in the distal ureter can be difficult to differentiate between pelvic calcifications. In these cases, the urologist needs to look for other signs of obstruction that indicate the presence of a stone, including ureteral dilation, inflammatory changes in the perinephric fat, hydronephrosis, and a soft-tissue rim surrounding the calcification within the ureter. The soft-tissue rim around a stone represents irritation and edema in the ureteral wall** (Dalrymple et al., 2000; Heneghan et al., 1997) (Fig. 3.18).

Stone patients are frequently subjected to radiation exposure as part of diagnosis, treatment, and follow-up. Increasing awareness of the potential long-term adverse effects of radiation exposure has encouraged urologists and radiologists to discover means to decrease the amount of radiation exposure. The low-dose unenhanced helical CT scan is gaining increasing popularity for initial diagnosis of renal colic suspected to be due to urolithiasis and for follow-up in stone patients. Using low-dose CT protocols, the specificity and sensitivity of unenhanced low-dose helical CT scan are approximately 96% and 97%, respectively. Low-dose techniques offer a 99% positive and 90% negative predictive value for urolithiasis. The end result is a 50% to 75% decrease in the patient's total radiation exposure for each CT obtained (Hamm et al., 2002; Kalra et al., 2005; Liu et al., 2000).

Cystic and Solid Renal Masses

The frequent CT imaging in emergency room patients has resulted in an increase in the detection of incidental renal masses. With use of CT imaging, the mass can be characterized as a simple or complex cyst or a solid mass. Based upon the Hounsfield unit attenuation scale, we would expect simple cysts to have Hounsfield units near zero (Fig. 3.19).

When the unenhanced CT images of a renal mass are compared with the enhanced images obtained in the cortical medullary or nephrogenic phase, an increase in Hounsfield units (measured in the area of the renal mass) by 15 to 20 HU confirms the presence of a solid enhancing mass, which is usually renal cancer.

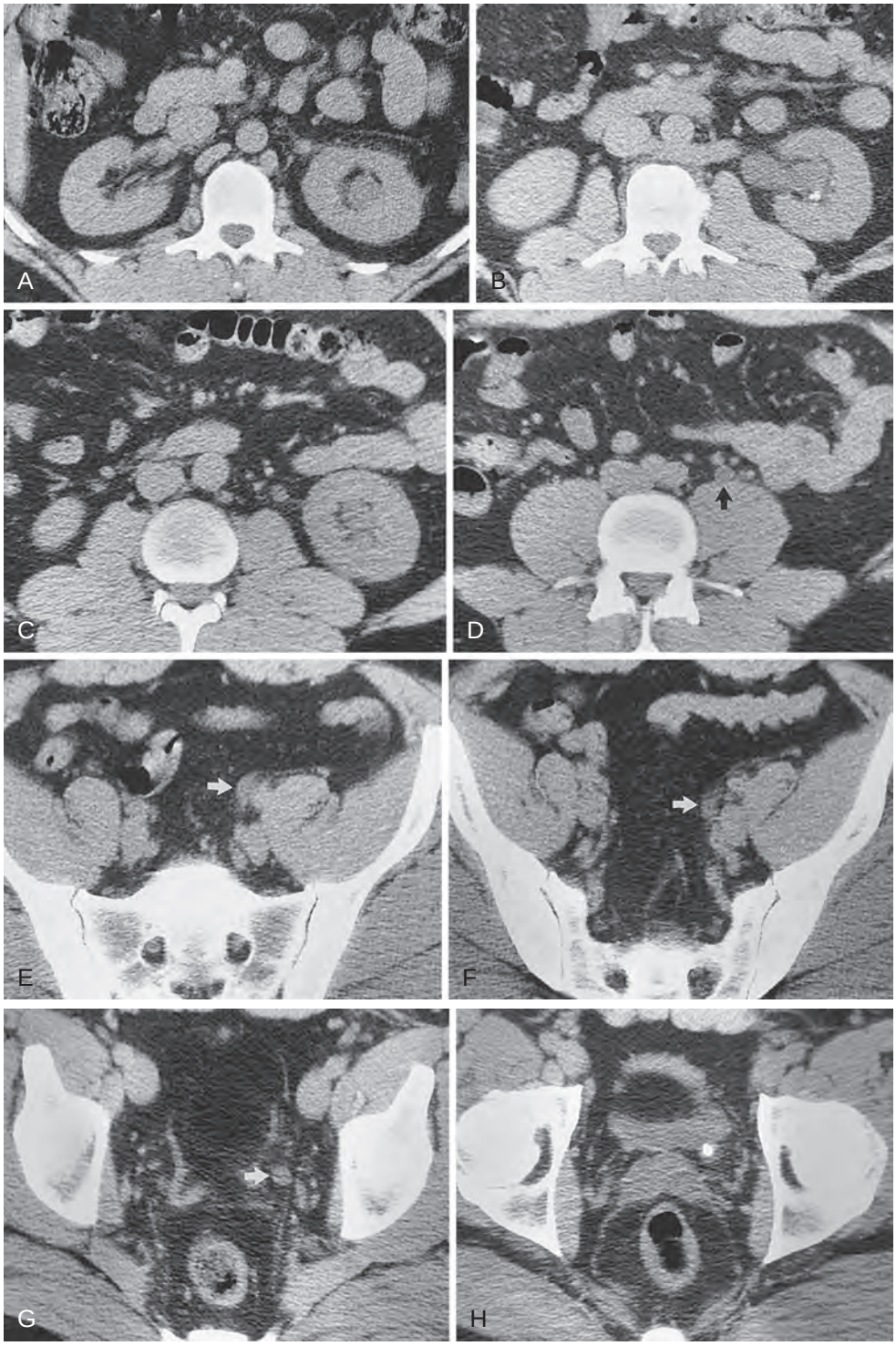


Fig. 3.18. CT of the abdomen and pelvis in patient with an obstructing ureteral stone at the level of the ureterovesicle junction. (A) Level of the left upper pole. Mild renal enlargement, caliectasis, and perinephric stranding are apparent. (B) Level of the left renal hilum. Left pyelectasis with a dependent stone, mild peripelvic and perinephric stranding, and a retroaortic left renal vein are shown. (C) Level of the left lower pole. Left caliectasis, proximal ureterectasis, and mild periureteral stranding are present. (D) Level of the aortic bifurcation. The dilated left ureter *(arrow)* has lower attenuation than do nearby vessels. (E) Level of the upper portion of the sacrum. A dilated left ureter *(arrow)* crosses anteromedial to the common iliac artery. (F) Level of the midsacrum. A dilated left ureter *(arrow)* is accompanied by periureteral stranding. (G) Level of the top of the acetabulum showing a dilated pelvic portion of the left ureter *(arrow).* (H) Level of the ureterovesical junction. The impacted stone with a "cuff" or "tissue rim" sign that represents the edematous wall of the ureter. (Reprinted from Talner LB, O'Reilly PH, Wasserman NF: Specific causes of obstruction. In Pollack HM, et al., eds: *Clinical urography,* ed 2, Philadelphia, 2000, Saunders.)

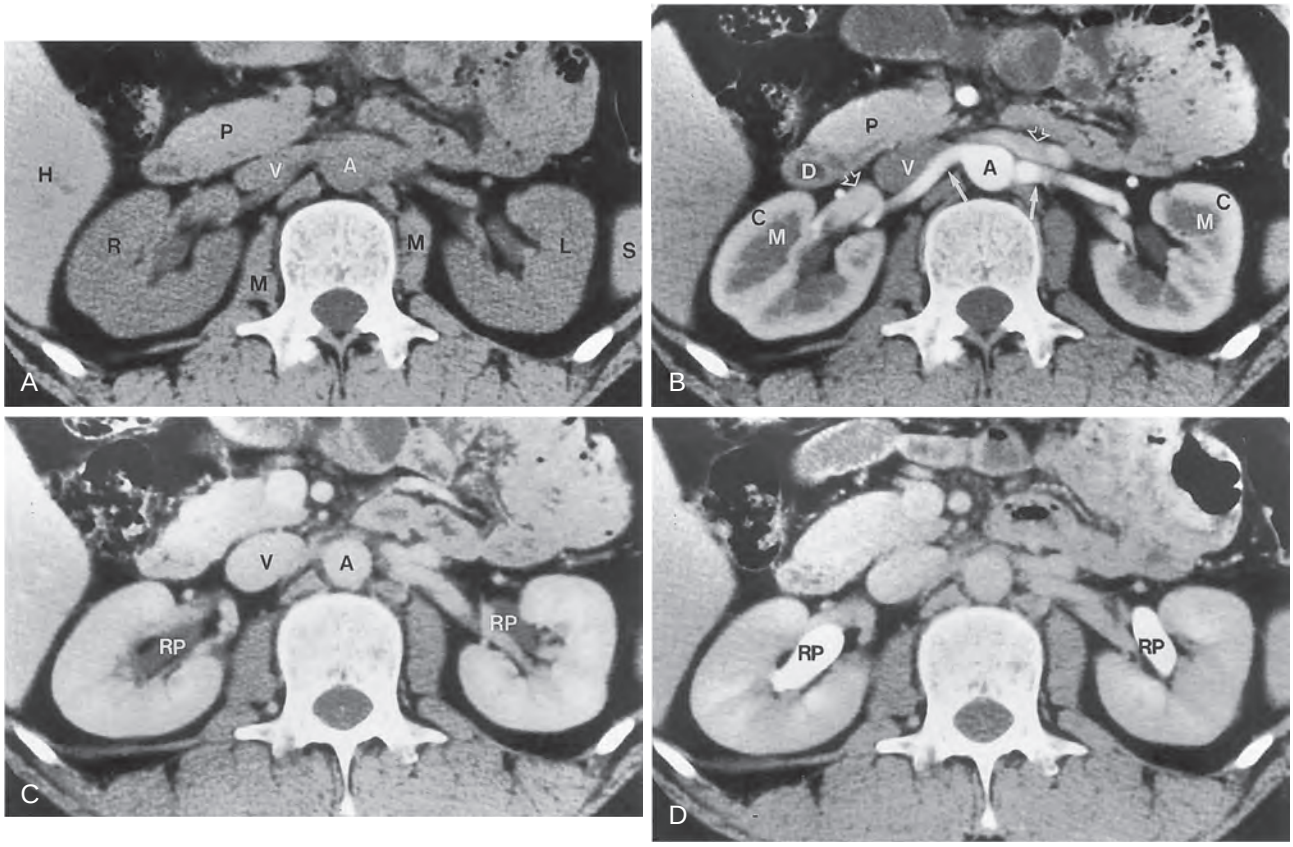


Fig. 3.19. Renal CT demonstrating normal nephrogenic progression. (A) Unenhanced CT scan obtained at the level of the renal hilum shows right *(R)* and left *(L)* kidneys of CT attenuation values slightly less than those of the liver *(H)* and pancreas *(P)*. *A,* Abdominal aorta; *M,* psoas muscle; *S,* spleen; *V,* inferior vena cava. (B) Enhanced CT scan obtained during a cortical nephrographic phase, generally 25 to 80 seconds after contrast medium injection, reveals increased enhancement of the renal cortex *(C)* relative to the medulla *(M).* The main renal artery is indicated with *solid arrows* bilaterally. Main renal veins *(open arrows)* are less opacified with respect to the aorta *(A)* and arteries. *D,* Duodenum; *P,* pancreas; *V,* inferior vena cava. (C) CT scan obtained during the homogeneous nephrographic phase, generally between 85 and 120 seconds after contrast medium administration, reveals a homogeneous, uniform, increased attenuation of the renal parenchyma. The wall of the normal renal pelvis *(RP)* is paper thin or not visible on the CT scan. *A,* Abdominal aorta; *V,* inferior vena cava. (D) CT scan obtained during the excretory phase shows contrast medium in the RP bilaterally; this starts to appear approximately 3 minutes after contrast medium administration.

Pseudoenhancement is maximal when small (≤1.5-cm) intrarenal cysts are scanned during maximal levels of renal parenchymal enhancement. The magnitude of this effect varies with scanner type but may be large enough to prevent accurate lesion characterization, despite use of a thin-section helical CT data acquisition technique (Birnbaum et al., 2002). **The presence of fat, which should enhance less than 10 HU, is diagnostic for angiomyolipoma. A hyperdense cyst shows no change in density between the postcontrast and delayed phase images.**

Complex cystic masses are usually characterized based upon the Bosniak classification system. The most important criterion used to differentiate a lesion that should be considered for surgery versus a nonsurgical lesion is the presence or absence of tissue vascularity or enhancement. Bosniak category I, II, and IIF lesions do not enhance to any measurable degree. Category I lesions are simple cysts and considered to be benign. Category II lesions are more complicated and may have calcifications, high attenuation fluid, and several thin septae. Category III lesions are more complex, have small areas of calcification, and may also have irregular walls or septate where there is measurable enhancement. Cystic lesions discovered on CT scan that are difficult to categorize as either II or III are now currently categorized as IIF. **Bosniak III lesions have been reported to be malignant renal cell carcinoma in 60% of cases and require close follow-up or surgical extirpation. Bosniak category IV lesions are cystic masses that meet all the criteria of category III but also have enhancing soft-tissue components adjacent or independent of the wall or septum of the cyst and have been reported to be malignant RCC in 100% of cases** (Bosniak, 1997; Curry, 2000; Israel and Bosniak, 2005).

Hematuria

The CTU is one of the most common studies ordered for the workup of gross or microscopic hematuria. With MDCT it is possible to perform a comprehensive evaluation of the patient with a single examination (Chai et al., 2001). The study images the abdomen and pelvis and typically includes four different phases. The first scan is an unenhanced CT to distinguish between different masses that can be present in the kidney and uncover kidney stones that would later be obscured by the excretion of contrast into the renal collecting system. At 30 to 70 seconds after contrast injection, the corticomedullary phase is captured with another pass through the MDCT, helping to define vasculature and perfusion. The nephrogenic phase occurs between 90 to 180 seconds after injection of contrast and, when compared with the nonenhanced images, allows sensitive detection and characterization of renal masses. The final phase is the excretory phase, imaged approximately 3 to 5 minutes after injection of contrast. The excretory phase allows complete filling of the collecting system and usually allows visualization of the ureter (Joudi et al., 2006).

CTU has been shown to be sensitive in detecting upper tract urothelial cancers. In one series of 57 patients with hematuria, 38 were found to have urothelial carcinoma. CT urography detected 37/38 urothelial cancers for a sensitivity of 97%, compared with retrograde pyelogram, which detected 31/38 lesions and had a sensitivity of 82%. Approximately 90% of malignant upper tract lesions can be detected with CT urography (Caoili et al, 2005; Lang et al., 2003; McCarthy and Cowan, 2002). CT urography is not as sensitive as cystoscopy for the detection of urothelial tumors in the bladder. Only large bladder tumors are visualized with CT imaging studies as filling defect in the lumen of the bladder. Carcinoma in situ cannot be visualized on CT scanning and therefore cystoscopy is still an important part of a comprehensive hematuria workup.

KEY POINTS: COMPUTED TOMOGRAPHIC IMAGING

- The CTU is an excellent imaging choice to evaluate the kidney, upper tract collecting system, and ureter.
- The CTU is highly sensitive and specific for upper tract urothelial carcinoma.
- A renal mass in the kidney seen on CTU that enhances more than 15 to 20 HU is most likely a renal cancer.
- With the exception of indinavir stones, all urolithiasis is visible on unenhanced CT of the abdomen and pelvis.

MAGNETIC RESONANCE IMAGING

CT imaging remains the mainstay of urologic cross-sectional imaging. Continued technologic improvements in MRI is narrowing the overall resolution quality gap between these two techniques. A significant advantage of MRI is the excellent signal contrast resolution of soft tissue without the need for intravenous contrast in many situations.

To obtain MRIs, the patient is placed on a gantry that passes through the bore of a magnet. When exposed to a magnet field of sufficient strength, the free water protons in the patient orient themselves along the magnetic field's z-axis. This is the head-to-toe axis, straight through the bore of the magnet. A radiofrequency (RF) antenna or "coil" is placed over the area of interest. It is the coil that transmits the RF pulses through the patient. When the RF pulse stops, protons release their energy, which is detected and processed to obtain an MRI. An MR sequence exploits the body's different tissue characteristics and the manner that each type of tissue absorbs and then releases this energy. Currently, most coils can transmit and receive signal, which is referred to as dual-channel RF.

Weighting of the image depends on how the energy is imparted through the physics of the pulse sequence and whether the energy is released quickly or slowly. Images are described as T1 or T2 weighted. The T1-weighted images are generated by the time to return to equilibrium in the z-axis. The T2-weighted images are generated by the time required to return to equilibrium in the xy-axis. **On T1-weighted MRIs, fluid has a low signal intensity and appears dark. T2-weighted MRIs have a high signal intensity and appear bright. In the kidney this translates into the cortex having a higher signal intensity or being brighter than the medulla, which gives off a lower signal and is darker.**

MRI has significant advantages over other imaging modalities. First, and most importantly, there are no risks associated with secondary malignancies from radiation exposure (Berrington de González and Darby, 2004). It is the modality of choice in patients who are pregnant, suffer from renal insufficiency, and/or have an iodine contrast allergy.

The contrast agents in MRI are noniodinated compounds. Iodinated compounds as used in CT imaging function by absorbing x-rays. **GBCAs shorten the relaxation times of water** (Lin and Brown, 2007). This results in an increase in signal intensity (enhancement), most commonly assessed in a T1 sequence. Gadolinium is a toxic heavy metal that is chelated to prevent cellular absorption and any associated toxicities (Lin and Brown, 2007). The dose of gadolinium is nontoxic for almost all patients, except ones with *severe* renal insufficiency.

Nephrogenic systemic fibrosis (NSF) occurs in patients with acute or chronic renal insufficiency with a GFR less than 30 mL/min/1.73 m^2 and was first described in 2000 (Cowper et al., 2000). Gadolinium is deposited in skin and muscle as an insoluble precipitate, which leads to the systemic fibrosis (Grobner, 2006). In response, the FDA has issued warnings regarding the association between NSF and GBCAs because there is no effective treatment available (US Food and Drug Safety Communication, 2010). The current guidelines are available at the FDA.gov official website and the US Food and Drug Administration website. In addition, there have been documented cases of gadolinium deposition (linear > macrocyclic) within deep brain tissue. However, the clinical significance of deposition is unknown, and no adverse events have been documented. Current recommendations include favoring the use of macrocyclic agents over linear GBCAs well as a continued analysis of possible future risks associated with GBCAs as the data continue to evolve (Gulani et al., 2017).

Adrenal Magnetic Resonance Imaging

One of the key differences between MRI and other imaging modalities is the ability of MRI to characterize soft tissues without the use of intravenous contrast. In the adrenal gland minute quantities of lipids can help differentiate between malignancies and benign adenomas. Most adrenal masses are identified incidentally and are nonfunctioning.

Adrenal adenomas are usually less than 3 cm and nonfunctional (Boland and Blake, 2008). Adrenal adenomas have a high lipid content (74%), which makes them more readily differentiated from malignant processes (Dunnick and Korobkin, 2002).

Inversion-recovery imaging, chemical shift imaging (CSI), and fat saturation imaging are three approaches to assess lipid content on masses. These approaches use the differences in the behavior of fat protons and water protons within the magnetic field. CSI is the most commonly used technique for urologic patients. Spectral presaturation with inversion recovery (SPIR) and spectral presaturation attenuated inversion recovery (SPAIR) can also be used to detect fat via selective excitation of the fat protons and T1 relation techniques (Ünal et al., 2016).

Adrenal Adenoma

Adrenal adenomas are characterized by assessing the lipid content within the cells. CSI uses the difference in the behavior of water protons (H_2O) versus fat protons ($-CH_2-$). The oxygen atom in water pulls on the electron cloud surrounding the hydrogen atom, whereas the carbon atom in fat is less electronegative and has a decreased effect on the hydrogen electron cloud (Pokharel and Macura, 2013). This difference in the magnetic field (shielding) for these two types of protons is the precession frequencies or the CSI (Pokharel and Macura, 2013).

CSI obtains images "in-phase" (IP) and "out-of-phase" (OP) regarding the water and fat protons. The signals detected for a given voxel can be additive or canceled out. The IP imaging refers to the contribution of fat and water, or additive, to the signal at a given voxel. This occurs when the echo time (TE) is set to align the fat and water protons.

In the OP imaging the TE is set to cancel the signals obtained, thus the subtraction of the protons results in a decrease, or canceling, in signal at that given voxel and produces a lower signal intensity if fat and water are present.

The next step is to compare the two data sets (IP and OP) obtained to determine if there is a loss of signal (decrease) on the OP images, which is indicative of intracytoplasmic fat (Fig. 3.21). If there is no change between the two data sets, then there is a lower probability that fat is present within the mass. This was initially determined on a qualitative basis by visually comparing signal intensities between the two sequences (Korobkin and Giordano, 1996). The loss of signal on CSI MRI is 92% sensitive and has a limited specificity of 17% for adrenal adenoma (Boland and Blake, 2008).

Other authors have attempted to determine signal intensity (SI) index by quantitatively comparing the IP and OP images. Nakamura and Namimoto (2012) reported that using a 5% SI yielded an accuracy of 100% (3 Tesla) in determining if intracytoplasmic lipid was present and thus a diagnosis of an adenoma. Although there are currently no set thresholds, cutoff ranges are reported to be between 1.7% and 20%