ATLAS OF Clinical Urology

SERIES EDITORS

E. Darracott Vaughan, Jr.

Aaron P. Perlmutter

VOLUME IV

Pediatric Urology

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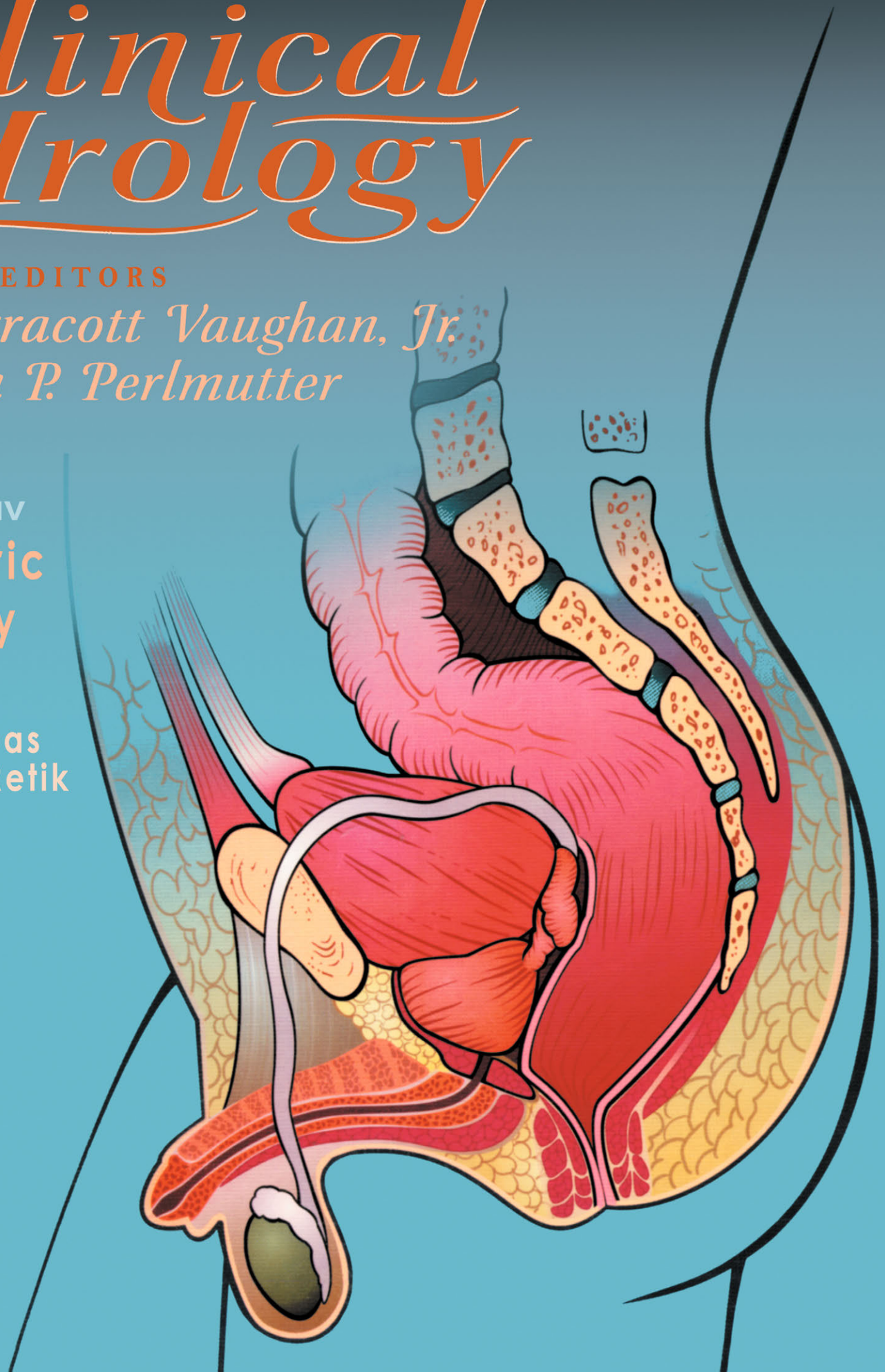
Dix Poppas

Alan B. Retik



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Dix P. Poppas, MD

The Richard Rodgers Family Assistant Professor of
Pediatric Urology;
Director, Laboratory for Minimally Invasive Urologic Surgery
Chief, Pediatric Urology and Reconstructive Surgery
The New York Hospital–Cornell Medical Center
New York, New York

Alan B. Retik, MD

Professor of Surgery (Urology)
Department of Surgery
Harvard Medical School;
Chief, Department of Urology
Children's Hospital
Boston, Massachusetts

SERIES EDITORS

E. Darracott Vaughan, Jr., MD

Professor
Department of Urology
Joan and Sanford I. Weill Medical College and
Graduate School of Medical Sciences of Cornell University
James J. Colt Professor and Chairman Emeritus
Department of Urology
New York-Presbyterian Hospital
New York, New York

Aaron P. Perlmutter, MD, PhD

Assistant Professor
Department of Urology
Joan and Sanford I. Weill Medical College and
Graduate School of Medical Sciences of Cornell University
Assistant Attending Urologist
New York-Presbyterian Hospital
New York, New York

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Developmental Editor . . . . . Elise M. Paxson
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Assistant Production Manager . . . . . Margaret La Mare

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SERIES PREFACE

As urology enters the 21st century, it is appropriate that the *Atlas of Clinical Urology* series captures and explains the major areas of modern urologic practice using a unique combination of images, schematics, tables, and algorithms. It does so in a compelling fashion, by combining a multilevel approach that includes the individual volumes and the internet. Urology is a specialty of great breadth, and visual images provide much of the backbone of urologic diagnosis and endoscopy and are key to surgical technique. The increasingly complex diagnostic and treatment paths are best depicted and understood as visual algorithms.

The editors of this five-volume series have not only contributed their world-renowned expertise to the chapters but have also assembled an outstanding group of individual chapter authors. Together, they provide each volume with completeness, depth, and—most important in this age of rapidly expanding science and technology—*current* urologic thinking.

In Volume I, Tom Lue and his contributors cover the expanding area of impotence from anatomic considerations through many of the new treatment modalities. As our population ages, urologists are evaluating and treating an expanding number of impotent patients. This section provides an excellent understanding and practical approach. In the second half of Volume I, Marc Goldstein and his expert colleagues provide a beautiful series of images that depict the important aspects of reproductive anatomy and endocrinology, as well as detailed surgical schematics demonstrating the ever-evolving "standard" surgery for infertility in addition to new assisted-reproduction techniques.

It would be fair to say that the 1990s are the decade of the prostate, and Volume II captures the paradigm changes that occurred in the management of both prostate cancer and benign disease. Management of prostate cancer is challenging, and the section by Peter Scardino provides a clear, concise, factual background for understanding prostate cancer and the myriad of treatment options. John McConnell's section on noncancerous diseases provides the background for understanding the new treatment modalities available for benign prostatic hyperplasia (BPH). The choices of pharmacologic management and device therapies continue to challenge even the most seasoned urologist, and the diagnostic and treatment schematics provided in the section have been constructed by leaders in the field.

Renal carcinoma is covered in Volume III by section editor Andrew Novick. Radiologic images play an increasing role in our diagnosis and management of renal cancer, and the visual image format of the Atlas is ideal. The challenges of nephron sparing and vena caval surgery are clearly illustrated and are combined with an understanding of the appropriate patient populations for these procedures. This section also includes the management of benign and malignant adrenal disorders. Michael Marberger has assembled an extremely diverse and important set of noncancerous diseases of the kidney. Nephrolithiasis management is covered from medical therapy to endoscopy to incisional surgery. The important role that laparoscopy has established in both excisional and reconstructive renal surgery is visually depicted and explained. The evolution of the techniques illustrated in this section will likely provide the basis for renal intervention in the 21st century.

Volume IV covers the diversity of pediatric urology under the editorship of Dix Poppas and Alan Retik. This volume provides images illustrating the most important diseases that confront the pediatric urologist. In addition, the changes in management and thinking in classic conditions such as vesicoureteral reflux and neurogenic vesical dysfunction are illustrated. This volume will not only be of great value to the practicing pediatric urologist, but also to general urologists as well as pediatricians and pediatric nephrologists.

Bladder diseases cause many patients to seek urologic care. In Volume V, Donald Skinner and John Stein have assembled state-of-the-art contributions to the management of bladder and urethral cancer. The combination of a better understanding of bladder cancer and new options in surgical urinary diversions is changing the management of bladder cancer. The role of surgery and surgical approaches to bladder cancer are illustrated in this volume by the innovative surgeons who contributed chapters to the section. Voiding dysfunction and incontinence as well as inflammatory and infectious conditions of the bladder are covered by Alan Wein's section. The excellent contributions to this section provide an illustrated understanding of the neuromuscular function of the lower urinary tract, and the images reproduced in this volume allow an easy understanding of the diagnosis and management of incontinence, inflammatory conditions, and fistulae.

These section editors and authors deserve tremendous credit for this *Atlas of Clinical Urology*, which was initiated by Abe Krieger, President of Current Medicine. We thank Abe, the developmental editors, and the excellent illustrators of Current Medicine for their outstanding efforts.

E. Darracott Vaughan, Jr.
Aaron P. Perlmutter

PREFACE

Pediatric urology is an exciting, challenging, and ever-changing specialty. New diagnostic tools, surgical modalities, and clinical and basic research combine to constantly keep our discipline on the cutting edge. This atlas brings the subject matter up to date in clear, concise formats highlighted with generous photographic illustrations.

This fourth volume in the *Atlas of Clinical Urology* series presents the broad spectrum of pediatric urology, from prenatal diagnosis through renal tumors. Office urology and medical management of urologic diseases, as well as the latest laparoscopic and other surgical techniques are presented. This atlas provides the reader with useful information in a quick reference format to assist in the care of pediatric urology patients. Although it is written primarily for the pediatric urologist, any healthcare practitioner who deals with pediatric urology conditions should find this atlas useful. Students of urology and residents preparing for examinations will find this atlas to be a useful study aid.

A distinguishing characteristic of this volume is its wealth of images. Each chapter contains up-to-date images using CT, MRI, or ultrasound. There are also detailed drawings of surgical procedures and tables containing diagnostic information and decision trees.

We are deeply indebted to our contributors for their effort and cooperation despite their busy professional commitments and personal responsibilities. Without their determination, this atlas would not have become a reality.

Dix P. Poppas, MD, FAAP, FACS
Alan B. Retik, MD

CONTRIBUTORS

Laurence S. Baskin, MD
Assistant Professor
Department of Pediatric Urology
University of California at San Francisco Medical School;
Chief, Pediatric Urology
University of California at San Francisco Medical Center
San Francisco, California

Mark F. Bellinger, MD
Clinical Professor
Department of Urology
University of Pittsburgh School of Medicine;
Pediatric Urology Associates
Pittsburgh, Pennsylvania

Joseph G. Borer, MD
Instructor in Surgery (Urology)
Department of Surgery
Harvard Medical School;
Assistant in Urology
Children's Hospital
Boston, Massachusetts

Douglas A. Canning, MD
Assistant Professor
Department of Urology
University of Pennsylvania;
Director
Department of Pediatric Urology
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Michael C. Carr, MD, PhD
Assistant Professor
Department of Surgery
University of Pennsylvania;
Attending Surgeon
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Anthony J. Casale, MD
Professor
Department of Urology
Indiana University School of Medicine;
Staff Pediatric Urologist
James Whitcomb Riley Hospital for Children
Indianapolis, Indiana

Linda M. Dairiki Shortliffe, MD
Professor and Chair
Department of Urology
Stanford University School of Medicine and Lucile Salter Packard Children's Hospital at Stanford
Stanford, California

David A. Diamond, MD
Associate Professor of Surgery (Urology)
Department of Surgery
Harvard Medical School;
Assistant in Urology
Children's Hospital
Boston, Massachusetts

Steven G. Docimo, MD
Professor
Department of Urology
University of Pittsburgh School of Medicine;
Director, Pediatric Urology
Children's Hospital of Pittsburgh
Pittsburgh, Pennsylvania

Kenneth I. Glassberg, MD
Professor
Department of Urology;
Director, Division of Pediatric Urology
State University of New York
Downstate Medical Center
Brooklyn, New York

David B. Joseph, MD, FAAP, FACS
Professor of Surgery
University of Alabama at Birmingham;
Chief, Pediatric Urology
Children's Hospital
Birmingham, Alabama

George W. Kaplan, MD, MS, FACS, FAAP
Clinical Professor
Departments of Surgery and Pediatrics
University of California at San Diego;
Chief of Urology
Children's Hospital
San Diego, California

Robert Kay, MD
Section of Pediatric Urology
Cleveland Clinic Urological Institute
Cleveland, Ohio

William A. Kennedy II, MD
Assistant Professor
Department of Urology
Stanford University School of Medicine and Lucile Salter Packard Children's Hospital at Stanford
Stanford, California

Barry A. Kogan, MD
Professor
Departments of Surgery and Pediatrics
Albany Medical College;
Chief, Division of Urology
Albany Medical Center
Albany, New York

Stanley J. Kogan, MD
Clinical Professor of Urology
Department of Urology
Weill Medical College of Cornell University
New York Medical College
New York, New York;
Attending pediatric urologist (private practice)
White Plains, New York

Irene M. McAleer, MD, FACS, FAAP
Assistant Clinical Professor
Departments of Surgery and Pediatrics;
Senior Attending (Urology Division)
Children's Hospital
San Diego, California

Emilio Merlini, MD
Chief, Department of Pediatric Surgery
Ospedale "Maggiore Della Caritá"
Novara, Italy

Michael E. Mitchell, MD
Professor
Department of Urology
University of Washington School of Medicine;
Chief, Division of Pediatric Urology
Children's Hospital and Regional Medical Center
Seattle, Washington

Hiep T. Nguyen, MD
Assistant Professor
Departments of Urology and Pediatrics
University of California at San Francisco;
Physician
University of California at San Francisco Medical Center
San Francisco, California

Dix P. Poppas, MD
The Richard Rodgers Family Assistant Professor of
Pediatric Urology;
Director, Laboratory for Minimally Invasive Urology Surgery
The New York Hospital–Cornell Medical Center
New York, New York

Alan B. Retik, MD
Professor of Surgery (Urology)
Department of Surgery
Harvard Medical School;
Chief, Department of Urology
Children's Hospital
Boston, Massachusetts

Richard C. Rink, MD
Robert A. Garrett Professor of Pediatric Urologic Research
Department of Urology
Indiana University School of Medicine;
Chief, Pediatric Urology
James Whitcomb Riley Hospital for Children
Indiana University School of Medicine
Indianapolis, Indiana

Jonathan H. Ross, MD
Head, Section of Pediatric Urology
Cleveland Clinic Urological Institute
Cleveland, Ohio

Michael P. Solliday, MD
Physician
Hudson Valley Urology, PC
Poughkeepsie, New York

Francis X. Schneck, MD
Clinical Assistant Professor
Department of Urology
University of Pittsburgh School of Medicine;
Pediatric Urology Associates
Pittsburgh, Pennsylvania

CONTENTS

1

Office Urology

George W. Kaplan and Irene M. McAleer

The office practice of pediatric urology is quite different from that of adult urology. First, the office setting in pediatric urology must consider the fact that patients are always accompanied by a parent (or parents), often by siblings as well, and sometimes by an extended family (*eg*, grandparents). Therefore, waiting rooms and examination rooms need to be larger than those for adults to accommodate the extra people. One also needs to provide diversions (*eg*, fish tanks, toys) for toddlers and younger children who are often impatient, as well as suitable reading material for both older children and adults. Examination rooms should be well lit, and the ambient temperature should be neither too hot nor too cold.

Far fewer procedures are performed on children in the office compared with adults because endoscopy is neither frequently necessary nor well tolerated without anesthesia by most children. However, the office visit is the best chance to establish rapport with parents and children and the best setting in which to educate parents regarding diagnosis and treatment and to enlist their support for the planned management. There should be, at a minimum, facilities for the collection of urine specimens and for the performance of chemical (dipstick) and microscopic urinalysis. The ability to perform ultrasound examination of the abdomen and urodynamics are desirable adjuncts. Most postoperative care is provided in the office setting.

It is essential that office personnel be friendly, helpful, and caring, but also efficient. The era of managed care has introduced layers of bureaucracy that present roadblocks to care. The office staff should be prepared to assist families to obtain needed records, imaging examinations, authorizations for treatment, and so on. Schedules must take into account the work habits of the physicians so that ample time is provided for counseling parents when necessary, but schedules should also avoid leaving practitioners idle.

The most common reasons for urologic consultation include prenatal counseling for antenatally diagnosed hydronephrosis; management of voiding dysfunction and incontinence; and evaluation of abdominal masses and hydronephrosis, hematuria or urinary infection, genital abnormalities (*eg*, hypospadias, epispadias, cryptorchidism, hydroceles, ambiguous genitalia, labial masses), and abdominal or testicular pain. Discussion of antenatal counseling, the management of most genital abnormalities, and urinary infection are covered elsewhere in this volume.

Causes of Abdominal Pain in Children

- Hydronephrosis
- Kidney stones
- Vesicoureteral reflux
- Distended bladder
- Constipation

◗ **FIGURE 1-1.** Causes of abdominal pain in children. Many children present to their primary care physicians with acute or chronic abdominal pain. It is sometimes suspected that the cause of the pain arises from the urinary tract; for that reason, urologist consultation is sought. The most common diagnoses producing pain that urologists encounter in children are shown here.

Hydronephrosis is usually not painful, but patients with ureteropelvic obstruction sometimes present with intermittent episodes of acute abdominal pain and vomiting. The pain may be located in the epigastrium rather than in the flank. Kidney stone disease is a cause of abdominal pain that is frequently overlooked in children. Calculus disease should be considered any time a child presents acutely with abdominal pain and hematuria. In our opinion, an intravenous urogram or a noncontrast spiral computed tomography scan at the time of acute presentation is the best method for diagnosing such kidney stones.

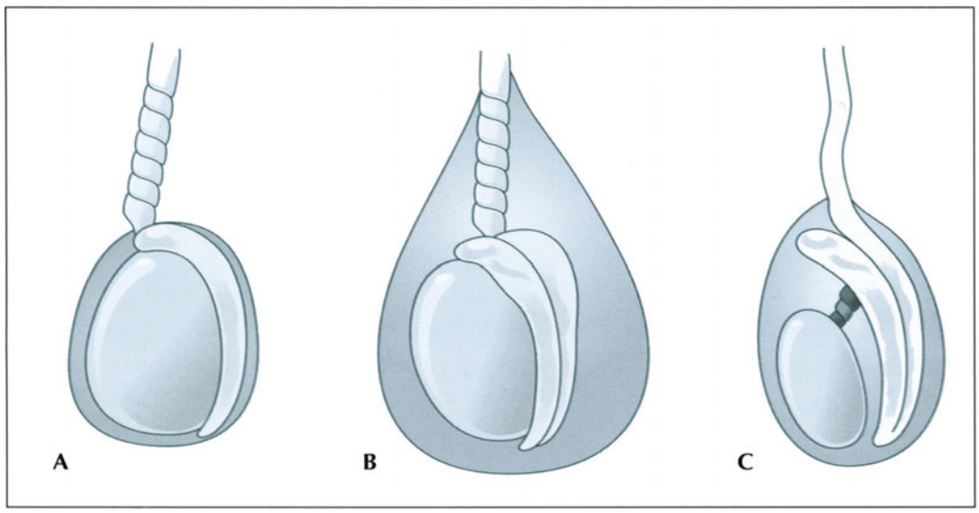
Vesicoureteral reflux is not usually thought to be painful; however, some children with reflux do complain of flank pain with a full bladder and during voiding. The pain is characteristically relieved by voiding. A distended bladder can be painful and is a frequent urologic cause of lower abdominal pain in toddlers. Upper abdominal pain produced by constipation is quite common in children and, even though it is not a urologic problem, it is a frequent diagnosis in pediatric urologic practice.

The history of the pain is quite important to diagnosis. Its location, timing, and nature can be clues to its cause. Because children do not characterize their pain well, the nature and frequency of the pain can be difficult to elicit. Whether nausea and vomiting accompany the episodes of pain is important. In addition, a history of incontinence, encopresis, or voiding dysfunction may point to constipation or bladder distention (or both) as diagnostic considerations. On physical examination, it is important to search for abdominal masses; rectal examination is an important but often omitted adjunct to the examination. Urinalysis is important in looking for white blood cells, red blood cells, and crystals. Imaging studies are essential and often include an ultrasound examination, a plain film of the abdomen, or an intravenous urogram. Intravenous urography is, in our opinion, the single best study for identifying urinary stone disease, and ultrasound is the best initial study for evaluating masses or hydronephrosis.

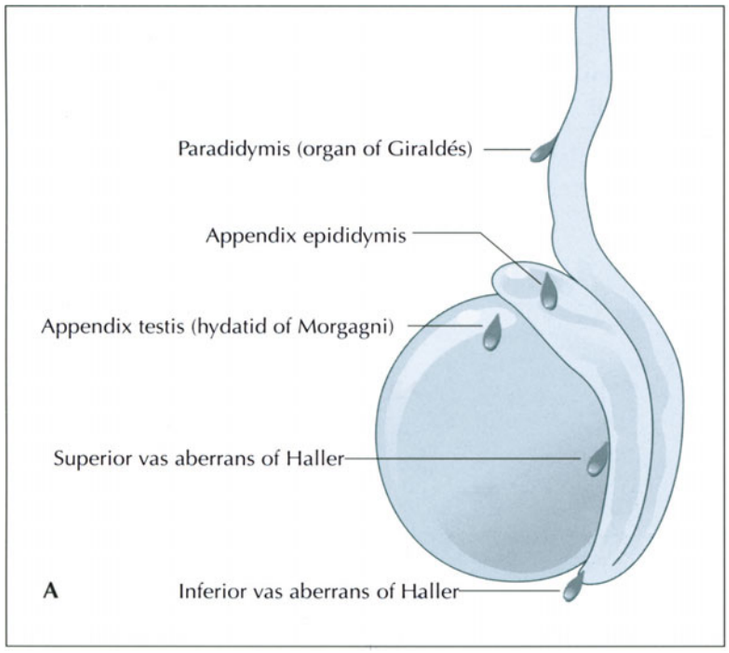
Causes of Testicular Pain

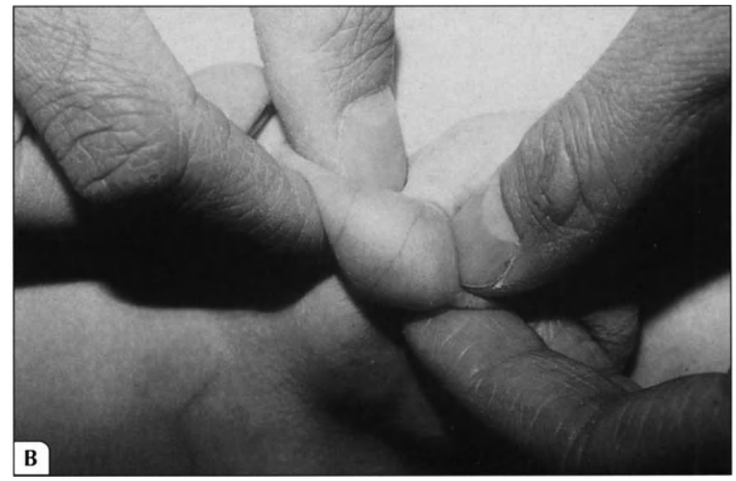
- Torsion of the spermatic cord
- Torsion of the testicular appendages
- Epididymitis
- Orchitis
- Acute idiopathic scrotal edema
- Henoch-Schönlein purpura
- Trauma
- Tumor
- Varicocele

◗ **FIGURE 1-2.** Causes of testicular pain. Acute onset of pain in a boy's scrotum is a frequent source of consternation and confusion to practitioners. Fortunately, most of the diagnoses are not time-related emergencies; however, torsion of the testis is such an emergency. It is essential that a tentative diagnosis be obtained quickly to determine if the problem requires a surgical solution. If surgery is indicated, it should be accomplished promptly.



◗ **FIGURE 1-3.** Testicular torsion. Testicular torsion is a lesion that presents by one of two mechanisms. In newborns, torsion occurs external to the tunica vaginalis because the tunica vaginalis is only weakly attached to the overlying dartos muscle (**A**). After 6 to 8 weeks of extrauterine life, these attachments become much stronger and extravaginal torsion is exceedingly uncommon. Torsion of the cord in an older child occurs because there is a lack of the normal attachments between the epididymis and the tunica vaginalis or because the mesorchium is somewhat longer than normal (**B** and **C**). Under these circumstances, the testis can twist on its blood supply within the confines of the tunica vaginalis. Although infants may have no pain and little if any swelling or erythema, older boys usually present with acute onset of scrotal pain, swelling, and erythema [1].





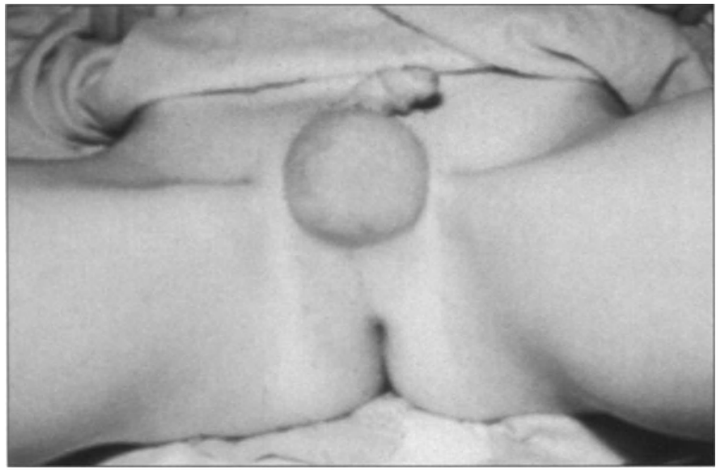
◗ **FIGURE 1-4.** Testicular appendage torsion. There are five testicular appendages [2] (**A**); only one (*ie*, the appendix testis) is of müllerian origin, and this is the one that most frequently tends to infarct, presumably by twisting on its blood supply. However, any of the other four can also infarct. The signs and symptoms of torsion of the appendix testis are the same as those for torsion of the spermatic cord but are usually of lesser intensity. If seen early in its course, a pathognomonic finding of torsion of a testicular appendage is the "blue dot" sign (**B** and **C**) in which the twisted and ischemic appendix testis is seen as a bluish area through the thin scrotal skin [3].

Causes of Epididymo-orchitis in Children

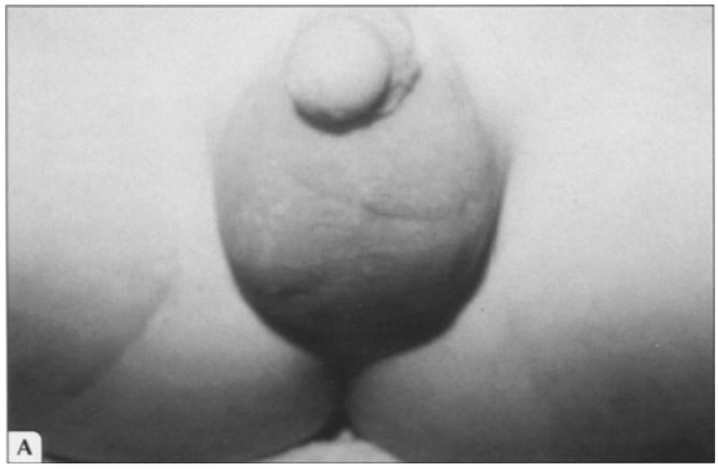
Bacterial
- Typhoid
- Scarlet fever
- Diphtheria
- *Staphylococcus* spp.
- *Klebsiella* spp.
- *Haemophilus* spp.
- *Salmonella* spp.
- Mediterranean fever
- Tuberculosis
- Syphilis

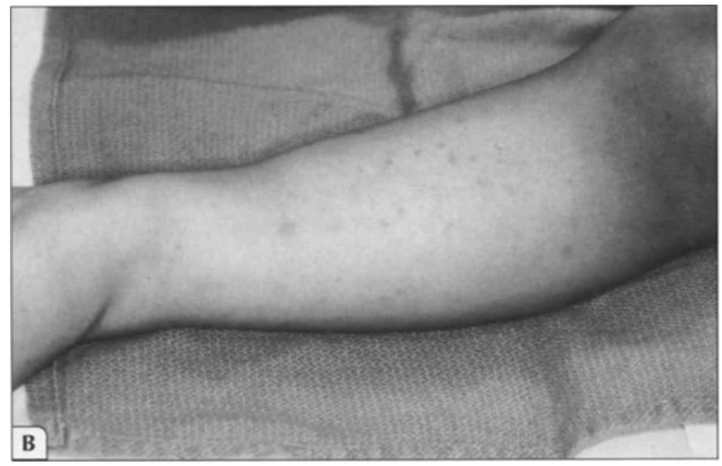
Viral
- Mumps
- Influenza
- Dengue
- Phlebotomy, fever
- Chicken pox
- Infectious mononucleosis
- Coxsackie
- Lymphocytic choriomeningitis
- Bat salivary gland virus
- Lymphopathic venereum

◗ **FIGURE 1-5.** Causes of epididymo-orchitis in children. Epididymitis is seen in children less commonly than it is in adults. In most cases, epididymitis is associated with urinary infection in a child, but it also can occur in association with a number of bacterial or viral diseases. In almost all instances, it occurs in the course of the acute illness.

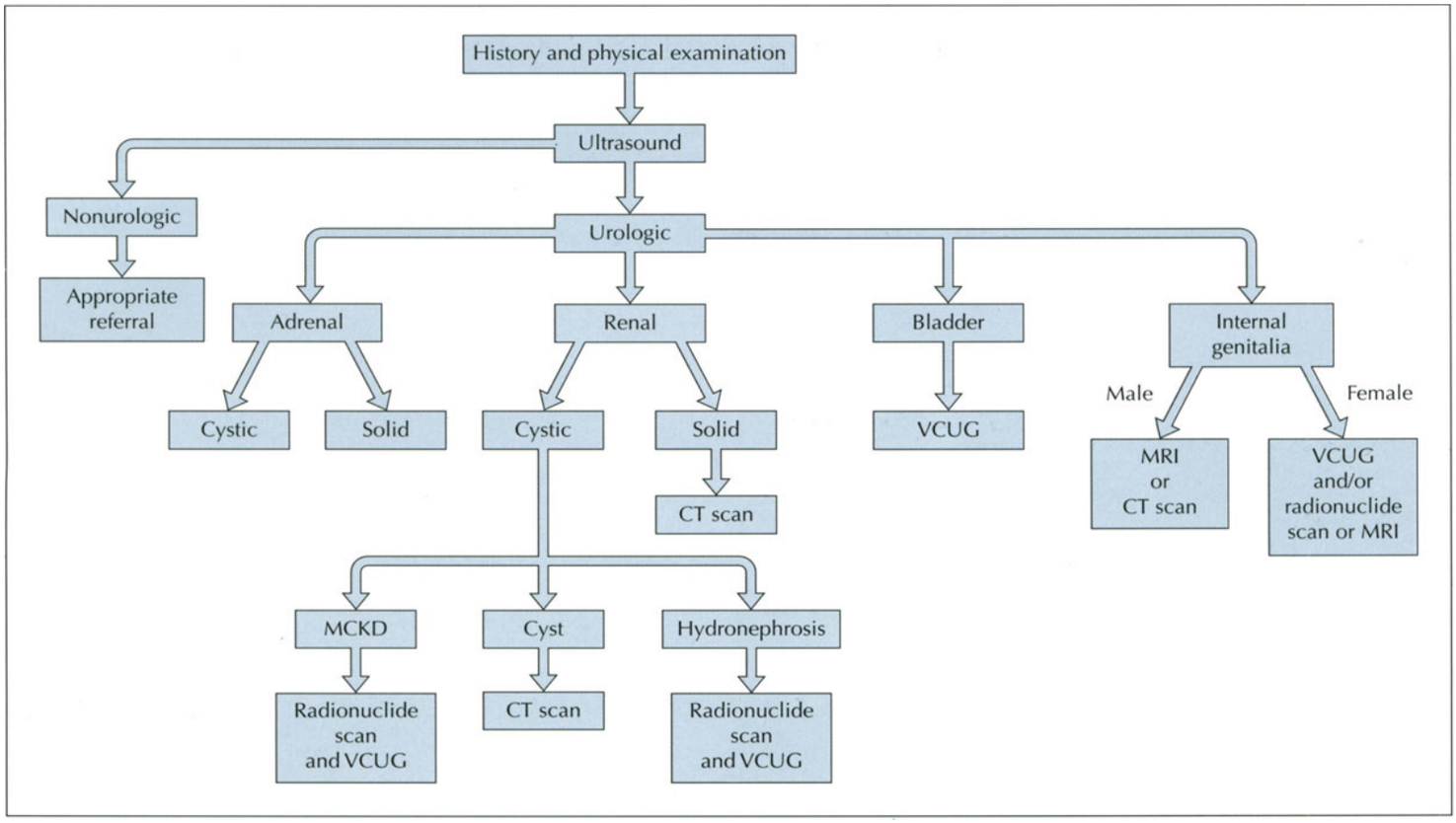


◗ **FIGURE 1-6.** Acute idiopathic scrotal edema. This is a poorly understood lesion seen in younger children that can mimic torsion of the spermatic cord [4]. However, in this instance, the redness extends beyond the scrotal margin and there is edema and tenderness of the scrotal skin, but the underlying tissues are perfectly normal. In a cooperative child, the testis itself can be felt through the reddened, edematous skin and can be noted to be normal and nontender.





◗ **FIGURE 1-7.** Henoch-Schönlein purpura. This vasculitis of unknown etiology occasionally presents with scrotal pain and at times with redness and swelling of the overlying scrotal skin. The characteristic skin lesions are best identified on the buttocks (**A**) and on the extensor surfaces of the arms and legs (**B**).

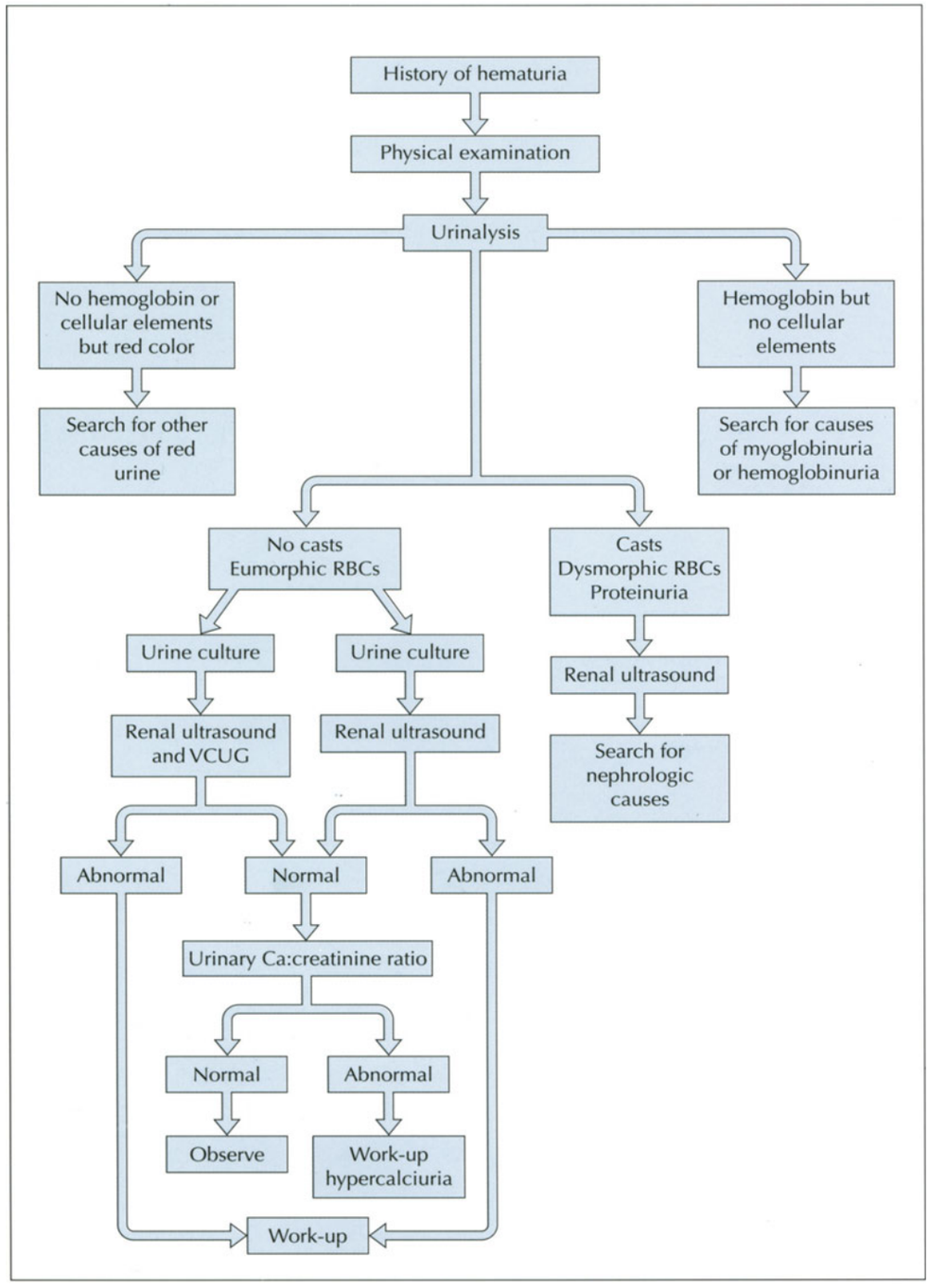


◗ **FIGURE 1-8.** Evaluation of abdominal masses in children. A common cause for presentation to the office is the evaluation of a child with an abdominal mass [5]. Although history and physical examination are important, an ultrasound examination is the cornerstone of diagnosis. This can establish whether the lesion is urologic or nonurologic. Between 50% and 75% of abdominal masses arise from the genitourinary system. If the lesion is urologic, it can originate from the adrenal glands, the kidneys, the bladder, or from the internal genitalia. CT—computed tomography; MCKD—multicystic dysplastic kidney; MRI—magnetic resonance imaging; VCUG—voiding cystourethrogram.

Differential Diagnosis of Incontinence

- Structural
  - Primary
    - Ectopic ureter
    - Single system
    - Duplex system
    - Exstrophy and epispadias
  - Secondary
    - Obstruction
      - Posterior urethral valves
      - Anterior urethral valves
      - Congenital strictures
    - Neurogenic lesions
      - Spinal dysrhaphism
      - Tethered cord
      - Spinal cord tumors
  - Trauma
    - Iatrogenic or external
- Nonstructural
  - Dysfunctional voiding (*eg*, lazy bladder syndrome, Beer-Hinman-Allen syndrome)
    - Psychogenic dysfunction
    - Giggle incontinence
    - Vaginal voiding
    - Nocturnal enuresis

◗ **FIGURE 1-9.** Differential diagnosis of incontinence. Incontinence and voiding dysfunctions are the mainstays of office practice in pediatric urology [6]. (Many of these lesions are discussed elsewhere in the text.) The overall differential diagnosis flows first from a determination of whether a structural cause exists for the incontinence. Admittedly, nonstructural causes account for far more cases of incontinence than do structural ones. Treatment of structural causes is much more satisfying than that of nonstructural causes and yet structural causes, in many ways, provide many more diagnostic and therapeutic challenges.



◗ **FIGURE 1-10.** Evaluation of hematuria. The evaluation of children with hematuria is another important area of pediatric urology office practice. History and physical examination are sometimes helpful, but often there are no clues to be found. Urinalysis is a cornerstone of diagnosis in that if red cell casts are present, the cause of the hematuria is most certainly from the parenchyma. The appropriate evaluation differentiates between the various nephritides, discussion of which is beyond the scope of this chapter. If no casts are present, a urine culture should be obtained to rule out urinary infection. If the hematuria is only microscopic and if evaluation as shown here does not yield any concrete diagnosis, it is highly unlikely that endoscopy will shed any further light on the subject [7]. Even if gross hematuria is present, the yield of endoscopy is small but a better case can be made for endoscopy under such circumstances. RBCs—red blood cells; VCUG—voiding cystourethrogram.

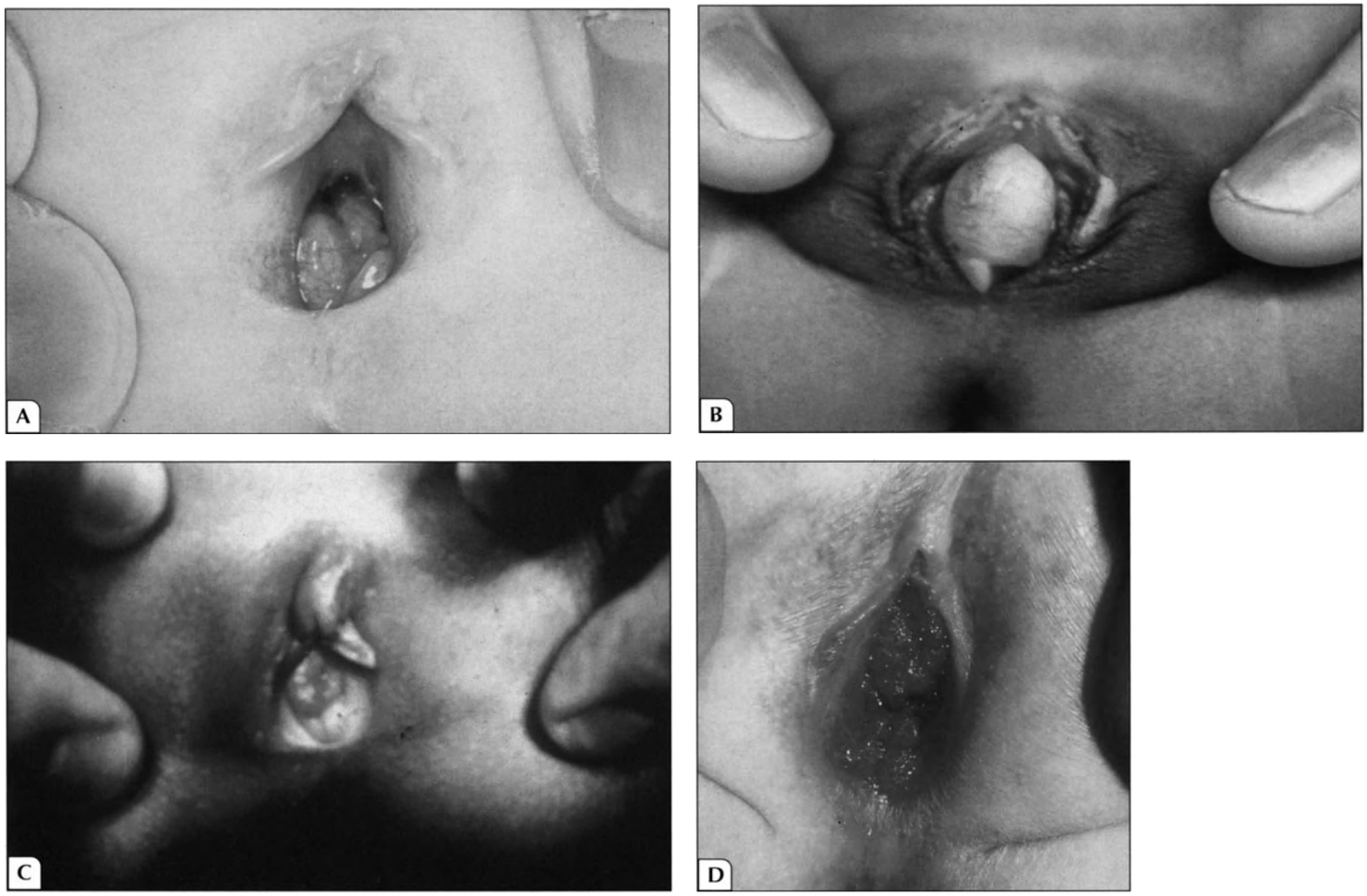
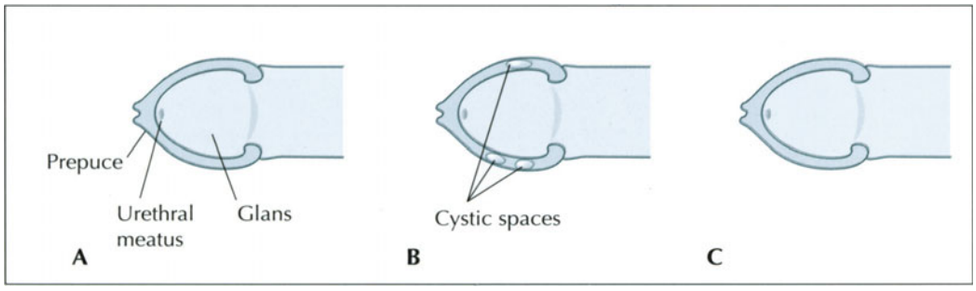
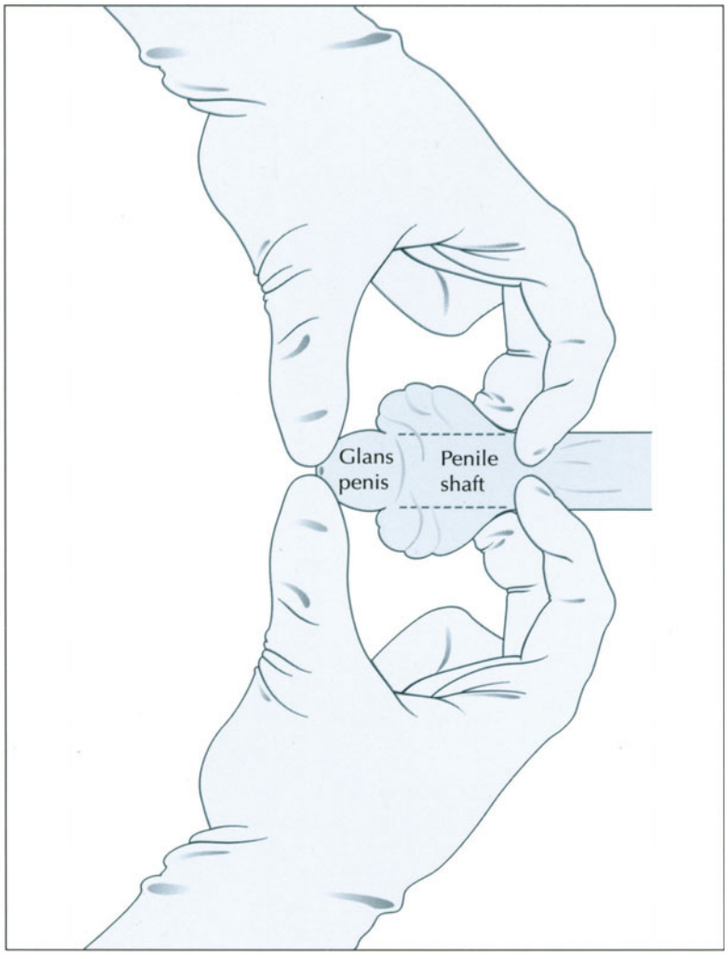


FIGURE 1-11. Interlabial masses. Yet another area of office consultation involves the differential diagnosis of interlabial masses in girls. Pediatric gynecology is an orphan area of medicine, so the management of these lesions often falls to urologists by default [8]. There are six lesions that may present as an interlabial mass. These include a prolapsed ureterocele (**A**), vaginal inclusion cyst (**B**), sarcoma botryoides urethral prolapse (**C**), condyloma acuminatum (**D**), and hydrocolpos (**E**). Ultrasound imaging aids in establishing the diagnosis of ureterocele, sarcoma, and hydrocolpos. Vaginal inclusion cysts usually appear in infants in the septum between the urethra and vagina and are under hormonal control such that they tend to involute as the maternal estrogen effect dissipates. Condyloma can sometimes be confused with tumor even though the appearance is usually sufficiently different. Urethral prolapse presents acutely, especially in blacks.



◗ **FIGURE 1-12.** Penile lesions. Penile lesions account for a large volume of office urology visits. However, the natural history of the foreskin is not well understood by many physicians in this country and, for this reason, many children are referred either because the foreskin is not retractable or because there are lumps of smegma encysted under the foreskin. In reality, the inner preputial epithelium and the glans are not separated from one another in uncircumcised boys for many months and sometimes years after birth [9] (**A**). The process of separation occurs by the formation of small cystic spaces (**B**), which sometimes fill with dead cells and oil (*ie*, smegma) that may become manifest as lumps under the penile skin. Untreated, these dissipate spontaneously (**C**) as the penis matures, and nothing needs to be done to hasten their maturation.



◗ **FIGURE 1-13.** Paraphimosis. Children with paraphimosis sometimes present to the urologist's office. Most episodes of paraphimosis are caused by ill-advised attempts at retraction of the foreskin. The paraphimosis can be reduced manually in many instances by grasping the shaft of the penis between the second and third fingers of both hands and pulling distally while simultaneously pushing the glans proximally with the thumbs of both hands. Hyaluronidase injected into the edematous prepuce sometimes facilitates this maneuver [10].

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2

Prenatal Urology

Hiep T. Nguyen and Barry A. Kogan

Approximately 3 million maternal ultrasound examinations are performed each year in the United States [1]. They are commonly performed as a routine examination during pregnancy, permitting the early identification of numerous congenital anomalies in the developing fetus. Based on large population studies, the incidence of congenital anomalies detected by prenatal ultrasound examinations is 1% to 2% [2], with urinary tract malformations being the most frequently detected anomalies [3]. Dilation of the collecting system (*ie*, hydronephrosis), the hallmark of urinary tract obstruction, represents approximately 50% of all abnormalities detected by ultrasound examination [4].

The early diagnosis of hydronephrosis has significantly affected the clinical presentation and management of patients with urinary tract obstruction. Before the advent of routine prenatal sonographic scanning, children with urinary tract obstruction commonly presented with abdominal masses, hematuria, pain, calculi, or urinary tract infection. Prenatal ultrasound imaging provides the opportunity to diagnose a urinary tract obstruction before the onset of these complications. With early diagnosis, urologists may now institute treatments to protect renal function and to permit normal renal growth and development.

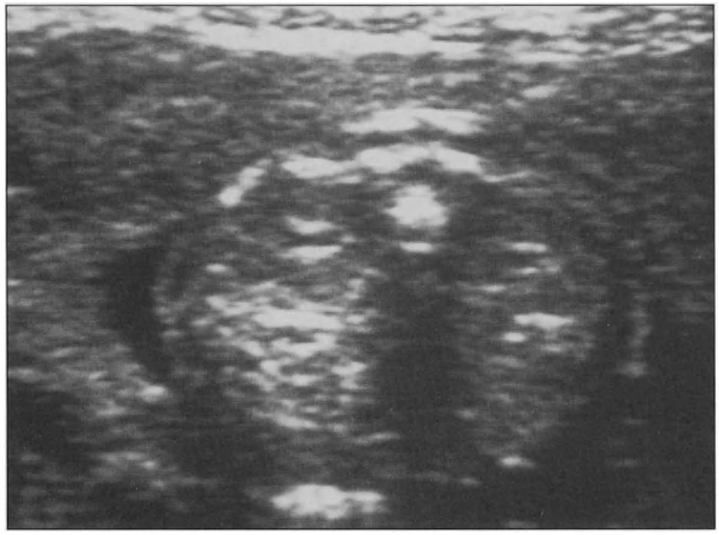
On the other hand, clinical experience has demonstrated that the presence of hydronephrosis does not necessarily indicate the presence of obstruction. During normal renal development, the collecting system may dilate transiently without much consequence to postnatal renal function. The dilemma is in determining which patients with hydronephrosis have clinically significant obstruction and, therefore, which patients require surgical intervention. This chapter addresses issues associated with prenatal ultrasonographic diagnosis of congenital uropathies and the evaluation and management of prenatally detected hydronephrosis.

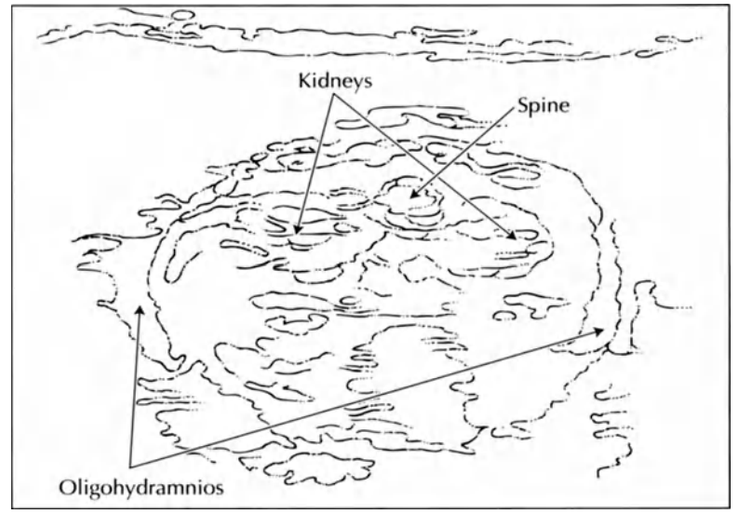
Maternal ultrasonography has allowed for the detection of genitourinary anomalies *in utero*, the most common being hydronephrosis. However, further research is needed to further refine this test for the determination of the clinical significance of these anomalies. To achieve this, we will have to further our understanding of the pathophysiology and natural history of these diseases, in particular of prenatal hydronephrosis. For now, it should be emphasized that prenatal hydronephrosis is not necessarily a normal condition but does not always indicate an obstruction. Regardless of the management options, careful monitoring is essential.

Important Sonographic Timepoints in the Development of the Urinary Tract in Humans

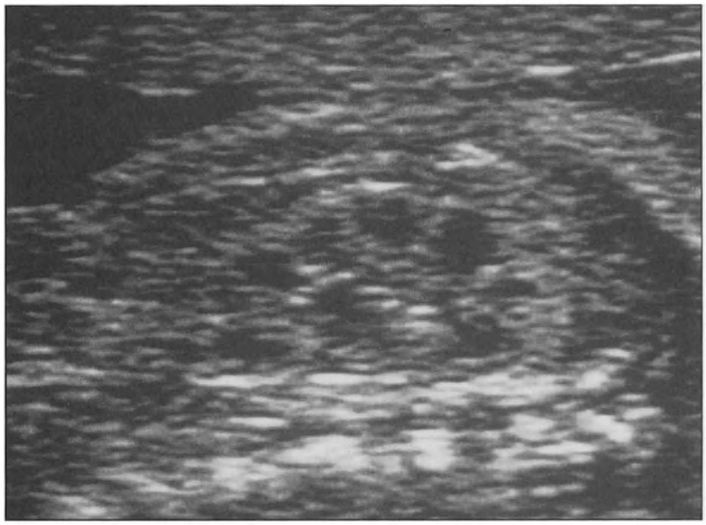
Event	*Time (wk of gestation)*
Ureteral bud formation in the fetus	5th
Urine formation by the fetal kidneys	8th
Fetal kidneys reliably visualized by ultrasound	15th
Emptying of the fetal bladder visualized by ultrasound	15th
Hydronephrosis visualized by ultrasound	
As early as	12th to 14th
On a regular basis	16th to 18th
Amniotic fluid dependent on fetal urine production	16th
Distinct appearance of internal renal architecture on ultrasound	20th

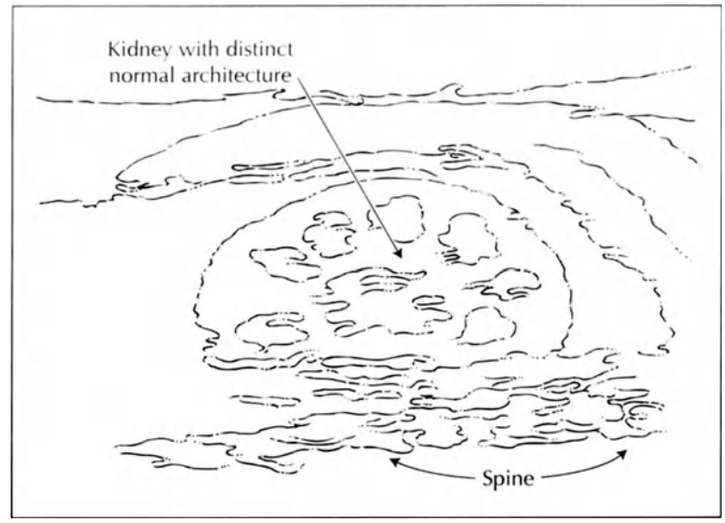
◗ **FIGURE 2-1.** Important sonographic timepoints in the development of the urinary tract in humans. In humans, the development of the urinary tract begins with the formation of the ureteric bud at the fifth week of gestation. The ureteric bud induces the differentiation of the metanephric blastema into mature renal elements; in turn, the ureteric bud differentiates into the collecting system. By the eighth week, the fetal kidneys become functional and produce urine [5]. The fetal kidneys and bladder can be visualized on maternal ultrasonograms by the fifteenth week of gestation [6]. The fetal bladder volume is approximately 4 to 5 cc, and the fetus typically appears to void every 30 to 60 minutes [7]. Dilation of the collecting system can be detected as early as the twelfth week of gestation but more reliably by the sixteenth to eighteenth week [8].





◗ **FIGURE 2-2.** Utrasound image of a fetus viewed in transverse section. Note the lack of amniotic fluid surrounding the fetus. Evaluation of the amniotic fluid is important after the sixteenth week of gestation because amniotic fluid volume largely depends on fetal urine production at this time [9]. The presence of oligohydramnios detected after the sixteenth week of gestation suggests problems with urinary production, drainage, or both.





◗ **FIGURE 2-3.** Fetus at the twentieth week of gestation showing a kidney with a distinct normal architecture. By the twentieth week of gestation, the internal fetal renal architecture appears distinct on maternal ultrasound images; this change is presumably caused by the deposition of fat in the perirenal space [10]. Failure to visualize the internal renal architecture suggests abnormal renal development and has a poor prognosis for normal postnatal renal function.

Specific Indications for Maternal Sonography to Detect Urinary Tract Anomalies

Indications	*Etiology*
Small fetus by clinical examination (fundal height)	Presence of oligohydramnios
Persistent breech presentation	Decreased urine production
Presence of oligohydramnios on routine ultrasound	Obstruction to urinary flow
Elevated α-fetoprotein level	Renal agenesis, congenital nephrotic syndrome, obstructive nephropathy, spina bifida
Family history of renal diseases	Renal agenesis, polycystic kidney disease, medullary cystic kidney disease, congenital nephrotic syndrome, prune belly syndrome, vesicoureteral reflux

◗ **FIGURE 2-4.** Specific indications for maternal sonography to detect urinary tract anomalies. There is a lack of consensus as to whether maternal fetal ultrasonography should be performed routinely during pregnancy. In some areas of the United States, the routine use of prenatal ultrasound imaging depends on the availability of in-office or nearby center-based ultrasound technology, the familiarity of health care providers with sonographic techniques and its clinical implications, and the willingness of insurance companies to pay for these examinations. Despite this lack of consensus, there are specific indications for genitourinary evaluation *in utero* [11].

Assessment of Prenatal Hydronephrosis

Subjective

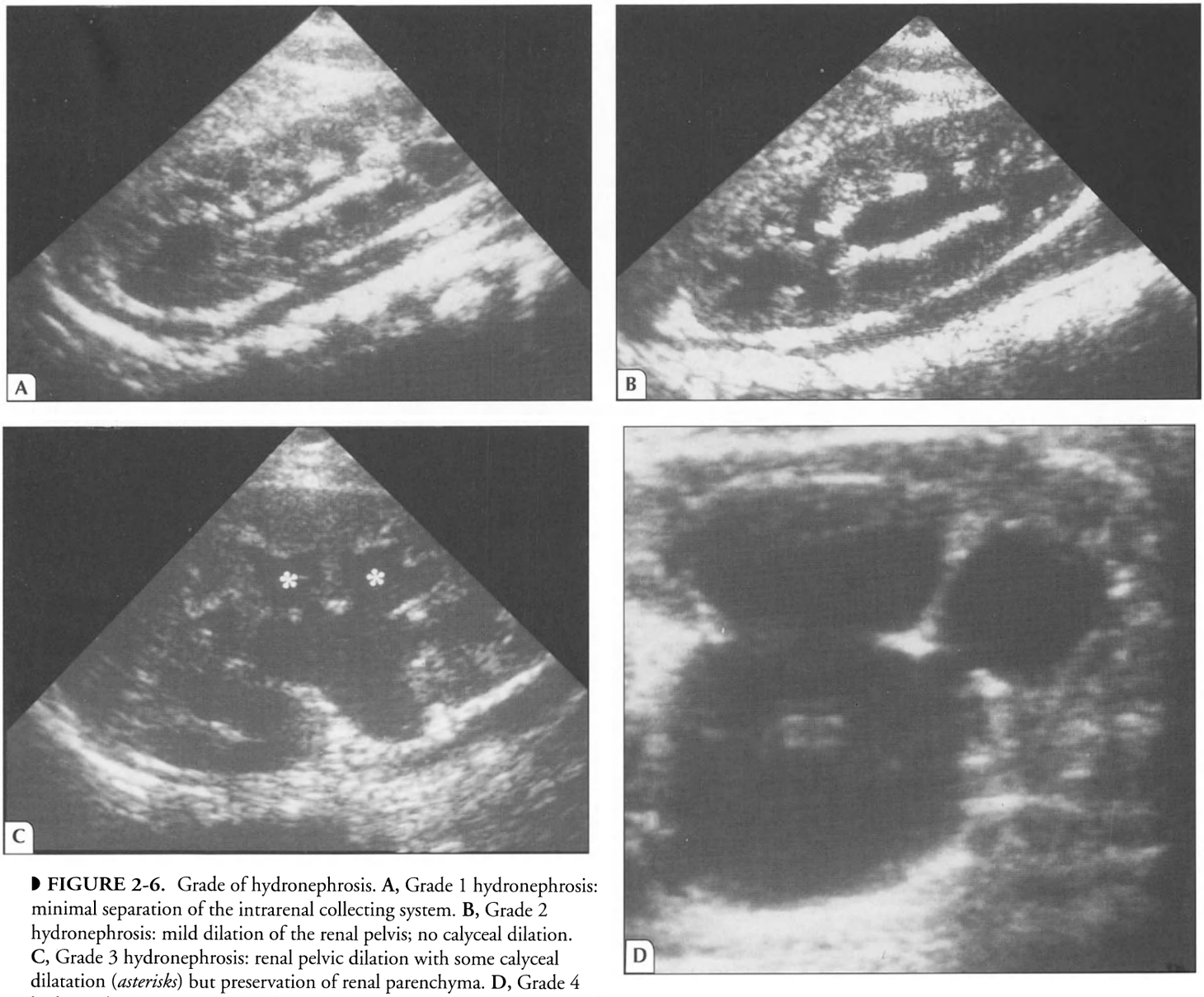
Grade 0	Normal echogenic central renal complex
1	Dilated renal pelvis splitting central renal complex
2	Dilated renal pelvis confined to the sinus and no calyces dilatation
3	Renal pelvis dilated beyond the sinus, dilated calyces but parenchyma not thinned
4	Dilated renal pelvis and calyces and parenchyma thinned (50% of normal side)

Objective

Date of Detection	*Severity*	*Renal Pelvis AP Diameter, mm*
2nd trimester	Mild	5–8
	Moderate	8–10
	Severe	>10
3rd trimester	Mild	10
	Moderate	10–15
	Severe	>15

◗ **FIGURE 2-5.** Assessment of prenatal hydronephrosis.

Hydronephrosis is the most common abnormality detected prenatally. Dilation of the urinary tract may be defined subjectively as in the system for grading the severity of hydronephrosis by sonography as adopted by the Society of Fetal Urology [12] or, more objectively, by accurate measurements of renal pelvic anteroposterior (AP) diameter [4,13]. Measurement of pelvic AP diameter should be correlated with the age of gestation at diagnosis because it has been shown to vary during gestation. It should be noted, however, that when a 10-mm pelvic dilation is used to define hydronephrosis, the false-positive rate ranges from 9% to 50% [14,15].



◗ **FIGURE 2-6.** Grade of hydronephrosis. **A,** Grade 1 hydronephrosis: minimal separation of the intrarenal collecting system. **B,** Grade 2 hydronephrosis: mild dilation of the renal pelvis; no calyceal dilation. **C,** Grade 3 hydronephrosis: renal pelvic dilation with some calyceal dilatation (*asterisks*) but preservation of renal parenchyma. **D,** Grade 4 hydronephrosis: not only significant hydronephrosis but also thinning of the renal parenchyma.

Ultrasound Evaluation of Prenatal Hydronephrosis

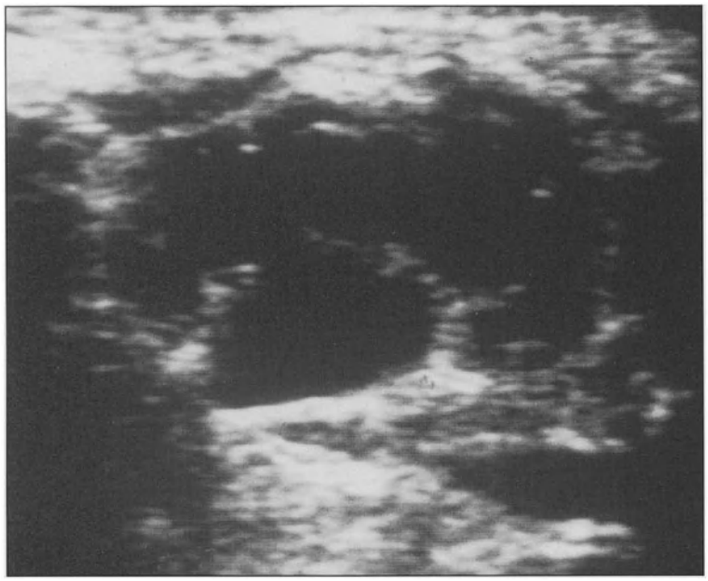
- Kidney and ureters
  - Renal parenchyma
    - Echogenicity
    - Thickness
  - Degree of upper tract dilatation
  - Unilateral versus bilateral
  - Ureteral dilatation
  - Variation in the degree of hydronephrosis
- Bladder and urethra
  - Bladder size and emptying
  - Posterior urethral dilatation
- Other
  - Amniotic fluid volume
  - Extrarenal fluid collection
  - Other anatomical anomalies
  - Gender
  - Overall growth and development

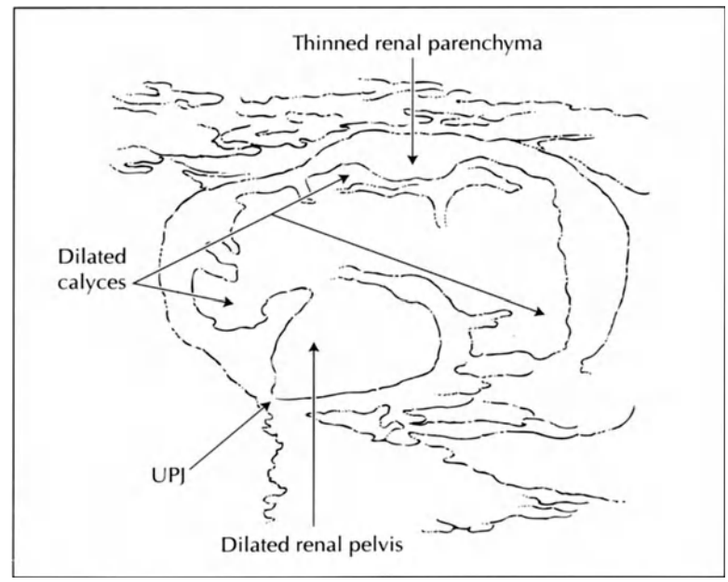
◗ **FIGURE 2-7.** Ultrasound evaluation of prenatal hydronephrosis. The simple finding of hydronephrosis is insufficient for diagnostic purposes. Complete characterization of the urinary tract is necessary to diagnose significant obstruction [16]. Together the findings help to characterize the functional importance of the urinary tract dilation, identify the etiology of the obstruction, and guide appropriate management of prenatal hydronephrosis.

Differential Diagnosis of Hydronephrosis

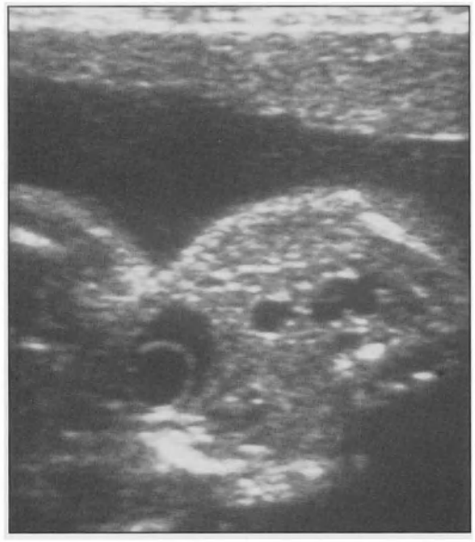
- Unilateral hydronephrosis
  - UPJ obstruction
  - UVJ obstruction
  - Ureterocele, ectopic ureter, duplex system
  - Multicystic dysplastic kidneys
  - Polycystic kidney disease
  - Vesicoureteral reflux
  - Physiologic
  - Extrarenal pelvis
- Bilateral hydronephrosis
  - Posterior urethral valves
  - Urethral aplasia
  - Prune belly syndrome
  - Megacystis–megaureter complex
  - Vesicoureteral reflux
  - Polycystic kidney disease
- Less common causes mistaken for hydronephrosis
  - Megacalicosis
  - Simple renal cyst
  - Urachal cyst
  - Ovarian cyst
  - Hydrocolpos
  - Sacrococcygeal teratoma
  - Bowel duplication
  - Duodenal atresia
  - Anterior meningocele
  - Renal tumors

FIGURE 2-8. Differential diagnosis of hydronephrosis. Ureteropelvic junction (UPJ) obstruction is the most common cause of hydro-nephrosis (39% to 64%) followed by reflux (33%), ureterovesical junction (UVJ) obstruction (9% to 14%), and posterior urethral valves (2% to 9%). The incidence of multicystic dysplastic kidneys ranges from 4% to 25% [17–19]. It is also important to recognize that not all anechoic masses detected in fetuses represent hydronephrosis; numerous other conditions may be misdiagnosed as dilation of the urinary tract.





◗ **FIGURE 2-9.** Ultrasound image of a fetus with right ureteropelvic junction (UPJ) obstruction (*see line drawing*). Note the dilation of the renal pelvis and calyces. As in this case, the renal parenchyma is usually thinned but has normal echogenicity (the exception occurs when there is severe obstruction resulting in cystic dysplasia). The ipsilateral ureter is not dilated; the bladder is normal in appearance and can be seen emptying periodically. In contrast to the fetuses with vesicoureteral reflux, those with UPJ obstruction have constant or worsening degree of pelvic and calyceal dilation on repeat scans.



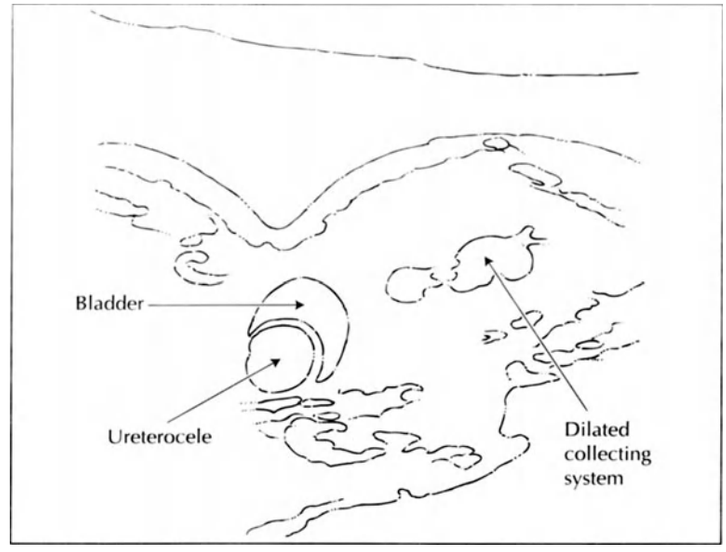
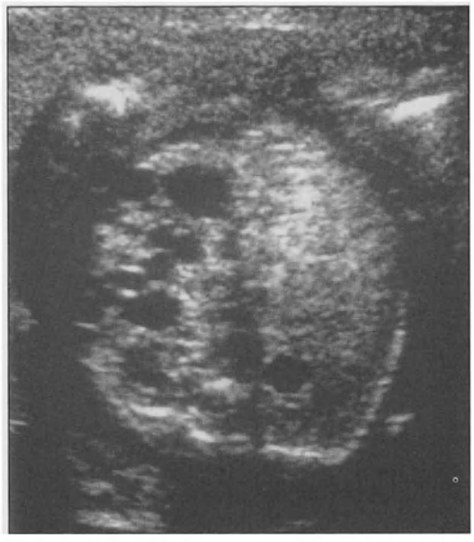


FIGURE 2-10. Ultrasound image of a fetus with a ureterocele. Note the cystic lesion in bladder. In most cases of ureteroceles, there is dilation of the ipsilateral collecting system.



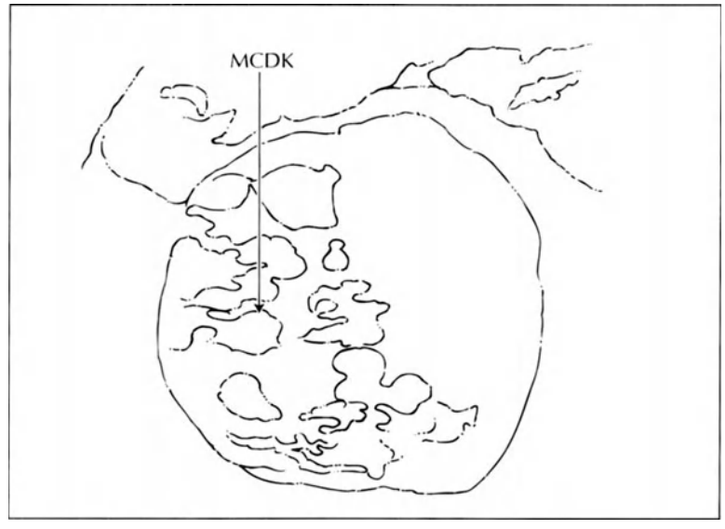
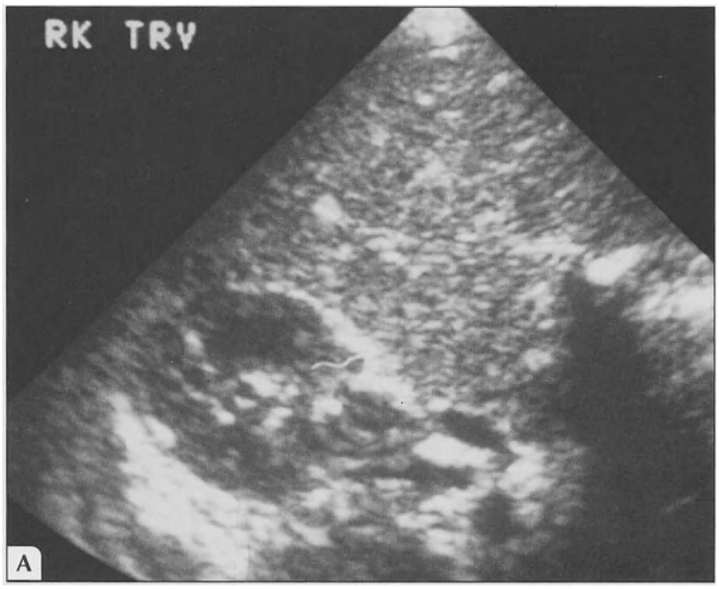


FIGURE 2-11. Ultrasound image of a fetus with a right multicystic dysplastic kidney (MCDK). Note that the renal parenchyma is echogenic, with multiple cysts dispersed throughout the kidney. As in this case, the dysplastic kidney can be very large, occupying the majority of the abdominal space. Often it may be difficult to distinguish MCDK from ureteropelvic junction obstruction sonographically.



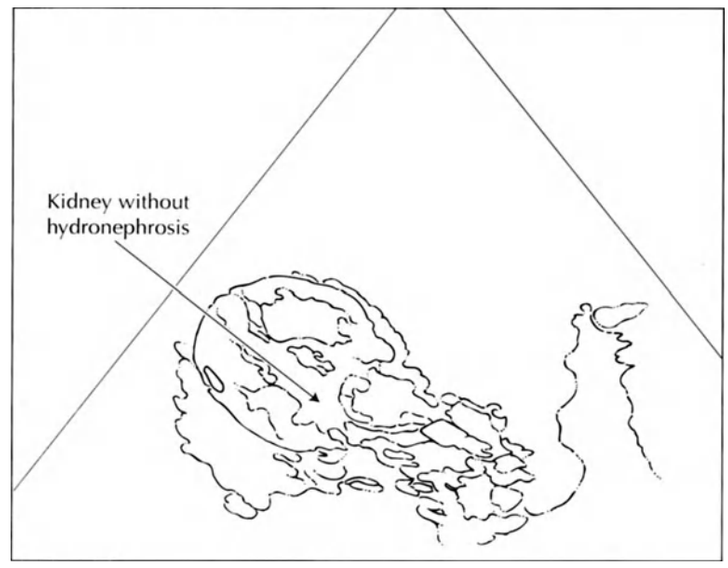


FIGURE 2-12. Ultrasound images (**A** and **B**) of a fetus with vesicoureteral reflux (VUR).

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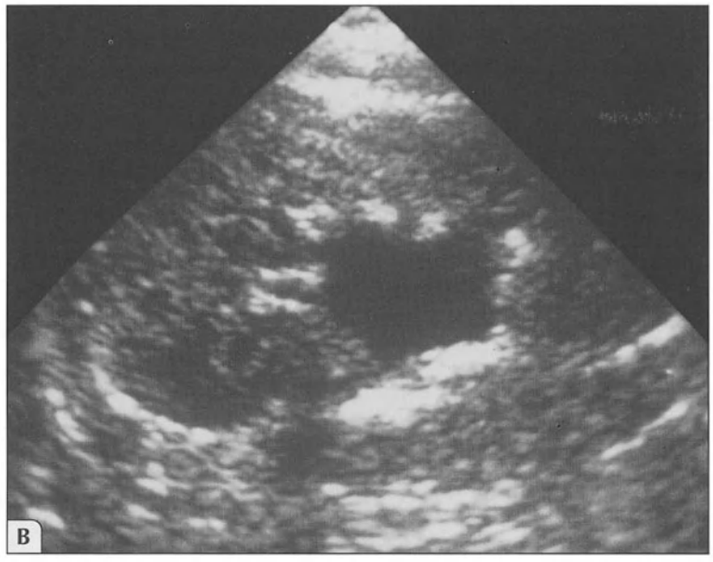
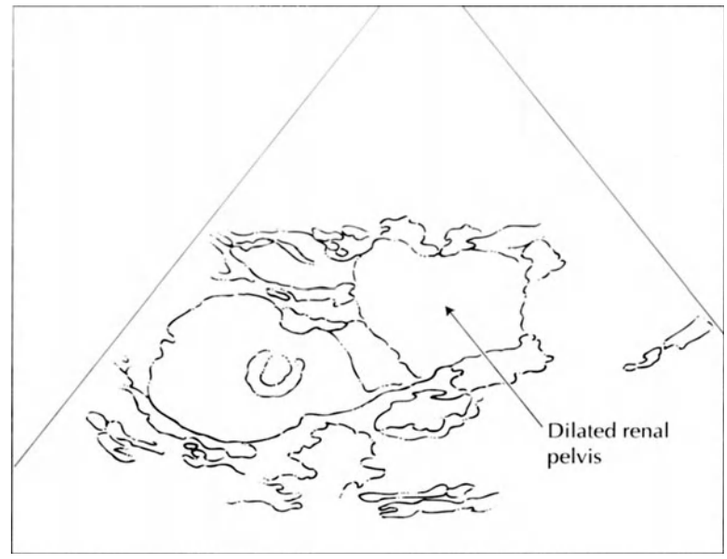
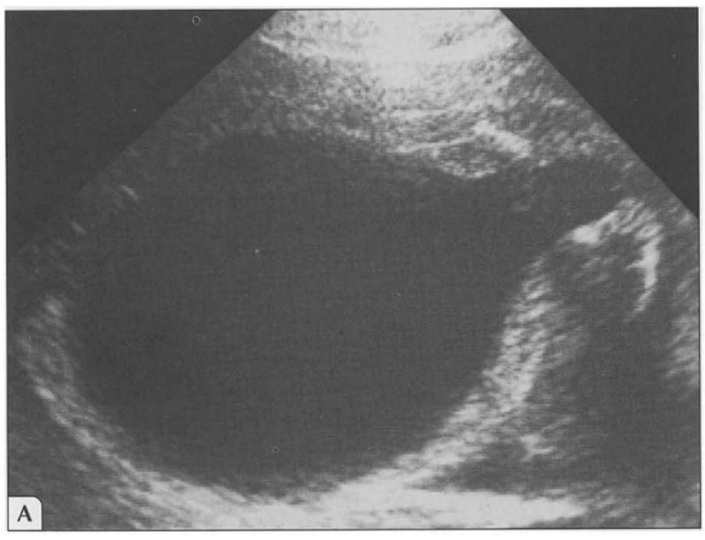
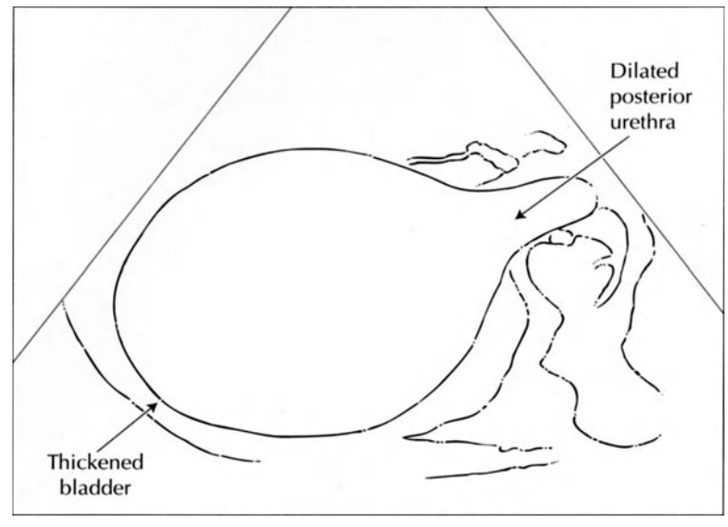




◗ **FIGURE 2-12.** (*Continued*) Note that on repeat scans, there is varying degree of hydronephrosis, diagnostic for VUR. The renal architecture is usually normal in appearance and the ipsilateral ureter is often dilated. In contrast to a fetus with bladder outlet obstruction, those with VUR have a thin-walled bladder that is dilated.





◗ **FIGURE 2-13.** Ultrasound images of a male fetus with posterior urethral valves (PUVs). **A,** Dilated posterior urethra and dilated thick-walled bladder. With repeat scans, it can be observed that bladder emptying is incomplete.

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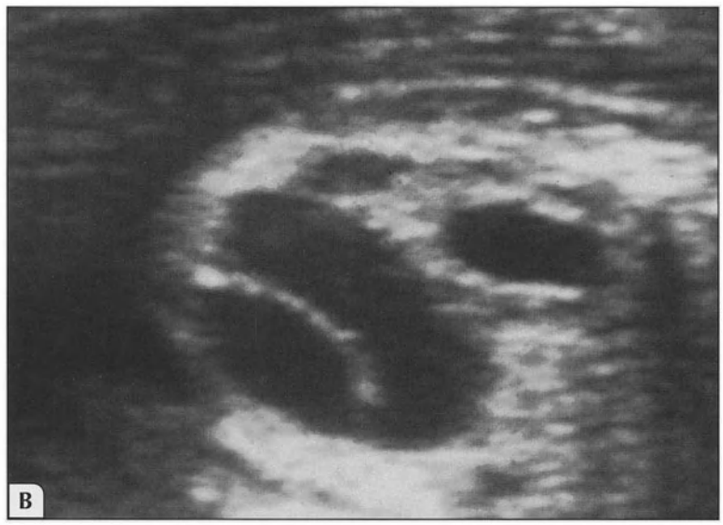
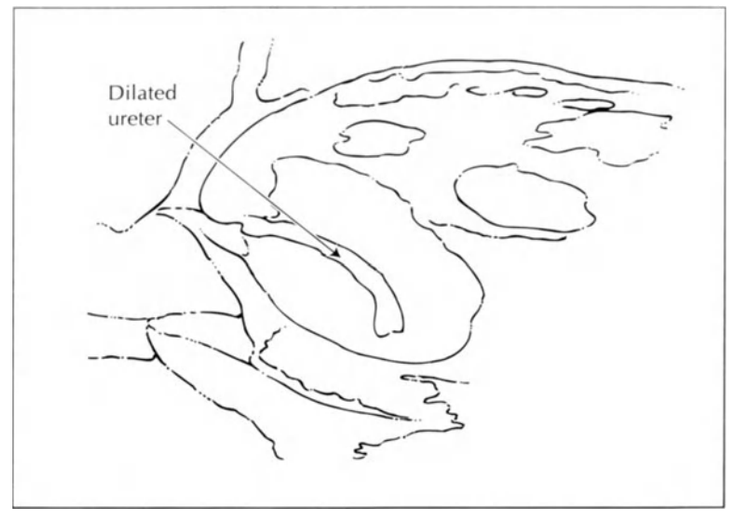
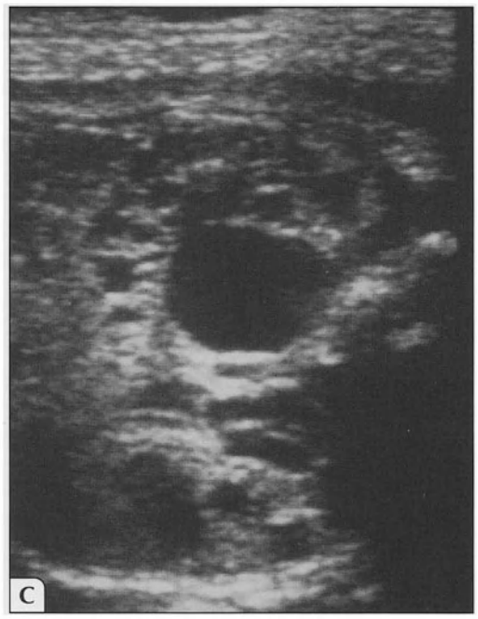
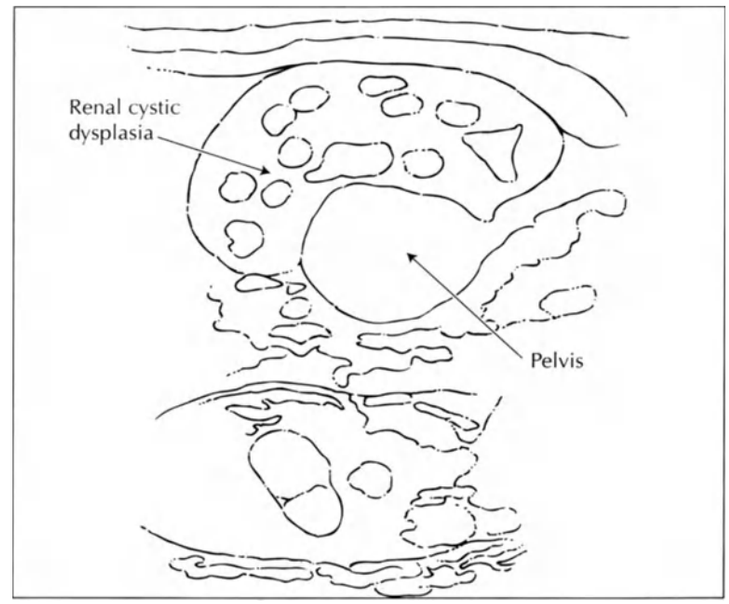






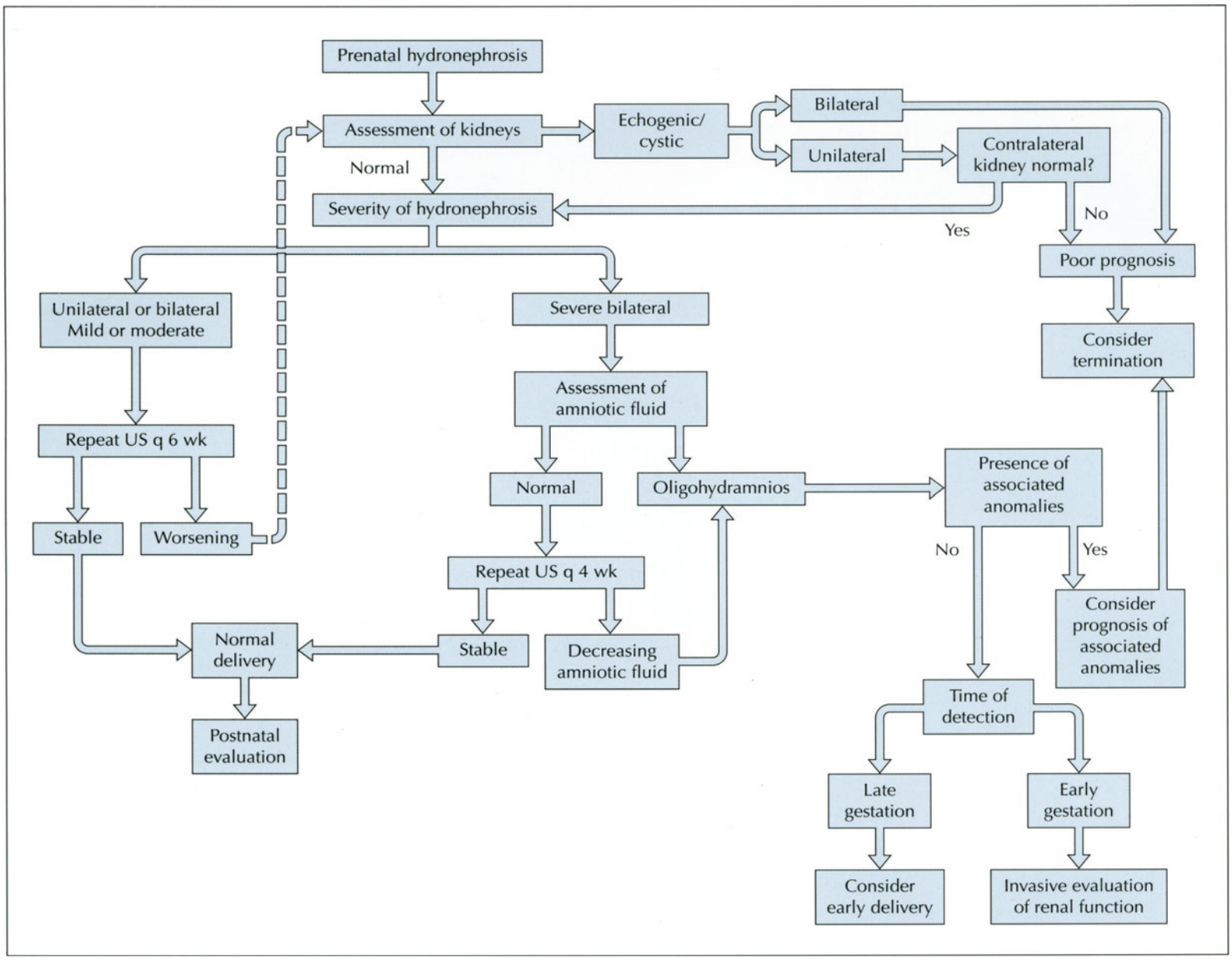


◗ **FIGURE 2-13.** (*Continued*) **B,** Both ureters are dilated. **C,** In some cases, PUVs may lead to cystic dysplasia.

Other Genitourinary Anomalies Detected on Prenatal Sonography

Anomaly	*Ultrasound Findings*
Renal cystic disease	
MCDK	Variable size cysts with no obvious communication with the collecting system
Polycystic disease (autosomal recessive)	Large echogenic kidneys and oligohydramnios
Renal hypoplasia	Small kidneys with increased echogenicity
Renal aplasia	Absent kidney but need to rule out renal ectopia
Renal tumor	Renal mass
Neuroblastoma	
Teratoma	
Congenital mesoblastic nephroma	
Extrophy	No bladder seen
Cloaca–imperforated anus	Intraluminal intestinal calcifications
Genital anomalies	
Hydroceles	
Chordee	
Ambiguous genitalia	

◗ **FIGURE 2-14.** Other genitourinary anomalies detected by prenatal sonography. These anomalies are more uncommon [11], so their identification requires a more thorough fetal evaluation by a skilled ultrasonographer and can be missed on routine surveillance ultrasound. MCDKs—multicystic dysplastic kidneys.



◗ **FIGURE 2-15.** Prenatal management of hydronephrosis. The fundamental goals in treating fetuses with prenatal hydronephrosis are to preserve renal function, permit normal renal and fetal growth and development, prevent the complications of urinary tract obstruction, and avoid unnecessary operations. There are several options in treating fetuses with hydronephrosis [20]. In general, the treatment of choice is careful observation with subsequent follow-up prenatal ultrasound (US) examinations. Prenatal intervention is rarely necessary, with the principle indication being progressive oligohydramnios. However, all infants with prenatal hydronephrosis require postnatal evaluation to identify those with clinically significant urinary tract anomalies.

One option is induction of early delivery. Again, this should be used only rarely, the particular indication being oligohydramnios that develops late in gestation. However, lung maturity should be assessed carefully to ensure the viability of the fetus. When necessary, prenatal maternal steroids or postnatal surfactant therapy have been shown to help accelerate lung maturity, decreasing the risk of early delivery. After the thirty-fifth to thirty-sixth weeks of gestation, delivery can usually be safely induced with minimal pulmonary risk; however, the true benefit of this is uncertain.

Another treatment option is elective termination. This option may be medically appropriate for fetuses with severe bilateral hydroureteronephrosis and cystic kidneys or fetal urinary biochemical abnormalities predictive of dysplasia, karyotypic abnormalities, or associated anatomic anomalies (*eg*, cardiac and neural). However, because of the seriousness of this option, careful evaluation by a team of physicians that includes obstetricians, perinatologists, pediatric urologists, and ethicists is recommended before this option is elected.

PRENATAL MANAGEMENT OF HYDRONEPHROSIS

Favorable Fetal Urinary Biochemical Values	
Sodium, *mEq/L*	< 100
Osmolality, *mOsm/kg of water*	< 210
Chloride, *mEq/L*	< 90
β_2-microglobulin, *mg/L*	< 2
Total protein, *mg/dL*	< 20

FIGURE 2-16. Favorable fetal urinary biochemical values [21]. The final alternative is some form of *in utero* fetal intervention, which is not common [20]. It is indicated in cases with the following criteria: bilateral (or unilateral hydronephrosis in a solitary kidney) and progressive hydronephrosis, oligohydramnios, no karyotypic or anatomic anomalies, favorable urinary indices, no sonographic evidence of renal dysplasia, and extensive informed consent. Types of fetal intervention include vesicoamniotic shunts, open fetal surgery, and fetoscopic surgery. However, these techniques should still be considered experimental. Although pulmonary function may be improved, many fear it will lead to an increased survival of infants with renal insufficiency. Furthermore, it should be remembered that any prenatal intervention puts the mother at risk, as well as the affected fetus.

POSTNATAL MANAGEMENT OF PRENATAL HYDRONEPHROSIS

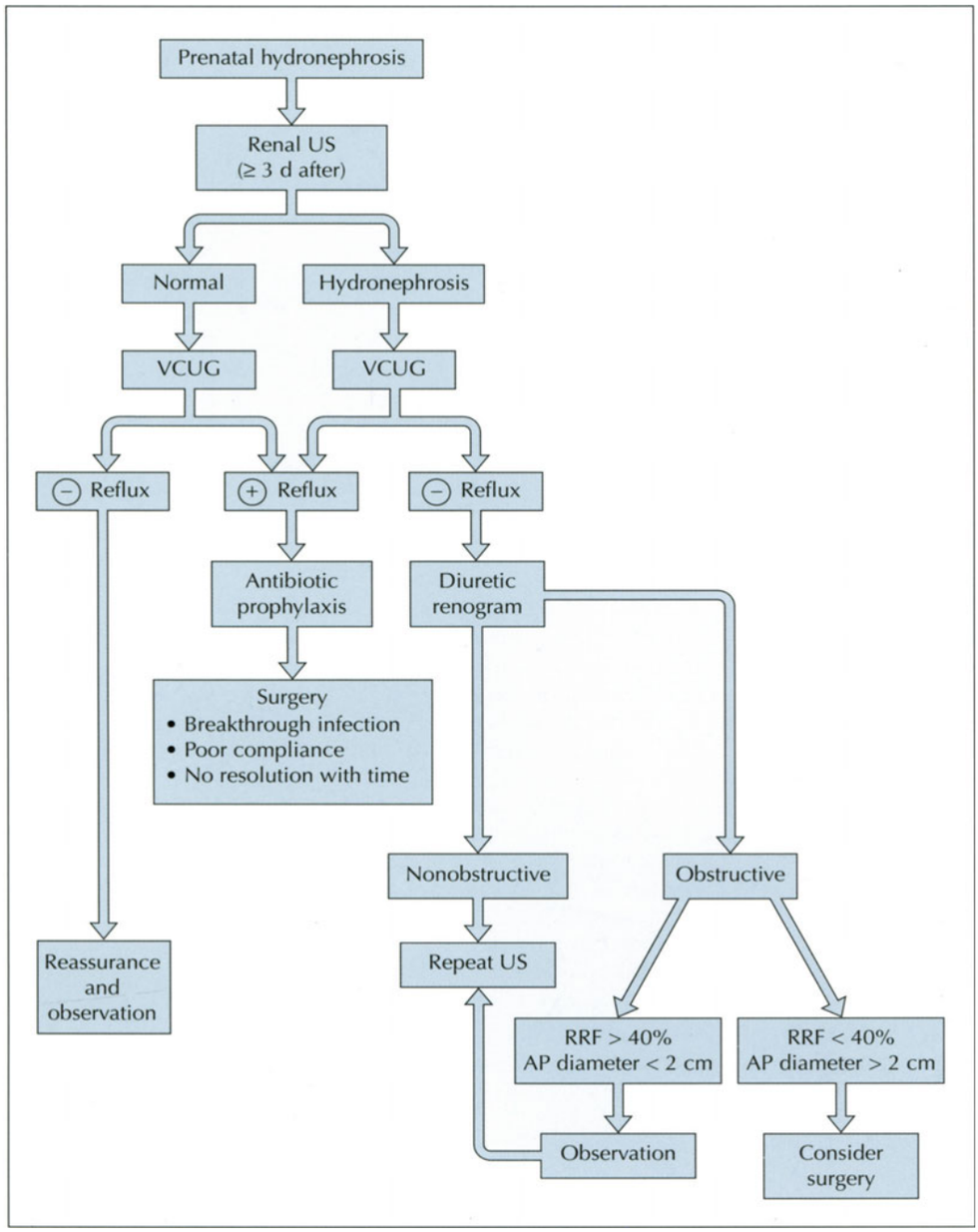
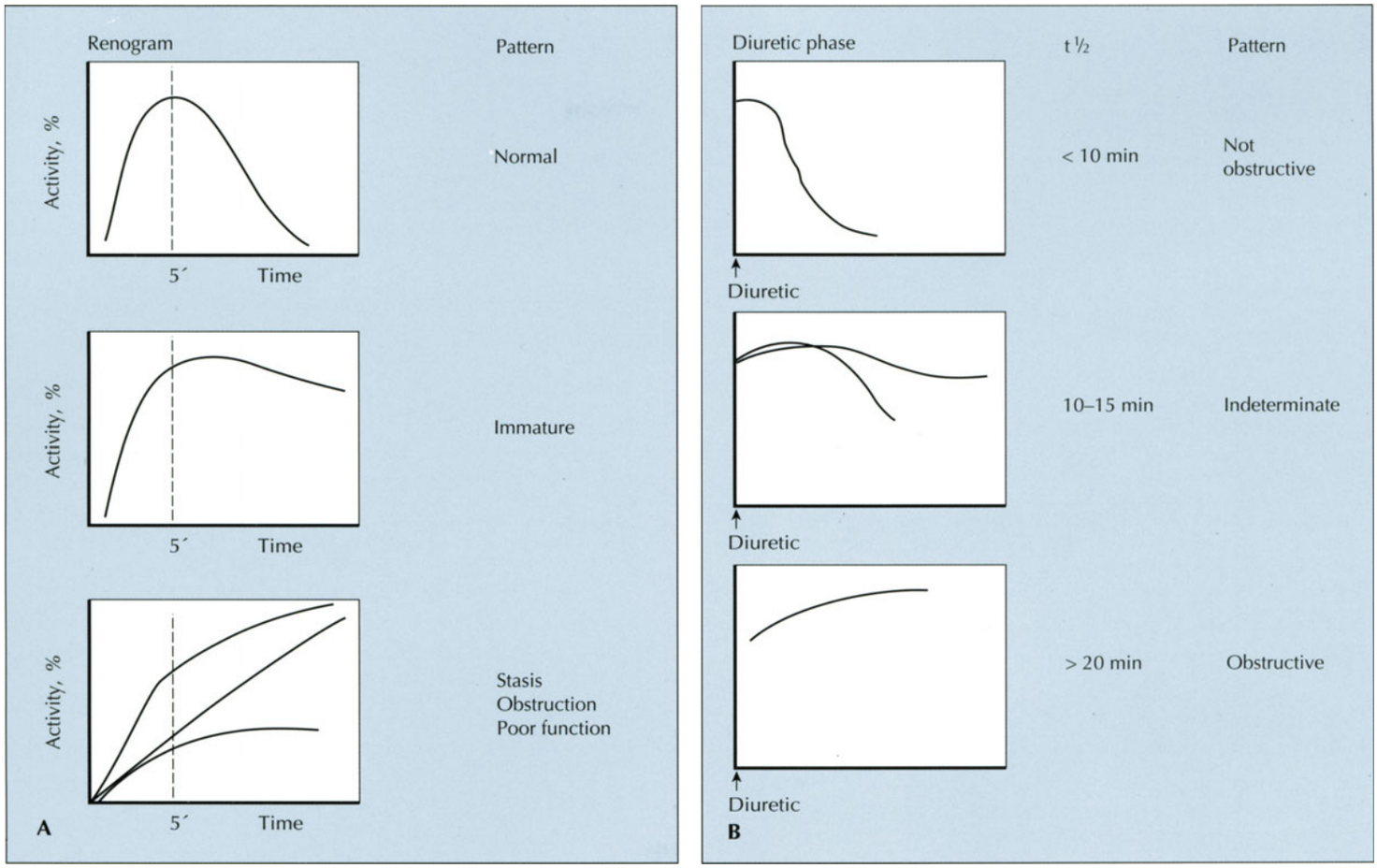


FIGURE 2-17. Postnatal management of prenatal hydronephrosis. Virtually all patients with hydronephrosis detected prenatally should have a postnatal evaluation to distinguish transient fetal hydronephrosis from significant disease. In cases of unilateral hydronephrosis, most pediatric urologists recommend waiting at least 3 days after birth before obtaining an ultrasound (US) image. The kidneys do not produce a large amount of urine during the first several days after birth. Thus, a postnatal US obtained in the first 2 days after birth often underestimates the ultimate severity [22].

A voiding cystourethrogram (VCUG) should also be obtained to evaluate for vesicoureteral reflux. Because up to 25% of patients with prenatally detected hydronephrosis and no hydronephrosis on postnatal US are subsequently found to have reflux, a VCUG is recommended even when postnatal US demonstrates no hydronephrosis [23].

In patients with significant postnatal hydronephrosis associated with caliectasis or thinned renal parenchyma, a diuretic radionuclide renogram should be obtained to help determine the degree of obstruction and relative renal function (RRF). Although there is still some controversy, the authors recommend surgical intervention in patients with less than 40% renal function, an obstructed pattern on renography, and marked hydronephrosis with an anteroposterior (AP) diameter of more than 2 cm on US [24] or clinical symptoms such as infections or renal colic. In contrast, observation is recommended when the RRF is more than 40% and the AP pelvic diameter is less than 2 cm in an asymptomatic infant. If observation is chosen for management, aggressive and careful urologic follow-up is required. Up to 25% of these patients may ultimately need surgery [25].

In contrast, patients with ureterovesical junction obstruction may be managed nonoperatively with little risk [26]. In one study [27], only 17% of the patients had subsequent deterioration of renal infection or urinary tract infection requiring surgery. In fact, it appears that the rate of spontaneous resolution is much higher with ureterovesical than with ureteropelvic junction obstruction.



◗ **FIGURE 2-18.** Stereotypical renogram and diuretic response patterns (time activity curves). Renogram (**A**) and diuretic (**B**) response patterns obtained from a diuretic radionuclide renogram help determine the presence of obstruction. However, it should be recognized that there are numerous potential technical pitfalls associated with nuclear renography. The renogram should be standardized with respect to the patient's state of hydration and bladder fullness, diuretic dosage and timing of administration, method used to calculate washout measurements, calculation of the background and region of interest, patient position, and radiopharmaceutical used [28]. However, when interpreting the results, it is important to consider other factors that cannot be standardized, such as the size and compliance of the collecting system, the differential response of the kidneys to diuretics, and volume dilutional effects.

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3

Vesicoureteral Reflux

Joseph G. Borer and David A. Diamond

In the normal state, the submucosal ureter is compressed against a firm detrusor muscle backing as the bladder fills with urine. This "flap valve" mechanism prevents retrograde flow of urine while permitting intermittent antegrade urine passage during ureteral peristalsis. Vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder to the upper urinary tract and is thought, in its primary form, to be the result of deficient submucosal tunnel length with deficient detrusor muscle backing. The prevalence of reflux in normal children has been reported to range from 1% [1] to 18.5% [2]. Approximately one third of siblings of children known to have the disorder are afflicted [3], as are 67% of offspring of a parent with VUR [4]. One of several causes within the broad spectrum of anatomic or functional bladder outlet obstruction or abnormalities in ureteral insertion may be responsible for secondary reflux.

In the majority of patients with VUR, the diagnosis is made during evaluation for a urinary tract infection (UTI) [5,6]. However, other common reasons for evaluation for and diagnosis of VUR include familial screening and prenatal hydronephrosis. Infants and younger children may present with fever, malodorous urine, dysuria, urinary frequency, lethargy, or gastrointestinal symptoms. Although newborns are typically nonspecific in their clinical presentation, failure to thrive and lethargy are worrisome signs. Diagnostic evaluation is recommended after the first documented UTI with or without fever. Traditionally, detection and grading of reflux have been based on the appearance of radiopaque contrast material in the upper urinary tract during a voiding cystourethrogram (VCUG), according to the International Classification System established by the International Reflux Study [7]. Although it does not provide as much anatomic detail, the use of radionuclide cystogram (RNC) has become a staple for familial screening and follow-up of patients who have been treated for VUR because of the increased sensitivity and decreased radiation exposure of RNC compared with conventional fluoroscopic cystography. The RNC grading system correlates closely with the International Classification System [8].

Cystoscopy has a limited role in the diagnosis of reflux because the ureteral orifice configuration has been found to be of little value in predicting the presence of reflux or prognosticating the likelihood of its spontaneous resolution. Urodynamic evaluation may be indicated for children suspected of having a secondary cause for reflux (*eg,* posterior urethral valves, neurogenic bladder, or non-neurogenic bladder) as an aid both in establishing a diagnosis and guiding therapy.

All patients suspected of having reflux should be placed on a prophylactic antibiotic regimen with or without an initial therapeutic antibiotic course, as dictated by presentation. Antibiotic prophylaxis is continued through diagnostic evaluation, which requires urethral catheterization for radiographic or scintigraphic study. If the diagnosis of VUR is established, a management plan is formulated based on many factors. These include (but are not limited to) the cause (primary vs secondary), mode of presentation, and grade of reflux, as well as age, gender, presence of renal scarring, and general health of the patient. Early surgical intervention may be necessary for treating the etiologic factors of patients with secondary reflux and for treating patients with primary high-grade reflux. More commonly, antibiotic prophylaxis is continued and serial examinations are performed with the knowledge of expected spontaneous resolution rates.

Medical or expectant management entails a concerted effort by the patient, the patient's family, and the clinician to protect the patient from VUR-related complications during the period of observation through his or her spontaneous resolution. This is the typical treatment approach for those patients with mild to moderate grades of reflux in whom spontaneous resolution is likely. Surgical intervention for the treatment of a patient with VUR should be recommended only after careful consideration of the all-important clinical factors involved for the individual patient. In the absence of indications for early intervention, surgery should be considered as an alternative to continued medical management of persistent reflux only after an appropriate length of time is granted for spontaneous resolution. Indications for early intervention include noncompliance with medical management, breakthrough UTI with pyelonephritis, and an associated paraureteral (Hutch) diverticulum.

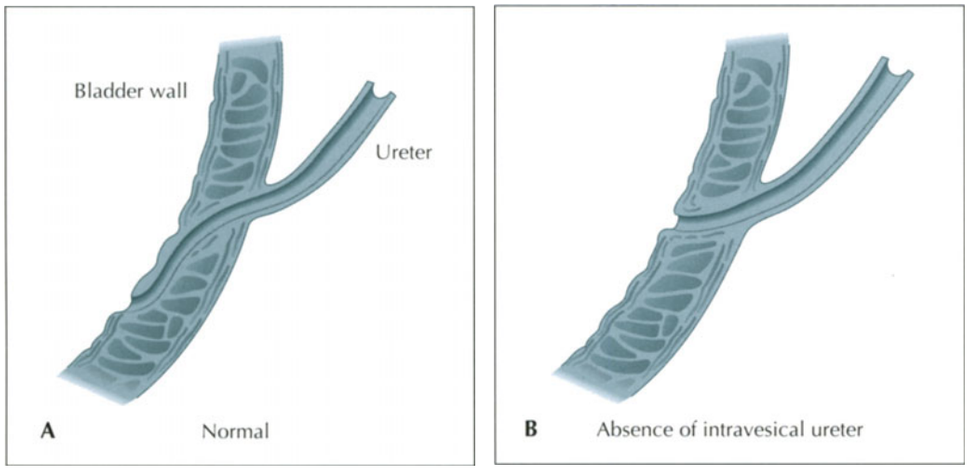
Grades I and II VUR (according to the International Classification System) have spontaneous resolution rates ranging from 56% to 90% over 2.5 to 5 years of follow-up [6,10–15]. Several investigators [13,16,17] have reported resolution of grade III reflux in approximately 50% of patients followed for up to 5 years. In a prospective randomized investigation [18], patients with grades III and IV VUR randomized to medical therapy were followed for 5 years in the International Reflux Study. Reflux resolution occurred in 25% of the 41 patients in the American arm [19]. In the European arm, reflux resolved in 61% with unilateral and 10% with bilateral reflux [20]. McLorie *et al.* [17] reported spontaneous resolution in 30% of patients with grade IV and 12% with grade V reflux followed up for 5 years.

Numerous techniques of ureteral reimplantation have been described, but the first to receive widespread acceptance was that by Politano and Leadbetter in 1958 [21]. Success rates, defined as correction of VUR without ureteral obstruction, have ranged between 88% and 99% for the Politano–Leadbetter ureteroneocystostomy [22–28]. A subsequent intravesical technique that achieved widespread acceptance was the transtrigonal ureteral advancement described by Cohen [29]. Excellent success rates ranging from 96% to 100% have been reported with this technique [25,27,29–35]. The Cohen reimplant, appropriately referred to as a transverse ureteral advancement, is currently the most commonly performed of all reimplantation techniques worldwide.

The anatomically appealing Lich–Gregoir extravesical technique [36,37] was originally associated with unsatisfactory success and complication rates. A renewed interest in this less invasive approach has resulted in improved success rates ranging from 90.2% to 98.2% [38–44]. Modifications of the original Lich–Gregoir technique have included a combination of the ureteral orifice advancing sutures as described by Daines and Hodgson [45] and a more liberal circumferential detrusor dissection at the ureteral orifice described by Zaontz *et al.* [46]. Success rates incorporating these modifications have ranged from 93% to 99.5% [28,46–48]. Burbige *et al.* [49] have reported a 100% success rate in 128 children with 174 refluxing ureters using either a dismembered (64 ureters) or nondismembered (110 ureters) extravesical technique.

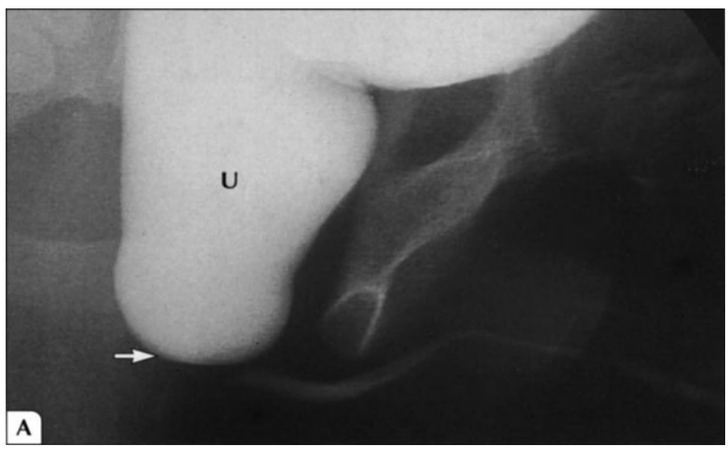
Endoscopic treatment of children with VUR was first introduced by Matouschek [50] when he injected polytef paste into the subureteric region of a patient. The transurethral treatment of patients with VUR is appealing to clinicians and patients because it can be performed on an ambulatory basis, is minimally invasive, and is highly successful. The search continues for the ideal injectable substance, *ie*, one that conserves its volume and is nonmigratory and nonantigenic. Currently, several materials and transurethral delivery systems are in use clinically or are undergoing evaluation for the treatment of patients with VUR. These include polytef paste, silicone microimplants, injectable bioglass, collagen, the deflux system, and a detachable membrane system. In addition, several autologous materials, including adipose tissue, chondrocytes, and muscle cells have been used or are under investigation as agents for endoscopic injection to correct vesicoureteral reflux.

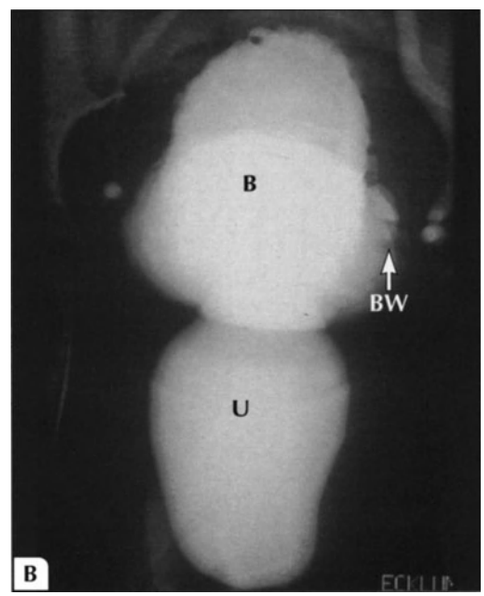
The endoscopic treatment of VUR has proven effective based primarily on the experience with transurethral delivery and subureteric injection of polytef. Other novel systems, using either autologous or nonautologous injectable substances, are currently under investigation for the treatment of patients with VUR. The safety and efficacy standards relevant to systems and substances used for treating an infant or child with VUR should be most stringent. In addition to efficacy and safety, durability of treatment in our young patient population is of vital importance. The long-term clinical results from the newer substances need to be critically reviewed. The next several years will be extremely interesting and important in determining which delivery systems and bulking agents are the most efficacious and safest for the treatment of patients with VUR.

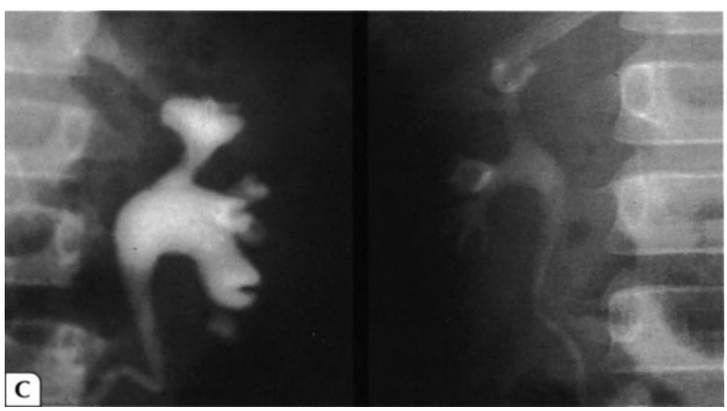


◗ **FIGURE 3-1.** Normal and abnormal ureters. **A,** The normal ureter depicted longitudinally in its distal course [9]. The normal intramural ureteral tunnel has a length that is approximately fivefold greater than the ureteral orifice diameter [51]. As the bladder fills with urine, the submucosal ureter is compressed against a firm detrusor muscle backing. As shown, this is facilitated by the oblique course of the distal ureter as it traverses the bladder wall. This "flap valve" mechanism prevents retrograde flow of urine while permitting intermittent antegrade urine passage during ureteral peristalsis.

B, Primary vesicoureteral reflux results from a congenital abnormality of the ureterovesical junction (UVJ) whereby an inadequate valvular mechanism allows the retrograde flow of urine from the bladder to the upper urinary tract [9,51]. An inadequate valvular mechanism may result when the distal ureter passes in a course near perpendicular to the bladder wall, as shown here. The embryologic relationship between the distal ureter and bladder during the first few weeks of gestation determines the development of the UVJ. A ureteral bud that has an abnormally caudal takeoff from the mesonephric duct inserts into the bladder at a lateral and cranial position relative to normal. This relationship offers an embryologic explanation for primary reflux [52].





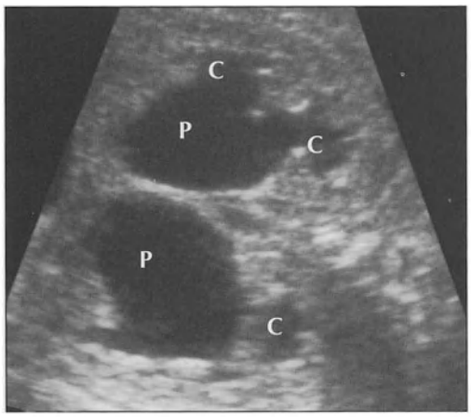


◗ **FIGURE 3-2.** Voiding cystourethrogram (VCUG) from an 8-year-old boy who presented with a history of nocturnal and diurnal enuresis, dysuria, and straining at micturition. **A,** Secondary vesicoureteral reflux (VUR) may result from several etiologies within the broad spectrum of anatomic or functional bladder outlet obstruction, including myelodysplasia and posterior urethral valves. This oblique view from the voiding phase of a VCUG depicts the typical dilated posterior urethra (U) and posteriorly placed pinpoint luminal opening of the urethra at the proximal extent of classic type I (Young's classification) posterior urethral valves (*arrow*).

B, Anteroposterior view showing a trabeculated bladder (B) with a thickened bladder wall (BW) and bilateral vesicoureteral reflux. Note the dilated posterior urethra (U) and the normal caliber urethra distal to the posterior urethral valves.

C, Anteroposterior view of kidneys obtained during the VCUG shows bilateral VUR of moderate grade. Reflux is present in approximately 50% of patients with posterior urethral valves at the time of diagnosis. VUR resolved in this patient after transurethral valve resection was performed, as it does in approximately 50% of patients with reflux preoperatively [53].

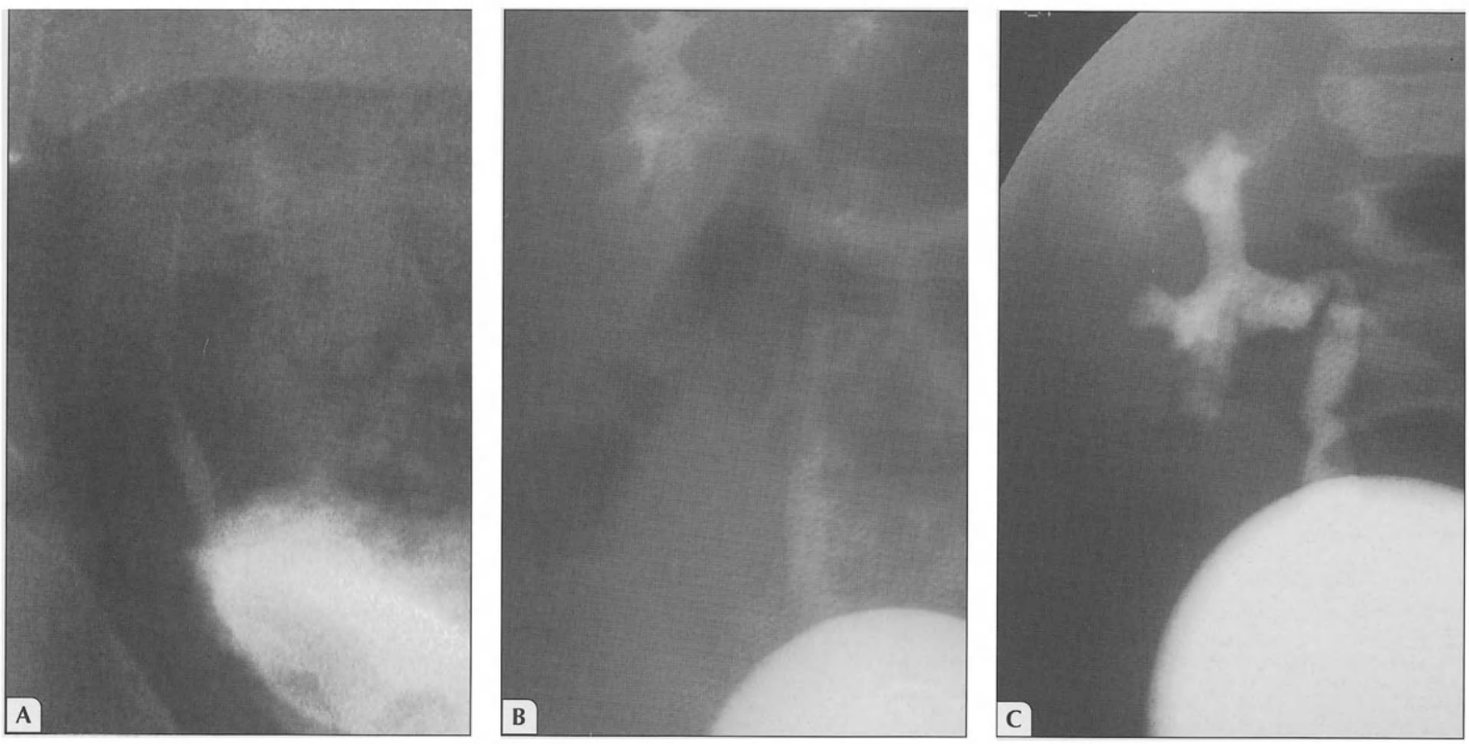
DIAGNOSIS



◗ **FIGURE 3-3.** Prenatal ultrasound (coronal view) showing moderate dilation of the renal pelvis (P) and calyces (C) bilaterally in a patient found to have bilateral vesicoureteral reflux (VUR) on postnatal evaluation. Moderate to severe prenatal hydronephrosis should be evaluated postnatally by ultrasound of the kidneys and bladder as well as by voiding cystourethrogram (VCUG). Newborns with moderate to severe upper tract dilation should be fully evaluated with VCUG, as should infants with significant intermittent hydronephrosis shown on prenatal or postnatal ultrasound. A urine culture should be included in the evaluation of any infant or child who presents with fever or malaise. Discussions about bowel status, urinary voiding schedules, and hygiene should be part of the initial interview of older children with urinary tract infections (UTIs) who are suspected of having VUR. Patterns of dysfunctional voiding should be identified because they appear to contribute to the persistence and clinical consequences of reflux [54,55].

A noninvasive ultrasound of the kidneys and bladder is the diagnostic study of choice in the setting of acute urinary infection. Ultrasonography can identify major malformations and severe obstructive processes of the urinary tract. In addition to ultrasonography, VCUG or radionuclide cystography is necessary to establish the diagnosis of VUR. Reflux is found in 29% to 50% of children with UTIs [7]. Evaluation is warranted for all children younger than age 10 years who have had a well-documented UTI and for all children who have had a febrile UTI, regardless of age. Adolescents who present with asymptomatic bacteriuria or UTIs that are manifested solely by lower tract symptoms can be initially screened with ultrasonography alone, reserving cystography for those with abnormal upper tracts and those with recalcitrant infections.

CLASSIFICATION



◗ **FIGURE 3-4.** Classification of vesicoureteral reflux based on voiding cystourethrogram (VCUG). The International Classification System established by the International Reflux Study provides the current standard for grading reflux and is based on the anatomic appearance of contrast in the ureter and renal collecting system during VCUG [7]. **A,** Grade I: reflux of radiopaque contrast into a nondilated ureter. **B,** Grade II: reflux of contrast into nondilated ureter, renal pelvis, and calyces. **C,** Grade III: reflux into ureter, renal pelvis, and calyces with mild to moderate dilation of the collecting system.

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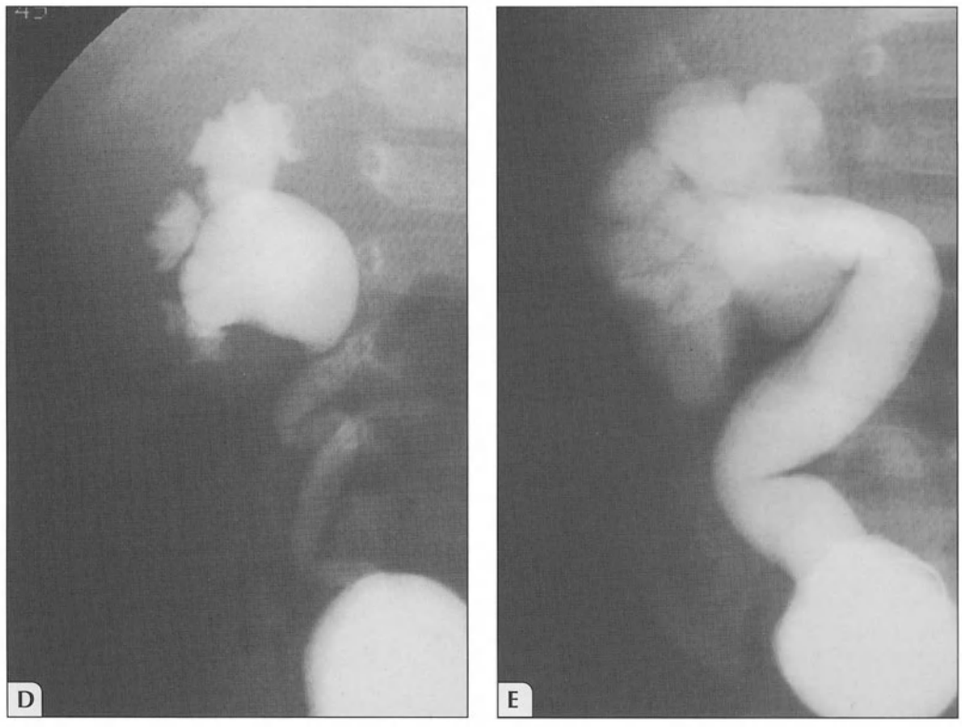
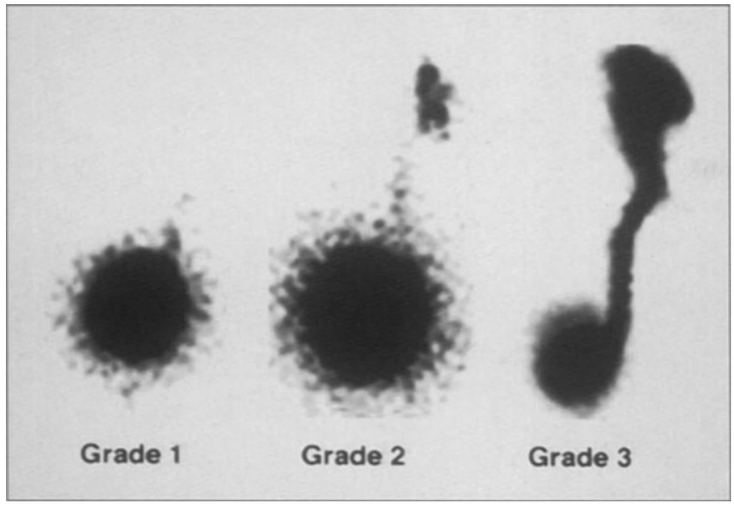
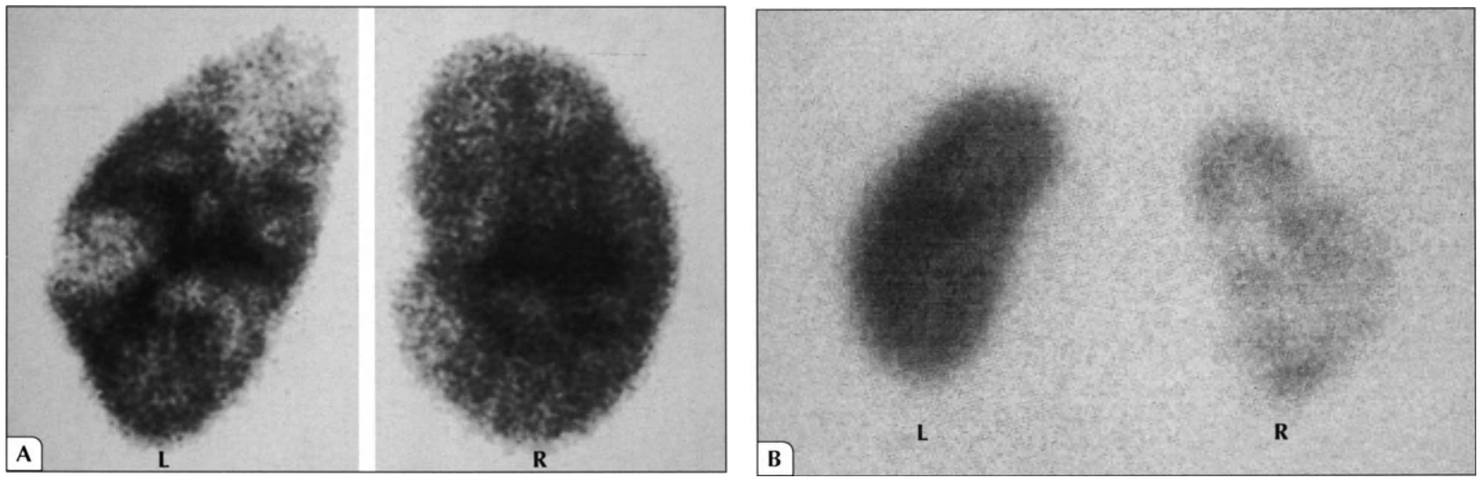


◗ **FIGURE 3-4.** (*Continued*) **D,** Grade IV: moderate to severe dilation of the collecting system with marked blunting of the calyceal fornices and, at times, mild to moderate ureteral tortuosity. **E,** Grade V: gross dilation of the entire collecting system and ureter with loss of papillary impressions.



◗ **FIGURE 3-5.** Classification of vesicoureteral reflux based on radionuclide cystogram. The radionuclide cystogram is the scintigraphic equivalent of conventional fluoroscopic cystography. Although the technique does not provide the anatomic detail of fluoroscopic studies, it is a sensitive method for detecting and following reflux using a markedly decreased radiation dose relative to standard voiding cystourethrography [8]. The classifications are defined as follows: grade 1, reflux of tracer into ureter only (correlates to grade I of the International Classification System); grade 2, reflux into the collecting system with or without impression of mild dilation (correlates to grades II and III of the International Classification System); and grade 3, reflux into a markedly dilated collecting system with ureteral tortuosity (correlates to grades IV and V of the International Classification System).



◗ **FIGURE 3-6.** An important adjunctive diagnostic modality used in the child with vesicoureteral reflux (VUR) is that of renal scintigraphy using ^{99m}Tc- labeled dimercaptosuccinic acid (DMSA). This is a sensitive technique for detecting acute pyelonephritis and cortical renal scarring. **A,** DMSA renal scan (pinhole image, posterior view) performed at the time of an acute febrile urinary tract infection in a 1-year-old girl. Acute pyelonephritis in the left kidney (L) with upper and midpole involvement is detected by decreased cortical uptake of the radionuclide tracer. There is no evidence of volume loss because the cortical outline is intact. Pyelonephritis impairs tubular uptake and causes areas of photon deficiency in the renal cortex. **B,** On DMSA renal scan, approximately 30% of patients with VUR show some evidence of renal parenchymal scarring that is usually proportional to the severity of reflux [7,14]. Reflux nephropathy is depicted in this DMSA scan (planar image, posterior view), which shows both focal scarring and globally decreased relative function in the right kidney (R) secondary to VUR. **C,** Global reflux nephropathy in the left kidney as well as a focal defect in the right kidney as imaged with high-resolution single-photon emission computed tomography. This technology incorporates 360° imaging and computer reconstruction, which enhance its sensitivity for identifying cortical defects.

TREATMENT OPTIONS

Possible Treatment Options for Patients with Vesicoureteral Reflux

Continuous antibiotic prophylaxis
Antibiotic prophylaxis and bladder training (timed voiding and behavioral techniques)
Antibiotic prophylaxis, bladder training, and anticholinergic medication
Open surgical repair
Endoscopic repair

◗ **FIGURE 3-7.** Possible treatment options (medical and surgical) for patients with vesicoureteral reflux [5].

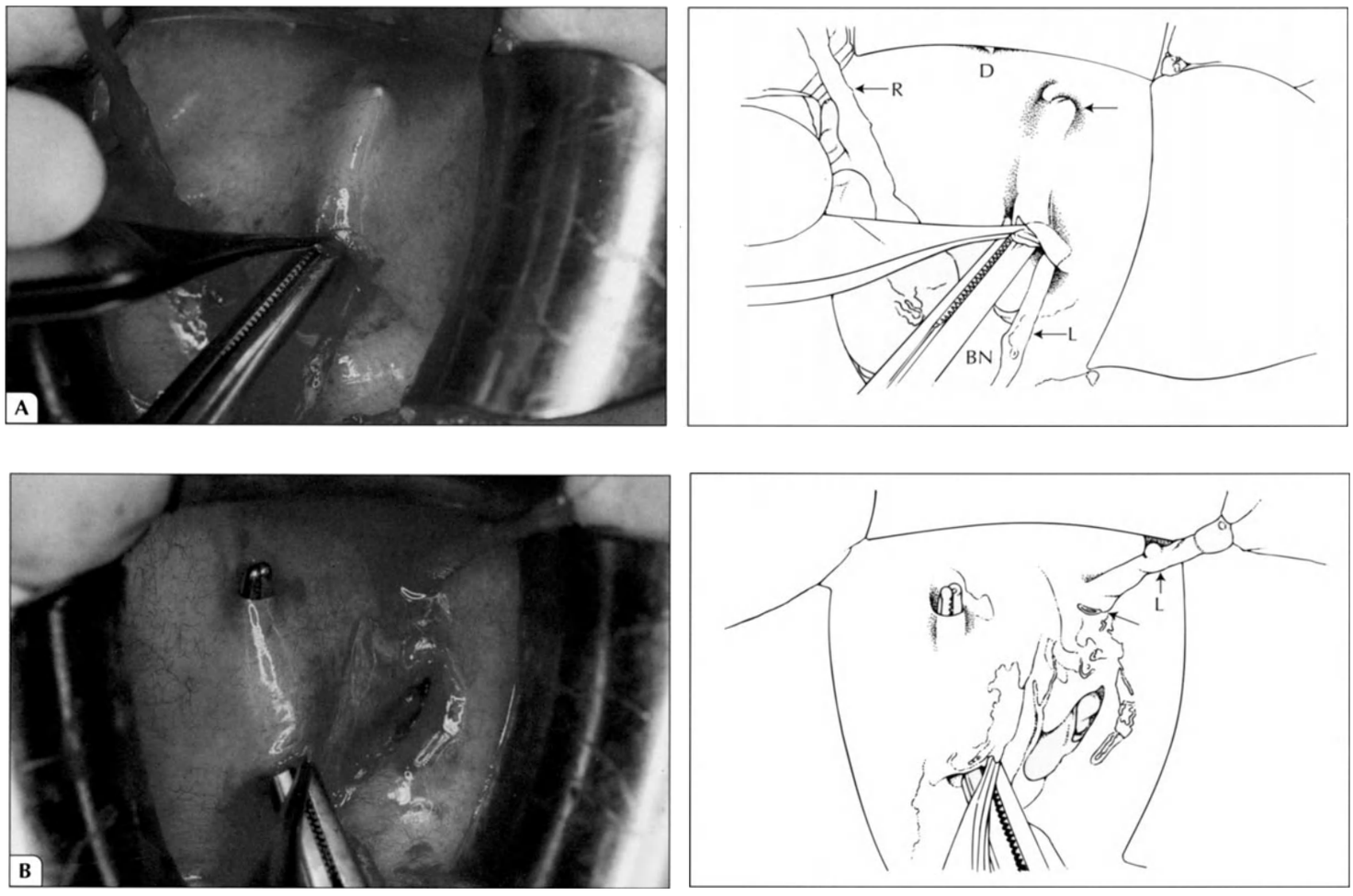
INDICATIONS FOR INTERVENTION

Indications for Surgical or Endoscopic Intervention in Patients with Vesicoureteral Reflux

Reflux of grade IV or V, especially when bilateral or associated with scarring
Noncompliance with medical management
Breakthrough urinary tract infections
Growth of existing or identification of new renal scars or deterioration of renal function on serial nuclear scintigraphy
Reflux that persists in girls as puberty approaches
Reflux associated with a paraureteral diverticulum

◗ **FIGURE 3-8.** Indications for surgical or endoscopic intervention in patients with vesicoureteral reflux.

SURGICAL CORRECTION OF VESICOURETERAL REFLUX



◗ **FIGURE 3-9.** Politano-Leadbetter technique. **A,** Both the right ureter (R) and left ureter (L) have been circumferentially dissected (*see* Fig. 3-11A), and their distal aspects are protruding through each respective native hiatus. A right-angle clamp has been passed in a cephalad direction through the left native hiatus, and the tips are elevating full thickness bladder wall at the proposed site of the neohiatus for the left ureter (*arrow*). At this point, the peritoneum is pushed off of the posterior bladder wall with the aid of the tips of a right-angle clamp and a Küttner dissector. This dissection is performed through the native hiatus of the ureter being reimplanted and is facilitated with the use of a lighted suction tip. The bladder neck (BN) and dome (D) are labeled for the purpose of orientation.

B, The left ureter has been passed from its respective native hiatus outside the bladder and then back into the bladder through its new hiatus (*arrow*). A right-angle clamp lies within the extravesical path prepared for the right ureter.

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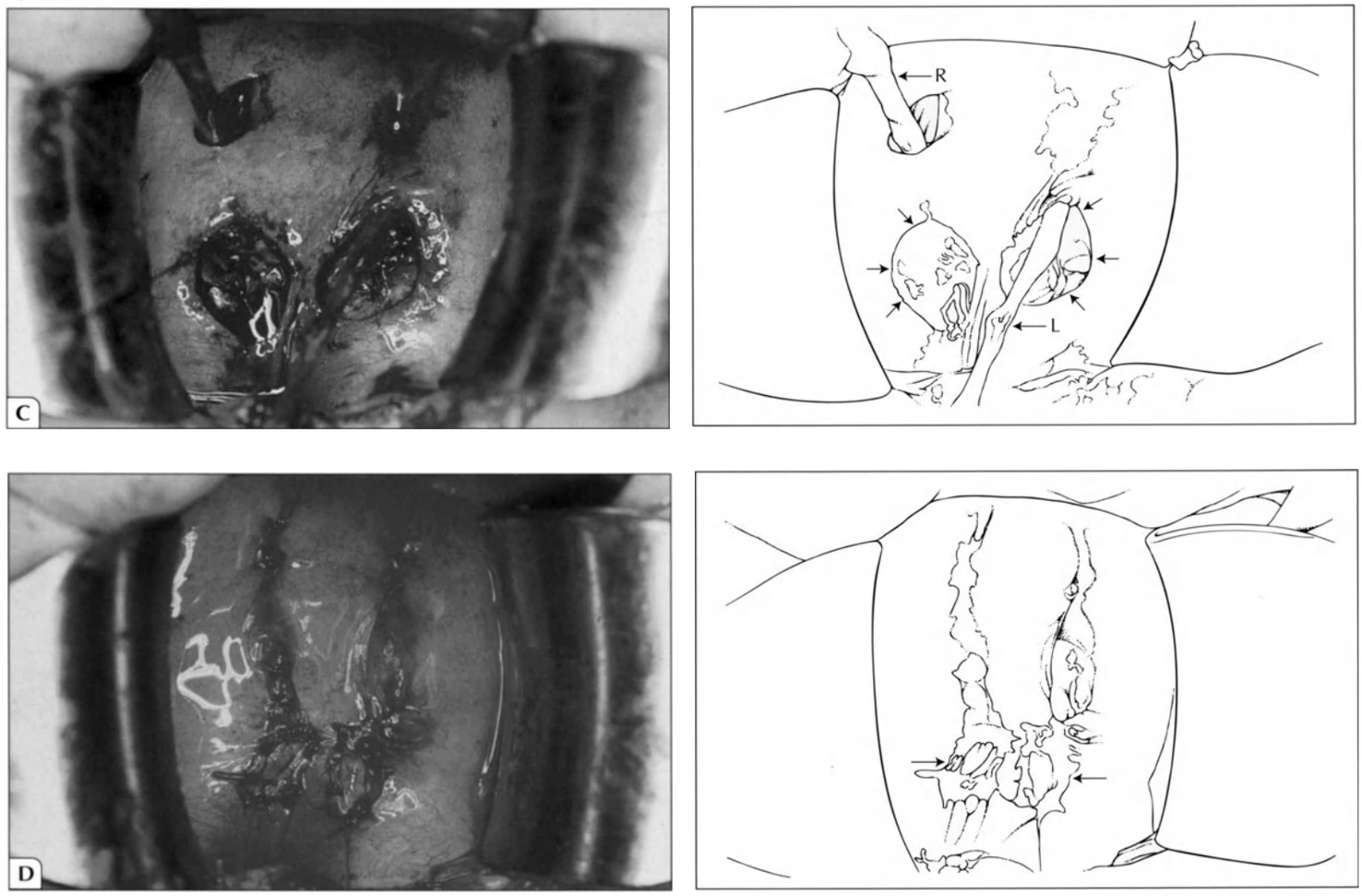


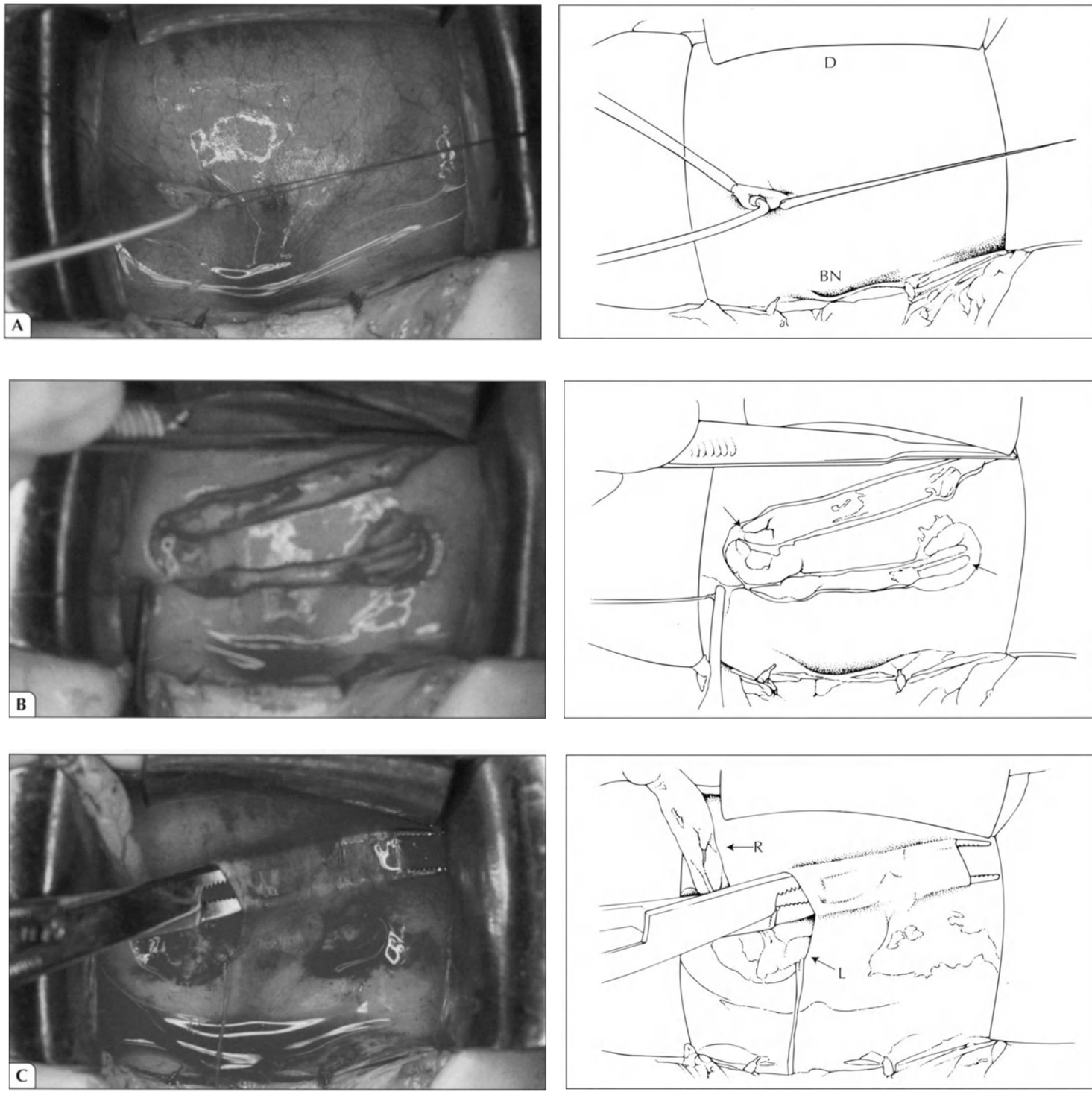
◗ **FIGURE 3-9.** (*Continued*) **C,** The left ureter has been passed through its submucosal tunnel (under the small section of mucosa that separates the new and native hiatus) on that side. The right ureter has reentered the bladder through its new hiatus. Mucosal defects at the site of the native ureteral meatus are clearly visualized (*arrows*). Both native hiatal defects have been approximated with absorbable suture in a simple interrupted technique. **D,** The ureters have been anastomosed at their new meatal sites (*arrows*) and the mucosa has been approximated over the reimplanted ureters, completing the repair.

Results of the Politano-Leadbetter Technique

Study	Patients, n	Ureters, n	Range or Time of Follow-up, mo	Success Rate, %*
Politano [22]	100	152	8–60	96.3
Hendren [23]	242	465	NA	99.0
Price *et al.* [24]	102	191	NA	97.4
Carpentier *et al.* [25]	70	100	6	88.0
Steffens *et al.* [26]	464	565	NA	90.4
Burbige [27]	70	88	12–48	96.7
Ellsworth and Merguerian [28]	27	43	6	95.3

*Ureters with resolution of reflux.

◗ **FIGURE 3-10.** Results of the Politano-Leadbetter technique. NA—not available.



◗ **FIGURE 3-11.** The Cohen technique. **A,** The bladder has been opened via a midline longitudinal incision. Note the bladder dome (D) and bladder neck (BN) with pooling urine. A catheter has been passed up the right ureter, and fine chromic sutures have been placed cephalad and caudad to the ureteral orifice. These traction sutures aid in dissection of the distal ureter and demarcate the margins of the 3- to 4-mm mucosal cuff to be preserved. Sharp dissection is carried out with tenotomy scissors or the use of low-current, cutting electrocautery with a pinpoint tip. **B,** The distal extent of each ureter has been dissected in this patient undergoing bilateral reimplantation. The ureters protrude from their respective native hiatus (*arrows*) and are laid transversly within the bladder, superficial to the site of the planned submucosal tunnel for each. **C,** A right-angle clamp has been passed from right to left through the mucosal defect that was the site of the native right ureteral orifice, illustrating the submucosal tunnel that has been prepared for the right ureter (R). The left ureter (L) has already been passed through its submucosal tunnel and the tip is visualized.

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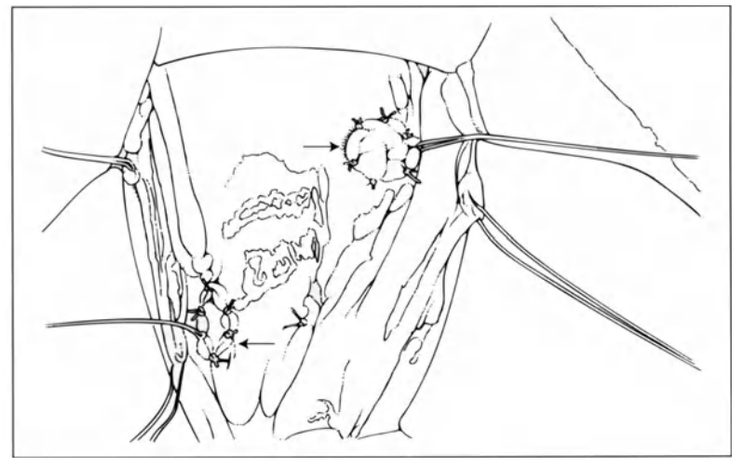


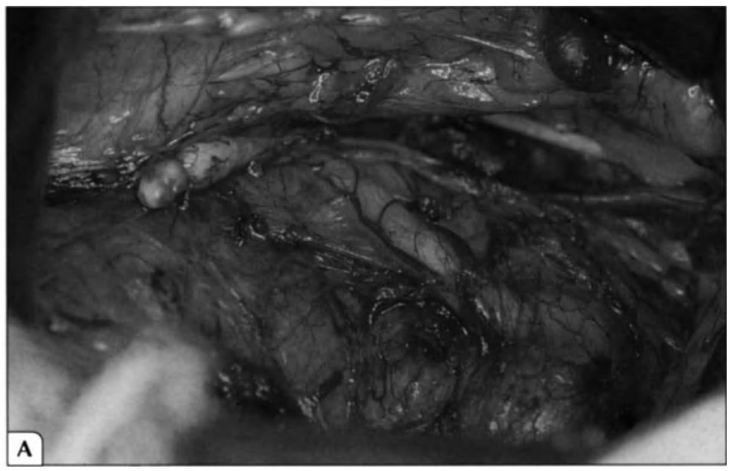
FIGURE 3-11. (*Continued*) **D,** Both ureters have been passed through their respective submucosal tunnels and the mucosal cuffs have been used to secure each ureteral orifice at its new site with simple interrupted fine chromic suture (*arrows*).

Results of the Cohen Technique

Study	Patients, n	Ureters, n	Range or Time of Follow-up, mo	Success Rate, %*
Cohen [29]	NA	189	NA	99.0
Ahmed [30]	92	131	3	99.2
Carpentier *et al.* [25]	71	100	6	97.0
Ehrlich [31]	135	229	NA	98.7
Wacksman [32]	NA	52	12	98.0
Glassberg *et al.* [33]	60	101	6–36	99.0
Burbige [27]	50	92	12–48	97.8
McCool and Joseph [34]	186	308	NA	96.0
Kennelly *et al.* [35]	110	182	6	98.3

*Ureters with resolution of reflux.

FIGURE 3-12. Results of the Cohen technique. NA—not available.



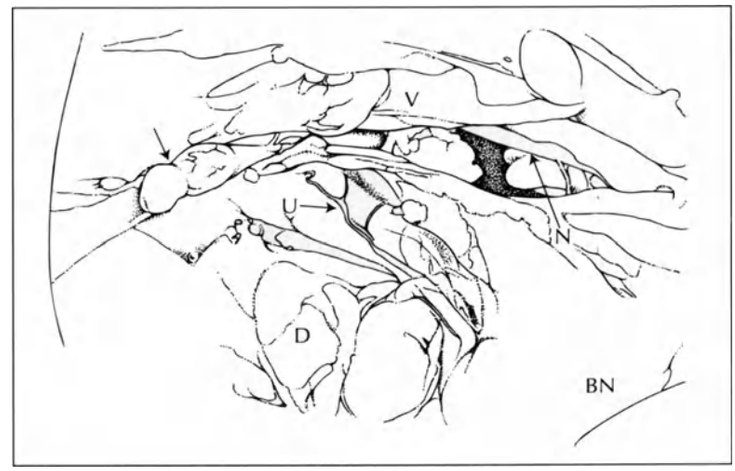


FIGURE 3-13. The extravesical (Lich-Gregoir) technique. **A,** After dissection to the level of the anterior bladder surface, the dissection is carried laterally toward the side of the ureter to be reimplanted, between the bladder and pelvic side wall. Structures visualized in this dissection for extravesical left ureteral reimplantation include the bladder neck (BN) and dome (D), external iliac vein (V), and obturator nerve (N). The distal left ureter (U) has been identified between the obliterated umbilical artery and the bladder side wall. The obliterated umbilical artery (*arrow*) has been ligated and divided to facilitate further dissection of the distal ureter.

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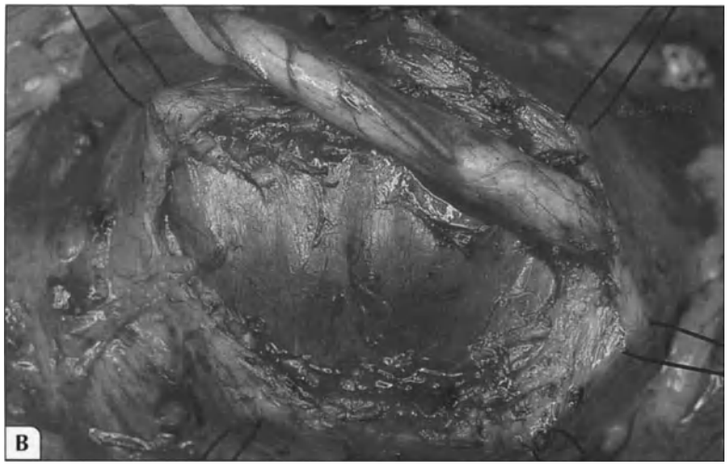

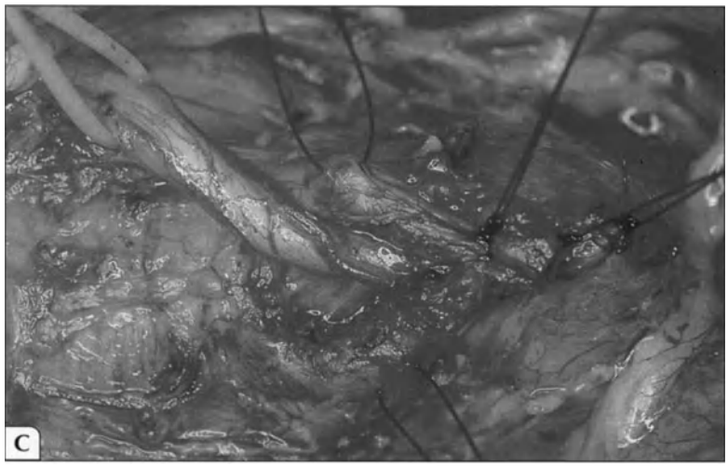

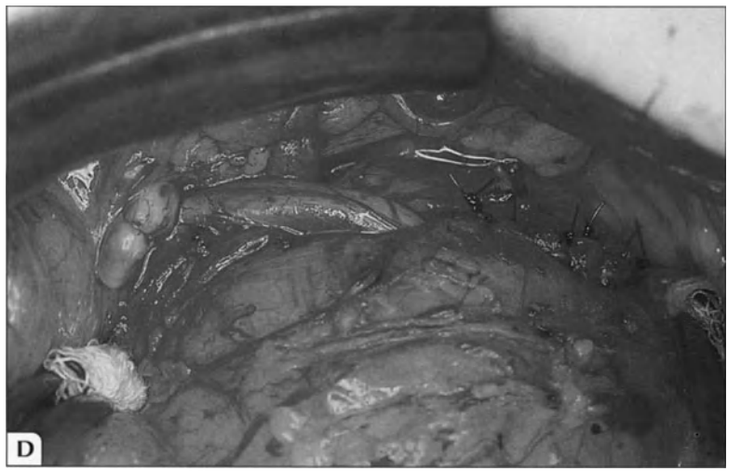

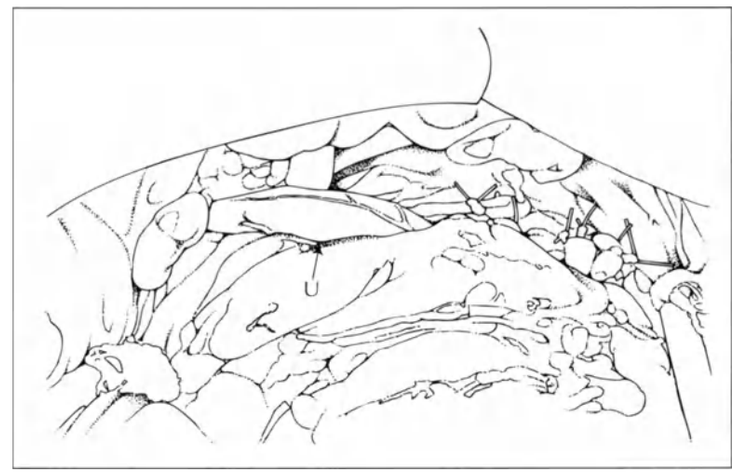

◗ **FIGURE 3-13.** (*Continued*) **B,** The bladder has been distended with saline via a catheter passed through the urethra and prepped in the field. Note the mucosa (M) protruding between the edges of the detrusor defect (D) and stay sutures (S) through muscle, which facilitate the dissection. A vessel loop has been passed around the left ureter (U). The dissection is carried to the level of the ureteral insertion (I). A more extensive and circumferential dissection around the ureteral insertion, as well as placement of an advancing suture, are modifications of the detrusorrhaphy technique [46]. **C,** The distal ureter (U) has been laid in the prepared mucosal trough and is then covered by approximation of the raised lateral and medial flaps of detrusor muscle (D). **D,** Note the relatively straight course of the distal left ureter (U) as it enters its new detrusor hiatus upon completion of detrusor flap approximation and release of bladder traction.

Results of the Lich-Gregoir Technique

Study	Patients, n	Ureters, n	Range or Time of Follow-up, mo	Success Rate, %*
McDuffie *et al.* [38]	51	76	6–156	96.0
Hampel *et al.* [39]	51	83	12–96	90.2
Marberger *et al.* [40]	371	429	6–36	97.7
Bruskewitz *et al.* [41]	62	82	2–81	93.9
Arap *et al.* [42]	300	520	6–168	99.0
Linn *et al.* [43]	70	135	12–120	92.5
Heimbach *et al.* [44]	225	283	23 (mean)	98.2

*Ureters with resolution of reflux.

FIGURE 3-14. Results of the Lich-Gregoir technique. NA—not available.

Results of the Detrusorrhaphy (Modified Lich–Gregoir) Technique

Study	Patients, n	Ureters, n	Range or Time of Follow-up, mo	Success Rate, %*
Zaontz *et al.* [46]	79	120	NA	93.0
Wacksman *et al.* [47]	132	211	6–12	99.5
Houle *et al.* [48]	45	65	6	95.4
Ellsworth and Merguerian [28]	29	38	6	94.7

*Ureters with resolution of reflux.

FIGURE 3-15. Results of the detrusorrhaphy (modified Lich–Gregoir) technique. Modifications of the original Lich-Gregoir technique, including a combination of the ureteral orifice advancing sutures as described by Daines and Hodgson [45] and a liberal circumferential detrusor dissection at the ureteral insertion described by Zaontz *et al.* [46]. NA—not available.

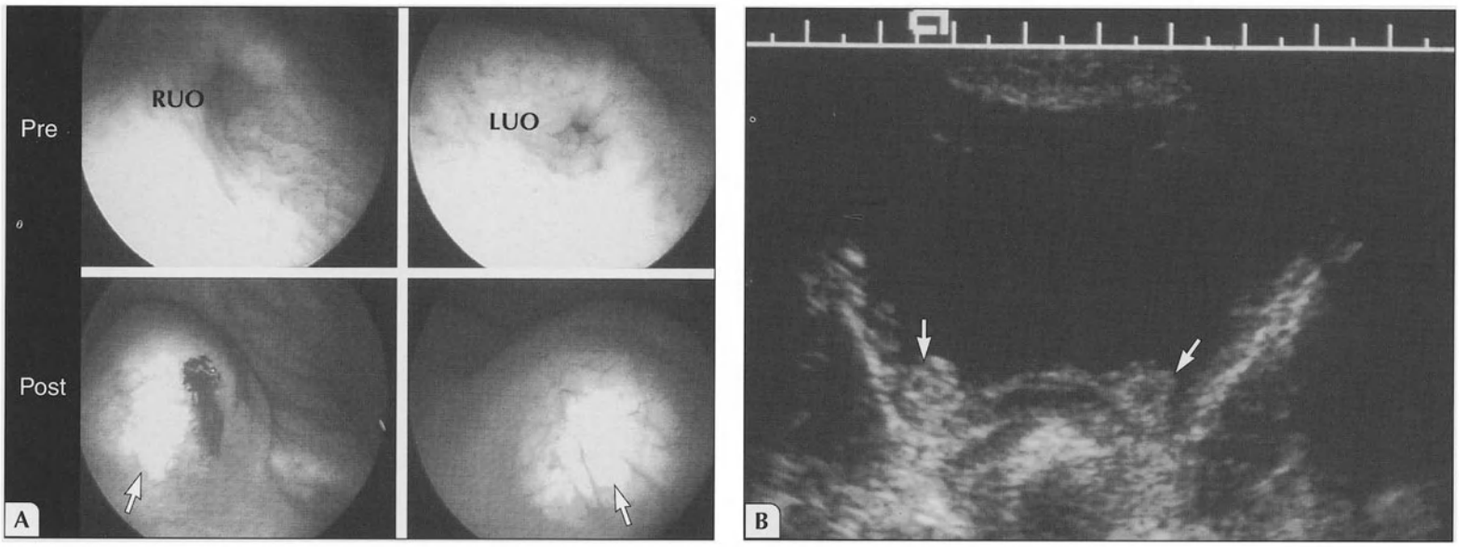

FIGURE 3-16. Endoscopic correction of vesicoureteral reflux. **A,** Cystoscopic view before transurethral subureteric chondrocyte injection (*top panels*) with an abnormal right ureteral orifice (RUO) and left ureteral orifice (LUO). Cystoscopic view after bilateral transurethral subureteric chondrocyte injection (*bottom panels*). **B,** Ultrasound (transverse bladder view at the trigone level) obtained 1 month after transurethral subureteric injection of chondrocytes. Note the mounds of injected chondrocyte mixture at the respective ureteral orifices (*arrows*).

Results of Transurethral Subureteric Injection

Study	Injectable Agent	Patients, n	Ureters, n	Success Rate, %*
Geiss *et al.* [56]	Polytef	844	1290	82.0
Dewan and Goh [57]	Polytef	47	60	82.0
Merckx *et al.* [58]	Polytef	68	100	75.0
Puri [59]	Polytef	4166	6216	76.3
Leonard *et al.* [60]	Collagen	57	92	61.4
Frey *et al.* [61]	Collagen	132	204	62.7
Stenberg and Lackgren [62]	Deflux system	75	101	68.0

**Ureters with resolution of reflux following a single injection.*

◗ **FIGURE 3-17.** Results of transurethral subureteric injection. NA—not available.

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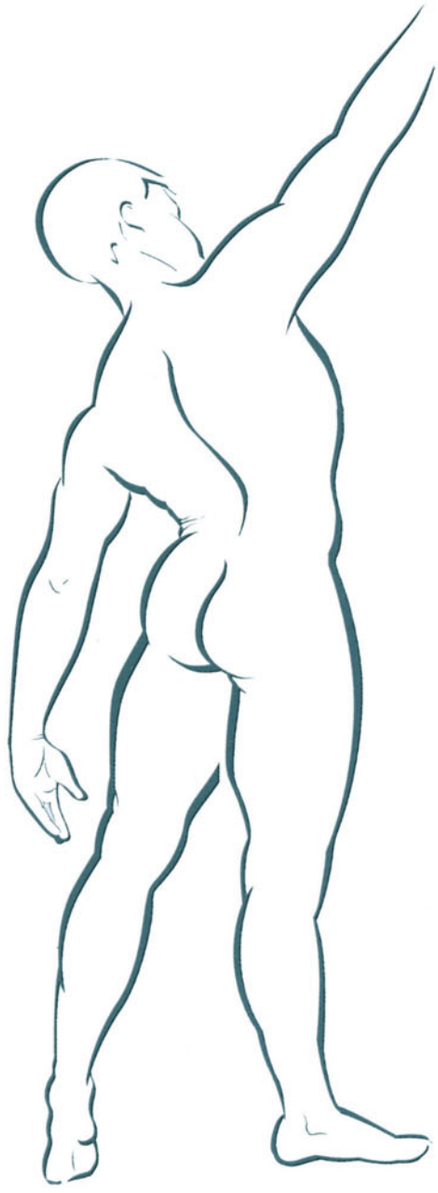
Ureteral Duplications and Ureteroceles

4

Emilio Merlini and Douglas A. Canning



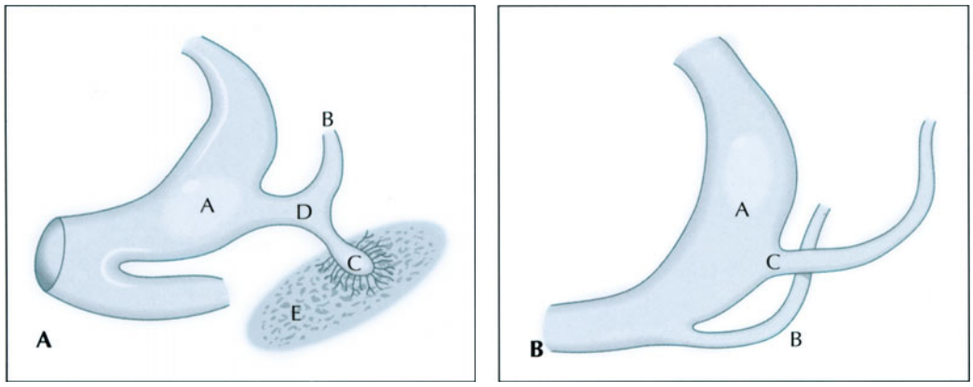
Abnormal development of the ureteric bud causes both ureteral duplication and ureterocele. Proximal branching of the ureteric bud is the cause of incompletely duplicated or bifid ureters, but completely duplicated ureters are caused by the development of two separate ureteric buds from the mesonephric duct. Ureteroceles are probably the result of abnormal distal ureteral canalization of Chwalla's membrane.

The incidence of ureteral duplication anomalies in the general population is 0.66% [1], with bifid ureters being five times more common than completely duplicated ones. Bilateral duplications are found in 39% of cases [2]. Patients with bifid ureters usually have no symptoms. In three situations, however, symptoms may occur 1) if vesicoureteral reflux (VUR) is present, 2) if a ureteropelvic junction obstruction exists in the inferior branch of the bifid ureter, or 3) (less commonly) if uretero-ureteric reflux occurs because of a functional obstruction distal to the branch point in the ureter.

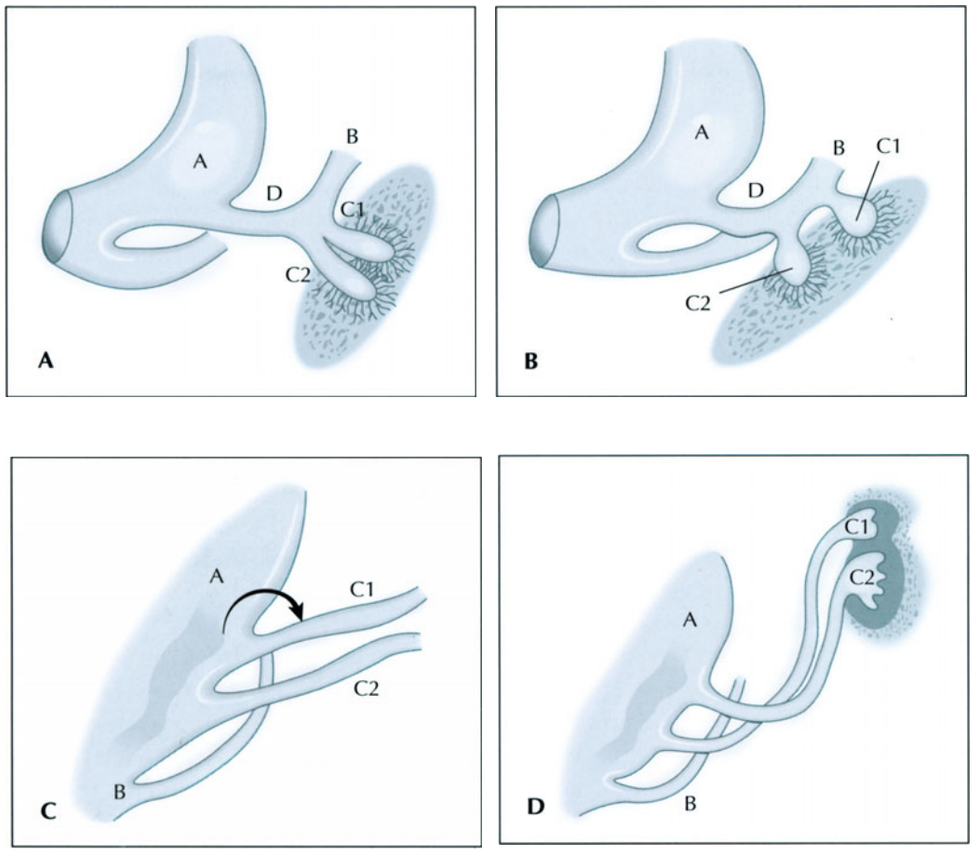
Complete ureteral duplications occur less commonly but are more likely to produce symptoms that require surgical attention. The most common anomalies in a duplex system are VUR into the lower pole ureter and ectopia of the upper pole collecting system with associated obstruction.

Ureteroceles are cystic dilatations of the intravesical portion of the terminal ureter. The incidence in autopsy studies is one in 500. Eighty percent of ureteroceles occur in duplex systems, and 10% of ureteroceles are bilateral. If a ureterocele occurs in a duplex system, the upper pole moiety is always affected. Single-system ureteroceles are relatively rare but are more common in males. Ureteroceles in the upper pole moiety of a duplex system are more common in females, occurring four to seven times more frequently than in males. In 70% of upper pole ureteroceles, the ureteric orifice is in an ectopic position at the bladder neck or in the proximal urethra.

The cause of ureteroceles is still unclear. Tanagho [3] believes that because of a late junction of the ureteric bud with the urogenital sinus, the ureter itself is involved in the expansion of the vesicourethral canal that ordinarily would take place after the ureter meets the bladder.



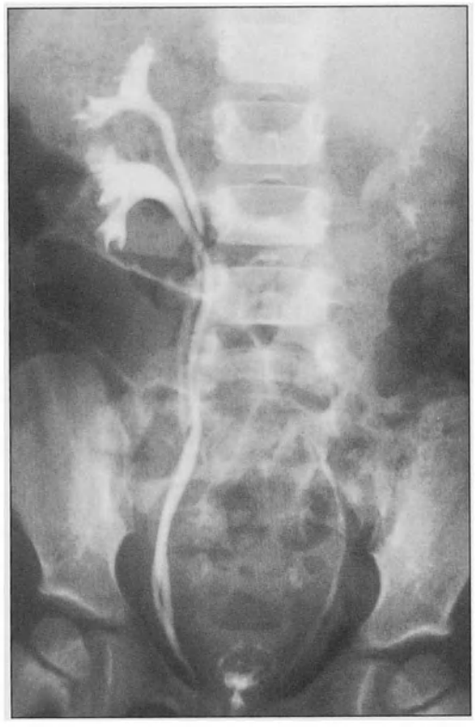
◗ **FIGURE 4-1.** Embryology. **A,** During the fourth week of embryonic life, the ureteric bud (C) originates as a diverticulum from the posterolateral aspect of the mesonephric duct (B), where it bends before entering the cloaca (A). The proximal end of the ureteric bud meets the metanephric blastema (E) and then undergoes a series of dichotomous branchings called ampullae. These later will form the collecting ducts, the calices, and the pelvis. The segment of the mesonephric duct that is located distal to the origin of the ureteric bud is called the common mesonephric or excretory duct (D). **B,** By 33 days of gestation, the common mesonephric duct dilates and is progressively incorporated into the developing urogenital sinus. During this process, the orifice of the mesonephric duct, which will give origin to the seminal vesicles (B), moves causally to open into the future posterior urethra, but the ureteric orifice ends in a more cranial position.



◗ **FIGURE 4-2.** **A,** Partial duplication. An early branching of the ureteric bud (C1, C2) causes an incomplete ureteric duplication or bifid ureter, which may vary in extension from bifid pelvis to an almost complete duplication with a short common limb limited to the intramural ureter. **B,** Complete duplication. A complete ureteric duplication or duplex ureter is caused by the development of two separate ureteric buds (C1, C2) that originate independently from the mesonephric duct (B) and induce the development of a duplex kidney. **C,** Rotation of the mesonephric duct. During the development of the trigone, the most cranial ureter (C1), which drains the upper moiety of the duplex kidney, rotates inward on its long axis (direction of the *arrow*) and crosses the lower ureter (C2). **D,** Demonstration of the Weigert-Meyer law. The upper pole ureter opens in the urogenital sinus in a more distal and medial position than the lower pole ureter; the relationship between the two ureteric orifices is constant.

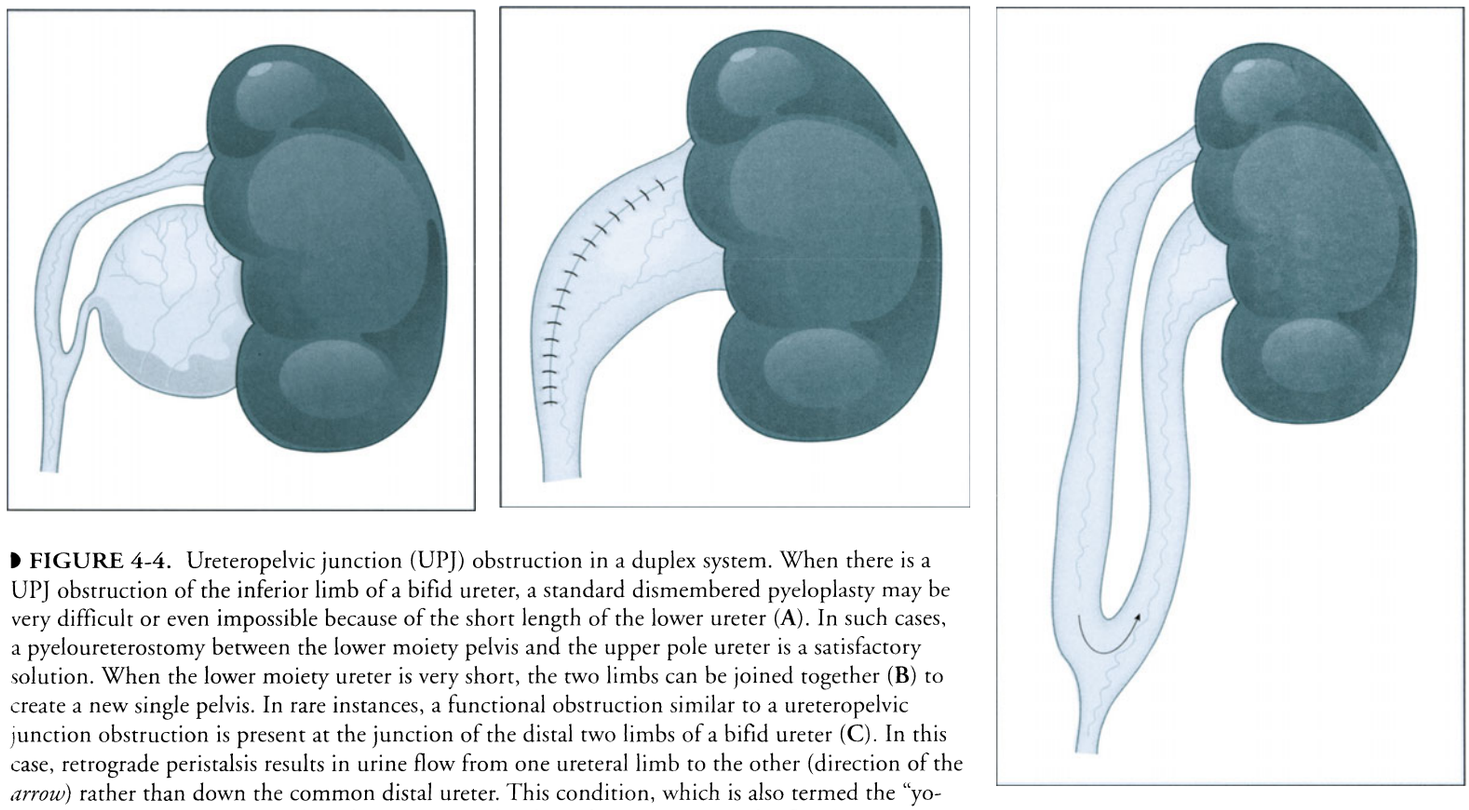
When two ureters originate close to each other and in a near-normal position, the ureteral orifice for both the upper and the lower pole end in a normal position on the trigone. In this case, a normal kidney develops. When the two ureteral buds originate at widely separate positions on the mesonephric duct, the upper pole ureter, which is located at a cranial position on the mesonephric duct, is later incorporated into the urogenital sinus. As a result, the ureteric orifice is situated in an ectopic position, inferior to the trigone. The lower pole ureter joins the mesonephric duct closer to the urogenital sinus. The lower pole orifice migrates cranially and laterally, leaving a relatively short intravesical tunnel. Vesicoureteric reflux into the lower pole ureter may be present because of the short tunnel length.

Mackie and Stephens [4] believe that stimulation of the metanephric blastema by the ureteral bud in the central position is critical to normal renal development. If the ureteral bud meets the metanephric blastema either too cranial or too caudal along the metanephric blastema, renal dysplasia results. That is why poor renal function of the renal moiety drained by a particularly ectopic ureter is the rule. Similarly, few severely refluxing ureters drain normal renal units.

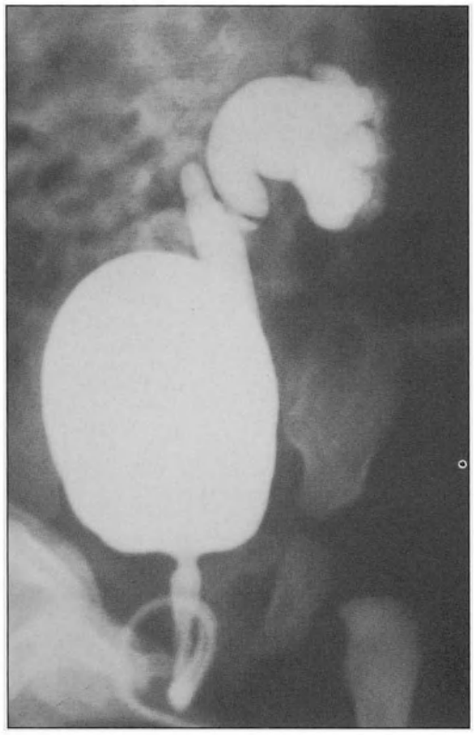


◗ **FIGURE 4-3.** Vesicoureteral reflux (VUR) in a duplex system. This voiding cystourethrogram (VCUG) shows VUR into a single ureter on the left and into the lower pole of a completely duplicated system on the right. VUR may affect the common limb of bifid ureters or it may be observed when the two ureters originate close together at a lateral position on the trigone.

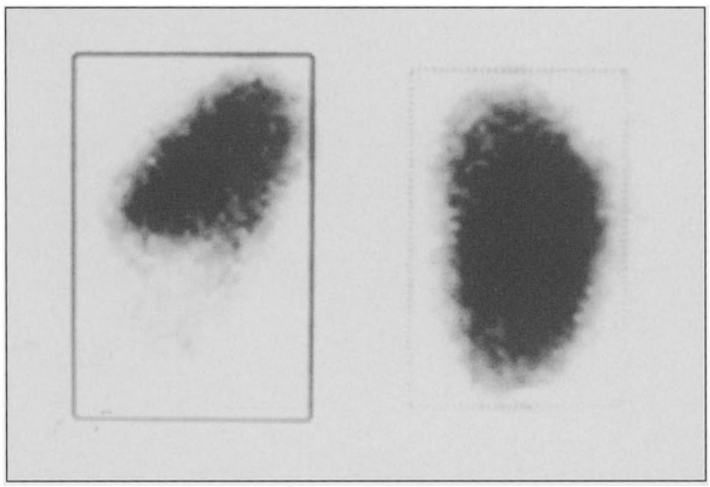
Occasionally, the decision is made to discontinue antibiotic prophylaxis in an older child if the reflux is low grade, if renal scarring has not occurred, and if the child has not had severe symptoms from a urinary tract infection (UTI). Antireflux surgery is often recommended if 1) UTI occurs despite treatment with antibiotic prophylaxis, or 2) high-grade reflux persists in an older child. Partially duplicated systems, even if the common limb is short, may be reimplanted in a standard cross-trigonal fashion.



◗ **FIGURE 4-4.** Ureteropelvic junction (UPJ) obstruction in a duplex system. When there is a UPJ obstruction of the inferior limb of a bifid ureter, a standard dismembered pyeloplasty may be very difficult or even impossible because of the short length of the lower ureter (**A**). In such cases, a pyeloureterostomy between the lower moiety pelvis and the upper pole ureter is a satisfactory solution. When the lower moiety ureter is very short, the two limbs can be joined together (**B**) to create a new single pelvis. In rare instances, a functional obstruction similar to a ureteropelvic junction obstruction is present at the junction of the distal two limbs of a bifid ureter (**C**). In this case, retrograde peristalsis results in urine flow from one ureteral limb to the other (direction of the *arrow*) rather than down the common distal ureter. This condition, which is also termed the "yo-yo reflux," is more apparent when the junction is distal or when vesicoureteral reflux (VUR) coexists. The yo-yo phenomenon is rare, even in cases in which distal obstruction exists. But urinary stasis in the proximal collecting system may cause urinary infection, flank pain, or hematuria. If VUR is present, reimplantation of the common stem is usually corrective. Rarely, a pyelostomy or a high pyeloureterostomy with excision of the upper ureter may be needed to relieve symptoms.



◗ **FIGURE 4-5.** "Drooping lily." This cystourethrogram reveals high-volume vesicoureteral reflux (VUR) with intrarenal reflux into the parenchyma of the lower pole moiety of a duplex kidney. Complete ureteral duplications may be affected by VUR into the lower pole ureter because the ureter enters the bladder in a more lateral and cranial position than normal. The resulting ureteral tunnel is short, predisposing the ureterovesical junction to incompetence. VUR then results. The most common presenting symptom is urinary tract infection (UTI). More than 60% of children with a previous UTI and a duplex kidney have VUR [5]. The voiding cystourethrogram sometimes shows reflux into a "drooping lily," the indirect sign of a duplex kidney. The "drooping lily" refers to the renal pelvis of the refluxing lower pole system: the pelvis is in a lower than normal position and is frequently laterally displaced, resulting in the appearance of the drooping pedals of a lily.



◗ **FIGURE 4-6.** Poor renal function in the refluxing lower pole. This image is taken from a 99m-technetium (99mTc)–labeled dimercaptosuccinic acid (DMSA) scan in the child shown in Figure 4-5. The renal scan demonstrates an absent uptake of isotope in the left lower pole. In this case of severe reflux, DMSA uptake may be absent or substantially reduced, indicating severe dysplastic changes or parenchymal scarring because of repeated episodes of urinary tract infection (UTI). In this case, the treatment of choice is lower pole partial nephrectomy; this is relatively rare. In most cases, the lower pole is worth saving, and a "double-barreled" reimplant is the best surgical treatment. Grade for grade, vesicoureteral reflux (VUR) resolves as frequently in the lower pole ureter in a duplex system as it does in a single system ureter. The reason that studies of patients with duplex kidneys show a smaller reflux resolution frequency is that duplex kidneys present with higher grades of reflux [6]. Therefore, a trial of medical management is warranted, particularly in children with low-grade reflux.

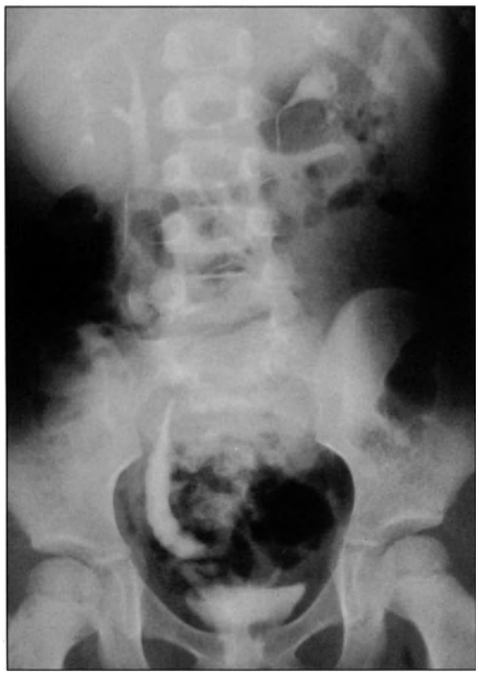
Considerations for surgical treatment are the same as for reflux in simple ureters and include 1) breakthrough infections despite appropriate medical management, 2) noncompliance with medical management, and 3) persistent high-grade reflux after years of medical management.

Endoscopic treatment of VUR in patients with duplicated systems is unsatisfactory, with a permanent resolution rate of only 46% [7]. The procedure of choice, when the refluxing ureter is not excessively dilated, is "double-barreled" ureteroneocystostomy. If the refluxing ureter is massively dilated, it may be tapered or tailored before reimplantation or, in select cases, a uretero-ureterostomy or pyelo-ureterostomy with excision of the distal refluxing ureter may be indicated.

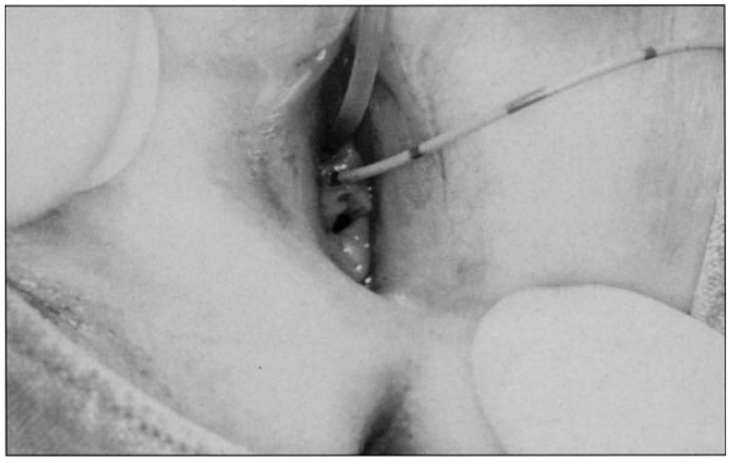
Locations of the Orifices of Ectopic Ureters

Male	*Female*
Bladder neck	Bladder neck
Posterior urethra	Urethra
Seminal vesicle	Uterus
Epididymis	Vagina
Rectum	Fallopian tube

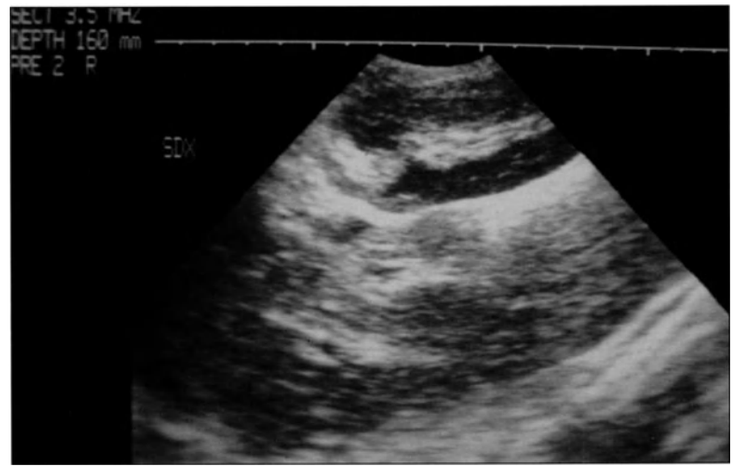
◗ **FIGURE 4-7.** Locations of the orifices of ectopic ureters. An ectopic ureter opens into a position that is more distal than normal along the path of the mesonephric duct. In males, the location of the ectopic orifice is along the pathway of the normal development of mesonephric duct. Although the developmental process that results in the ureteric bud opening into müllerian derivatives in females is not clear, it has been proposed that ectopic ureters may rupture into the adjacent müllerian structure along the path of Gartner's duct.



◗ **FIGURE 4-8.** Ectopic upper pole with incontinence. This intravenous pyelogram shows a bilateral duplex system in a 4-year-old girl, with continuous wetting from an ectopic right upper pole ureter. The right upper pole ureter is slightly dilated and ends at the introitus. Ectopic ureters in males are almost always obstructed and dilated. Sometimes ureters terminating at the bladder neck reflux during micturition. In these cases, urinary tract infection (UTI) may develop. In females, the ureters ending in the bladder neck or urethra are usually dilated and may reflux. UTI is common in this case. Conversely, ureters that drain distal to the bladder neck or urethra, at the vaginal introitus, or along the path of Gartner's duct usually are found during an evaluation for continuous urinary incontinence.

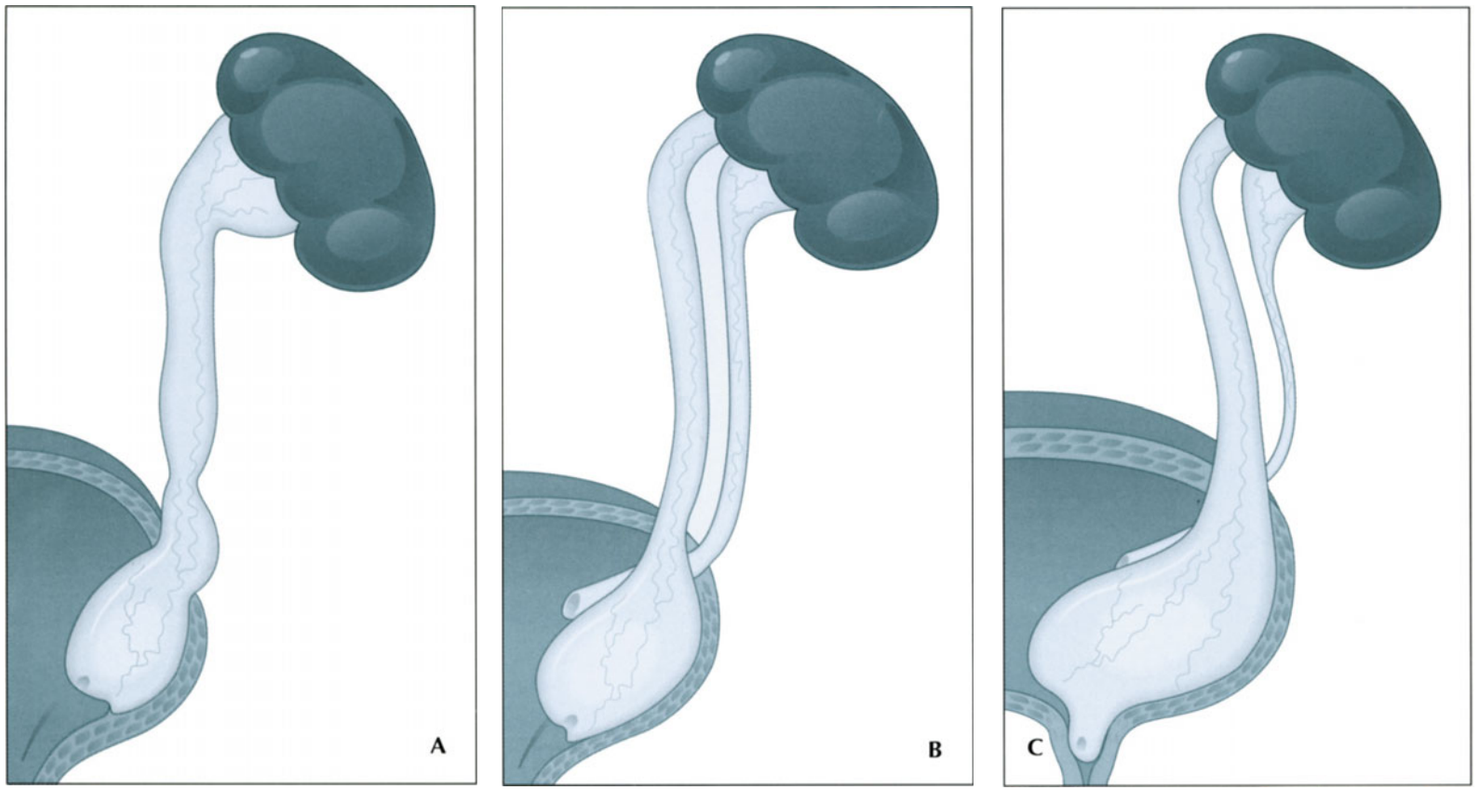


◗ **FIGURE 4-9.** Ectopic ureteral orifice to the introitus. Sometimes ectopic ureters end inferiorly on the anterior vaginal wall or in the septum between the urethra and vagina. The ureteral orifice in these cases can sometimes be seen and cannulated with a ureteral catheter, as shown here.



◗ **FIGURE 4-10.** Upper pole dysplasia. In some cases, the ureter and the collecting system are not dilated. If the upper pole function is so poor that it cannot be visualized on excretory urograms, identification of an ectopic upper pole ureter in a patient presenting with urinary incontinence may be exceedingly difficult. In such cases, an accurate renal ultrasound may sometimes show a small, echogenic upper pole renal segment that was not visible on the intravenous pyelogram.

In nearly all cases, the function of the upper pole segment is poor, usually less than 5% total function. If the function is poor, the upper pole of the kidney may be removed along with the upper pole ureteral segment. Rarely, upper to lower ureteropyelostomy will effectively decompress the system. Alternatively, lower ureteroureterostomy may be performed.



◗ **FIGURE 4-11.** Ureteroceles. A ureterocele is a cystic dilatation of the intravesical ureter. Ureteroceles may be associated with a single system ureter (**A**); in such cases, they are also called adult type ureteroceles because they are frequently found in adults. In most cases, single system ureteroceles are associated with less hydronephrosis and minor obstructive renal changes than the duplex system ureteroceles that are more commonly seen in children. Approximately 80% of ureteroceles are associated with the upper pole of a duplex system. The ureterocele may reside completely inside the bladder (an intravesicle ureterocele; **B**), or part of the ureterocele may extend distal to the bladder neck (an ectopic ureterocele; **C**). In most cases, the ureterocele obstructs the upper pole ureter. The upper pole renal segment is dysplastic in 50% of cases. In duplex systems, the ipsilateral lower pole ureteric orifice is displaced superolaterally by the ureterocele. The ipsilateral lower pole ureter refluxes in more than 50% of cases [8].

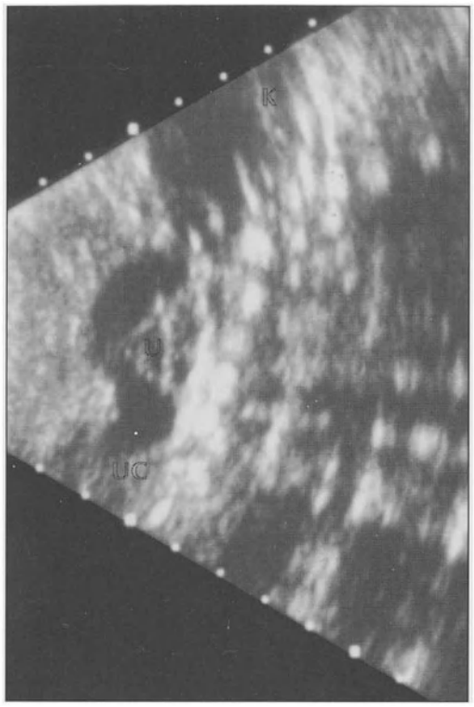
Classification Of Ureteroceles

Study	*Types*
Ericsson [9]	Simple or orthotopic
	Ectopic
Stephens [10]	Stenotic
	Sphincteric
	Sphinctero-stenotic
	Caecoureterocele
	Blind ureterocele
Glasssberg *et al.* [11]	Intravesical
	Ectopic
	Simple
	Duplex

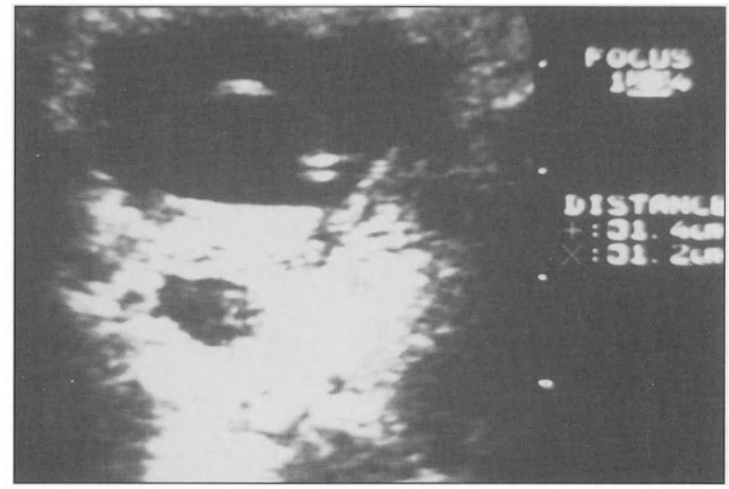
◗ **FIGURE 4-12.** Classification of ureteroceles. In the past, the classification of ureteroceles has been inaccurate and confusing. Ericsson [9] divided ureteroceles into simple or adult type when they are associated with a single ureter and ectopic when they are associated with the upper pole of a duplex system. This classification is inaccurate because ureteroceles associated with a duplex system may reside completely inside the bladder.

Stephens [10] classified ureteroceles based on the location and morphology of the orifice. In Stephens' system, a ureterocele is stenotic when the ureteral orifice is small or nonvisible and located within the bladder. When the orifice is patulous and distal to the bladder neck, the ureterocele is referred to as sphincteric. When the orifice is both ectopic and stenotic it is called spincterostenotic. If the orifice is inside the bladder but has a "tonguelike" extension into the urethra, Stephens [10] calls it a caecoureterocele. If the upper pole is hypoplastic and the afferent ureter is nondilated or atretic, it is called a blind ureterocele.

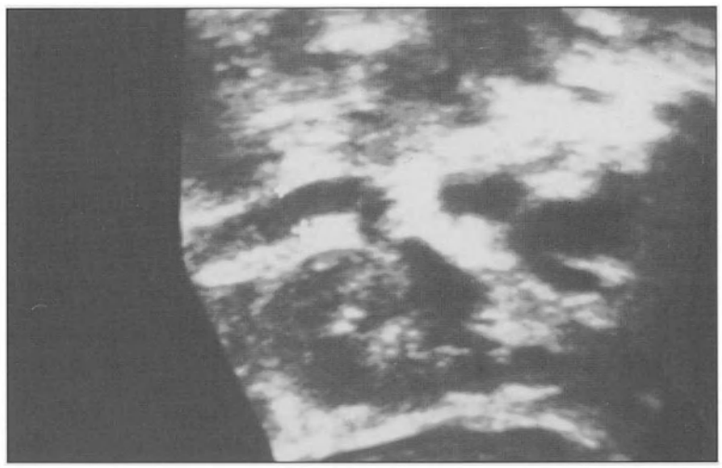
On behalf of the Committee on Terminology, Nomenclature and Classification of the Section of Urology of the American Academy of Pediatrics (AAP), Glassberg *et al.* [11] simplified the classification of ureteroceles. In the AAP system, ureteroceles are divided into intravesical and ectopic. Ureteroceles are further defined according to the number of ureters (simple or duplex) and the type and location of the orifice: stenotic, sphinteric, sphinterostenotic, or caecoureterocele. From a practical standpoint, the distinction between intravesical and ectopic ureteroceles has most relevance when surgical therapy is considered. Simple ureteroceles are almost always successfully treated with endoscopic puncture. Ectopic ureteroceles usually require subsequent trigonal surgery to correct associated vesicoureteral reflux or incontinence.



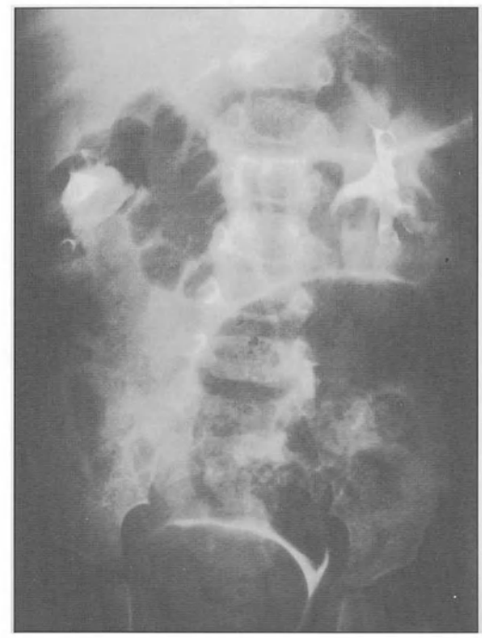
◗ **FIGURE 4-13.** Fetal ultrasound. This prenatal ultrasound shows, from *left* to *right*, the ureter (U) ending in an ureterocele (UC) located inside the bladder, the dilated collecting system, and the fetal kidney (K). Third trimester fetal ultrasound studies have resulted in an increasing number of ureteroceles that may be treated immediately after birth before infection supervenes.



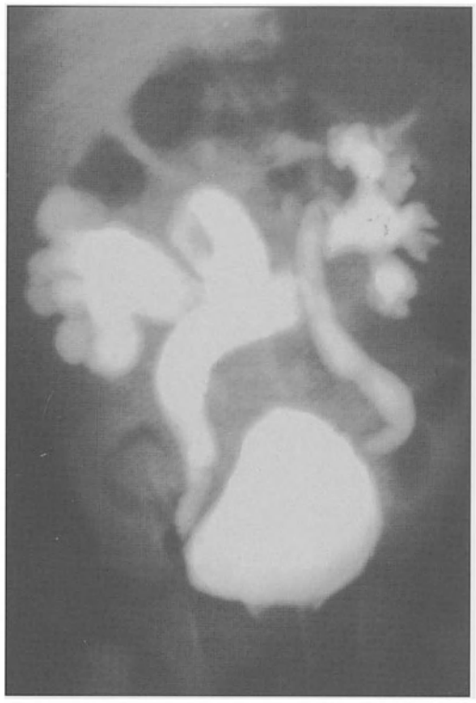
◗ **FIGURE 4-14.** Ultrasound of the bladder demonstrating an intravesicle ureterocele. Unfortunately, despite prenatal imaging, a number of patients are still diagnosed after an episode of pyelonephritis. In these cases, a renal and bladder ultrasound is usually the first study ordered. The ureterocele appears as a cystic, echolucent mass within the bladder.



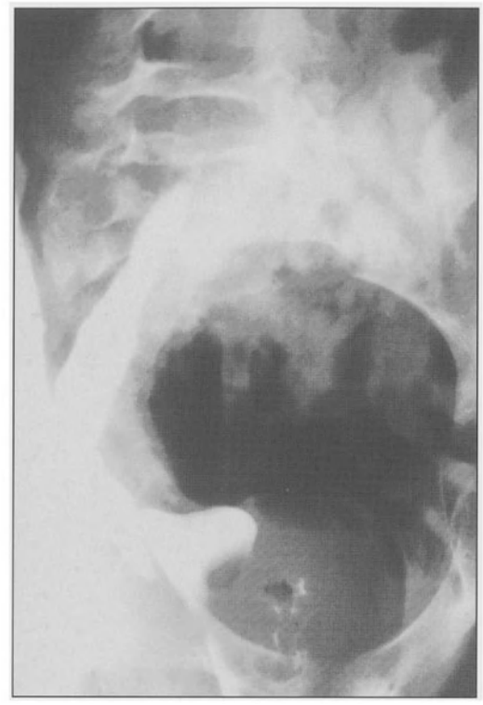
◗ **FIGURE 4-15.** Duplex system with upper pole ureterocele. This renal ultrasound shows a duplex collecting system with a dilated upper moiety and thinning of the renal parenchyma. Increased echogenicity and the presence of cortical cysts in the upper pole indicate parenchymal dysplasia and usually mean that renal function in the affected segment is not recoverable even after decompression.



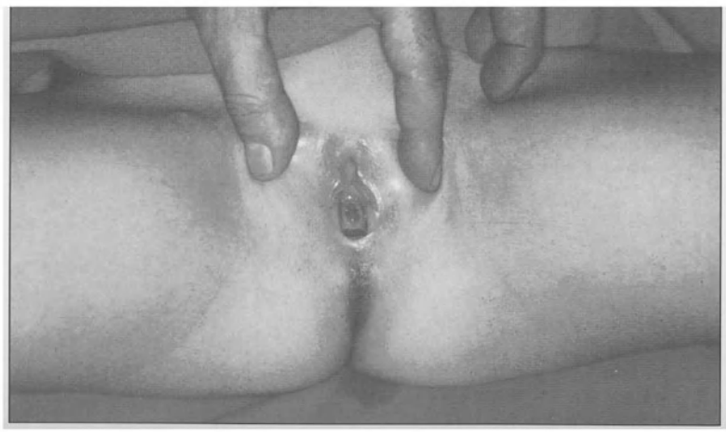
◗ **FIGURE 4-16.** Duplex system with upper pole ureterocele. This intravenous pyelogram reveals a right duplex kidney with a nonopacified upper pole ureter draining into a large ureterocele. The lower pole pelvis is laterally displaced by the dilated upper ureter. Intravenous urography still plays an important role in the imaging of ureteroceles. In the initial postinjection views, a filling defect in the bladder, sometimes occupying most of the bladder, is evident as a radiolucent mass surrounded by faint contrast. In later views, the ureterocele, if small, may be obscured by the contrast that fills the bladder. If the upper pole function is poor, the lower pole pelvis and ureter will not opacify initially. With delayed imaging, the upper pole pelvis will be visible about 50% of the time. Rarely, an ipsilateral lower pole ureter and (less frequently) a controlateral ureter may be obstructed by the ureterocele. The controlateral kidney must be imaged carefully to identify an occult duplication or lower pole reflux. Bilateral ureteroceles are found in about 10% of cases.



◗ **FIGURE 4-17.** Voiding cystourethrogram (VCUG) showing high-volume bilateral vesicoureteral reflux in a patient with a right upper pole ureterocele. Contrast refluxes into the right lower pole ureter and into a single system on the left. The ureterocele is visible only at the beginning of bladder filling because intravesicle contrast obscures the view of the ureterocele as the bladder fills. Fifty percent of ipsilateral lower pole ureters reflux. The controlateral side refluxes about 25% of the time.



◗ **FIGURE 4-18.** Eversion of the ureterocele. By the end of the voiding phase of the cystourethrogram, the ureterocele flattens or may even evert, appearing as a diverticulum because of poor muscular backing offered within the bladder wall lateral to the ureterocele. The cystourethrogram shows also the coexistence of a vesicoureteric reflux into the ipsilateral lower pole ureter.



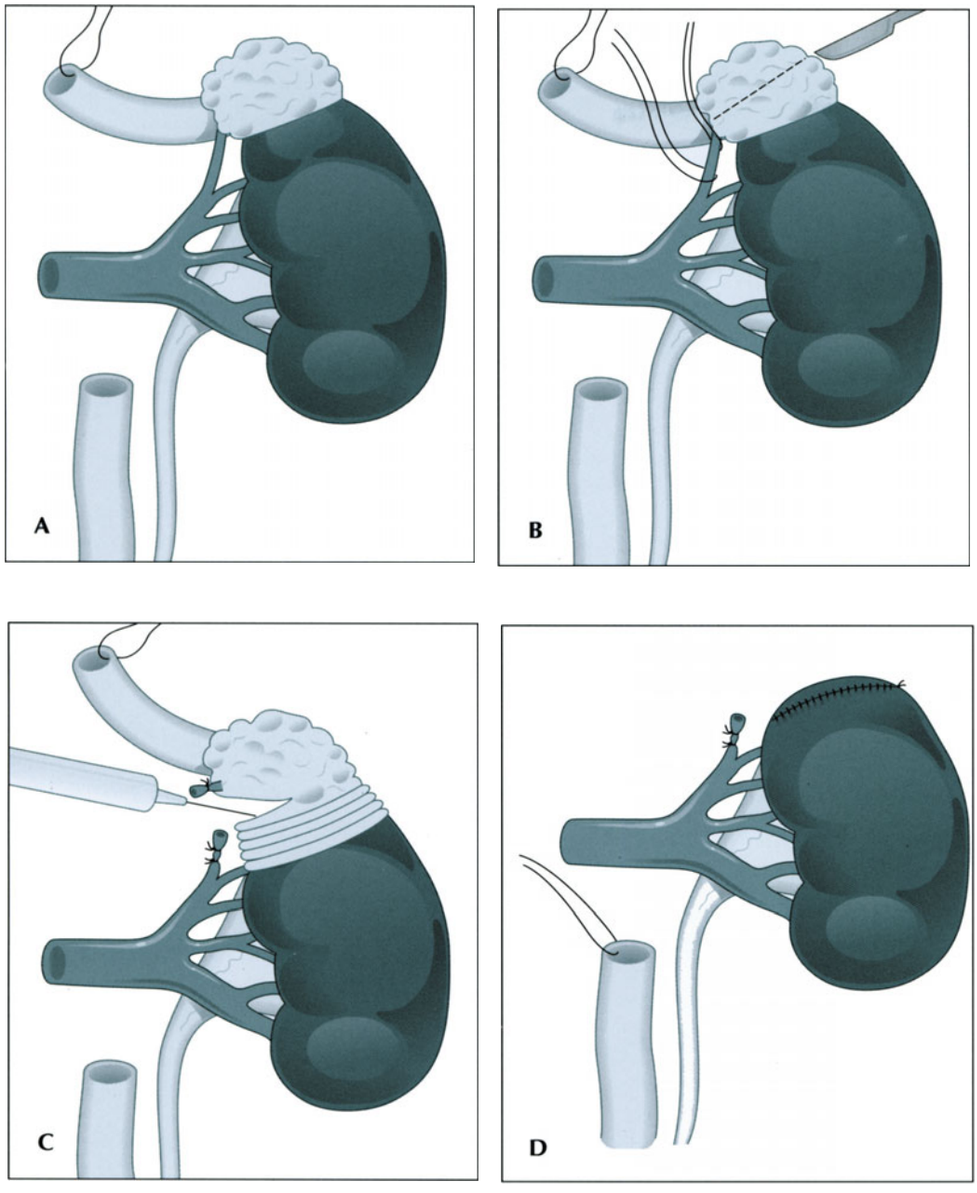
◗ **FIGURE 4-19.** Prolapsed ureterocele. Rarely, a ureterocele may present in a female as a cystic mass that has prolapsed through the urethral meatus. This phenomenon may be caused by a large intravesical ureterocele that protrudes through the bladder neck and urethra. In some cases, the ureterocele is compressed at the level of the bladder neck and may appear as a cyst inferolateral to the urethra. In other cases, the prolapsed portion is the urethral extension of a caecoureterocele that appears pink and nontense. A prolapsed ureterocele is the most common cause of urinary retention in girls and must be distinguished from other perineal masses such as rhabdomyosarcoma, hydrometrocolpos, and periurethral cysts. Rhabdomyosarcoma often has a grapelike appearance. In patients with hydrometrocolpos, the urethra is anterior to the protruding mass. Rarely, a prolapsed ureterocele requires emergency drainage when it results in acute urinary retention. In these cases, an in-office incision of the protruding mass is sufficient to relieve the obstruction.

Principles of Treating Patients with Ureteroceles

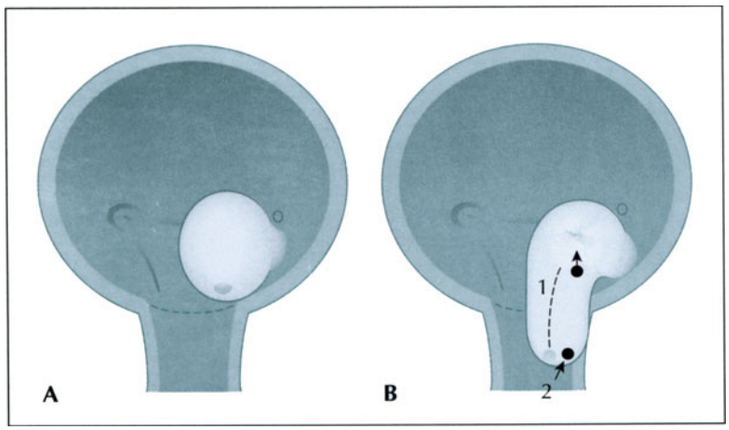
Type of Approach	*Methods*
Low	Ureterocelectomy and reimplantation of the ureters
	Transurethral endoscopic incision of the ureterocele
High	Upper pole partial nephrectomy and partial ureterectomy
	Upper pole to lower pole uretero-ureterostomy or uretero-pyelostomy
Combined	Upper pole nephrectomy and ureterocele removal with or without lower ureteral reimplant in one or two stages

◗ **FIGURE 4-20.** Principles of treating patients with ureteroceles. The goals in treating ureteroceles are to relieve obstruction, correct associated vesicoureteral reflux, and maintain urinary continence. Ureteroceles may have many anatomic variants, so treatment must be individualized.

Combined upper and lower surgery for ureteroceles includes upper pole partial nephrectomy, excision of the ureterocele, reconstruction of the bladder neck, and reimplantation of the ipsilateral, and often the controlateral, ureter. This is an extensive operative procedure, particularly in infants.



◗ **FIGURE 4-21.** Upper pole partial nephrectomy. In 1974 a "simplified" approach (**A**) was suggested [12] that consists of an upper pole partial nephrectomy, leaving in place the distal ureteral stump leading to the ureterocele. In most cases, no further surgery is needed. The ureterocele commonly decompresses and does not need to be removed. This approach can be very effective if vesicoureteral reflux (VUR) is not present. The surgical procedure is straightforward. First, the upper pole ureter is identified and dissected off the lower pole ureter with great care not to compromise the medial blood supply. The upper ureter is then detached from the renal vessels and lifted up in order to define the anatomy and the boundaries of the upper pole. Light traction on the upper pole ureter helps to identify the vessels supplying the upper pole. In general, the incision into the renal parenchyma is made before tying off the vessels. In this way, the chance of inadvertent ligation of a lower pole vessel is minimized. After the upper pole vessels are identified, they are tied with synthetic absorbable sutures (**B**). If there is any doubt about the area perfused by a vessel, the vessel should be left untied. The dissection may then proceed with finger dissection along the base of the upper pole collecting system. Bleeding is minimal in this plane. If bleeding vessels are present within the parenchyma of the superior lower pole, they can be oversewn with fine chromic or polyglycolic acid suture. The renal capsule is incised approximately 1.5 cm above the proposed line of section of the parenchyma and detached from the renal tissue with the handle of the scalpel. The capsule is used later to cover the cut surface of the kidney. The upper pole is then removed using diathermy (**C**). The capsule is then secured over the cut surface with a running suture (**D**). After removal of the upper pole and decompression of the ureterocele, the need for subsequent intravesical surgery (excision of the ureterocele with repair of VUR) varies from 10% to 50% [13]. Ipsilateral reflux resolves in 60% of cases. Controlateral reflux nearly always resolves [14].



◗ **FIGURE 4-22.** Endoscopic puncture of a ureterocele. Endoscopic incision or puncture of the ureterocele is minimally invasive. Endoscopic decompression of the urinary tract has recently become very popular [15] because it can be easily performed with minimal morbidity on neonates with prenatally detected ureteroceles. The ureterocele is punctured using a wire electrode or a 3-F Bugbee electrode, with cutting current set high enough to ensure a clean incision.

For intravesical ureteroceles (**A**), the puncture is made on the inferior wall of the ureterocele, near where the ureterocele meets the bladder wall. Ectopic ureteroceles (**B**) are punctured low in the lateral sulcus with the bladder wall, immediately superior to the bladder neck. It is important to be sure that the incision is superior to the bladder neck (1). An incision at or inferior to the bladder neck (2) fails to decompress the system because the internal sphincter compresses the ureterocele and prevents drainage of the ureter through the puncture site.

The treatment of the intraurethral extension of the ureteroceles is still debated. Some pediatric urologists prefer to vertically incise the intraurethral tongue of the ureterocele, but others recommend a single puncture in the most dependent portion of the sac to avoid creating a valve flap that can obstruct urine outflow. We have had experience with both of these approaches and have also omitted puncturing the urethral extension of the ureterocele with equal results. We now believe that there is no compelling reason to make a second puncture or incision in the urethral portion of the ectopic ureterocele.

In many cases, endoscopic treatment may be the only procedure necessary. In the Children's Hospital of Philadelphia experience [16,17], endoscopic incision has been the only treatment in 93% of intravesical ureteroceles and in 50% of ectopic ones. In our series, the upper moiety has regained its function in 96% and 50% of cases, respectively. After endoscopic treatment, reflux in the ureterocele has developed in 32% of cases, most commonly in those with ectopic ureteroceles.

We now believe that the surgical algorithm for the treatment of ureteroceles depends primarily on the patient's anatomy. Intravesicle ureteroceles appear to disrupt the trigonal and bladder neck function less extensively than do ectopic ureteroceles. Conversely, because of increased distortion of the bladder neck and trigone, patients with an ectopic ureterocele have a higher incidence of associated ipsilateral lower pole and controlateral reflux. As a result, patients with an ectopic ureterocele require reconstruction of the bladder neck and trigone much more frequently than do those with an intravesicle ureterocele regardless of the initial surgery to decompress the ureterocele. In our opinion, the need for secondary trigonal surgery depends on the anatomy of the ureterocele. We now treat all ureteroceles initially with endoscopic incision. If high-volume reflux occurs or persists after incision, we usually recommend ureteral reimplantation with excision of the ureterocele with bladder neck reconstruction, if necessary at about 18 months of age or sooner if urinary tract infection occurs despite antibiotic prophylaxis. We believe that the patients who would be effectively treated with upper pole nephrectomy alone are, in most cases, the same patients who would be effectively treated with incision alone—namely, those with intravesicle ureteroceles or ectopic ureteroceles with minimal trigonal distortion.

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Ureteropelvic Junction Obstruction

5

David B. Joseph

Developmental changes in the region of the ureteropelvic junction (UPJ) may result in hydronephrosis, which is frequently identified in the antenatal period. Hydronephrosis occurs in approximately one in 1000 fetuses and is the most common urinary abnormality seen in the newborn by the pediatric urologist [1]. Fetal ultrasonography has had a great impact on the diagnosis and subsequent management of hydronephrosis, especially that related to obstruction of the UPJ. Prior to fetal ultrasonography, ureteropelvic junction obstruction (UPJO) was most often identified in a child after evaluation revealed an abdominal mass, intermittent abdominal or flank pain and vomiting, or a urinary tract infection. Identification of the obstructed UPJ in a symptomatic child is relatively straightforward, with treatment resulting in improvement of the obstructive process and resolution of symptoms.

In regions where fetal ultrasonography is routine, hydronephrosis is frequently identified and asymptomatic neonates present to the pediatric urologist. It has become apparent that asymptomatic infants with hydronephrotic changes significantly outnumber symptomatic children seen prior to fetal ultrasonography. This finding has had a dramatic impact on current management of hydronephrosis. It is obvious now that many infants with fetal hydronephrosis never become symptomatic and may experience natural resolution of the abnormality. Although operative intervention for hydronephrosis in the neonate has excellent results, surgery is unnecessary in most neonates with hydronephrosis.

The UPJ is the most common site for obstructive uropathy in the urinary system. This finding may be due to an intrinsic abnormality of the renal pelvis and proximal ureter or extrinsic compression.

Evaluation and management of hydronephrosis are more challenging in the asymptomatic neonate than in the symptomatic child. The goals of assessment are to determine the significance of the obstruction, identify any compromise of renal function, and provide a foundation for subsequent comparisons. Unfortunately, when assessing the significance of a UPJO, no imaging or functional study can be relied upon as the "gold standard." The objective in treating obstruction is to preserve and improve renal function and to avoid urinary tract infection and pain.

When operative intervention is deemed appropriate, a variety of exposures and techniques may prove valuable. Open operative repair continues to be the consensus approach to UPJO in a child. This procedure results in a small incision, a limited hospitalization, mild postoperative discomfort, and a success rate greater than 95%. Alternative laparoscopic and percutaneous procedures are available for children but provide limited benefit over an open approach. These alternative procedures are better suited to the adult population.

Epidemiology

Before fetal ultrasonography
- 75% of cases diagnosed at > 1 y of age
  - Symptomatic (fever, UTI, abdominal pain, abdominal mass)
- UPJO diagnosed in 22% of patients with hydronephrosis at 4 wk of age

Fetal ultrasonography evaluation
- Hydronephrosis in 1:1000 births
  - Asymptomatic
  - 41% of cases related to UPJO
  - < 15% of patients have abdominal mass
  - Male:female ratios 2:1
  - 60% of UPJO cases on left side
  - Bilateral UPJO in 20% of patients < 1 y of age, in 5% > 1 y of age
  - Coexisting VUR in 15% of patients

FIGURE 5-1. Epidemiology. Prior to fetal ultrasonography, most children in whom ureteropelvic junction obstruction (UPJO) was diagnosed were older than 1 year of age [2]. A UPJO was diagnosed in infants most often after evaluation for a urinary tract infection (UTI), fever, or unusual fussiness [3]. At 4 weeks of age, approximately 20% of children with hydronephrosis were found to have a UPJO. With the advent of fetal ultrasonography, the number of infants presenting with hydronephrosis has significantly increased. Approximately 40% of newborns with hydronephrosis are now noted to have a UPJO [1]. Only a small percentage of infants have any abnormal physical findings, and fewer than 15% have a palpable abdominal mass [4]. Bilateral UPJO has been noted in approximately 20% of asymptomatic infants younger than 1 year of age [5]. Vesicoureteral reflux (VUR) coexists in 20% of asymptomatic infants [6], and for that reason all infants with a diagnosis of antenatal hydronephrosis should also undergo voiding cystourethrography.

Etiology

Intrinsic
- Narrowed segments
- Muscular discontinuity
- High insertion
- Valves

Extrinsic
- Crossing vessel, 20% to 35% of cases
- Kinks

Acquired
- VUR
- Polyps
- Urolithiasis
- Tumor

FIGURE 5-2. Etiology. Intrinsic narrowed segments may persist owing to a failure in recanalization of the metanephric cord during the 5th to 6th week of fetal development [7]. The ureteropelvic junction (UPJ) obstruction may appear grossly normal. Microscopic and electron microscopic examination of the UPJ, however, shows a variable degree of disorganized muscle cells [2,8–12]. The normal spiral musculature is replaced by abnormal longitudinal muscles with an abundance of intercellular ground substance and increased collagen. In addition, smooth muscle dysplasia has been noted proximal to the obstructed segment. All of these features result in limited peristaltic activity, delayed emptying, and obstruction. True ureteral valves have been reported but rarely occur.
Extrinsic compression due to a lower pole crossing vessel has been implicated in 20% to 30% of children with a ureteropelvic junction obstruction (UPJO) [5,13]. However, it is doubtful that a crossing vessel is the primary cause of obstruction. More likely, the crossing vessel is a contributing factor when an intrinsic UPJ abnormality already exists. Proximal ureteral folds (Ostling's folds)[14] can be seen in infants when intravenous urography is performed. Although these folds may cause some resistance, they rarely lead to obstruction [14].
A UPJO may coexist with or result from vesicoureteral reflux (VUR)[6,15]. High-grade VUR can cause proximal ureteral kinking and renal pelvic dilatation. It is important to determine whether these changes are primarily related to the VUR or to independent problems. Ureteral polyps are a rare cause of obstruction. Stone formation and tumors are more commonly seen in the adult population.

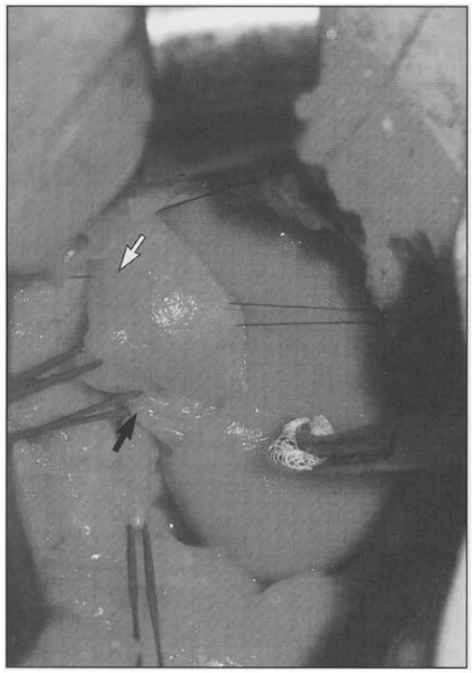
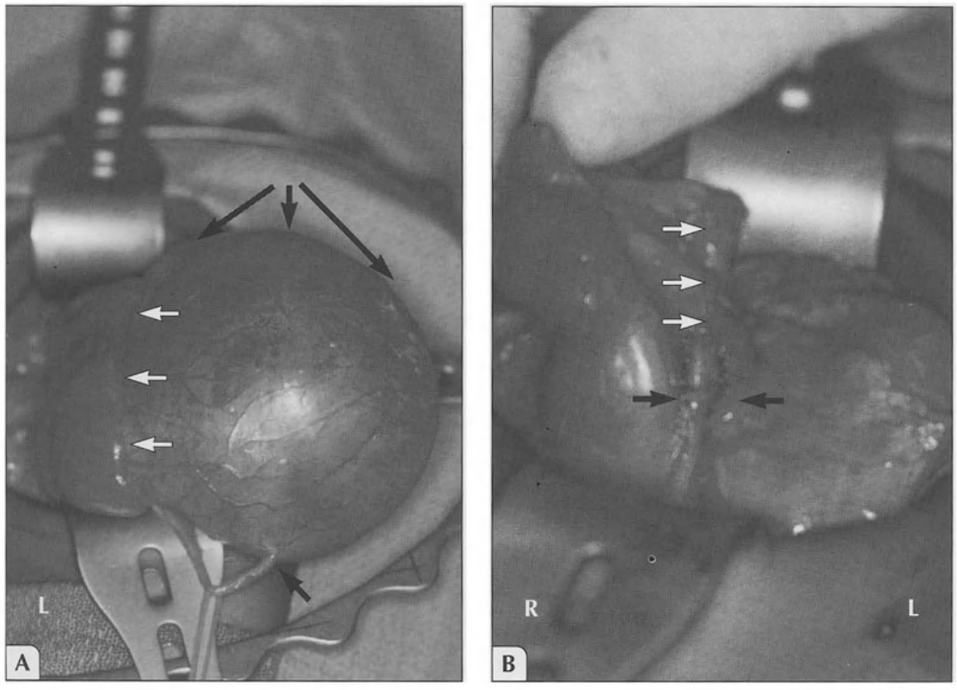


FIGURE 5-3. Lower pole crossing vessels. The *solid arrow* identifies lower pole vessels traveling anterior to the ureteropelvic junction (UPJ) and proximal ureter. The *open arrow* identifies the UPJ. Renal arteries are end arteries, and therefore transection would result in loss of renal parenchyma. Appropriate treatment requires a dismembered pyeloplasty with excision of the UPJ and proximal ureter. A dependent ureteral pyelostomy is fashioned anterior to the lower pole vessel.



◗ **FIGURE 5-4.** Stenotic ureteropelvic junction obstruction (UPJO). **A,** The *solid arrows* indicate a stenotic UPJO. The *long arrows* identify a large extrarenal pelvis. The *open arrows* show the medial border of the renal parenchyma. This segmental stenosis of the ureteropelvic junction resulted in significant enlargement of the renal pelvis, with preservation of the renal parenchyma. **B,** The *open arrows* indicate pelvic reduction with midline closure. The *solid arrows* show sutures from a spatulated dismembered pyeloplasty.

Evaluation

- Renal ultrasonography
  - Parenchyma
  - Hydronephrosis
  - Resistive index
- Renal scintigraphy
  - ^{99m}Tc DTPA
  - ^{99m}Tc MAG3
    - Differential uptake
    - Time to peak activity
    - Excretion
    - Half-time for renal pelvis drainage
- Upper tract urodynamic evaluation
  - Whitaker study
  - Pressure-performance study
- Voiding cystourethrography
  - Coexisting VUR
- Postoperative studies
  - Renal ultrasonography
  - Renal scintigraphy

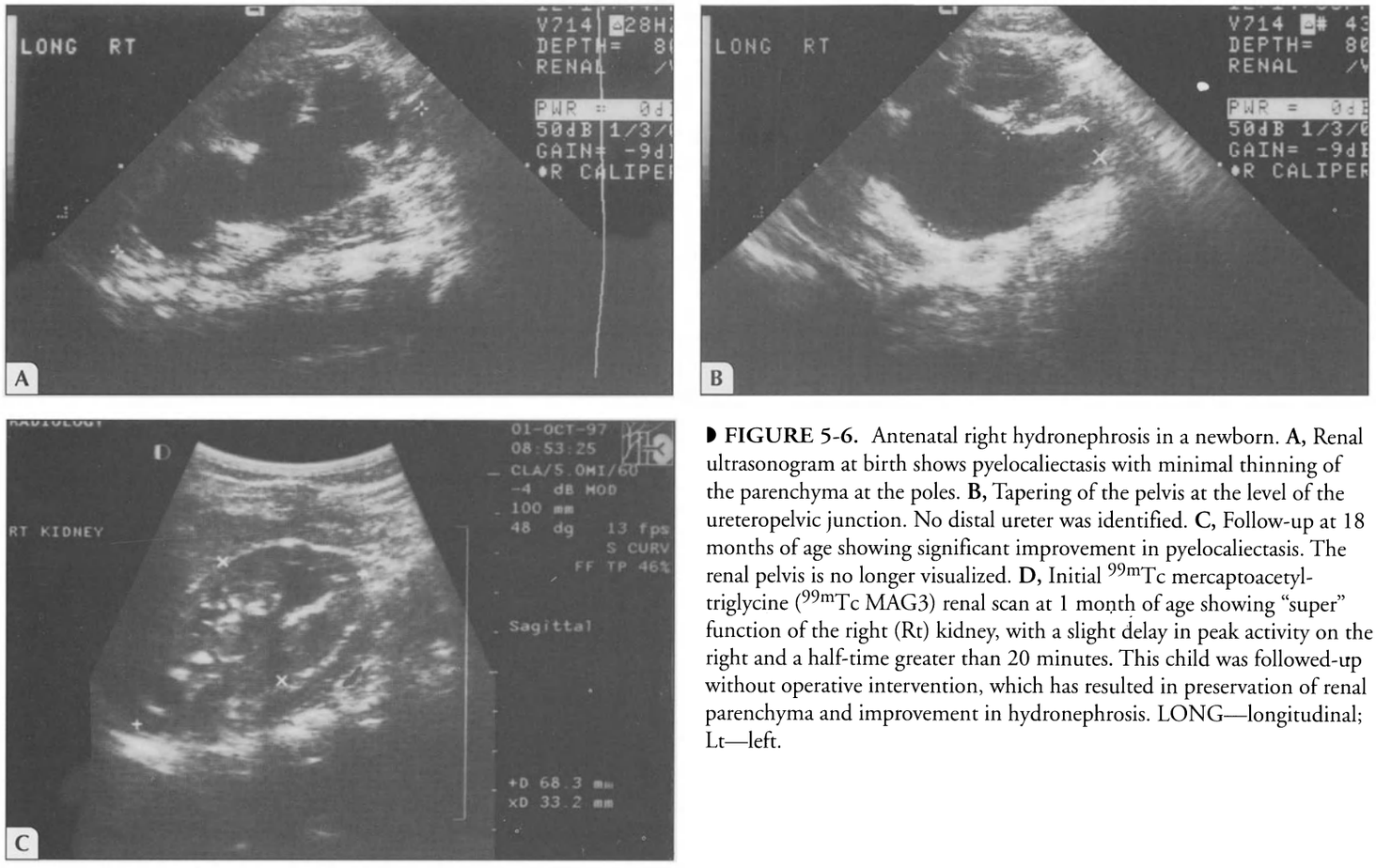
◗ **FIGURE 5-5.** Evaluation. Most children are first imaged by renal ultrasonography. Although ultrasonography cannot directly assess function and obstruction, several variables, when considered in association, can be predictive of a ureteropelvic junction obstruction (UPJO). These variables include increased echogenicity of the renal parenchyma, contralateral hypertrophy, a decreased rim of parenchyma of less than 5 mm, and a resistive index ratio of greater than 1:1 [16].

Nuclear renal scintigraphy remains the most reliable imaging study in the assessment of a UPJO, but it is not definitive. When determining the significance of hydronephrosis, several parameters are calculated, including the differential uptake of activity between the two kidneys, the time to peak activity, excretion, and the half-time for drainage of the renal pelvis. No one particular feature of the renal scan indicates obstruction. There are multiple pitfalls when using nuclear scintigraphy, and for that reason, standardized protocols have been established to eliminate as many variables as possible [3].

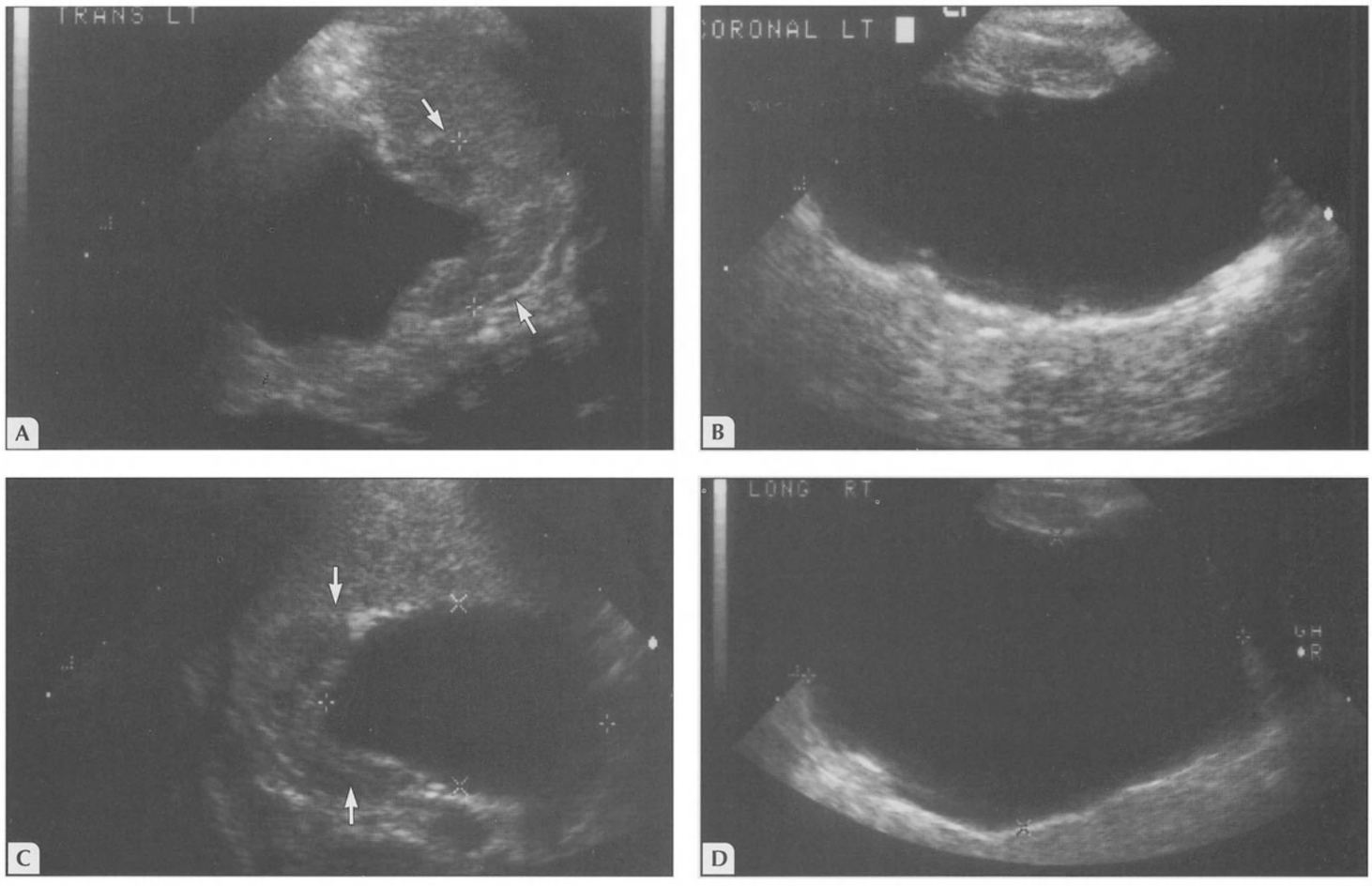
Upper urinary tract urodynamic evaluation combining fluoroscopic assessment of the ureteropelvic junction and pressure manometry has been helpful in selected cases to further delineate the UPJO. The Whitaker study is performed by infusing the testing medium into the renal pelvis at a constant rate. The change in pressure is recorded as the renal pelvis fills and drains [17–19]. The pressure perfusion study is an alternative to constant infusion [20]. In this study, a preselected filling pressure is used to fill the renal pelvis, and the change in renal pelvic pressure is determined as the pelvis fills and drains. This technique eliminates the infusion rate as a variable.

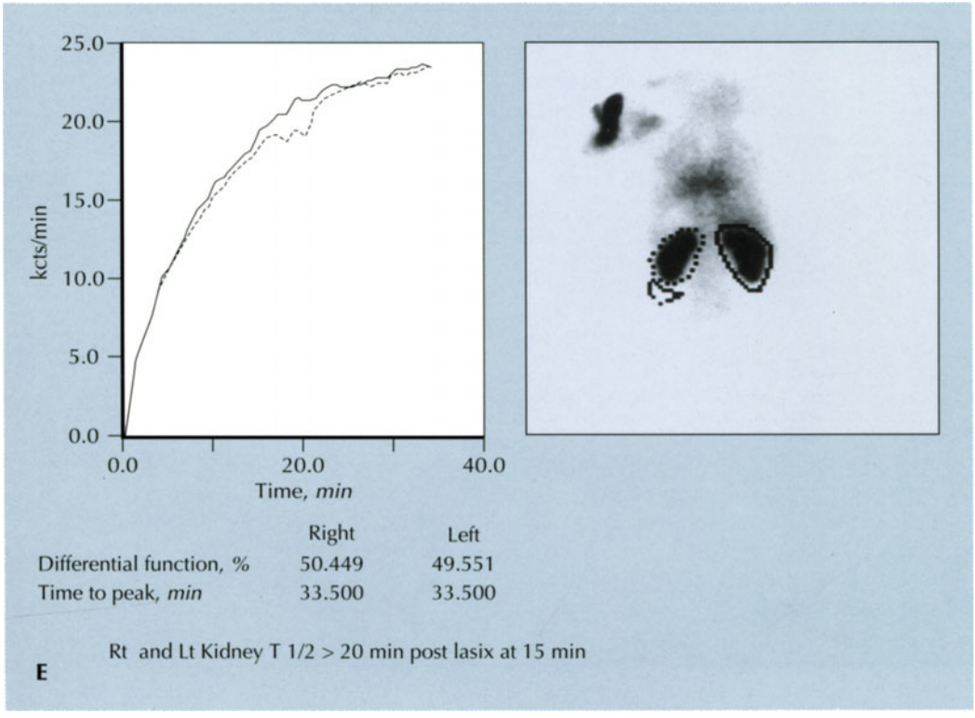
Vesicoureteral reflux (VUR) occurs in approximately 20% of children [6,15] with a UPJO. It is important to determine whether a true UPJO exists or whether hydronephrosis is due to significant tortuosity and dilatation of the ureter and renal pelvis. The difference in the density of contrast between the renal pelvis and the ureter can help in defining a true obstruction. When an obstruction exists, the renal pelvis is usually much less dense than the ureter because refluxed contrast is mixed with retained urine. When a dilated renal pelvis is secondary to VUR, the contrast density in the pelvis and in the ureter is similar. Delayed images show poor drainage with true obstruction.

Both ultrasonography and renal scintigraphy are helpful in postoperative assessment. If imaging studies are obtained within 4 weeks of the repair, it is not unusual to see either no apparent change or a small increase in hydronephrosis. This finding can be due to operative edema at the site of the anastomosis. It may take several months for improvement to be visible on renal ultrasonography. ^{99m}Tc DTPA—^{99m}Tc diethylene triamine penta-acetic acid; ^{99m}Tc MAG3—^{99m}Tc mercaptoacetyltriglycine.



◗ **FIGURE 5-6.** Antenatal right hydronephrosis in a newborn. **A,** Renal ultrasonogram at birth shows pyelocaliectasis with minimal thinning of the parenchyma at the poles. **B,** Tapering of the pelvis at the level of the ureteropelvic junction. No distal ureter was identified. **C,** Follow-up at 18 months of age showing significant improvement in pyelocaliectasis. The renal pelvis is no longer visualized. **D,** Initial ^{99m}Tc mercaptoacetyltriglycine (^{99m}Tc MAG3) renal scan at 1 month of age showing "super" function of the right (Rt) kidney, with a slight delay in peak activity on the right and a half-time greater than 20 minutes. This child was followed-up without operative intervention, which has resulted in preservation of renal parenchyma and improvement in hydronephrosis. LONG—longitudinal; Lt—left.





◗ **FIGURE 5-7.** Antenatal massive bilateral hydronephrosis in a newborn. On physical examination, bilateral flank masses were palpated. **A,** Renal ultrasonogram showing renal parenchyma with large extrarenal pelvis. The *arrows* show the extent of parenchymal tissue. **B,** Large left (Lt) extrarenal pelvis. **C,** Right (Rt) renal system showing dilated extrarenal pelvis. The *arrows* indicate renal tissue. **D,** Massive dilatation of the right renal pelvis. **E,** ^{99m}Tc mercaptoacetyltriglycine (^{99m}Tc MAG3) renal scan showing relatively equal function with no established peak activity and no excretion or apparent drainage after administration of furosemide (Lasix; Hoechst-Roussel Pharmaceuticals, Somerville, NJ). LONG—longitudinal; TRANS—transverse.

Treatment

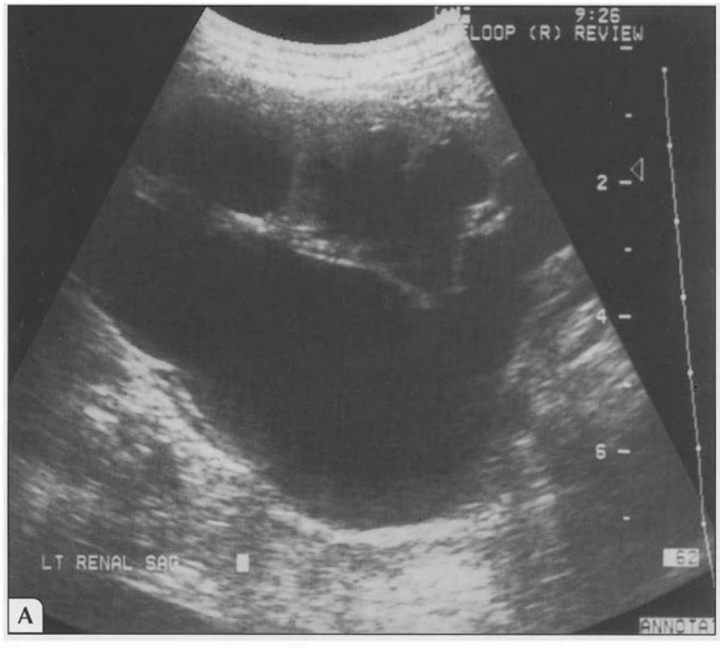
- Indications
  - Symptomatic
    - Abdominal pain, nausea, vomiting (Dietl's crisis), fever, UTI, stones
  - Asymptomatic
    - Progressive loss of renal function
    - Subsequent pain, UTI
- Technique
  - Open
    - Anderson-Hynes dismembered pyeloplasty
    - Foley Y-V pyeloplasty
    - Culp-DeWeerd flap
  - Percutaneous
  - Endoscopic
- Approach
  - Anterior subcostal
  - Flank
  - Dorsal
- Postoperative hospitalization
  - Complication rate, < 3%
  - Success rate, > 97%

◗ **FIGURE 5-8.** Treatment. Children presenting with symptoms such as abdominal pain, intermittent nausea and vomiting, and urinary tract infections (UTIs) benefit from operative intervention. It is not unusual to see an adolescent who has had a gastrointestinal workup for intermittent abdominal pain, nausea, and vomiting (Dietl's crisis). Often the results of imaging studies are normal when the child is asymptomatic. It may be necessary to obtain imaging studies when the child is experiencing colicky pain. The finding of renal pelvic stones coexisting with a ureteropelvic junction obstruction (UPJO) requires intervention to remove the stones and correct the obstruction. Pelvic stones are not simply a result of a UPJO and can recur postoperatively in a decompressed system [21]. It is a challenge to determine when operative intervention is required for the asymptomatic infant. The child's health, findings on the physical examination, and results of imaging studies play a combined role in determining when correction is to be undertaken. Children with hydronephrosis are candidates for repair if progressive renal pelvic dilatation is noted on ultrasonography and is associated with a decrease in renal function calculated by nuclear imaging. Any specific expression of abdominal discomfort or the occurrence of a UTI is also an indication for intervention.

The most common technique for repair of the UPJO is the Anderson-Hynes dismembered pyeloplasty, with excision of the ureteropelvic junction (UPJ) and proximal ureter [22]. The ureter is then spatulated laterally and secured to the renal pelvis. It is important to preserve the blood supply to the proximal portion of the ureter. Key points in the repair are to provide a dependent UPJ without twisting or applying tension to the ureter. Both percutaneous and retrograde endoscopic procedures for the repair of a UPJO have been reported in children but at the present time offer only marginal benefits over an open technique [23].

The anterior subcostal and flank approaches to the kidney for repairing a UPJO are the most common [24]. Both offer excellent access to the UPJ and renal pelvis, with adequate mobility of the kidney. Recently, the dorsal approach has gained in popularity, particularly for infants [24]. The dorsal approach offers excellent exposure of the renal pelvis but provides limited mobility of the kidney. Concern regarding the presence of a crossing vessel may deter some surgeons from this approach, but the presence of such a vessel is not a contraindication. The dorsal approach can be advantageous when doing bilateral repairs. Retrograde ureteropyelography prior to a repair can rule out a potential second distal ureteral obstruction. It is also helpful in detecting a crossing vessel.

The postoperative hospitalization of children undergoing a procedure done with open technique is limited, with many children discharged on the morning of the 1st postoperative day [25]. The limited use of a nephrostomy tube or stent has allowed for an earlier discharge. A nephrostomy tube and ureteral stent are not required in every case and may be a disadvantage in a young child or an infant. A nephrostomy tube and stent should be considered in the setting of chronic infection or significant operative edema and in older children. Postoperative recovery is usually uneventful with a less than 3% complication rate and a 97% success rate in our series of 115 children undergoing repair [25].



◗ **FIGURE 5-9.** Findings in a 6-year-old child undergoing evaluation for intermittent nausea and vomiting and abdominal pain. **A,** Renal ultrasonogram showing marked pyelocaliectasis and thinned renal parenchyma.

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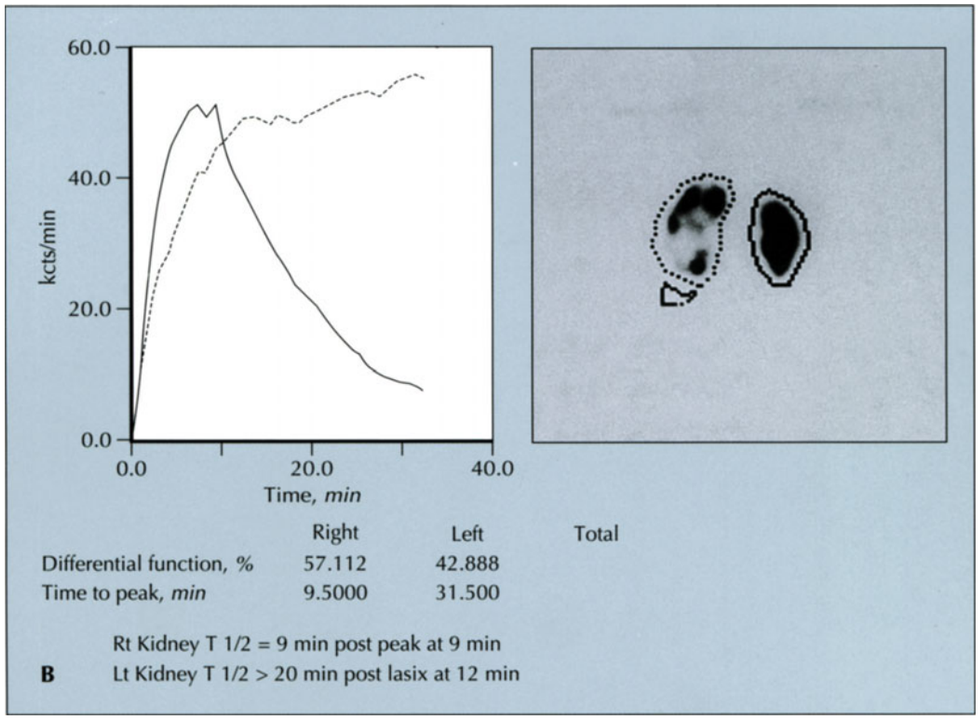
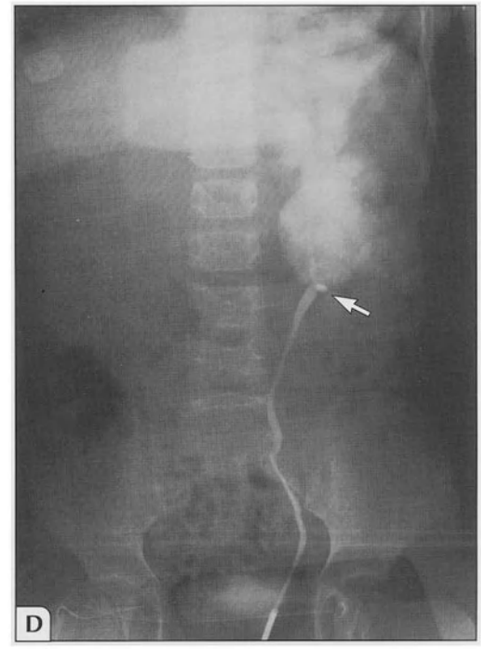
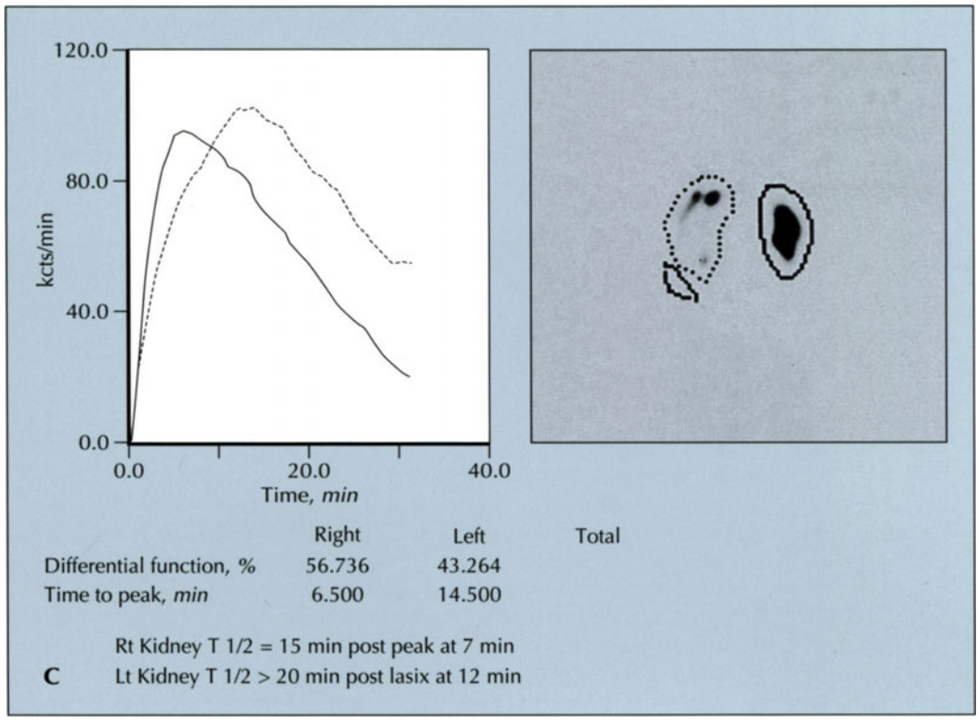
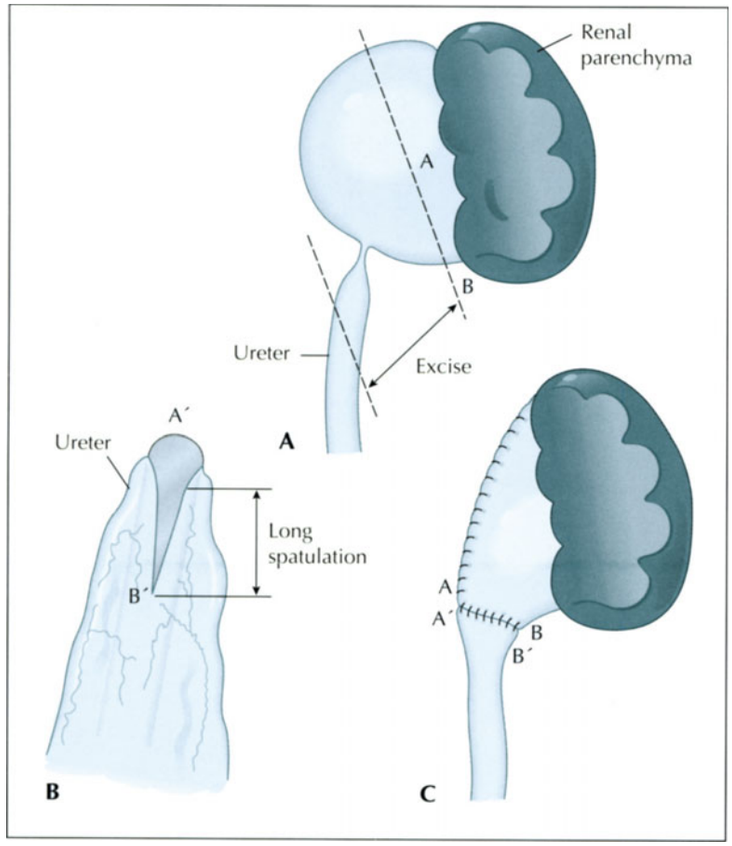


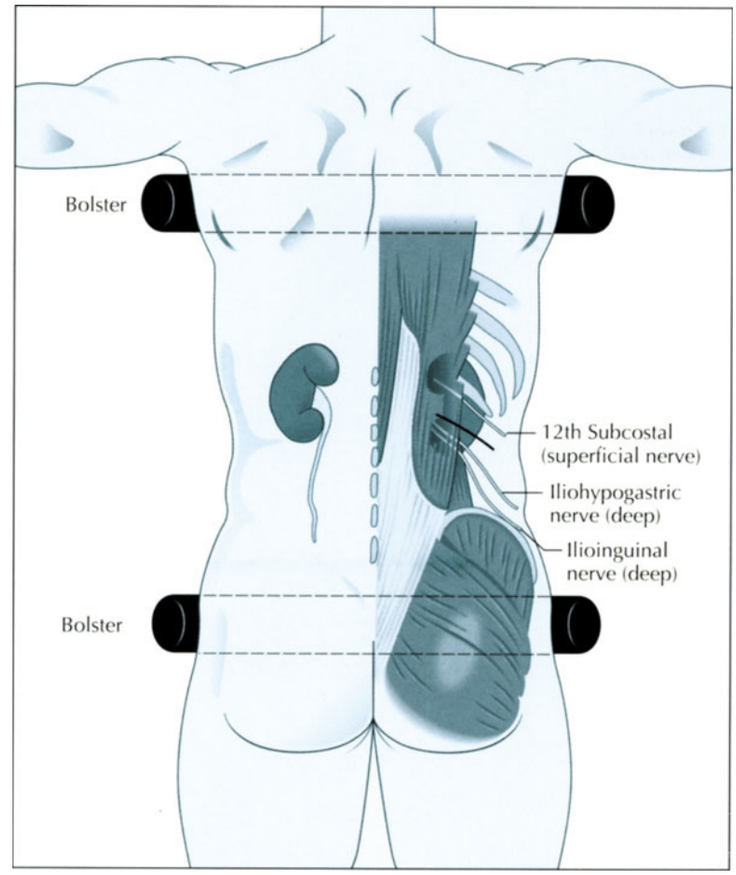




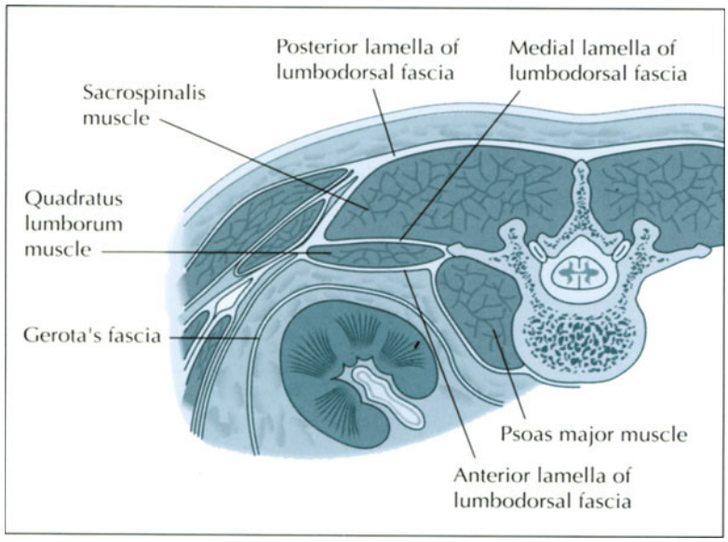
◗ **FIGURE 5-9.** (*Continued*) **B,** Renal scan obtained at the time of pain showing minimal drainage of the right (Rt) system. **C,** Post-operative imaging showing improved drainage of the right system. **D,** Retrograde ureteropyelogram obtained at the time of the repair. The *arrow* indicates lateral horizontal kinking of the ureter secondary to a crossing vessel. L—left; SAG—sagittal.



◗ **FIGURE 5-10.** The classic Anderson-Hynes dismembered pyeloplasty. **A,** Excision of the redundant renal pelvis and proximal ureter. **B,** Long lateral spatulation of the ureter. When mobilizing the ureter, care should be taken to prevent devascularization. **C,** Ureteropyelostomy placing the ureteropelvic junction in a dependent location, which prevents tension or torsion of the ureter. The remaining renal pelvis is simply closed.



◗ **FIGURE 5-11.** Prone positioning for a dorsal approach. Bolsters are placed under the thorax and pelvis, which straightens the spine and drops the peritoneal contents to a dependent location. The incision for a pyeloplasty is placed within Langer's lines, one third of the distance between the 12th rib and the crest of the iliac spine. The medial limit of the incision begins over the middle of the sacrospinalis muscle and is continued approximately 3.5 cm laterally. The 12th subcostal nerve may be encountered superficially while achieving the exposure. The iliohypogastric and ilioinguinal nerves are noted deep and should be avoided when opening the anterior lamella of the lumbodorsal fascia.



◗ **FIGURE 5-12.** The fascial and muscle layers encountered in a dorsal approach. After a skin incision is made, the plane between the subcutaneous tissue and posterior lamella of the lumbodorsal fascia is developed, creating superior and inferior skin flaps. The posterior lamella is opened parallel to the sacrospinalis muscle from the 12th rib to the posterior iliac spine. The sacrospinalis is next mobilized medially to identify the medial lamella of the lumbodorsal fascia, which is opened in a similar fashion to expose the quadratus lumborum muscle. This is then mobilized medially to identify the anterior lamella of the lumbodorsal fascia. An incision is made here between the iliohypogastric and ilioinguinal nerves. Gerota's fascia is opened, and the lower portion of the kidney and the renal pelvis are easily approached. (*Adapted from* Liu *et al.* [25].)

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6

Hypospadias

Laurence S. Baskin

Hypospadias remains one of the few pediatric urologic anomalies solely treated by surgical reconstruction. The number of published repair techniques must be unmatched for this common congenital anomaly. The term *hypospadias* is derived from the Greek word *spadon* and refers to a vent on the ventral surface of the penis. Hypospadias results from incomplete development of the anterior urethra. The abnormal urethral opening may be anywhere along the shaft of the penis, along the scrotum, or even in the perineum (see Fig. 6-1). Hypospadias is associated with penile curvature, depending on the severity of the anomaly.

The goal of hypospadias surgery is to correct the penile curvature, to reposition the meatus to allow for intercourse and proper delivery of semen, and to reconstruct a forward-directed stream. Each hypospadiac penis is different; therefore, one operation will not solve all the reconstructive problems. When planning hypospadias surgery, the issues to consider are reconstruction of a new urethra, correction of penile curvature, creation of a new meatus, skin coverage, and finally correction of any penile scrotal transposition or bifid scrotum. These issues must be assessed prior to surgery, but flexibility needs to be maintained because the quality of the hypospadiac urethra may be difficult to evaluate until the patient is under anesthesia. An anterior hypospadias may therefore turn into a proximal hypospadias, especially after the correction of penile curvature and resection of abortive or inadequate urethral tissue. A surgeon's approach to hypospadias depends on his or her personal preference, skill, and experience. The father of modern hypospadias surgery, Dr. John W. Duckett, coined the term *hypospadiology*, building his knowledge and technique on an extensive familiarity with the work of those who have come before him. My approach is to divide hypospadias into two categories: 1) penises that require a vascularized flap procedure (posterior) and 2) those that can be managed with a meatus-based procedure (anterior).

The treatment of anterior hypospadias depends on the cultural preference of the child's family. Many patients with anterior hypospadias do not have a functional defect, are without significant penile curvature, and will be able to stand and void with a straight stream. Therefore, the goal of placing the meatus in its normal position within the glans is essentially cosmetic. The outcome needs to be as close to perfect as possible. At present, it is standard to perform the surgery on an outpatient basis, typically without the need for urethral stents. Because the surgery is elective, the optimum time as recommended by the American Academy of Pediatric Consensus Panel on genital surgery is between 6 months and 18 months of age [1]. The tech-

nique chosen depends on the anatomy of the hypospadiac penis. The most common accepted procedures are the meatal advancement glansplasty (MAGPI), the glans approximation procedure (GAP), the pyramid procedure, the Mathieu or flip-flap procedure, and the tubularized incised plate urethroplasty [2–5].

The most feared complication of hypospadias surgery is meatal stenosis, which may be accompanied by fistula and proximal urethral diverticulum. Extreme care should be taken to create a glandular urethra of adequate caliber by satisfactorily forming the glans wings and performing a tension-free glansplasty. Simple fistulae after hypospadias, on the other hand, that are not accompanied by distal obstruction are easily repaired as an outpatient procedure with a 90% success rate. Although the presence of a fistula is initially upsetting to the family and surgeon, a well-performed hypospadias repair with a resulting fistula that is subsequently fixed has an excellent chance of long-term success without the need of further surgery.

Long-term follow-up of patients with hypospadias is difficult to assess because procedures have changed and techniques have improved [6]. It is clear, however, that the surgeon's assessment of hypospadias outcome is decidedly different from the patient's assessment [7]. Therefore, all patients should be followed-up into adolescence and offered the option of further cosmetic correction if they are not satisfied.

In summary, the patient with hypospadias has an excellent chance of normal sexual function, normal voiding, and acceptable cosmetic results with our present management techniques. The surgeon treating patients with hypospadias should have a clear understanding of penile anatomy and be well versed in multiple reconstructive procedures. Optimum results will be achieved by those who continue the study of "hypospadiology."

CLASSIFICATION

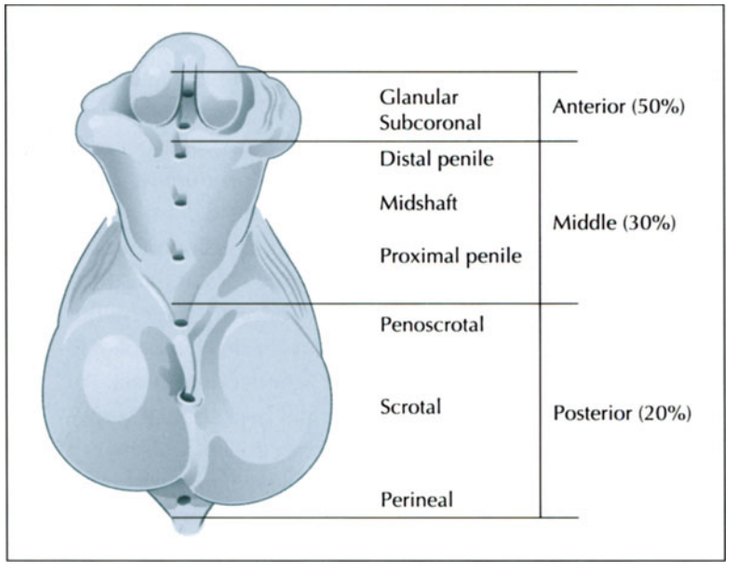
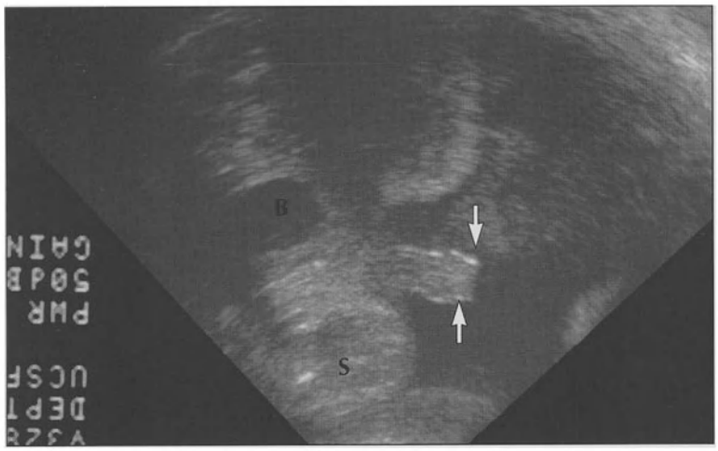


FIGURE 6-1. Classification of hypospadias. Classification is based on the location of the urethral meatus after release of penile curvature. Fifty percent of patients will have anterior hypospadias, subclassified as either glandular or subcoronal; 20% will have midshaft hypospadias, classified as distal penile shaft, midpenile shaft, or proximal penile shaft; and the remaining 30% of patients will have posterior hypospadias, classified as penoscrotal, scrotal, or perineal hypospadias. (*Adapted from* Baskin and Duckett [8].)

INCIDENCE AND ASSOCIATED ANOMALIES

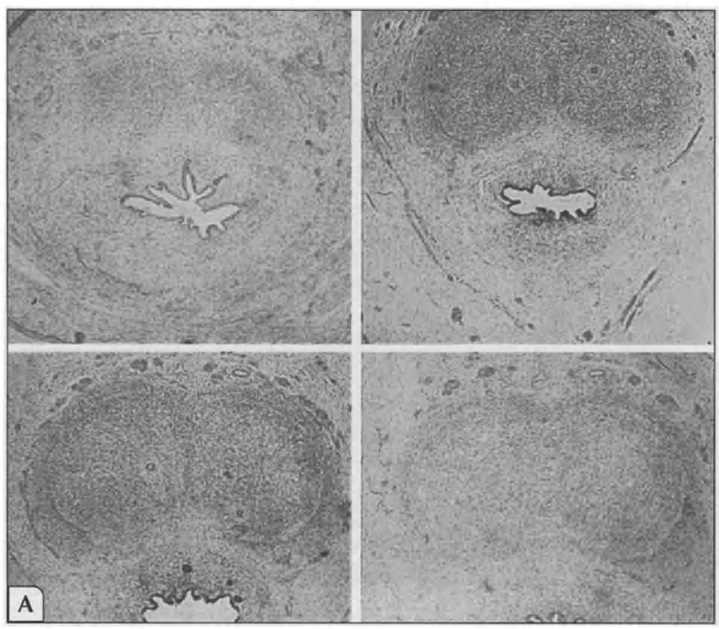


◗ **FIGURE 6-2.** Ultrasonographic image of hypospadias. Hypospadias occurs in 0.3% of healthy male newborns [9]. Urinary tract anomalies are infrequent in patients with hypospadias because the external genitalia are formed much later than the supravesical portion of the urinary tract. Undescended testes and inguinal hernias are the most common associated conditions, occurring in slightly fewer than 10% of patients. An enlarged utriculus masculinus (utricle) is also found in patients with hypospadias, but typically in those who have either scrotal or perineal openings. A utricle is significant only if it causes difficulty in catheterization at the time of surgery. Patients with isolated anterior hypospadias and no other congenital anomalies detected on physical examination, such as a cardiac murmur or symptoms of pyloric stenosis, do not need further evaluation of their urinary tract. Patients with posterior hypospadias, however, or an associated nonpalpable testis should have a karyotype obtained to assess the possibility of intersex, the most common type being mixed gonadal dysgenesis.

The diagnosis of hypospadias is typically straightforward at the time of birth. Classic findings are the abnormal position of the urethral meatus and the dorsal hooded foreskin, which results from incomplete fusion of the foreskin secondary to the absence of the urethral spongiosum. An accurate diagnosis of hypospadias is critical; circumcision is certainly contraindicated in these patients because the foreskin will be needed for subsequent reconstruction. Typically, a dimple is present at the glans penis, which represents an attempt at ectodermal intrusion or distal formation of the urethra. This dimple ends blindly and should not be confused with urethral duplication. Recently, with the advent of more sophisticated ultrasonography and higher-quality equipment, hypospadias has been diagnosed in utero [10]. The classic finding at the time of prenatal fetal ultrasonography is a wide distal end of the penis, which correlates with the excess dorsal prepuce.

This prenatal fetal ultrasonographic image at 31 weeks of gestation reveals a wide distal end of the penis (*arrows*), which represents the abnormal dorsal hooded prepuce, consistent with the diagnosis of hypospadias. B—fetal bladder; S—scrotum. (*From* Duckett and Baskin [9]; with permission.)

NORMAL ANATOMY AND EMBRYOLOGY



◗ **FIGURE 6-3.** Neurovascular anatomy of the normal human penis. Surgical repair of hypospadias requires an expert understanding of the anatomy of the normal penis as well as the hypospadiac penis. The human penis consists of paired corpora cavernosa covered by a thick, elastic tunica albuginea, with a midline septum [11]. The urethral spongiosum lies in a ventral position, intimately engaged between the two corporal bodies. Buck's fascia surrounds the corpora cavernosa and splits to contain the corpus spongiosum in a separate compartment. Recent work has shown that the neurovascular bundle lies deep to Buck's fascia and where the two crural bodies join to form the corporal bodies, the neurovascular bundle completely fans out around the corpora cavernosa, all the way to the junction of the corpus spongiosum (see Figs. 6-3 and 6-4) [12]. This concept is in contradistinction to the classic belief that the neurovascular bundle lies in the 11 and 1 o'clock positions. Superior to Buck's fascia is the dartos fascia, which lies immediately beneath the skin. This fascia contains the blood supply to the prepuce. The prepuce is supplied by two branches of the inferior external pudendal arteries, the superficial penile arteries [13]. These arteries divide into the anterolateral and posterolateral branches. The island flap is typically based on the anterolateral superficial vessels. The onlay island flap and tubularized island flap are dependent on careful preservation of these blood vessels. In hypospadias surgery, the outer skin survives from remaining subcutaneous vessels.

A, Top left, Transverse section. **Top right,** Distal penile shaft. **Bottom left,** Midpenile shaft. **Bottom right,** Proximal penile shaft. Note the localization of S-100 nerve marker completely surrounding the cavernous bodies up to the junction with the urethral spongiosum along the penile shaft, except at the 12 o'clock position.

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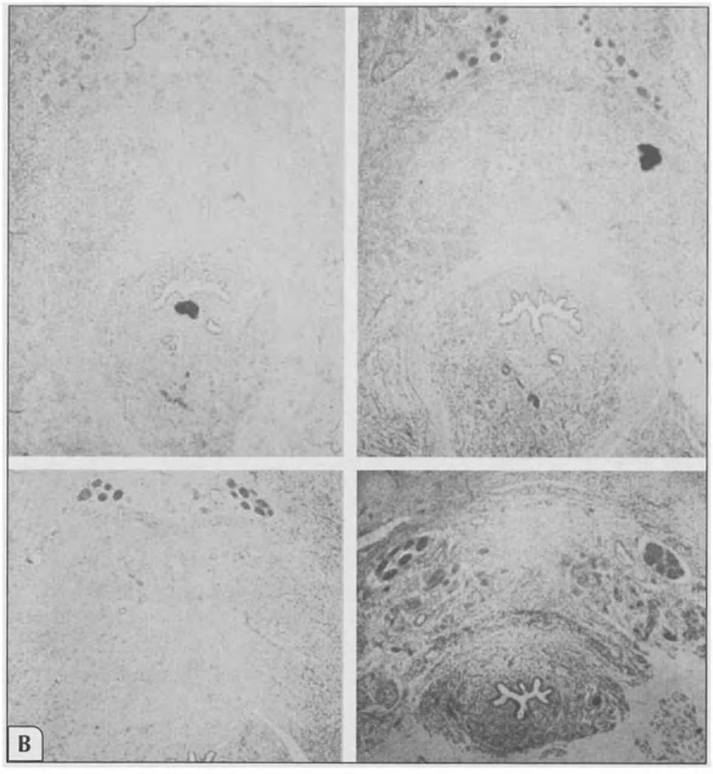
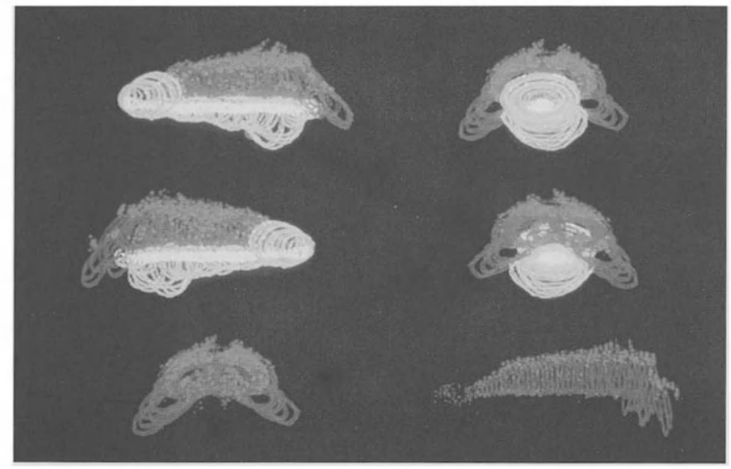
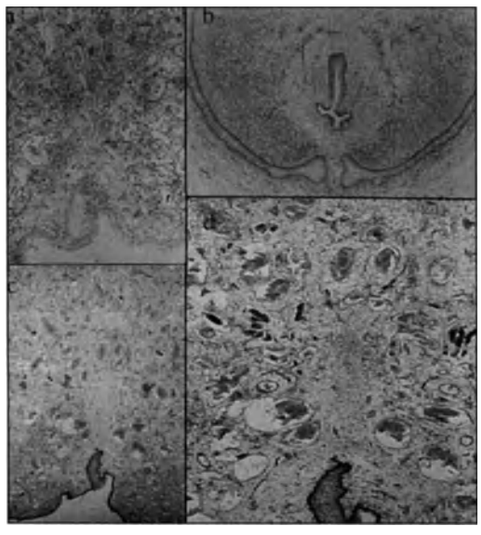


◗ **FIGURE 6-3.** (*Continued*) **B,** On the proximal penis at the point where the corporal bodies split into two and continue in a lateral fashion inferior and adjacent to the pubic rami, the nerves localize to an imaginary triangular area at the 11 and 1 o'clock positions. At this point (**top left**), the nerves reach their farthest vertical distance from the corporal body (approximately one half the diameter of the corporal body) and continue (**top right** and **bottom**) in a gradually tighter formation at the 11 and 1 o'clock positions well away from the urethra. (*From* Baskin *et al.* [14]; with permission.)



◗ **FIGURE 6-4.** (***See Color Plate***) Three-dimensional computer reconstruction of a normal human fetal penis at 25 weeks of gestation. **Top left,** Side view. **Top right,** Front view. **Middle left,** Side view. **Middle right,** Back view. **Lower left,** Front view without the urethra. **Lower right,** Side view without the urethra. The nerves are represented in *red*. Note their absence in the 12 o'clock position and the extensive distribution around the corporal cavernosal bodies to the junction of the urethral spongiosum. The tunica is represented in *blue*; the urethral lumen in *yellow*; and the urethral spongiosum and prepuce in *green*. The three-dimensional reconstruction was created by serial sectioning of a human fetal penile specimen. Immunohistochemical staining was performed using S-100, a nonspecific neuronal marker, with reconstruction accomplished with Adobe PhotoShop image enhancement and the NIH Image program. (*From* Baskin *et al.* [14]; with permission.)

NEUROVASCULAR ANATOMY



◗ **FIGURE 6-5.** Anatomy of the hypospadiac and normal penis. The anatomy of the normal penis can be compared with that of the hypospadiac penis [14]. Except at the region of the abnormal urethral spongiosum and glans, hypospadiac and normal penises show no difference in neuronal innervation, in architecture of the corpora cavernosa and tunica albuginea, and in blood supply. The nerves in both normal and hypospadiac penises start as two well-defined bundles superior and slightly lateral to the urethra. As the two crural bodies converge into the corporal cavernosal bodies, the nerves diverge, spreading around the cavernosal bodies up to the junction with the urethral spongiosum, not limiting themselves to the 11 and 1 o'clock positions. The 12 o'clock position in the hypospadiac penis is spared of any neuronal structures, as in a normal penis. The most striking difference between the normal penis and the hypospadiac penis is that of vascularity. The hypospadiac penis has huge endothelium-lined vascular channels filled with erythrocytes. In contrast, the normal penis has well-defined, small capillaries around the urethra, fanning into the glans. The vascularity under the urethral plate is also quite extensive in the hypospadiac penis, and the nerve distribution in the abnormal glans is less extensive when compared with that in the normal penis. In this figure, note that the hypospadiac penis has huge endothelium-lined vascular channels filled with erythrocytes (**top left**) compared with the normal penis, which has well-defined small capillaries around the urethra and fanning into the glans (**top right**). The nerve distribution in the abnormal glans is also less extensive (**bottom left** and **bottom right**). (*From* Baskin *et al.* [14]; with permission.)

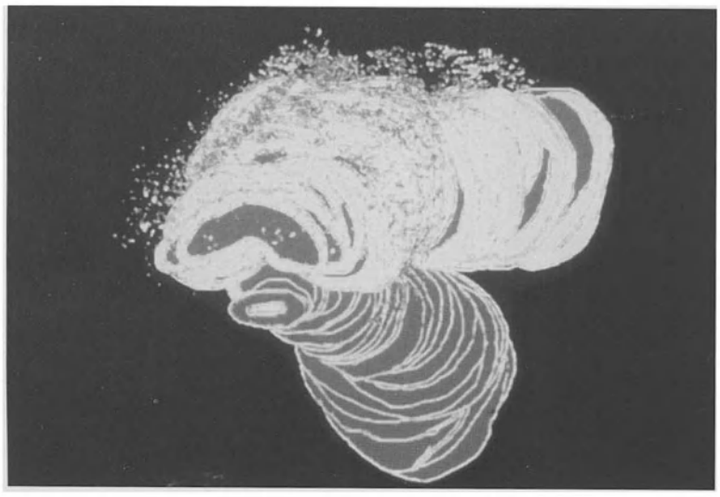


FIGURE 6-6. (*See Color Plate*) Three-dimensional computer reconstruction of hypospadiac penis at 33 weeks of gestation. Note the nerves in *light blue* and their absence at the 12 o'clock position, as in the normal penis. The tunica of the corporal bodies is represented in *yellow* and the urethral spongiosum in *green*. The hypospadiac penis has the same innervation and anatomy as the normal penis except for the abnormal urethral spongiosum.

TREATMENT

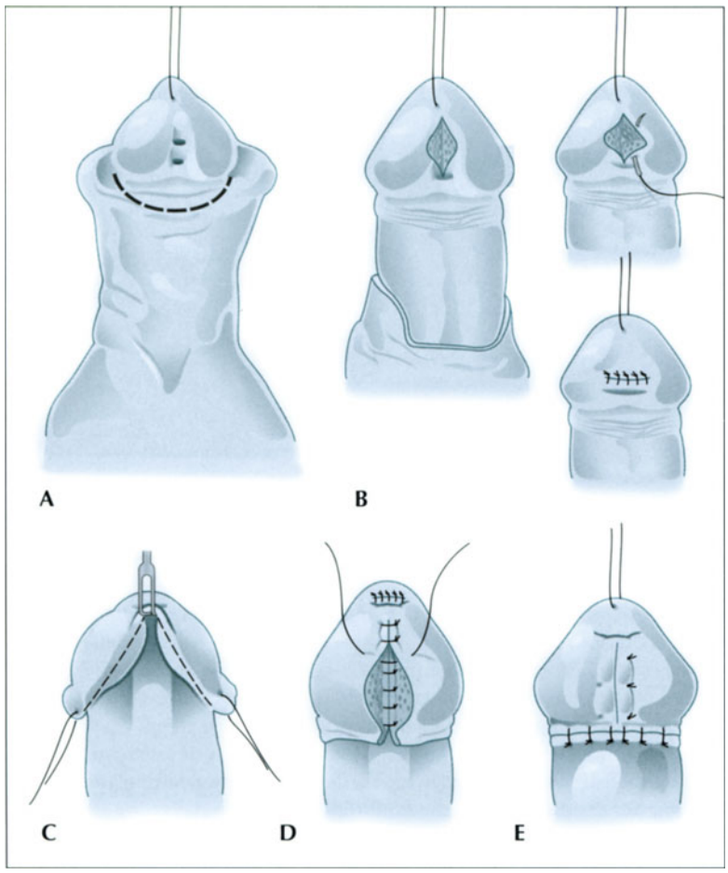


FIGURE 6-7. Meatal advancement glansplasty (MAGPI) hypospadias technique. The MAGPI technique was devised by Duckett [2] in 1981. This technique will provide outstanding results if patient selection is appropriate. The hypospadiac penis that is amenable to the MAGPI is characterized by a dorsal web of tissue within the glans that deflects the urine from either a coronal or a slightly subcoronal meatus. Once the patient is anesthetized, the urethra itself must be shown to have a normal ventral wall, without any thin or atretic urethral spongiosum. The urethra also must be mobile so that it can be advanced into the glans.

A, The initial maneuver of the circumferential subcoronal incision. **B,** The Heineke-Mikulicz closure of the dorsal meatus after excision of the dorsal web skin bridge. **C,** The most critical step, which is exposure of the glans mesenchyme by trimming excess skin, illustrated by the *dashed lines* in the figure, and advancing the mobile urethra with the use of a 6-0 chromic suture or, as shown here, a skin hook. **D,** A two-layer closure of the glans mesenchyme over the advanced urethra, allowing for a normal-appearing glans with excellent support of the urethra. **E,** Skin closure with a sleeve approximation of the penile shaft skin. When a ventral skin deficiency is present, a Byers flap skin rearrangement with a standard midline seam is appropriate.

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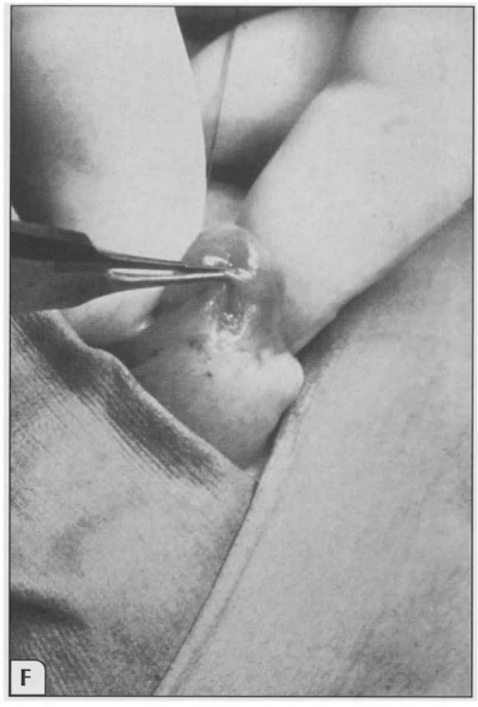
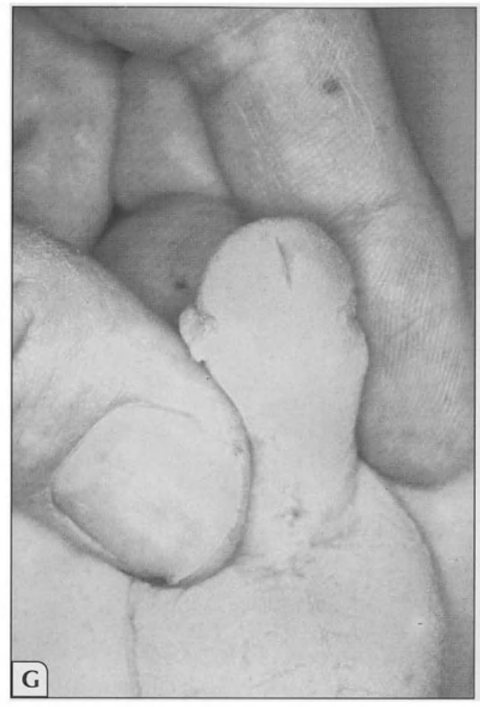
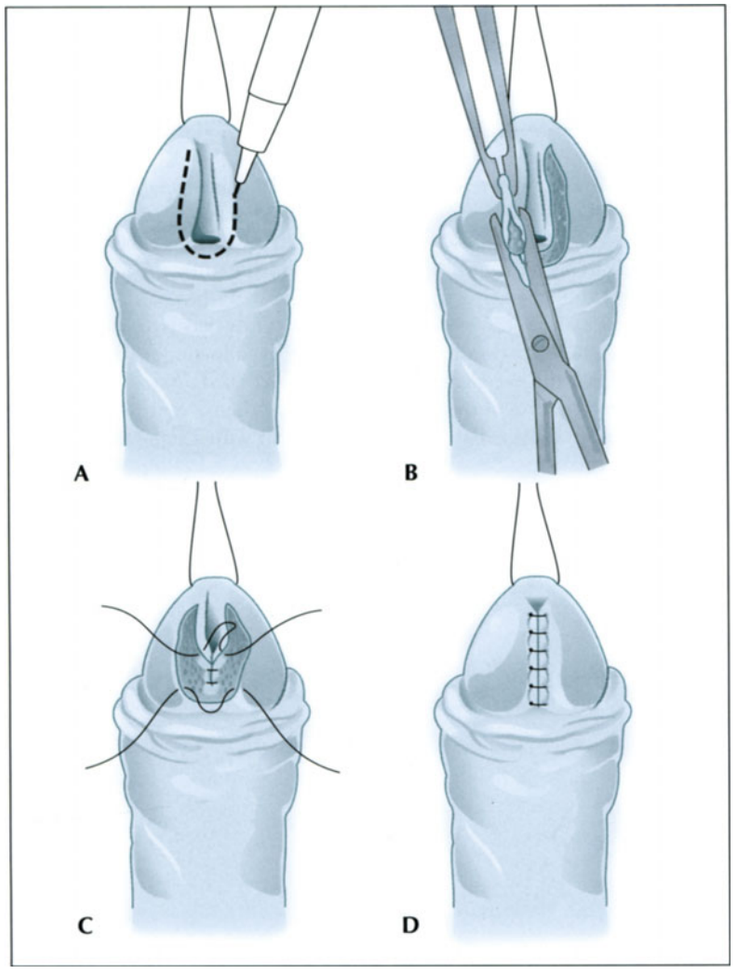


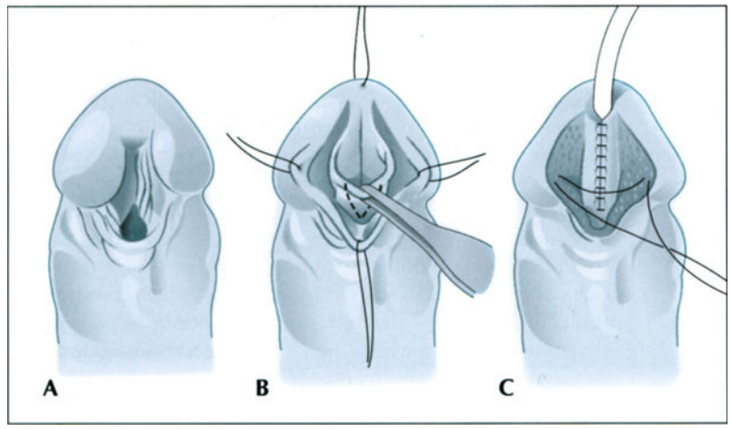


◗ **FIGURE 6-7.** (*Continued*)
F, Preoperative view of anterior hypospadias amenable to the MAGPI procedure. Note the dorsal web of tissue in the forceps. **G,** Postoperative result of the MAGPI procedure. (*Parts A through E adapted from* Hinman [15].)

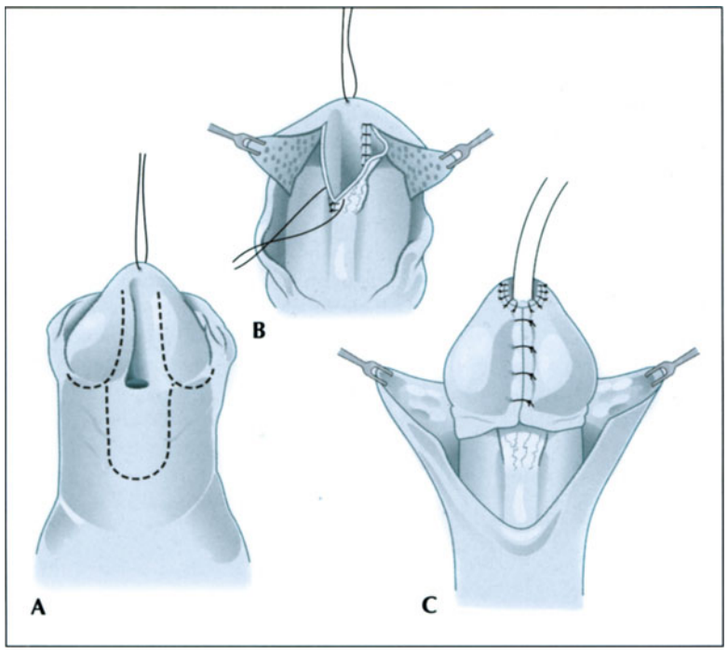


◗ **FIGURE 6-8.** Glans approximation procedure (GAP) hypospadias technique. The GAP is applicable in a small subset of patients with anterior hypospadias who have a wide and deep glandular groove [3]. These patients do not have a bridge of glandular tissue that typically deflects the urinary stream, as seen in patients who would be more appropriately treated with the meatal advancement glansplasty procedure. In the GAP, the wide-mouth urethra is tubularized primarily over a stent.

A, The initial incision. **B,** The exposure of the glans mesenchyme by deep epithelialization of tissue, which is critical for a two-layer glans closure, allowing for good support of the urethroplasty. **C,** Tubularization of the neourethra followed by glans closure. **D,** The completed repair. **E,** Anterior hypospadias with a patulous fish-mouth urethra amenable to the GAP.

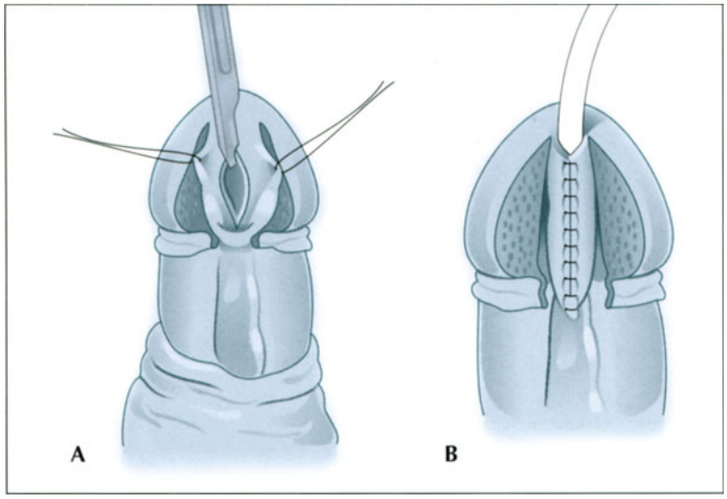


◗ **FIGURE 6-9.** Pyramid procedure for repair of megameatus hypospadias. Another small subset of patients present with a unique form of anterior hypospadias in which the foreskin is intact and a megameatus exists under the normal foreskin [16]. Patients with a megameatus have a very wide glandular defect and no penile curvature (**A**). Calibration reveals that the meatus is 22- to 24-F in a newborn baby versus the normal caliber of 12 to 14 F. Often this anomaly is recognized only after circumcision. Correction, however, is the same as if the foreskin is intact in that the technique involves careful periurethral dissection (**B**), exposing the urethra as well as glans tissue, and then removing a wedge of the abnormally enlarged urethra and closing the exposed glans tissue over the newly closed neourethra (**C**). Technically, the nuance of this procedure involves careful dissection down the shaft and distal penis by way of a four-quadrant exposure; hence the name "pyramid technique." Tapering the urethra and burying it into the glans is similar to the technique used for epispadias. **D**, Anterior hypospadias noticed after circumcision. Note the huge-caliber urethra classic for the megameatus and amenable to the pyramid procedure. (***Parts A to C adapted from*** Duckett and Baskin [9]; ***part D from*** Duckett and Baskin [9]; with permission.)

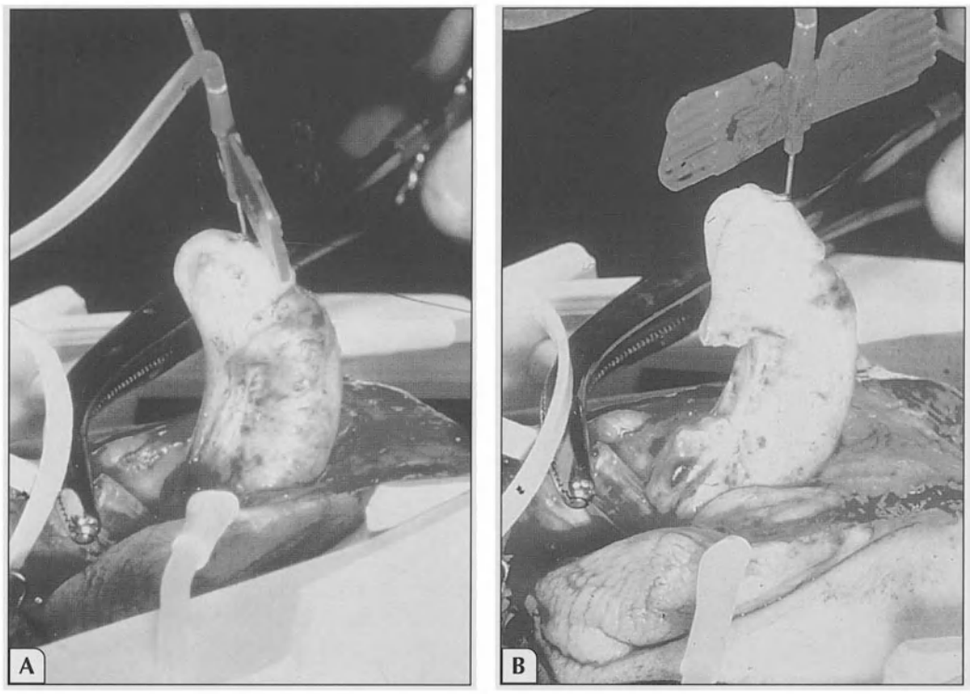


◗ **FIGURE 6-10.** Mathieu hypospadias technique. When the meatus is too proximal on the shaft to use a meatal advancement glansplasty procedure, or there is not a deep glandular groove appropriate for a glans approximation procedure or in situ tubularization technique (see next section), the meatus is advanced onto the glans using the procedure described in 1932 by the French surgeon Mathieu [5]. This technique involves the use of a randomly based perimeatal skin flap, created in accordance with the intrinsic blood supply. To ensure viability, the length-to-width ratio of the skin flap should not exceed 2:1. The flap has also been used essentially as a free skin graft, with no attempt made to preserve any of the subcutaneous tissue, but a pedicle of foreskin is brought around as in a vascularized flap technique and is used as a recipient bed [17]. In designing the Mathieu repair, the ventral skin needs to be outlined so that it can be advanced to its new location on the glans. Newer modifications of the Mathieu procedure have involved a second layer as a subcutaneous pedicle.

A, Distal hypospadias with schematic outline prepared for Mathieu flap. **B**, Mobilization of glans wings and urethroplasty. **C**, Completion of urethroplasty, glansplasty closure, and preparation for skin closure. Note that because the ventral skin is sacrificed for the urethra, a Byers flap skin rearrangement technique with a midline suture will be necessary. (*Adapted from* Hinman [15].)



◗ **FIGURE 6-11.** Tubularized incised plate urethroplasty. Historically, if the urethral groove was not wide enough for tubularization in situ, as in the glans approximation procedure or Thiersch-Duplay procedure [18,19], then an alternative approach such as the Mathieu procedure or, for more severe hypospadias, a vascularized pedicle flap procedure was performed. A more recent concept of incision in the urethral plate with subsequent tubularization and secondary healing was introduced by Snodgrass [4]. Short-term results have been excellent, and this procedure has extensive popularity [20]. One appealing aspect is the slitlike meatus that is created with the dorsal midline incision. More recently, this technique has been applied to posterior forms of hypospadias. Theoretically, there is a possibility of meatal stenosis from scarring as occurs in patients with urethral stricture disease, in whom direct-vision internal urethrotomy often leads to recurrent stricture. In hypospadias, the native virgin tissue with excellent blood supply and large vascular sinuses [14] appears to respond to primary incision and secondary healing without scar.
A, The deep incision in the urethral plate down to corporal tissue.
B, Tubularization of the neourethra, with subsequent glansplasty.



◗ **FIGURE 6-12.** Urethral plate and penile curvature. Duckett has popularized the concept of preserving the urethral plate, which is now standard practice for posterior as well as more severe anterior hypospadias surgery [21,22]. The urethral plate serves as the dorsal urethral wall, and the ventral urethra is created by a vascular onlay flap of tissue from the inner prepuce. Extensive experience has shown that the urethral plate is rarely the cause of penile curvature. This knowledge was obtained by repetitive resection of the urethral plate with subsequent repeat artificial erections showing no gain in correction of penile curvature [23]. Further efforts and experience showed that the urethral plate appeared to be supple and that ancillary penile-strengthening procedures with preservation of the urethral plate led to decreased complications, such as fistula and stenosis at the proximal anastomosis [21]. The concept of preserving the urethral plate, yet undermining the plate, exposing the corporal bodies with the idea that chordee tissue could be released, has not held true. In fact, careful anatomic studies have shown an extensive network of blood vessels supplying the urethral plate in the hypospadiac penis, and lifting of the urethral plate defeats the purpose of preservation by destroying this intricate blood supply [12,14]. The technique of mobilizing the urethral plate should be abandoned. Historically, posterior hypospadias was approached by complete resection of the abnormal urethra and all tissue down to normal corporal bodies. The urethra was replaced by a tubularized vascular preputial flap, from either the inner prepuce or the outer prepuce [24,25]. Currently, in the majority of cases of posterior hypospadias, including perineal hypospadias, the urethral plate can be preserved and a vascularized flap used in an onlay fashion. In the rare situation in which the urethra is so abnormal that it should be discarded, the tubularized flap can bridge a long gap or a two-stage technique can be employed [26].

A, Penile curvature with preservation of the urethral plate. **B,** Resection of the urethral plate with continued severe curvature.

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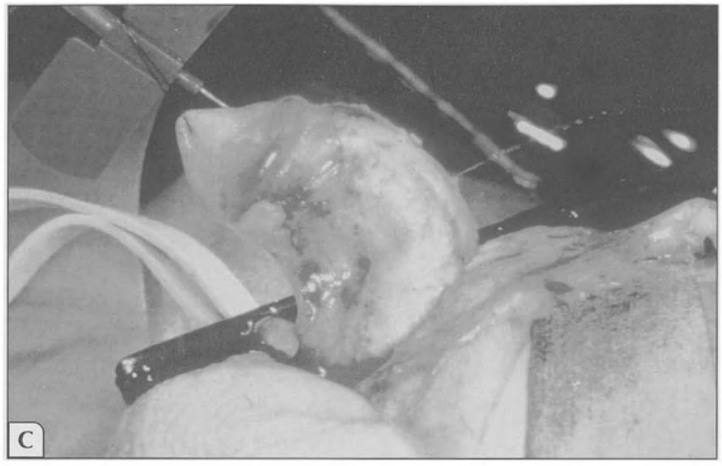
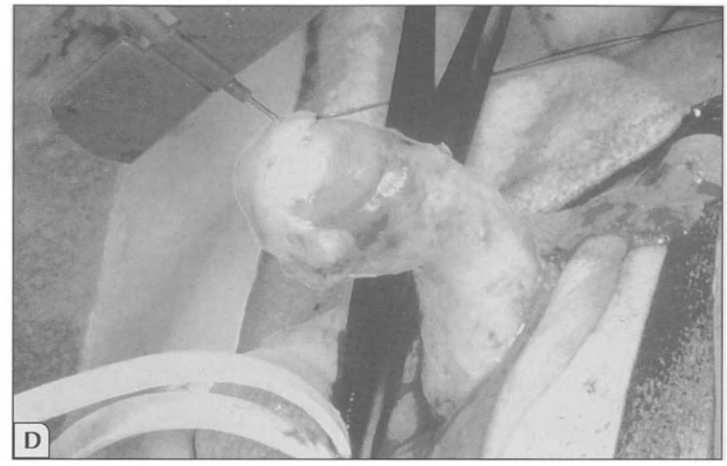
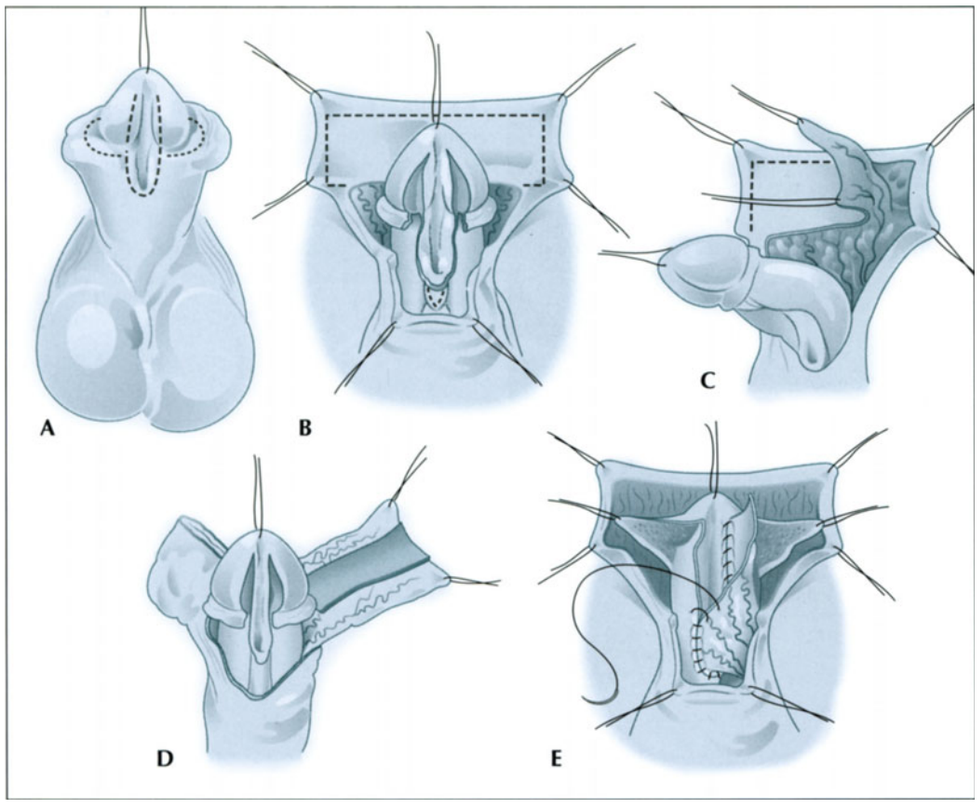




◗ **FIGURE 6-12.** (*Continued*) **C,** Penile curvature with preservation of the urethral plate. **D,** Resection of the urethral plate with continued severe curvature. Extensive experience as illustrated by these examples has shown that the urethral plate is rarely the cause of penile curvature. This knowledge was obtained by repetitive resection of the urethral plate with subsequent repeat artificial erections showing no gain in correction of penile curvature despite extensive "chordee" resection.



◗ **FIGURE 6-13.** Onlay island flap hypospadias repair. All cases of posterior hypospadias, including those with and without penile curvature, are approached initially by leaving the urethral plate intact. The onlay island flap repair can be applied to penile shaft as well as scrotal and perineal hypospadias. The intact dorsal plate essentially avoids complications of proximal stricture, and the excellent blood supply has decreased the fistula rate to approximately 5% to 10% for all cases of onlay island flap hypospadias repair [21]. For shorter repairs, the flap may be dissected from one half of the prepuce, as described by Rushton and Belman [27], leaving the remaining half of the foreskin available for a second layer of coverage. Long-term results with the onlay island flap have been highly durable [6,9,21,22]. For very severe hypospadias, the prepuce can be designed in a horseshoe style to bridge extensive gaps (see parts **H** and **I**) [22].
A, A U-shaped incision is made around the urethral plate, preserving a dorsal urethral strip approximately 8-mm wide. **B,** Take-down of the skin and subcutaneous tissue, as well as outlining of the inner prepuce for the onlay island flap. The glans wings are mobilized along the plane of the corporal body and the glans mesenchyme. **C,** Preservation of the urethral plate with penile curvature in a case of penoscrotal hypospadias. **D,** The split prepuce in situ technique for dissection of a short vascularized onlay island flap. This method is useful for shorter onlays, leaving the remaining half of the foreskin available for a second layer of coverage. **E,** Suturing of the onlay flap with running 7-0 suture to the urethral plate. The flap is trimmed to obtain a 12-F caliber bougie in a child of 1 year of age, to prevent the complication of urethral diverticulum, which results from leaving excess tissue. The glans wings are approximated over the new urethra after maturing the meatus, and then the skin is closed by a classic Byers flap skin rearrangement.

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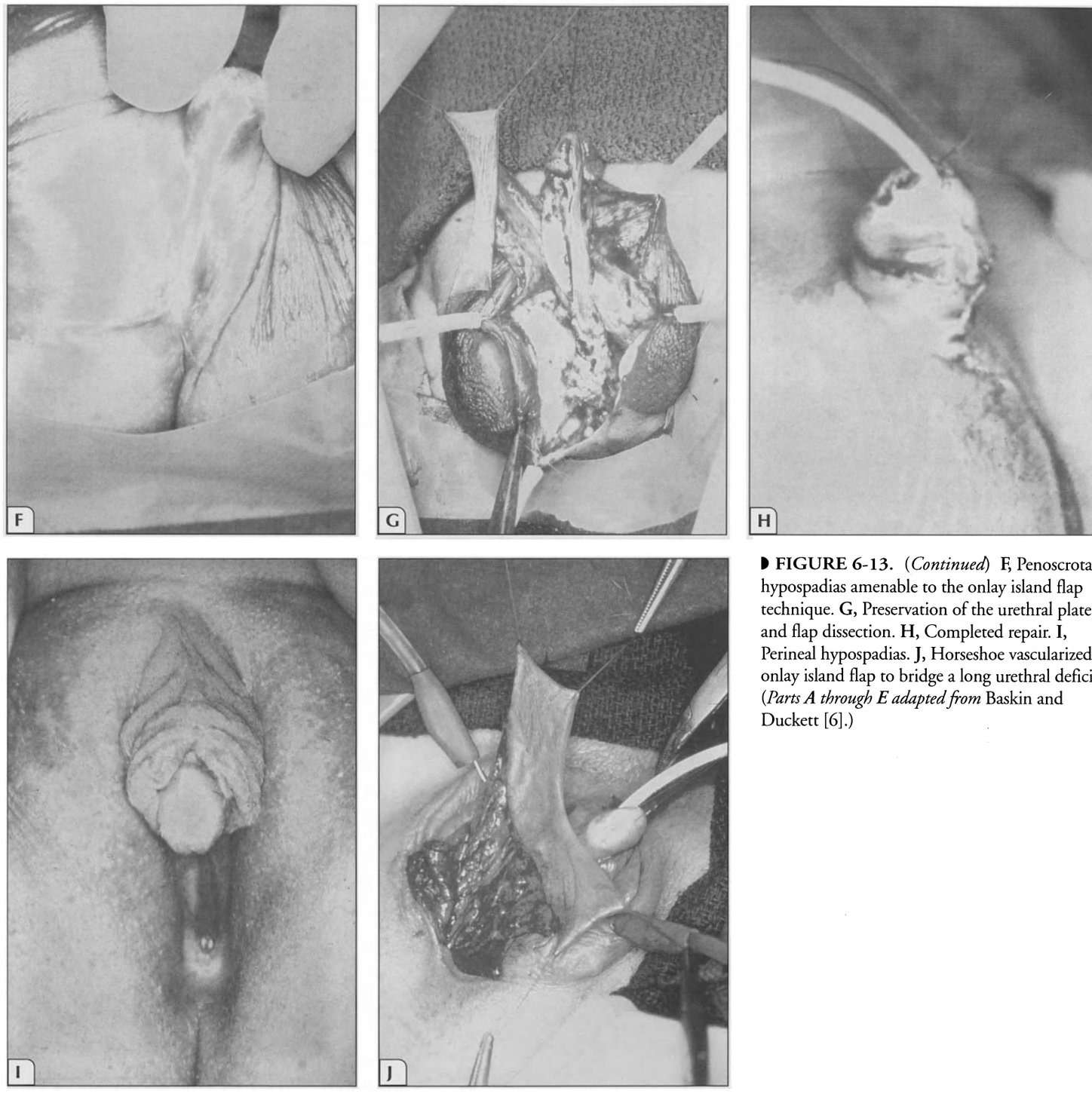
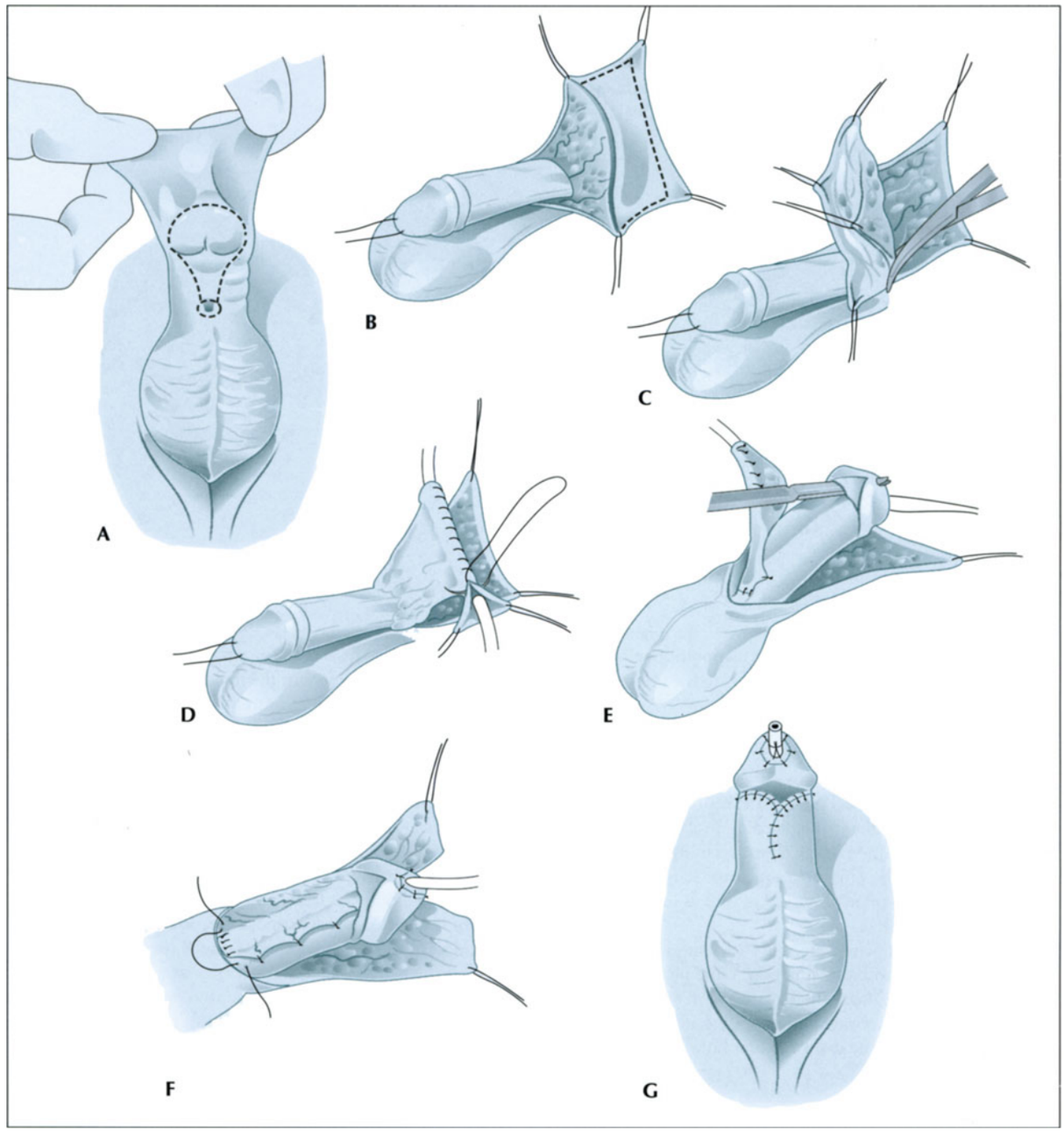
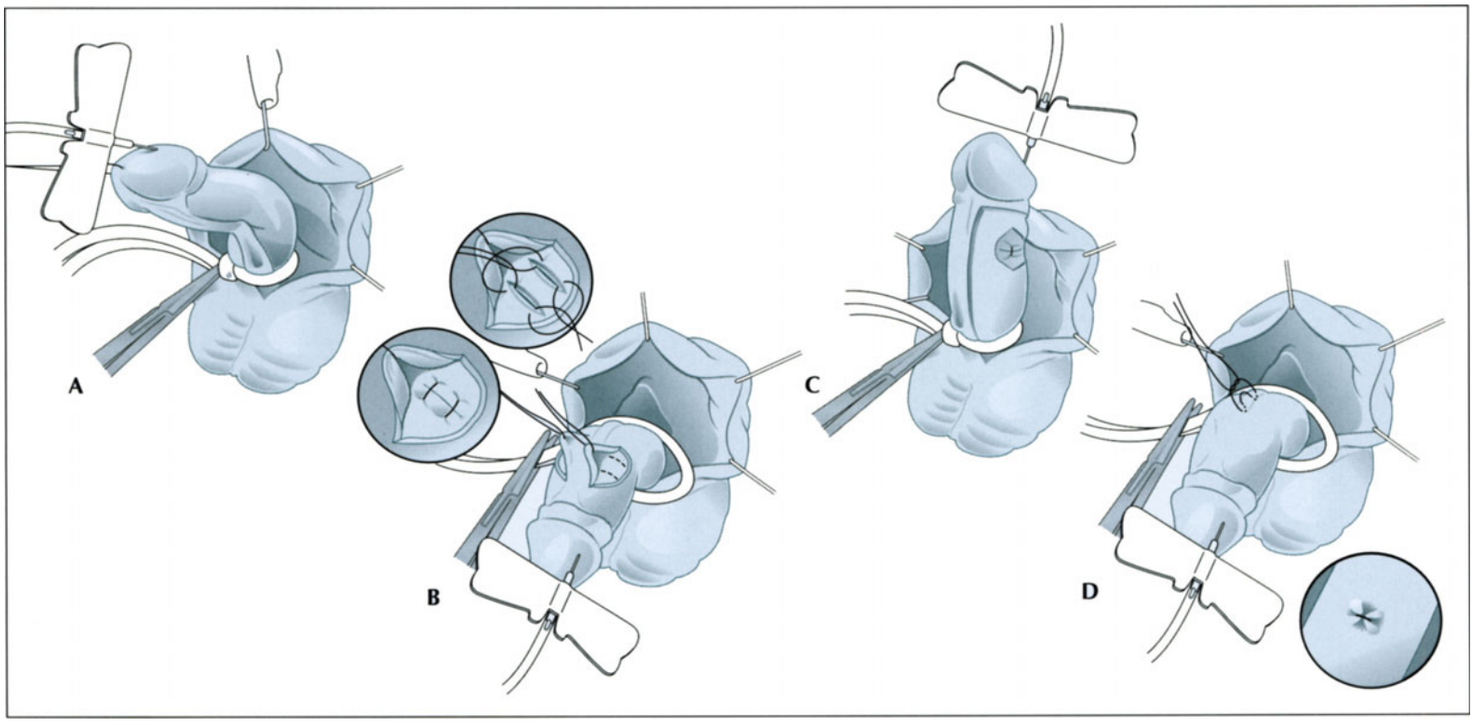


FIGURE 6-13. (*Continued*) **F,** Penoscrotal hypospadias amenable to the onlay island flap technique. **G,** Preservation of the urethral plate and flap dissection. **H,** Completed repair. **I,** Perineal hypospadias. **J,** Horseshoe vascularized onlay island flap to bridge a long urethral deficit. (*Parts **A** through **E** adapted from* Baskin and Duckett [6].)



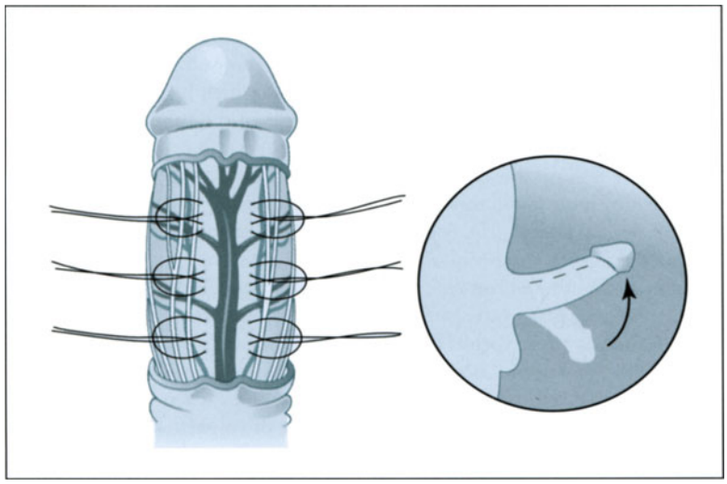
◗ **FIGURE 6-14.** Transverse preputial island flap with glans channel hypospadias repair. The transverse tubularized island flap technique was extensively used prior to the concept of preserving the urethral plate. It is still successful for severe cases when the urethral plate needs to be resected. Technical nuances involve an oblique proximal anastomosis with interrupted sutures to avoid stenosis, fixation of the neourethra to the corporal bodies to prevent diverticulum and improve ease of catheterization, and a wide glans channel made under the glans cap against the corporal bodies to avoid meatal stenosis.

A, Release of penile curvature by surgical release of the skin and dartos fascia and ancillary straightening procedures as needed. **B,** The transverse island flap is designed. **C,** Development of the island flap by dissecting subcutaneous tissue from dorsal penile skin. **D,** The transverse preputial island flap is developed and tubularized to 12 F, which is monitored by a bougie à boule. The distal edges of the tube are sewn with interrupted sutures so that the edges can be trimmed to fashion the appropriate length. **E,** Rotation to the ventrum must avoid torsion of the shaft by freeing the base of the flap adequately. A proximal oblique anastomosis is made, fixing the urethroplasty to the tunica albuginea along its posterior anastomosis. A wide glans channel is made under the glans cap against the corporal bodies by removing glans tissue within the channel. **F,** The neourethra is tacked to the corporal bodies. **G,** Lateral transposition of Byers' flaps of dorsal penile skin to the midline and excision of the tips. A 6-F catheter is used as a stent for the repair. (*Adapted from* Hinman [15].)



◗ **FIGURE 6-15.** Tunica albuginea plication. Correction of penile curvature has also evolved along with the concept of preserving the urethral plate. Artificial erection, introduced by Gittes and McLaughlin in 1974, has provided the mechanism by which to check for penile curvature and for the immediate success of correction at the time of surgery. The standard technique is to take all skin and subcutaneous tissue down to the penile scrotal junction, with preservation of the urethral plate. At this time artificial erection will determine the need for ancillary straightening procedures. If after these maneuvers the penis remains curved, the classic technique of tunica albuginea plication can be used [28]. This technique can be applied in patients who have had the urethral plate preserved as well as in those who have had it resected.

A, Penoscrotal hypospadias with penile curvature after surgical release of the skin and dartos fascia to the penoscrotal junction. Note preservation of the urethral plate. **B,** With the penis erect, Buck's fascia is elevated at the point of maximum curvature on either side of the midline at the 10 and 2 o'clock positions to avoid damage to the neurovascular bundle. Parallel incisions 4 to 6 mm apart and about 8 mm long are made through the tunica albuginea. The outer edges of the incisions are approximated with permanent sutures (5-0 polypropylene sutures in infants) in a way that buries the knot. **C,** The straightness of the penis is confirmed by repeat intraoperative artificial erections. **D,** Midline dorsal plication technique for penile curvature. Based on more recent anatomic studies, we now advocate the midline dorsal plication. This procedure is performed by dissecting the skin and subcutaneous tissue aggressively to the penile scrotal junction to release any tethering tissue responsible for curvature. Two 5-0 polypropylene sutures are placed at the point of maximum curvature. The sutures are placed directly in the midline through Buck's fascia and 1 to 2 mm into the corporal tissue so that the knot is buried. Repeat artificial erection confirms resolution of the curvature and in more severe cases, two parallel rows of plication sutures may be placed. If the penis remains curved after two rows of plication sutures, select an alternative approach, such as a ventral graft of dermis or synthetic material. After placing the sutures, loosely approximate Buck's fascia over the repair for additional coverage. (*Adapted from* Baskin and Duckett [28].)



◗ **FIGURE 6-16.** Multiple parallel suture plication technique at the 12 o'clock position for the correction of ventral penile curvature. This technique has the theoretic advantage of not injuring any nerves or vessels.

Although this technique has stood the test of time, recent anatomic studies question the concept of disturbing the tunica at the 10 and 2 o'clock positions because of possible damage to the nerves [12,14]. A newer technique that involves plication sutures at the 12 o'clock position is now advocated, although long-term results in children are lacking. In this technique, parallel plication sutures are placed in the tunica albuginea in the 12 o'clock position, which is free of both nerves and vascular structures. This technique causes a minimum amount of manipulation to the penis. If the curvature is severe, rows of parallel plications at the 12 o'clock position can be placed. I question the routine use of dermal grafts as well as tunica vaginalis patches because of the inherent damage caused to the neurovascular bundle and the aesthetic problem of violating the corporal bodies at an early age when growth potential and long-term complications are unknown. Ventral dermal grafting or the use of synthetic material is reserved for the most severe cases, typically in conjunction with a two-stage approach.

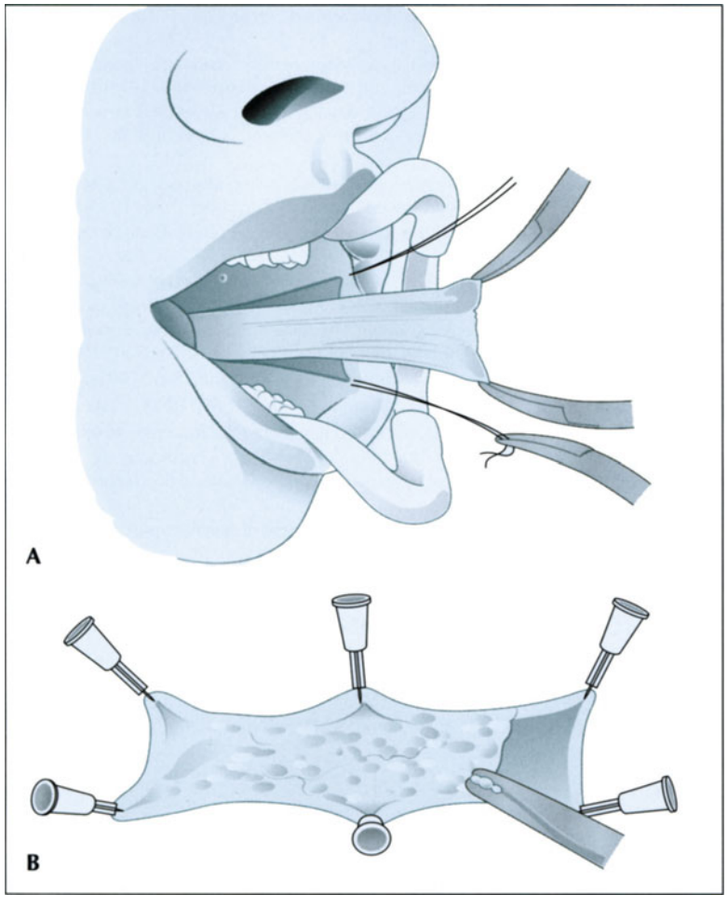


FIGURE 6-17.
Harvesting buccal mucosa for complicated hypospadias. For patients who have had multiple previous procedures, often the best option is to discard the abnormal urethra and replace the tissue with a vascularized pedicle graft, if skin is available, or in rare cases, a free graft. Buccal mucosa has enjoyed impressive success and is now the free graft material of choice when adjacent well-vascularized skin is not available [29]. From a graft biology viewpoint, buccal mucosa is an ideal graft material in comparison with both skin and bladder mucosal grafts. The epithelial layer of a buccal graft is four times thicker, and the relatively thin lamina propria allows efficient transfer of nutrients by diffusion (imbibition) from the recipient site to the new graft. The extensive vascularity in the lamina propria also allows new capillaries to grow into the graft (inosculation). At first, buccal mucosa was used in a tubular form as a complete urethral replacement. At present, however, the best results have been obtained with preservation of the urethral plate, using the buccal mucosa in an onlay fashion [29].

A, Harvesting of the buccal mucosa graft. The graft may be harvested from the inner cheek, with care taken to avoid Stensen's duct. The muscle of the inner cheek should be left in situ. **B,** Once the graft is harvested, the fat is removed. Then the graft can be sewn in place in either onlay or tube fashion. Buccal mucosa may also be harvested from the inner lip, and in extensive cases, grafts can be taken from both sides of the mouth. (*Adapted from* Baskin [30].)

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7

Exstrophy and Epispadias

Michael E. Mitchell and Michael C. Carr

Bladder exstrophy represents a deformation of the bladder, urethra, external genitalia, and pelvis with anterior displacement of these structures. This condition was believed to result from abnormal development of the cloacal membrane. We believe that the pathophysiology can best be explained by ventral herniation of these structures. The timing of this herniation then leads to the spectrum of deformations seen, which include cloacal exstrophy, classic exstrophy, and epispadias. In its most severe form, cloacal exstrophy represents an anterior herniation before the formation of the urorectal septum so that bladder halves are separated by an intestinal plate. This occurs before 7 weeks' gestation. Later herniation results in classic bladder exstrophy or epispadias.

Contemporary management of classic exstrophy has involved a number of stage procedures, with the goals of surgery being 1) preservation of renal function, 2) restoration of normal bladder function, 3) achievement of urinary incontinence, and 4) restoration of normal external genitalia.

Jeffs *et al.* [1] championed this approach and demonstrated that a large number of patients could maintain good renal function and achieve continence. The first stage involved closure of the abdominal wall, pelvis, and bladder, with bilateral pelvic osteotomies being performed to facilitate closure. It has also been demonstrated that this type of closure could be performed without iliac osteotomies on newborns because of the presence of maternal relaxin. No attempt was made to correct vesicoureteral reflux, the continence mechanism, or epispadias in male patients. Female patients, though, had complete closure of the bladder and urethra and restoration of the clitoris. The males were incontinent, but their kidneys were protected because of the low-pressure egress of urine. The second operative stage consisted of bladder neck reconstruction and ureteroneocystostomies using a crossed-trigonal technique [2,3]. This required the bladder to grow and develop in the interim, with a volume greater than 60 mL being necessary before attempting bladder neck reconstruction. The third stage involved the epispadias repair as favored by the Cantwell-Ransley technique. Modifications of the staged reconstruction were made as greater experience was obtained. Thus, epispadias repair was subsequently performed as the second stage when the patient was 3 to 5 years old. The idea was to further increase urethral resistance to promote the bladder's growth.

The planned multiple stage anatomic closure yielded a continence rate of 60% to 92% with an average of 73% [4]. This approach also led to fewer complications to the kidneys, such as renal scarring or persistent elevation of serum creatinine. Several surgeries were necessary in the

patient's first 5 to 7 years of life in order to accomplish these goals in the best of hands, with some patients suffering bladder dehiscence that required reclosure of the bladder along with iliac osteotomies. Failed reconstruction of the bladder neck by the Young-Dees-Leadbetter technique necessitated revisions or bladder augmentation (or both) or techniques that would improve continence, but this reconstruction came at the expense of allowing volitional voiding (Kropp procedure) [5]. Multiple failures would lead to complete abandonment of the bladder, necessitating continent diversion.

Several recent developments have allowed us to reassess the notion of stage reconstruction. The first is a new technique for epispadias repair that involves complete disassembly of the phallic component parts into the urethral plate and the right and left hemicorporal glandular bodies [6]. This penile disassembly facilitates tubularization and ventralization of the entire urethra, as the corporal bodies are rotated and positioned anteriorly. When combined with exstrophy closure, urethral continuity is maintained and correct positioning of the bladder neck and proximal urethra occurs posteriorly.

The second area involves a better understanding of bladder growth and development. The exstrophic bladder is a defunctionalized bladder that has no ability to store urine. The growth and development of a newborn's bladder is mediated by its response to stretch. A bladder that does not cycle normally can only grow passively rather than achieve full potential because of the cycling process. An exstrophic bladder that has no continence after closure will grow only passively. The earlier the bladder is allowed to cycle normally, the greater the potential for it to grow and develop. That is why newborn female patients with exstrophy who underwent the closure procedure with the bladder neck and urethra moved to its correct posterior location tended to achieve successful continence and develop a normal bladder. The complete anatomic repair of a patient with exstrophy restores the anatomy and provides the greatest chance for normal bladder development, continence, and normal external genitalia.

PRIMARY ANATOMIC REPAIR: MALE

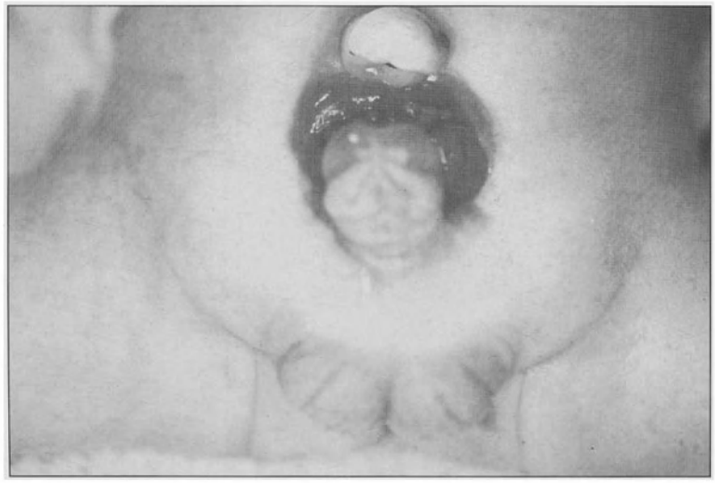
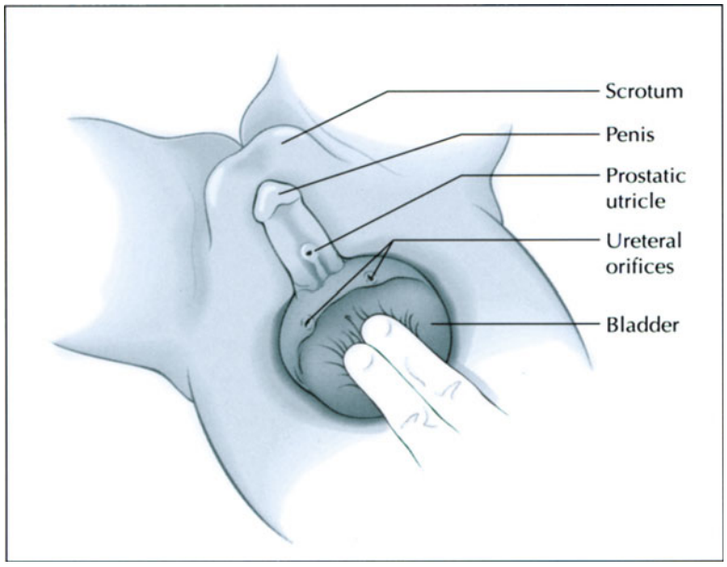
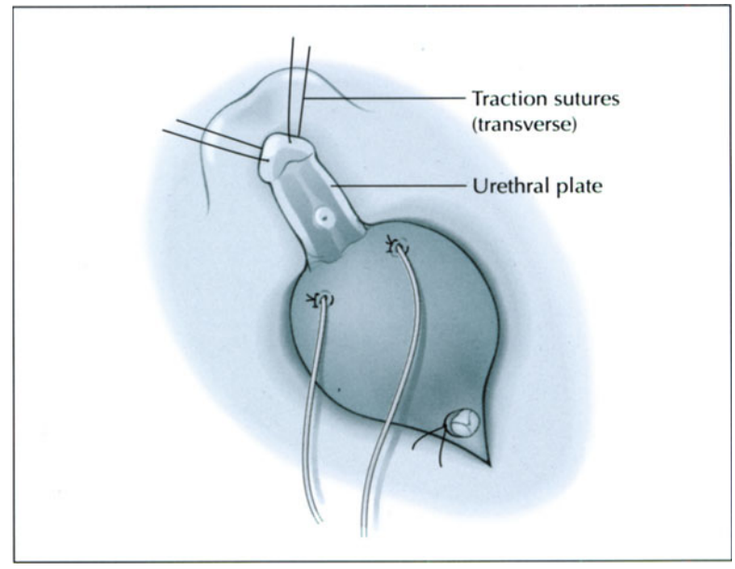


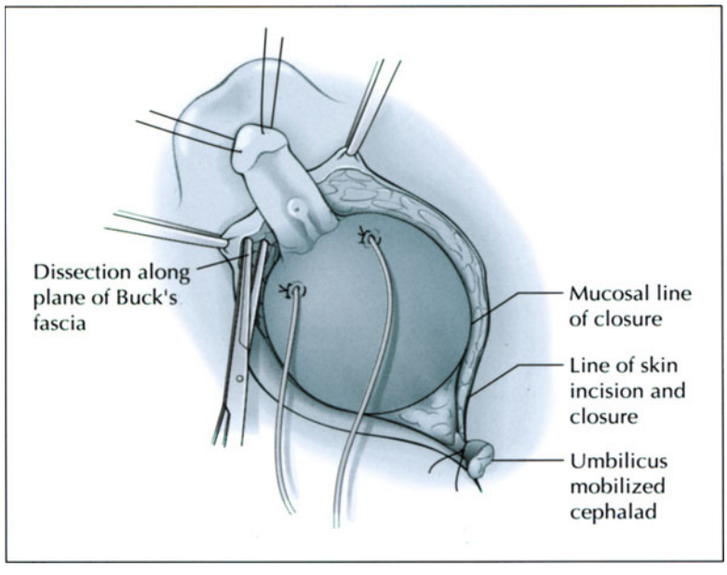
FIGURE 7-1. Newborn male with bladder exstrophy. Newborns who are discovered to have bladder exstrophy are often admitted to the neonatal intensive care unit. The majority have normal pulmonary and renal function. A screening renal ultrasound confirms the presence of two normal kidneys. After initial assessment, it is helpful to cover the exposed bladder mucosa with a nonadherent covering such as Vigilon (CR Bard, Inc., Covington, GA). Plans can then be made for bladder closure on the first day of life.



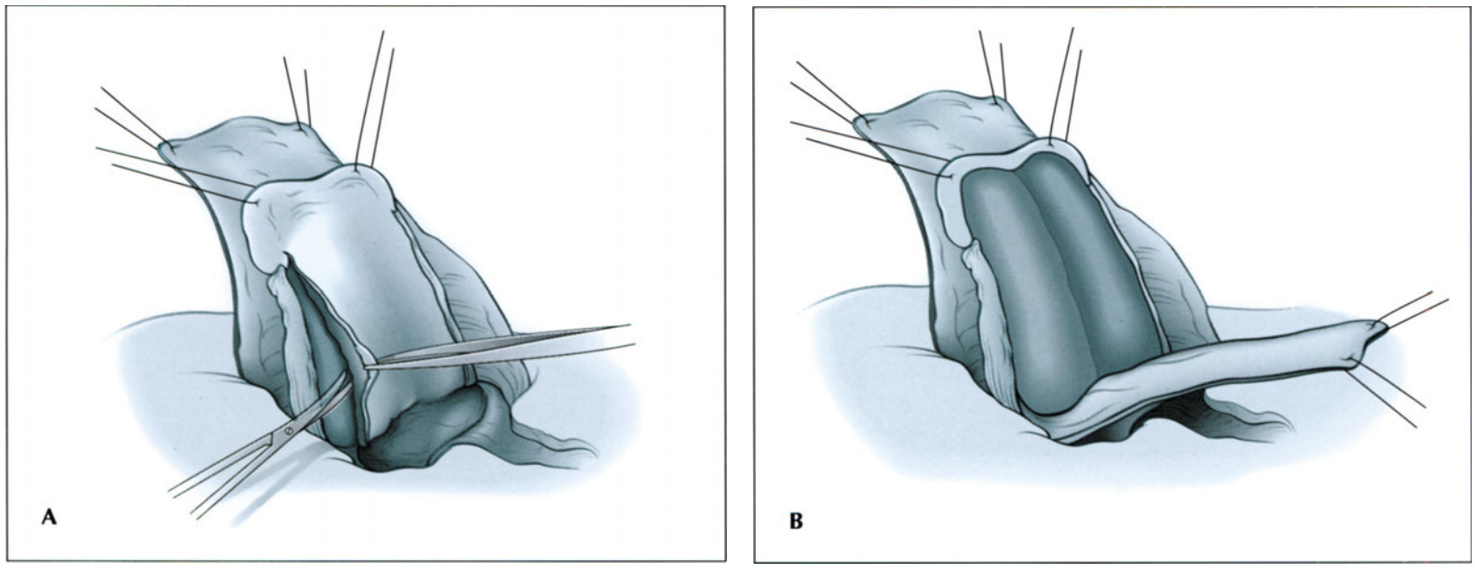
◗ **FIGURE 7-2.** The anatomy of bladder exstrophy. An anterior herniation of the entire bladder occurs. The bladder plate can be depressed into the pelvis to provide an assessment of bladder size. The prostatic utricle is identified just distal to the bladder neck region, and the urethral plate can be identified separate from the remainder of the penis. The glans is splayed out such that separate halves are seen. In addition, the "intersymphyseal ligament" (coalescence of pelvic diaphragm) is found beneath the bladder neck and prostatic urethra in male patients or the distal urethral plate and vagina in female patients. In order to successfully close the bladder, these structures need to be moved posteriorly. The "intersymphyseal ligament" beneath the bladder neck and prostatic urethra in male patients or the bladder neck in female patients must be incised. Furthermore, the complete penile disassembly used in epispadias repair facilitates this aggressive dissection at the prostatic urethra and bladder neck.



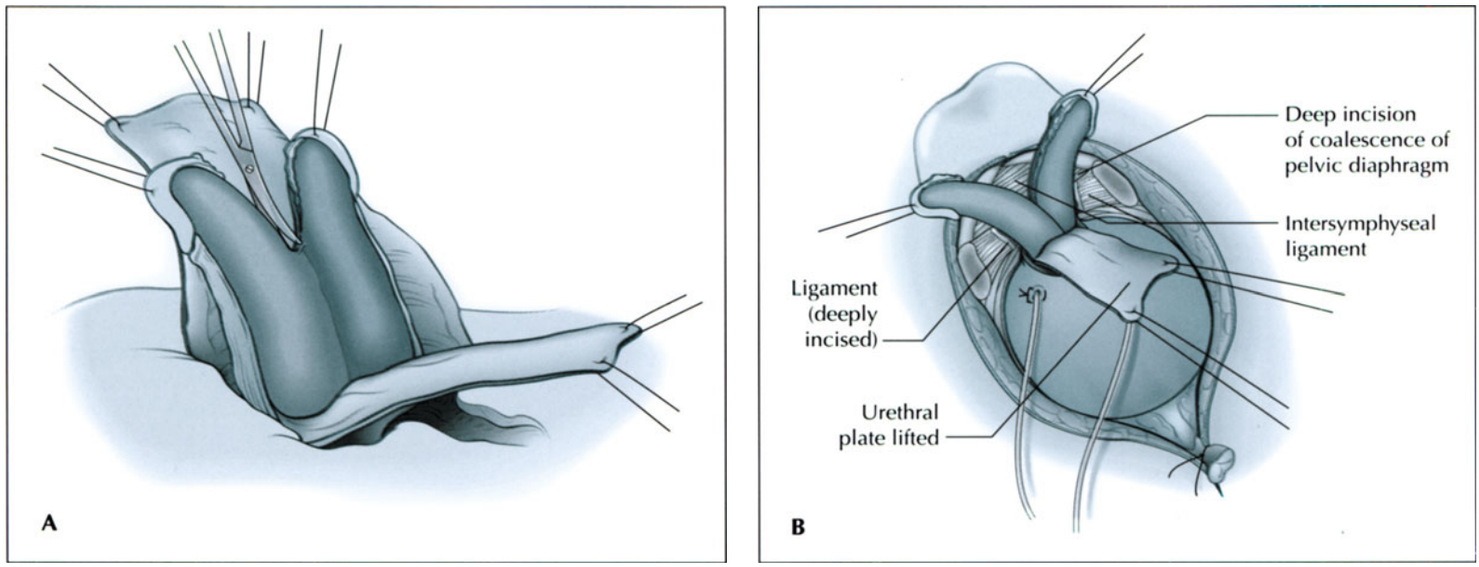
◗ **FIGURE 7-3.** Repair for a newborn male patient with exstrophy. A 2-0 silk suture is placed around the umbilical cord. Traction sutures of 5-0 monocryl are placed transversely through each glans half. The urethral plate is marked with marking pen to facilitate the dissection. Feeding tubes are placed into each of the ureteral orifices and sutured into place.



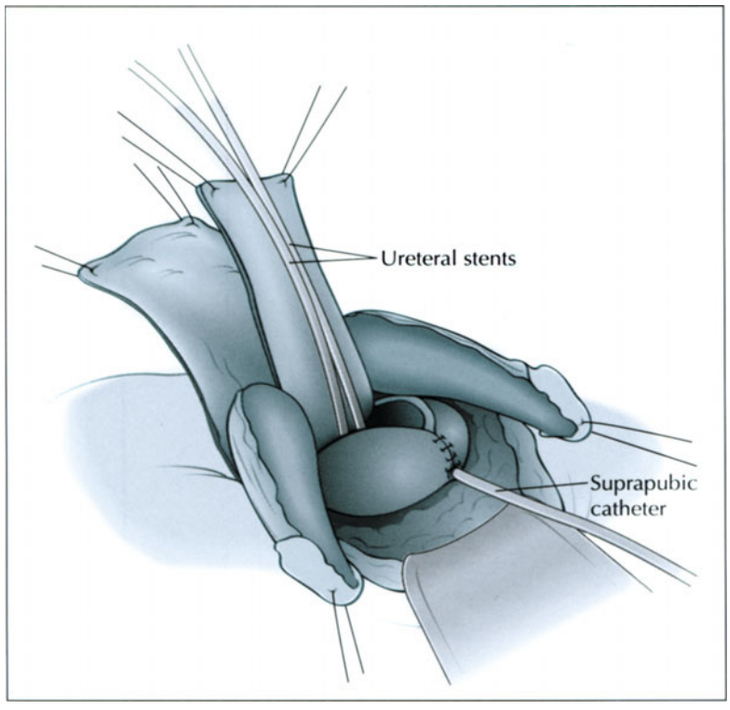
◗ **FIGURE 7-4.** Exstrophy repair continued. The urethral plate and bladder plate are circumscribed by using the Colorado-tip cautery. This gives very fine control for incising the tissue with limited thermal energy dispersion. The dissection is continued deeply until the peritoneum is identified. The umbilical cord structures are dissected and moved cephalad.



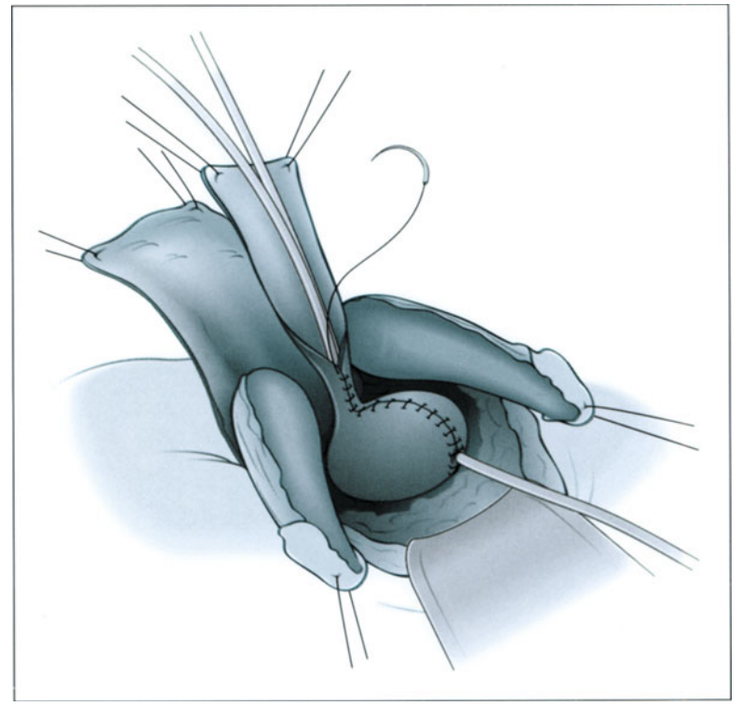
◗ **FIGURE 7-5.** Exstrophy repair continued. **A,** The dissection is then continued caudally by freeing the urethral plate from the underlying corpora cavernosa. This is facilitated by dissection on both the dorsal and ventral aspects of the corpora. A vessel loop can be brought around the urethral plate to aid in the dissection. In addition, traction sutures are placed on the shaft skin ventrally. **B,** The urethral plate shown completely dissected free from the underlying corpora.



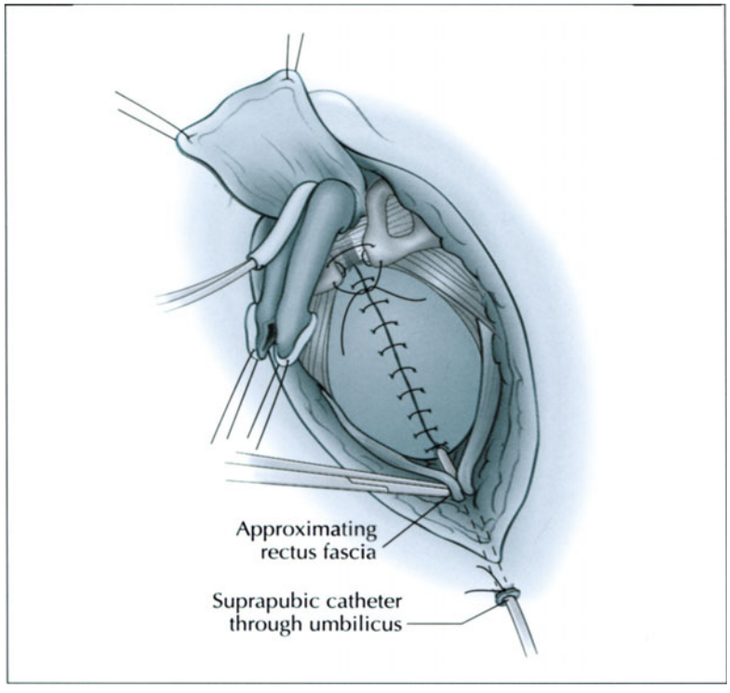
◗ **FIGURE 7-6.** Exstrophy repair continued. **A,** The critical dissection involves dissecting each of the corporal bodies proximally toward the prostatic urethra, where the corpus spongiosum is better developed. The corpora and two hemiglans are separated by dividing the midline. **B,** This facilitates the dissection of the prostatic urethra and division of the intersymphyseal ligament, which extends between the pubic bone. This intersymphyseal ligament actually extends beneath the prostatic urethra and must be divided. After aggressive dissection, the bladder neck and prostatic urethra are now moved posteriorly.



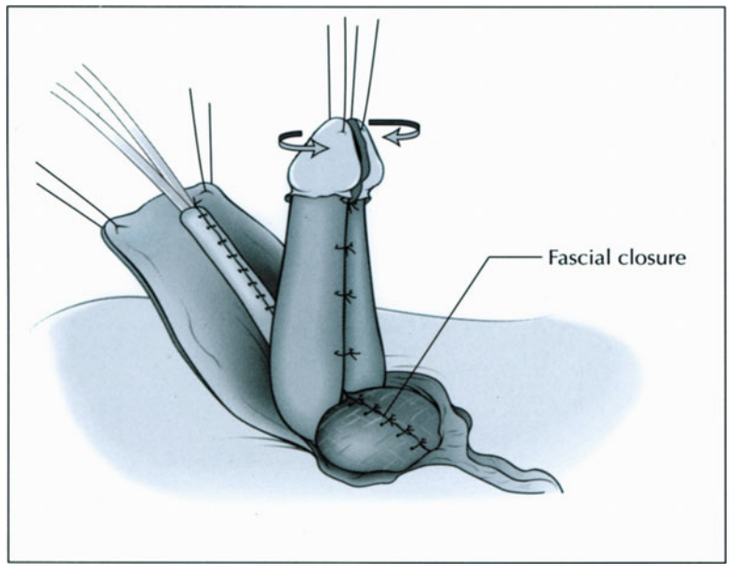
◗ **FIGURE 7-7.** Bladder closure. Bladder closure is accomplished in two layers with the mucosa and muscularis incorporated in the first layer using 7-0 Maxon (Sherwood-Davis and Geck, St. Louis, MO) suture. A second layer of running 6-0 PDS (Sherwood-Davis and Geck, St. Louis, MO) suture is used beginning at the dome and ending at the bladder neck. An 8-F or 10-F Malecott catheter is placed in the dome of the bladder after it is brought through the skin and the anterior abdominal wall. This will heal as the umbilicus. A chromic pursestring suture is placed around the catheter on the outside of the bladder wall.



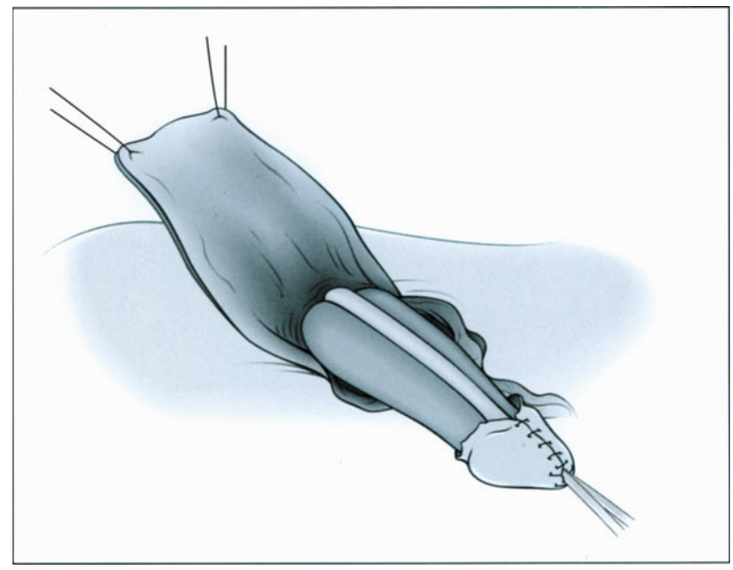
◗ **FIGURE 7-8.** Tubularizing the urethral plate. The urethral plate is tubularized by using a running 7-0 Maxon suture. The feeding tubes exit through the neourethra. A second layer of 6-0 PDS completes the closure of the urethra. Interrupted 5-0 PDS sutures are placed at the bladder neck complex to provide further support.



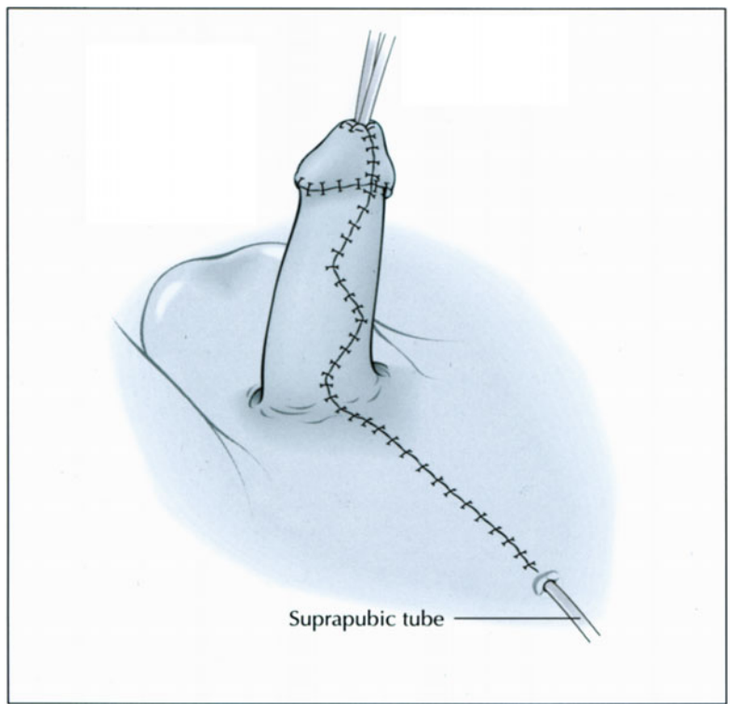
◗ **FIGURE 7-9.** The neourethra is brought below the corpora as the bladder neck and prostatic urethra have been moved posteriorly. The rectus fascia is identified and dissected out using electrocautery. The edges of the pubic bone are brought together by using several interrupted 0 or 2-0 PDS sutures in a figure-eight fashion. The goal is to move the pubic bone medially.



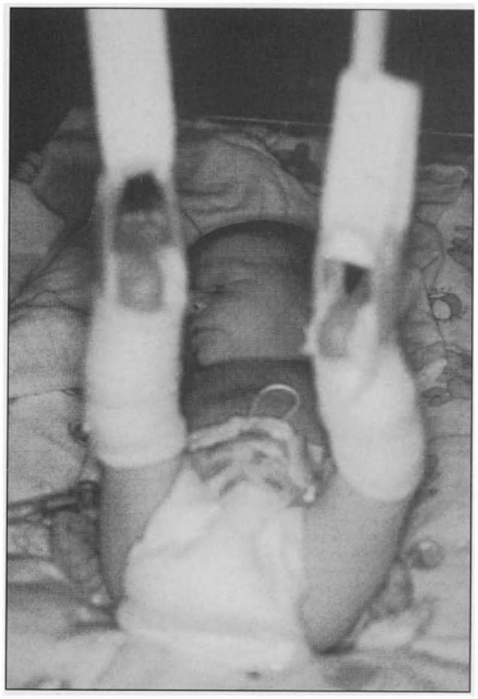
◗ **FIGURE 7-10.** The corpora are rotated toward the midline with interrupted 5-0 PDS sutures starting at the base of the penis and working distally. The neurovascular bundles are rotated to their dorsal location and the traction sutures in the glans halves now have a vertical orientation.



◗ **FIGURE 7-11.** Suturing. The urethral meatus is then sutured to the glans using 7-0 Vicryl (Ethicon, Inc., Somerville, NJ) sutures. The glans halves are approximated by using deep 6-0 PDS suture followed by 7-0 Maxon in a vertical mattress fashion. If the neourethra does not extend to the end of the glans, it is left in a hypospadiac position.



◗ **FIGURE 7-12.** Fascial closure. Fascial closure is performed by using a running 3-0 or 4-0 PDS suture followed by a second layer of 5-0 Monocryl (Ethicon, Inc., Somerville, NJ) in the subcutaneous tissues. The tacking of sutures between the penoscrotal junction, both dorsally and ventrally, is important to prevent the penis from becoming buried. Final closure of the abdominal skin is accomplished with a 6-0 Monocryl suture in a subcuticular fashion. The penile skin is reapproximated dorsally with interrupted 6-0 mild chromic suture. A dressing of Telfa (The Kendall Company Ltd., Mansfield, MA), thin Duoderm (ConvaTec, Skillman, NJ), and, finally, Tegaderm (3M Healthcare, Minneapolis, MN), is applied. The penis is taped down to the abdomen so that it is in a dependent position with the ureteral catheters placed to gravity drainage. The suprapubic tube is sutured in place with a 5-0 nylon suture.

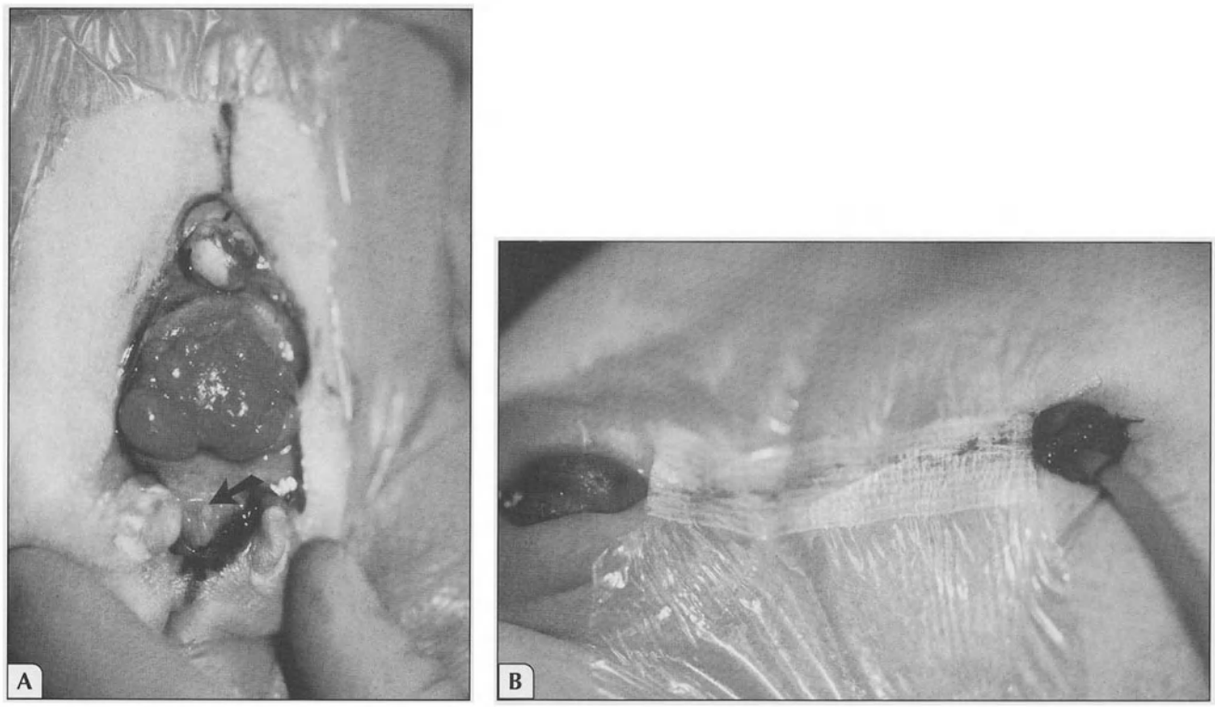


◗ **FIGURE 7-13.** Modified Bryant's traction for a patient who underwent repair of exstrophy. The newborn boy is left in traction for a period of 5 to 7 days. The legs are suspended by applying moleskin and then wrapping with Webril (BBA Nonwovens, Simpsonville, SC). The suprapubic catheter is left to drain via gravity and the ureteral catheters are left to drain into the diaper. Very little weight is required to keep the buttocks just off the bed.

Infants are then transitioned to a "bucket" device for an additional week and are often able to be discharged home at this point. The ureteral catheters, if still in place, are removed. The suprapubic tube, which has been kept to gravity drainage postoperatively, is then clamped on or around postoperative day 10 to allow the bladder to begin to cycle. Diaper weights are recorded and an assessment of postvoid residual is noted. After it has been determined that voiding is occurring well, the suprapubic tube can be removed (generally after several weeks of clamping the suprapubic tube). The day the suprapubic tube is removed, a renal and bladder ultrasound examination is made to assess any degree of hydronephrosis. The infants are left on antibiotic prophylaxis because of the inherent risk of infection in the face of presumed vesicoureteral reflux. Periodic ultrasounds in the first year of life are helpful to assess renal growth, the degree of hydronephrosis, and bladder capacity. Initial hydronephrosis usually resolves in 3 to 4 months. A careful history that elicits intermittent voiding rather than continuous urinary dribbling suggests bladder cycling and bladder neck and proximal urethral sphincteric function.

At 6 months postoperatively, a repeat ultrasound and voiding cystourethrogram study are performed to assess the patient's kidneys and the bladder. These give an idea of bladder capacity, bladder neck function, and degree of reflux. Several patients have shown complete resolution of reflux in this first year of life; antibiotic prophylaxis can be discontinued in these cases.

PRIMARY ANATOMIC REPAIR: FEMALE



◗ **FIGURE 7-14.** Repair for a newborn female patient with exstrophy. Neonatal closure of female patients born with classic bladder exstrophy mimics closure in male patients. The urethral plate and bladder neck are moved with the vagina en bloc posteriorly, and no attempt is made to dissect the urethra off the vagina. **A,** A newborn female patient with exstrophy has been marked to show where the incision will be made. The umbilicus will be moved cephalad and the urethral–vaginal complex will be moved posteriorly, yet a normal perineal body will be maintained. The *arrow* denotes the vaginal introitus.

B, Primary anatomic closure has been completed and the suprapubic tube is seen exiting through the umbilicus while the feeding tubes exit through the neourethra. Because the urethral–vaginal complex has been moved posteriorly, the bifid clitoris is brought together and the vagina assumes a normal anatomic location. Bladder neck function and continence are immediately achieved with this closure. It was the early successes achieved in female patients, some of whom who did not require later bladder neck reconstruction, that paved the way for the complete anatomic repair in male patients.

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Controversies Regarding Treatment of Undescended Testes

8

Stanley J. Kogan

Undescended testes are one of the most commonly encountered problems in pediatric urologic practices. Despite this prevalence and the long clinical interest in this problem, management of patients with cryptorchidism continues to undergo refinement and improvement. Recent discoveries regarding mechanisms of testicular descent, improved methods of diagnosis, and new innovative specialized surgical techniques have drastically improved the overall management of patients with this condition, often allowing a streamlined approach. This chapter addresses controversies that relate to these issues. In some instances, solutions will not be evident, but the discussion will enlighten the reader and help formulate improved approaches to management.

Controversy exists about the mechanisms of testicular descent. Theories explaining these mechanisms are abundant and have undergone continuous evolution over the years. Theories based on mechanical, anatomic, hormonal, and biochemical findings have been postulated. Whereas no one theory alone explains all circumstances encountered clinically, knowledge of each is helpful in interpreting the findings during surgery, and clinicians should be familiar with each. In a similar fashion, existing classifications of cryptorchidism have not adequately acknowledged these disparate findings encountered clinically. Classifications based on testis position are useful because position generally dictates the choice of treatment to follow. Recently, a useful classification based on underlying cause that acknowledges the heterogenicity of cryptorchidism and has some prognostic value regarding ultimate outcomes of treatment has been described. This classification emphasizes that cryptorchidism is not one disease; rather, there are multiple causes, each with a potentially varied prognosis. Besides these classically described forms of cryptorchidism, delayed ascent and iatrogenic secondary cryptorchidism are two more recently described causes of undescended testes. It is important to note clinically that in these instances the testes are subject to the same deterioration that normally occurs in patients with primarily undescended testis, although at a seemingly slower rate.

Diagnosis and treatment of patients with palpable undescended testes are well described in many textbooks and are straightforward. Impalpable undescended testes are distinctly different than palpable undescended ones. In general, they are more structurally abnormal (*ie*, they have a higher frequency of associated hernias, shortened spermatic cord, higher frequency of vasoepididymal abnormalities, smaller size) and sometimes require additional special diagnostic tests. Also, the surgical approach is more complex and detailed. The important questions to answer when dealing with impalpable testes are 1) is the testis present or absent? and 2) what is the best ther-

apeutic response? Historically, a variety of invasive diagnostic tests have attempted to localize an impalpable testis, each with its own limitations and less-than-desired accuracy. More recently, ultrasound has been used because it is noninvasive, relatively inexpensive, easily available, and painless, but it too lacks adequate sensitivity to be used reliably. Sometimes the clinical examination is actually more accurate and useful than any imaging modality. Proper patient relaxation in a warm, quiet examining environment is helpful. Positioning the patient in a cross-legged, leaning-forward position or supine with maximal hip abduction relaxes the cremasteric muscles and may coax an initially impalpable testis into a palpable position, precluding completely the need for any imaging modality. Placing an older child with an impalpable testis in a full squatting position accomplishes the same results. Demonstrating contralateral testicular hypertrophy in a boy younger than 2 years of age may also indicate that the impalpable undescended testis is absent. In some instances, diagnostic laparoscopy may be used to determine the presence and position of an impalpable testis. Published series indicate that laparoscopy is safe and reliable when used in this context and that laparoscopy is the most accurate diagnostic test that can be done to diagnose the absence or presence of an impalpable undescended testis.

Bilateral impalpable undescended testes pose a special problem. In this instance, distinction must be made between bilateral impalpable cryptorchidism (*ie*, testes present) and bilateral anorchia (*ie*, testes absent). Conventional imaging techniques previously mentioned can be used to show testis presence, but hormonal testing measuring serum gonadotropins and the response to human chorionic gonadotropin (HCG) stimulation has a unique application in this clinical setting. When hormonal testing demonstrates elevated gonadoptropin levels and a failed response to HCG stimulation, surgical exploration for confirmation of testis absence is unnecessary. Diagnostic laparoscopy can be performed for confirmation at the time of testicular prosthesis placement.

The goals of treating cryptorchid testes have remained unchanged over the years: placing the testis in the scrotum at an early-enough age maximizes fertility and potentially diminishes the risk of testicular cancer later in life, lessens the risk of testicular torsion in the undescended testis, allows for repair of the often-accompanying hernia, and maximizes body image by having a natural testis filling the scrotum. Hormonal and surgical treatments have been used historically, with each approach having advantages and disadvantages. Specific controversies exist regarding age of treatment and the role of hormonal treatment. Recent studies emphasize that treatment at or around 1 year of age is ideal because rapid germ cell depletion and failure of normal germ cell maturation occurs otherwise. Detractors have argued otherwise: that location is far more important than age, with abdominally located testes having a poorest fertility prognosis.

The role of early orchidopexy and its potential lessening of the increased cancer risk in cryptorchid testes is exceedingly controversial. Testis cancer occurs with an increased risk calculated at about 50 per 100,000, which is estimated as 10 to 30 times the normal risk, although the *absolute risk* is still small. The risk is increased six times over testes located in other undescended positions when the testis is intra-abdominal. Although traditional teaching indicates that orchidopexy (at any age) does not reduce the subsequent risk of germ cell testis tumor formation, recent data indicate that testicular cancer risk in patients treated for cryptorchidism increases as the age of orchidopexy increases. Whether or not *early* orchidopexy lessens the risk is an unanswered question. Conclusive data are inadequate, and answers will have to wait until the current generation of boys who have undergone early orchidopexy have matured.

Whereas the data supporting early or later orchidopexy are each convincing, it seems prudent to offer early repair when the testis has not descended by 1 year of age because the likelihood of spontaneous descent lessens significantly afterwards. Conversely, orchidopexy should not be denied at older ages based on fertility reasons alone because some prospect for fertility may be present, especially when the additional benefits provided by newer assisted reproductive techniques (*eg*, intracytoplasmic sperm injection; round spermatid nuclei injection) are considered.

Historically, HCG has been used to effect testicular descent for decades; it was first used in this manner in 1931. Markedly disparate success rates varying between 5% and 99% have been noted. Introduction of gonadotropin-releasing factor (GNRH) therapy for testicular descent offered another potentially beneficial approach. Just as results with HCG treatment have varied, so too treatment results with GNRH have ranged from 13% to 78% for successful induction of testicular descent. The proven efficacy of orchidopexy must be weighed against these results.

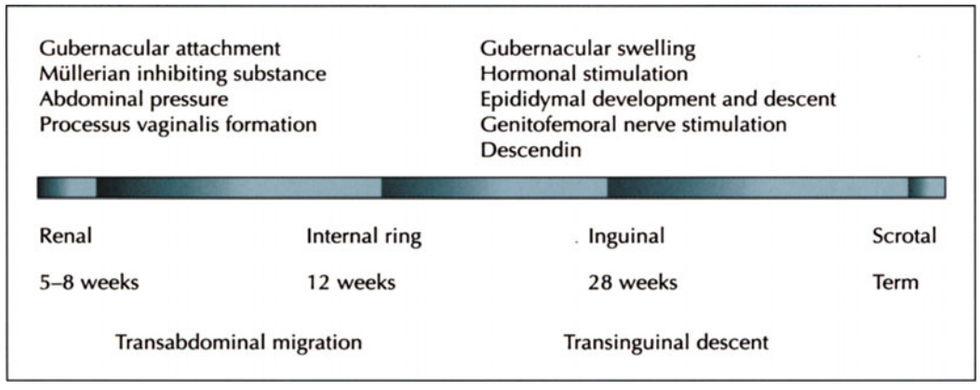
Orchidopexy for patients with palpable undescended testes is performed in a single stage through an inguinal incision by well-described techniques and should achieve success rates in excess of 95%. Most controversy and discussion involve treatment of those with higher impalpable testes whose treatment is more demanding and complex and in which, by necessity, considerable creativity and refinement in surgical techniques has emerged. Considerable experience is necessary in managing these testes because there are no guidelines described. Experience indicates that a "radical" high retroperitoneal dissection is often successful for descending testes that seem to initially require more extensive procedures. When this is impossible, a single-stage procedure sparing division of the spermatic vessels is preferred. Laparoscopic orchidopexy in either a single or deliberate two-stage fashion is another approach and is an inevitable and logical extension of diagnostic laparoscopy. Initial experience indicates that the success rates using laparoscopic orchidopexy for descending these testes are at least as good, if not better, than with open surgical techniques.

If the testis is found to be absent, testicular prostheses may be placed. These provide a definite cosmetic and psychologic benefit to boys with absent testes. Prosthesis placement in adolescent boys in particular is essential and is usually highly desired in this age

group. Preadolescent placement in boys with absent testes is more controversial, although I personally recommend this approach. Early placement provides a sense of "normality" for the parents and, later, for the child. Scrotal growth and appearance are normal. In adolescence, the prosthesis is exchanged for an adult-sized one. In the past, testicular prostheses have been made with a silicone interior and an outer silicone shell, but the Food and Drug Administration now mandates that previous models be replaced with a saline-filled model with a silicone envelope exterior. Health concerns regarding the safety of silicone testicular implants have not stood the test of scientific scrutiny.

These observations indicate the continued interest and change occurring in the management of patients with cryptorchidism. Although the incidence of cryptorchidism has remained stable, the number of orchidopexy procedures has tripled in recent years. Additional numbers of boys are treated hormonally. Technical and surgical innovations have significantly improved the success rate in dealing with the higher, more difficult testes. Concomitantly, the number of subfertile adults resulting from untreated or inadequately treated cryptorchidism has decreased. Early orchidopexy may prove to reduce this number further in time. Because there does not seem to be any added risk when surgery is performed by a skilled pediatric urologist and skilled pediatric anesthesiologist, early orchidopexy at or about 1 year of age has been recommended as optimal treatment by the Action Committee of the American Academy of Pediatrics, when these criteria can be met. To date, there is encouraging evidence that the risk for testicular atrophy is not increased by this approach.

MECHANISMS OF TESTICULAR DESCENT



◗ **FIGURE 8-1.** Factors influencing normal and disordered testicular descent. Anatomic, hormonal, and biochemical theories have been postulated to explain the diverse findings encountered in normal and disordered testicular descent [1]. Formation of the processus vaginalis and attachment of the gubernaculum to the lower end of the epididymis (at 5 to 8 weeks' gestation) occurs, delivering the testis to a position adjacent to the internal inguinal ring by the twenty-first week (this is known as transabdominal migration). Differential body growth may also play a role in this process. No additional descent occurs until 26 to 28 weeks' gestation, when gubernacular swelling distends the inguinal canal, possibly facilitating entry of the testis. Descendin, an androgen-independent factor promoting gubernacular cellular growth, has been described experimentally. The gubernaculum subsequently atrophies as the testis descends through the canal (*ie*, the transinguinal phase of descent), allowing passage. Hormonal factors are important during this phase: increasing testosterone levels occur and, experimentally, anti-androgens often block this phase of descent. Epididymal growth, elongation, and descent precede the testis into the scrotum. A neural role may be important here as well: evidence suggests that the genitofemoral nerve spinal nucleus located in the anteromedial aspect of the L3-4 spinal segment is "masculinized" by fetal androgens, causing it to release a neurotransmitter (*ie*, a calcitonin gene–related peptide), which stimulates rhythmic gubernacular contractions, helping to deliver the testis through the inguinal canal [2].

Disorders of testicular descent occur commonly in association with derangements of the above processes. Gonadotropin-releasing factor deficiency or pituitary disorders with resultant gonadotropin deficiency (*ie*, Kallmann's syndrome, Prader-Willi syndrome, pituitary hypoplasia) are associated with cryptorchidism. Absence of müllerian inhibiting factor results in retained müllerian ductal structures and abdominal cryptorchidism. Abnormalities of the abdominal muscles with diminished abdominal pressure (*ie*, prunebelly syndrome, gastroschisis) are associated with an increased frequency of cryptorchidism. Epididymal anomalies are commonly associated with undescended testes, and the higher the testis, the more severe and frequent the anomalies encountered. Finally, boys with spina bifida have a higher frequency of cryptorchidism, especially those with lower defects (*ie*, potentially affecting the L3-4 segments). Whereas no one theory alone explains all circumstances encountered clinically in patients with cryptorchidism, it is apparent that diverse factors each contribute something to the overall process of descent and that different mechanisms may be operative in each circumstance.

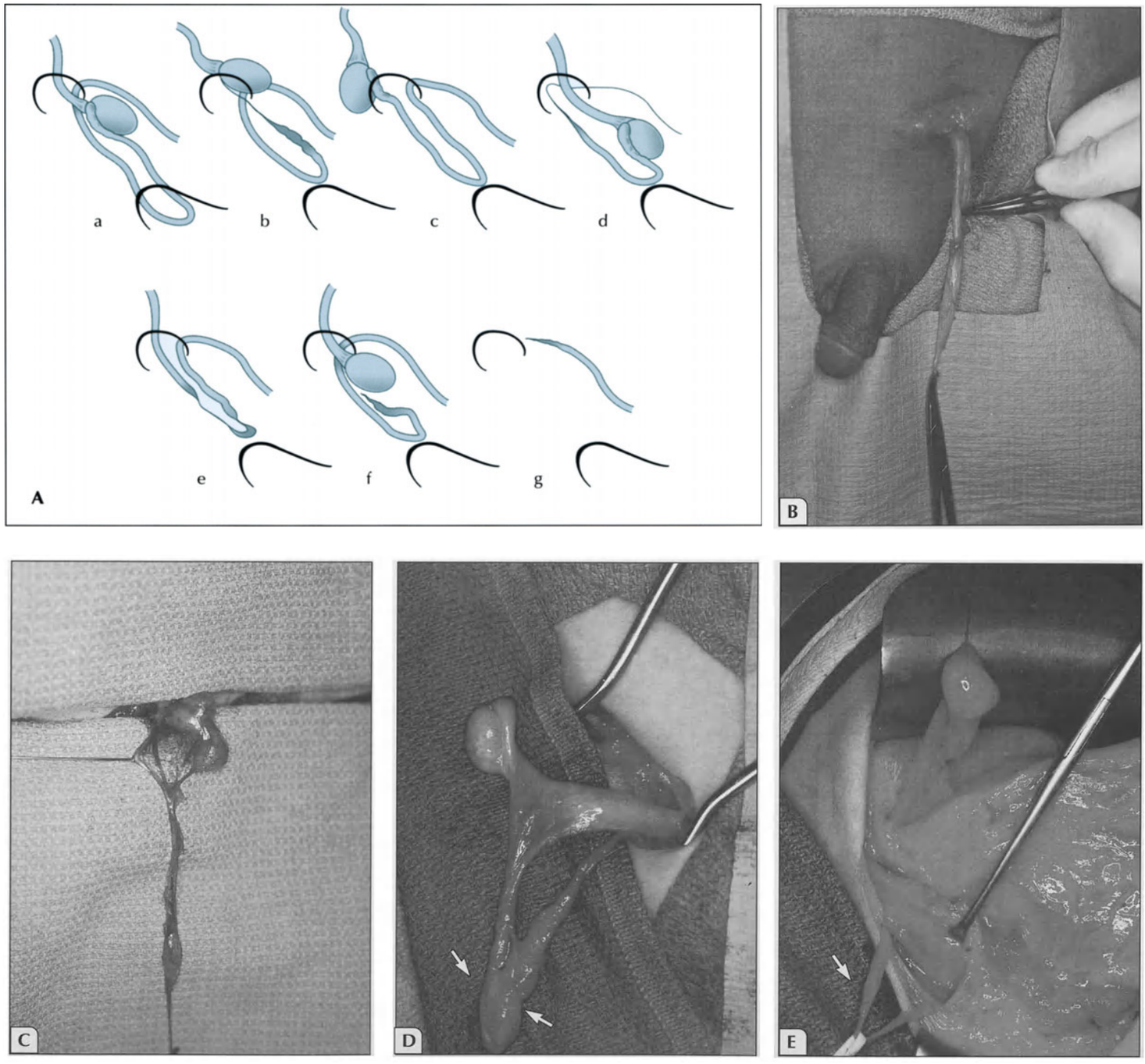
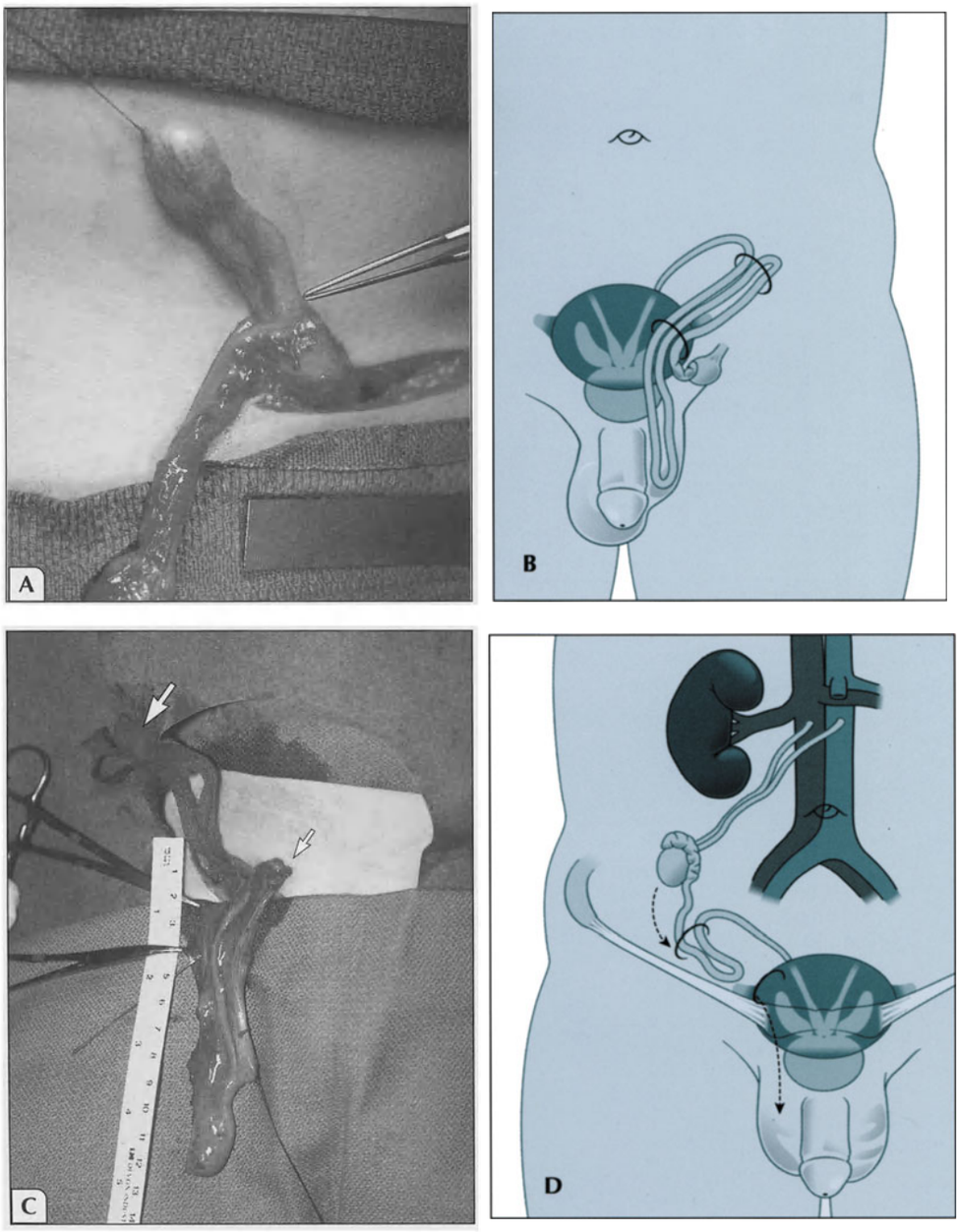


FIGURE 8-2. Epididymovasal abnormalities in cryptorchidism. Epididymal abnormalities are encountered commonly in patients with cryptorchid testes. Gross ductal abnormalities are seen in at least one third of those with cryptorchid testes, with an increased frequency in higher (*ie*, abdominal) testes. Distal looping of the vas deferens and epididymal tail ("long-looped vas") is the most frequent finding; other abnormalities of ductal fusion or suspension also occur [3]. Besides having significance regarding the underlying potential reason for testicular maldescent, accurate identification of these structures during surgery is exceedingly important because surgical errors may result from misinterpretation of the gross findings. For example, a looped epididymis may simulate the appearance of a blind-ending spermatic cord and may be accidentally excised, leaving an abdominal testis above. Intraperitoneal exposure and thorough mobilization and definition of the structures is essential to prevent errors in these instances [4].

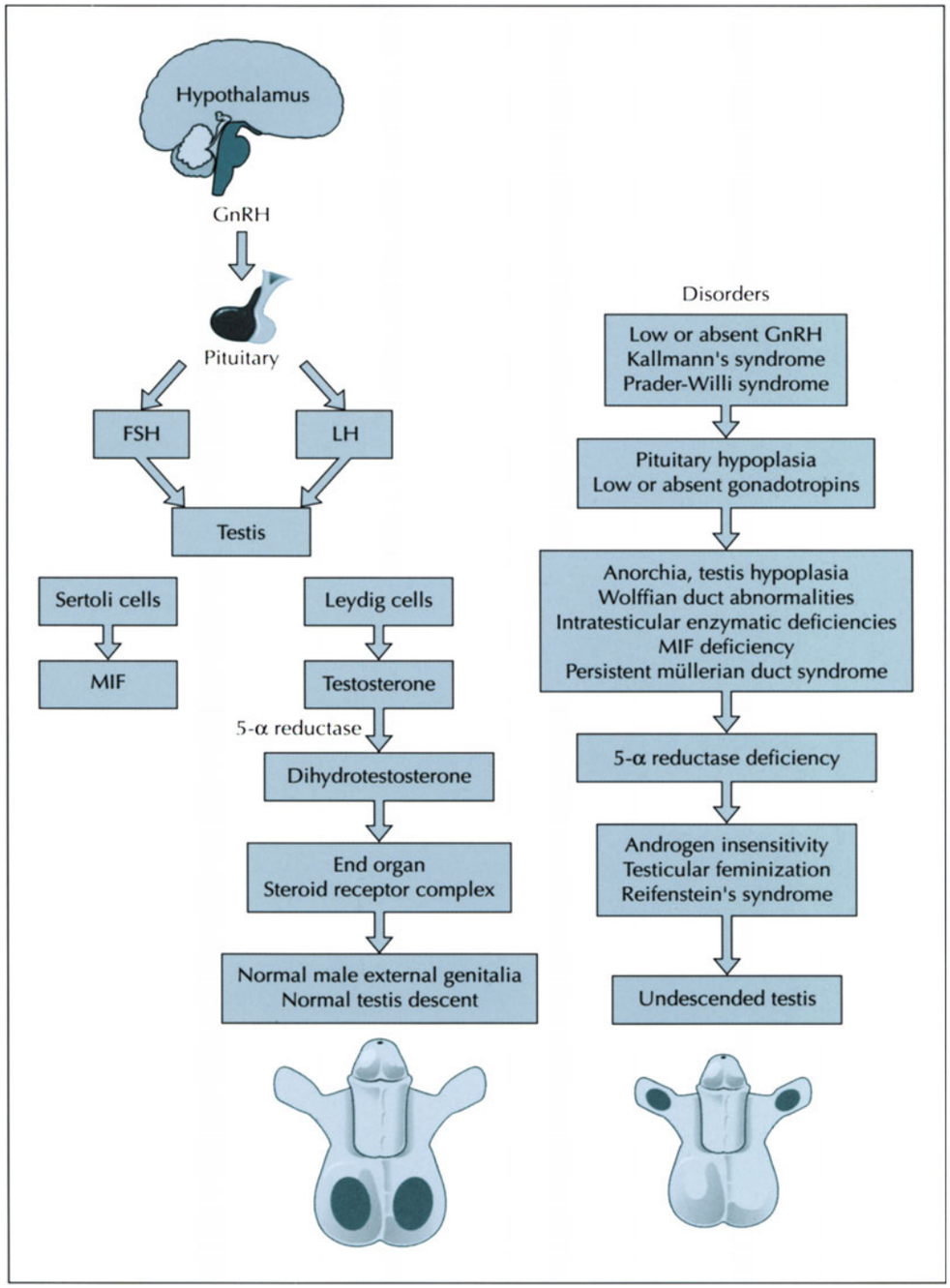
A, Epididymovasal abnormalities in patients with cryptorchidism. Small letters are defined as follows: a: Long-loop vas deferens preceding the testis through external inguinal ring. b: Atresia of distal epididymis with threadlike communications to the intra-abdominal testis. c: Intra-abdominal testis with descended long-loop vas deferens. d: Atresia of the proximal vas deferens. e: Blind-ending vas deferens and spermatic pedicle with unidentifiable testicular tissue. f: Failure of union of vas deferens and testis. g: Blind-ending distal vas deferens with absent testis and spermatic vessels.

B, Long-looped vas deferens with "nubbin" at end extending down the inguinal canal. **C,** Similar example with long-looped vas and presumed "nubbin" at end, extending down the inguinal canal. The testis shown above was intra-abdominal. **D,** Older child with structure mimicking atrophic testis with collapsed surrounding tunica vaginalis at end (*arrows*) that had exited through the external inguinal ring. Retroperitoneal testis above. **E,** Blind-ending gubernaculum-like structure passing down through the inguinal canal (*arrow*). The testis lies above within the abdomen. (Part A *adapted from* Kogan [4]. Parts B to D *from* Kogan [4]; with permission.)

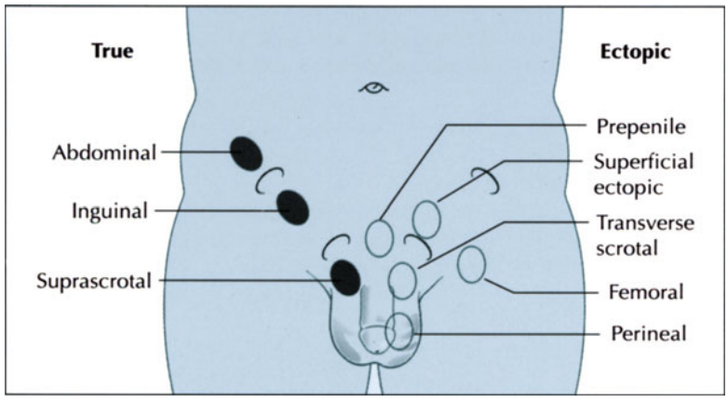


◗ **FIGURE 8-3.** Epididymal descent in two patients with cryptorchidism. **A** and **B**, Lesser example of elongated epididymis descending toward or into the scrotum with cryptorchid testis. **C** and **D**, Extreme example of epididymal descent with cryptorchid testis tethered to the lower pole of the kidney by epididymis attachment. Despite fixation at renal level, complete epididymal descent has occurred (*large arrow* indicates the point of previous attachment to the kidney; *small arrow* indicates the testis).

Controversy has raged between theorists of testicular descent regarding the role of the epididymis in normal and abnormal descent [5]. In both of the cases shown here, epididymal descent has occurred to a varying degree, "leading" the testis, which remains cryptorchid. Those that support the role of the epididymis in effecting testicular descent cite examples such as these to support their beliefs that epididymal descent is an integral part of normal descent and that an abnormally developed epididymis occurs frequently when maldescent is present.



◗ **FIGURE 8-4.** Hormonal abnormalities associated with normal and disordered testicular descent. Boys with cryptorchidism are suspected of having an abnormal postnatal hormonal environment, with hypogonadotropic hypogonadism and impaired testosterone secretion early in life. A corresponding abnormal prenatal hormonal milieu is inferred [6,7]. A variety of clinical syndromes exist in which cryptorchidism is associated with hormonal abnormalities and a disordered hypothalamic–pituitary axis. FSH—follicle-stimulating hormone; GnRH—gonadotropin-releasing hormone; LH—luteinizing hormone; MIF—müllerian inhibiting factor. (*Adapted from* Gill and Kogan [8].)



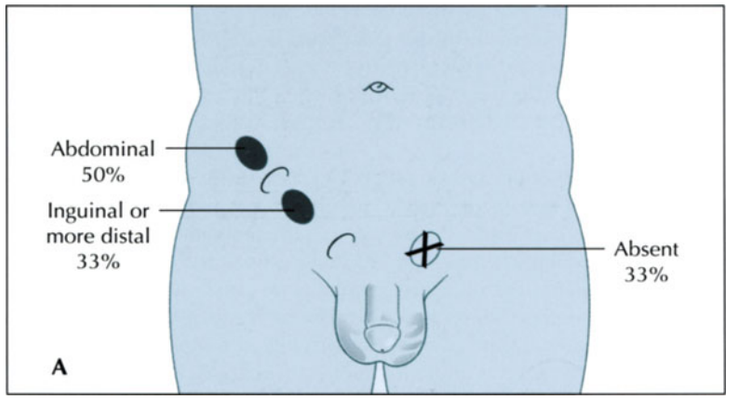
◗ **FIGURE 8-5.** Classifications of cryptorchidism by location. Classification of cryptorchidism based on location is useful because description in this fashion indicates the appropriate subsequent treatment. Palpable undescended testes may be retractile, suprascrotal, or "gliding" (within a wide patent processus vaginalis), secondarily ascended to an extrascrotal location after previous documented descent, ectopic, or inguinal in location. Virtually every palpable testis may be surgically descended by conventional orchidopexy techniques. Adequate spermatic cord length is present and special techniques are not needed for this reason. Impalpable testes occur when they are within the abdomen, sometimes within the inguinal canal, or when they are atrophic or absent. In these circumstances, more involved surgical procedures are often needed.

Clinical observations indicate that descended testes, whose dependent position is often well documented on multiple occasions, may subsequently ascend to an extrascrotal location. Differential body growth, fixation to surrounding structures, and shortening of an accompanying processus vaginalis have all been suggested as potential causes. Iatrogenic cryptorchidism occurs most often when the testis adheres to the internal aspect of an inguinal scar (*ie*, after herniorrophy or hydrocelectomy). Ensuring that the testis is properly dependent and fully "seated" at the termination of the repair minimizes this occurrence. It is important to note clinically that the testes are subject to the same deterioration in these instances that normally occurs in a primarily undescended testis, although at a seemingly slower rate [9,10]. (*Adapted from* Kogan [4].)

Multifactorial Classification of Cryptorchidism by Underlying Cause

Abnormality	*Effect on Fertility*	*Early Orchidopexy*
Abnormal end organ (rudimentary testis)	Impaired sperm production	Unhelpful
Ductal abnormality (dysjunction, long-looped vas deferens)	Impaired sperm transport	Unhelpful
Ectopia (abnormal gubernaculum, closed scrotal space)	Normal initial development Secondary germ cell depletion	Helpful
Abnormal hormonal milieu (hypogonadotropism)	Normal initial development Secondary germ cell depletion	Early hormonal treatment with or without orchidopexy
Diminished abdominal pressure (prunebelly, gastroschisis)	Normal initial development Secondary germ cell depletion	Helpful
Complete nondescent	Impaired initial development Secondary germ cell depletion	? Helpful
"Acquired" cryptorchidism (secondary ascent, scar fixation)	Secondary germ cell depletion	N/A

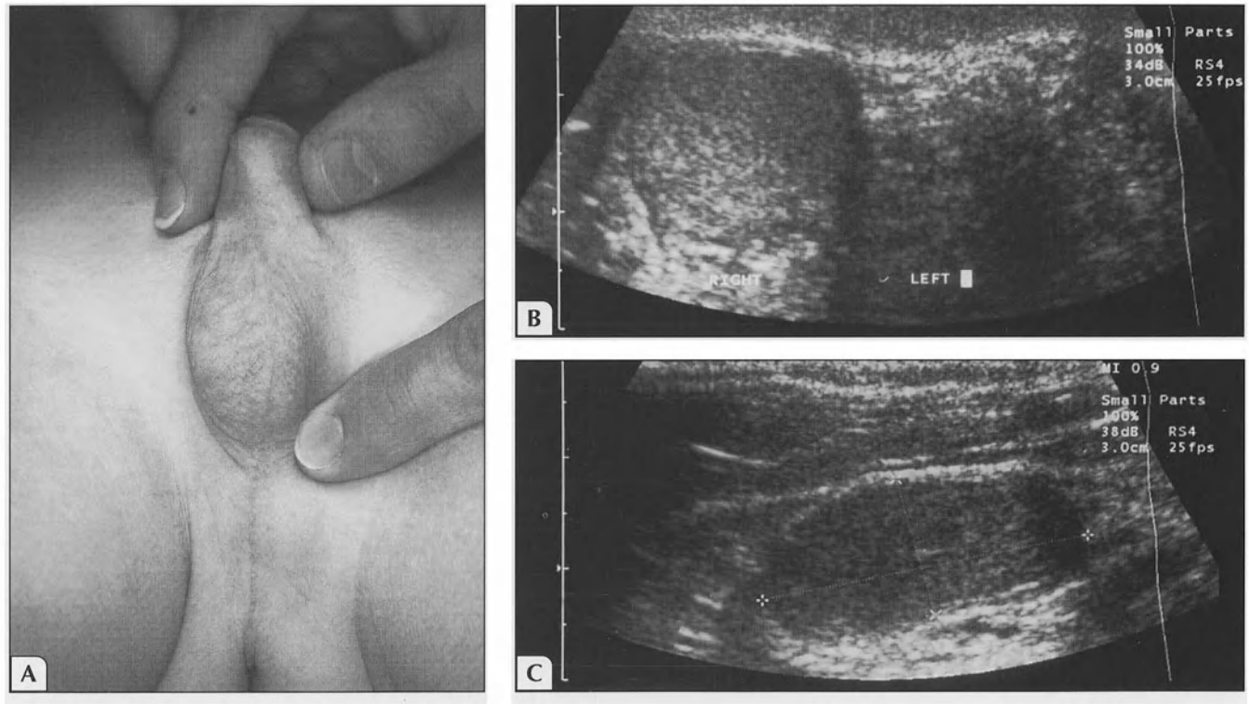
◗ **FIGURE 8-6.** Multifactorial classification of cryptorchidism by underlying cause. This classification system emphasizes that cryptorchidism is not one disease; rather, there are multiple causes, each with a differing underlying process involved and each with a potentially varied prognosis. This classification also stresses the heterogenicity of cryptorchidism and has prognostic value regarding the outcome of treatment. For example, early treatment may have little or no value for treatment of rudimentary testes because there is inadequate testicular tissue present. Similarly, hormonal supplementation might be necessary for patients with severe hypogonadotropism to achieve full fertility potential, in addition to early successful surgery (King LR, Personal communication).



B. Findings in Boys with Unilateral Absent Testes

Finding	*Patients, n(%)*
Minispermatic vessels	47(72)
Wolffian structures	54(83)
Vessels and wolffian structures	45(69)
Vessels and vas deferens	20(31)
Vessels, vas deferens, epididymis	12(18)
Vessels, vas deferens, epididymis, terminal nubbin of tissue	13(20)
Vas deferens only	9(14)
Vessels only	2(3)
Absence of all structures	9(14)
Total	65(100)

◗ **FIGURE 8-7.** Surgical findings in boys with impalpable testes. **A,** Locations of impalpable undescended testes. **B,** Surgical findings demonstrated with absent testes [11]. Figures vary widely according to which references are cited regarding the frequency and locations of impalpable undescended testes. Impalpable undescended testes constitute about 20% of all cryptorchid testes. About 30% to 60% of impalpable testes are absent: when the testis is impalpable, it is present in about 40% to 70%[12]. Overall, about 10% of cryptorchid testes are abdominal, 50% to 70% are high scrotal or ectopic, 3% to 4% are absent, and the remainder are intracanalicular. When impalpable, the distribution figures change: about 50% are abdominal and about 33% each are inguinal or absent [11]. (*Data from* Kogan *et al.* [13].)



◗ **FIGURE 8-8.** Ultrasound evaluation for impalpable cryptorchidism. Historically, a variety of invasive diagnostic tests have been described attempting to localize an impalpable testis, each with its own limitations and less-than-desired accuracy. Previously used modalities such as gonadal venography or arteriography, herniography, routine computed tomography, or magnetic resonance imaging examination are of limited use and of historic note only. The latter two approaches are useful in selected cases in older boys but should not be used routinely. None of these tests can reliably diagnose a vanishing testis or small testicular nubbin; for these, direct observation is necessary by laparoscopy.

A, Impalpable left testis. **B** and **C,** Testis impalpable but ultrasound shows testis in left inguinal canal.

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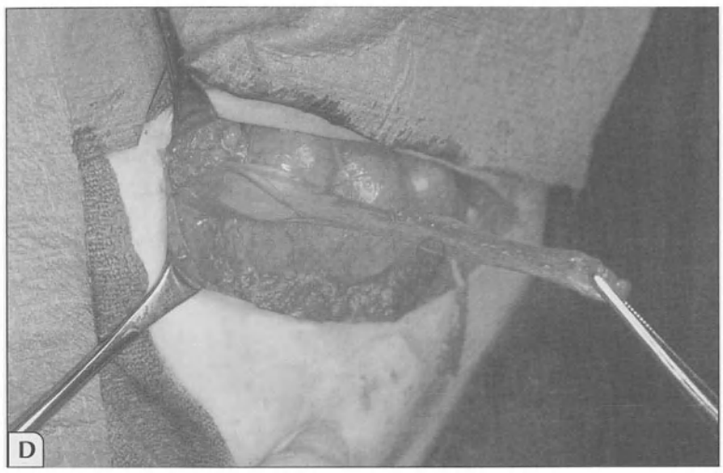
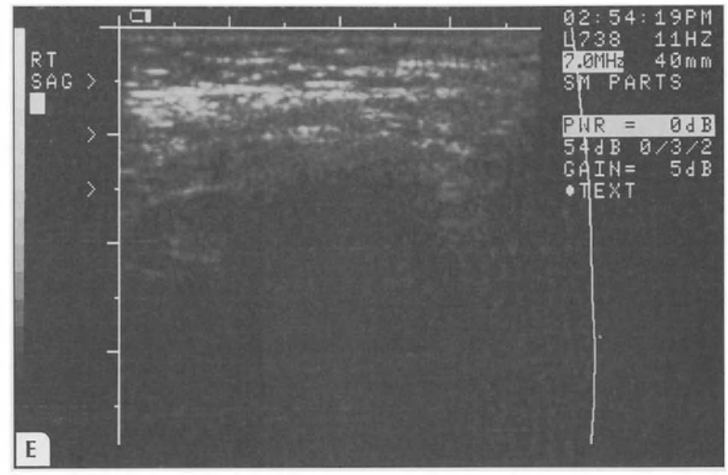
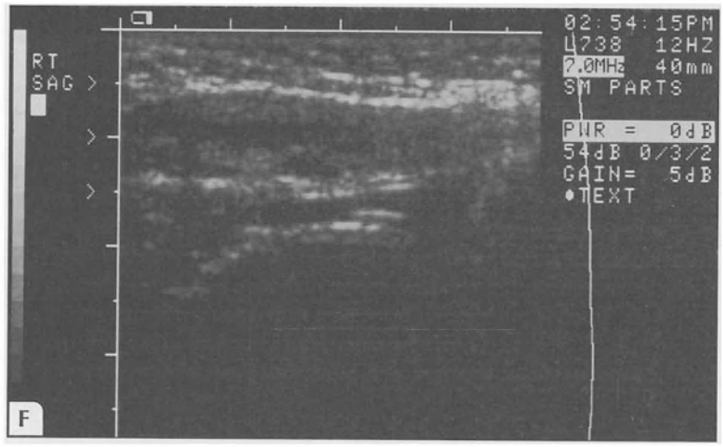
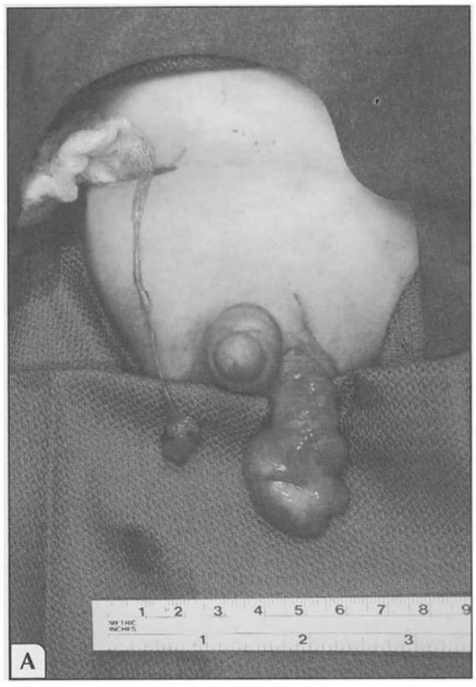


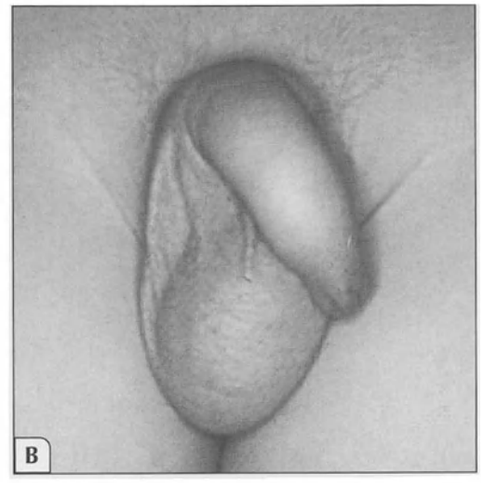


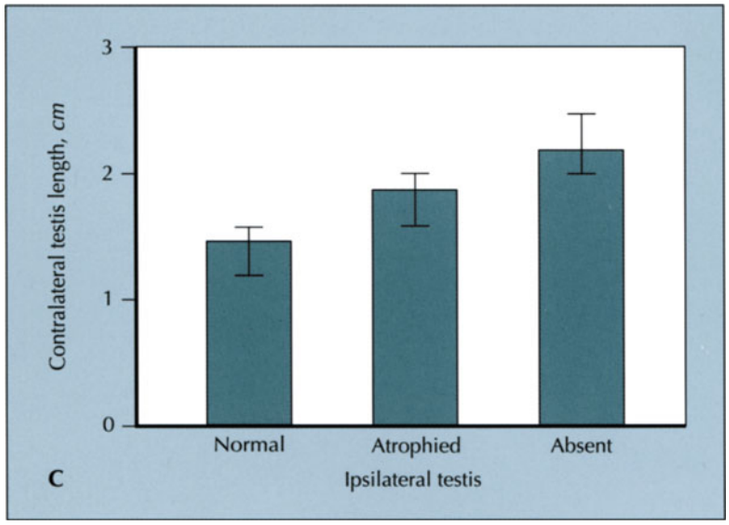


◗ **FIGURE 8-8.** (*Continued*) **D** through **F**, Testis easily palpable in groin, but ultrasound fails to demonstrate testis.

Ultrasound is noninvasive, relatively inexpensive, readily available, and painless, but is lacking in sensitivity, especially in prepubertal boys in whom the testis is often 2 cm in size or smaller. False-positive examinations (showing a testis falsely to be present) are rare, but false-negative examinations, failing to show a testis when it is actually present, are quite common [14]. If an ultrasound in a prepubertal boy fails to demonstrate a testis, laparoscopy and exploration are still needed, so the utility of this examination is limited in prepubertal boys. On the other hand, in older pubertal boys with impalpable testes, ultrasound is often useful because false-negative examinations are much less common. Laparoscopy should still be done to confirm testis absence when the ultrasound fails to demonstrate a testis in a pubertal boy.





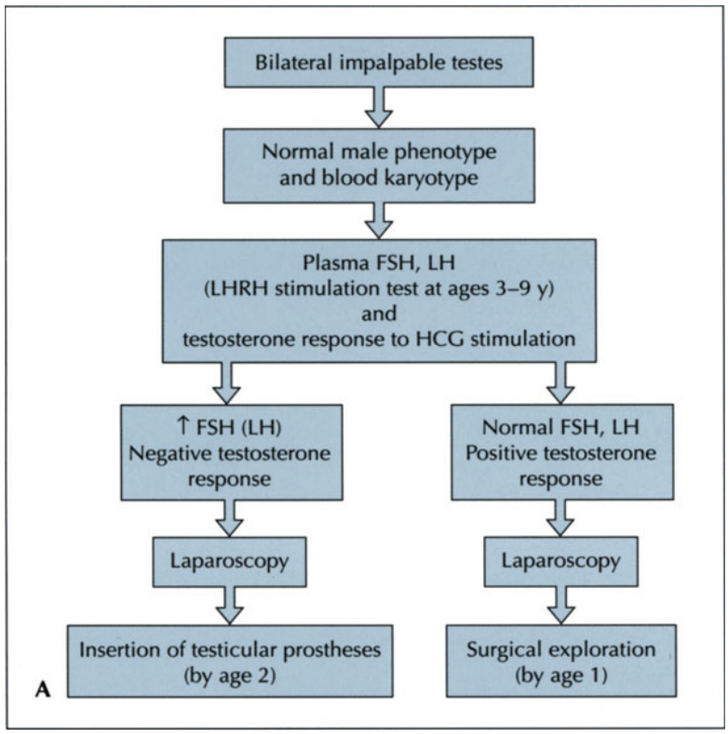


◗ **FIGURE 8-9.** Contralateral testis hypertrophy in impalpable cryptorchidism. Unilateral testicular hypertrophy occurs in boys with absent testes. **A,** A 1-year-old boy with an impalpable right testis was found to have an atrophic nubbin in the scrotum. Pathologic examination of the excised nubbin demonstrated hemosidirin and calcification but no testicular tissue, compatible with antenatal torsion and infarction. Left solitary testis greater than 2 cm. **B,** Massive contralateral testis hypertrophy (testis 50 mL in volume) in an early pubescent boy with monorchia. **C,** Size of contralateral descended testis in boys with unilateral absent testis, atrophic testis, and normal testis [15].

In boys younger than 3 years of age, contralateral testis hypertrophy equal or greater than 2 cm length when present has been shown to be an accurate predictor of testicular absence (*ie*, monorchia) [15]. This finding is useful clinically to predict testicular absence before laparoscopy or open surgical exploration. In older boys, contralateral descended testis hypertrophy occurs as well with monorchia, but also may occur when the other testis is abnormally developed (*ie*, cryptorchid or atrophied, so one should not assume testis absence in this circumstance). **D,** Cautionary statements.

D. Cautionary Statements Regarding Contralateral Testis Hypertrophy in Impalpable Cryptorchidism

1. Only findings of a testis equal or greater than 2 cm length in boys younger than 3 years of age indicates strongly that the opposite (*ie*, impalpable) testis is absent.
2. This rule does not hold true for older boys.
3. If a testis is smaller than 2 cm in size, it does not confirm that the contralateral impalpable testis is necessarily present, nor does it exclude monorchia. In other words, a normal size testis does not exclude monorchia.



B. Interpretation of Hormonal Findings in Boys Undergoing Hormonal Evaluation for Bilateral Congenital Anorchia

	FSH, LH	*Testosterone After HCG*
Testes absent		
Bilateral congenital anorchia	↑	0
Possible in prepubertal bilateral congenital anorchia (*ie*, ages 3 to 9 years)	Normal	0
LHRH →	↑	0
Testes present		
Bilateral impalpable cryptorchidism	Normal	↑
Possible in hypogonadotropic hypogonadism	Low	0
Prolonged HCG →	—	↑
Possible in postpubertal bilateral hypoplastic/damaged testes present	↑	0

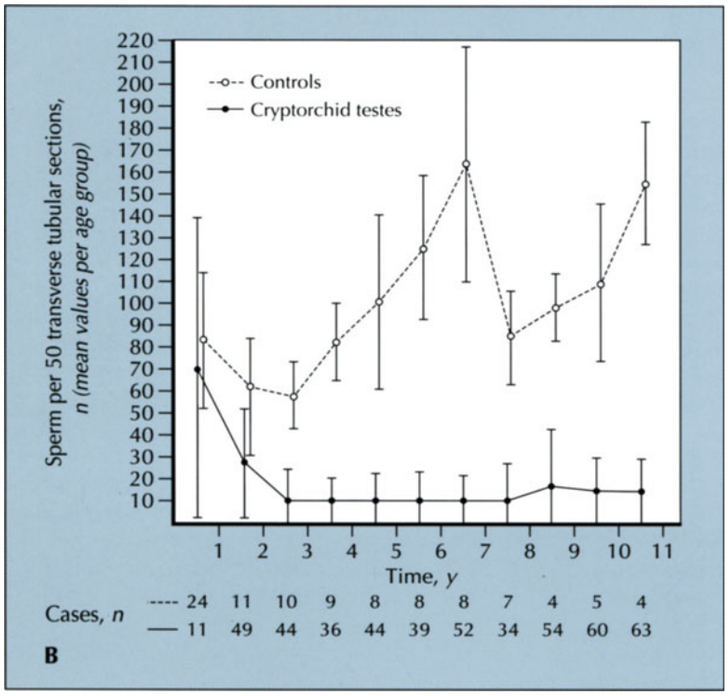
◗ **FIGURE 8-10.** Diagnosis and treatment of patients with bilateral impalpable testes. **A,** Algorithm for diagnosis and management of boys with bilateral impalpable testes. **B,** Interpretation of hormonal findings in boys undergoing hormonal evaluation for bilateral congenital anorchia.

When bilateral impalpable undescended testes are present in a boy with a normal phenotype, distinction must be made between bilateral impalpable cryptorchidism (*ie*, testes present) and bilateral anorchia (*ie*, testes absent). Conventional imaging techniques previously mentioned can be used to show testis presence, but are unreliable in demonstrating absent testes. Hormonal testing measuring serum gonadotropins and the response to human chorionic gonadotropin (HCG) stimulation has a unique application in this clinical setting because follicle-stimulating hormone (FSH) levels (and sometimes luteinizing hormone [LH] levels) are elevated in boys with absent testes, even early in life, and the testes are responsive to testosterone as well at this time. Elevated gonadotropin levels and a failed response to HCG stimulation in this context indicates bilateral absent testes (*ie*, bilateral anorchia), and surgical exploration for confirmation of diagnosis is unnecessary. Diagnostic laparoscopy can be performed for confirmation at the time of testicular prosthesis placement [16].

Although there is controversy regarding the accuracy and interpretation of these tests, careful review will identify potential pitfalls in interpreting these data and clarify this confusion [17]. When both components of this test are present, namely increased levels of FSH or LH (or both) and failure of testosterone response to HCG, bilateral anorchia is present, although postpubertal boys with damaged testes conceivably may have similar endocrine findings. Besides this, bilaterally anorchic boys between the ages of 3 to 9 years, when the hypothalamic-pituitary "gonadostat" is relatively inactive, may not elevate their gonadotropin levels. In this circumstance, a luteinizing hormone–releasing hormone (LHRH) stimulation test will unmask this inactivity. In all other circumstances, when either or both of the endocrine components are not fulfilled, a testis may be present and a thorough exploration must be undertaken. (*Adapted from* Kogan [16].)

A. Major Landmarks in Normal Testis Development and Disturbed Landmarks in Cryptorchid Testis Development

	Normal Development	*Abnormal Development*
Fetal testis	Gonocyte to Ad-spermatogonia; normal number of gonocytes initially	
Postnatal	Gonocytes disappear by 6 months	Impaired transformation of gonocytes to Ad-spermatogonia
Age 1 year	Main cell is Ad-spermatogonia	
Age 2 years	Virtually all testes have normal germ cell number	One third normal, one third subnormal, one third absent germ cells
Age 5 years	Primary spermatocytes appear (first meiosis)	Impaired primary spermatocyte appearance
Puberty	Progression of normal spermatogenesis	Impaired progression of spermatogenesis



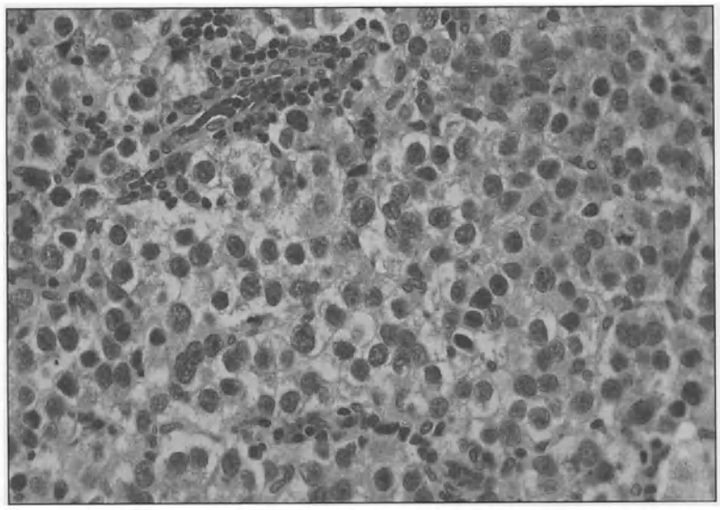
C. Semen Analysis in Men with Unilateral Palpable and Impalpable Undescended Testes Who Had Orchidopexy Performed Between Ages 7 and 13.5 Years

		Normal	*Subnormal*
	WHO Standards	*Mean (n)*	*Mean (n)*
Volume, *mL*	>1.5	2.9 (101)	0.9 (18)
Density, *X* 10^6*/mL*	>20	74.3 (88)	10.3 (27)
Abnormal forms, %	<50	34 (96)	69 (19*)
Motility, %	>50	61 (97)	29 (18)

*Four azoospermic.

◗ **FIGURE 8-11.** Testicular histology according to age and location. **A,** Major landmarks in normal testis development and disturbed landmarks in cryptorchid testis development. **B,** Germ cell counts in cryptorchid testes according to patient age and location of the testis [18]. **C,** Semen analysis in men with unilateral palpable and impalpable undescended testes who had orchidopexy performed between ages 7 and 13.5 years [19].

Based on extensive histologic analysis of the cryptorchid testis, the age that treatment is provided has continually lessened because it was noticed that "the younger the child's age, the less the histological appearance differed from a normal testis" [20]. Cryptorchid testes do not develop properly. The three major landmarks in histologic development are arrested: transformation of gonocytes to Ad-spermatogonia at or around 6 months age; failure of transformation to primary spermatocytes at or around 5 years of age; and failure of primary spermatocytic meiotic division at puberty [21]. Failure of nomal transformation is suspected to be associated with increased risk of subsequent infertility and neoplasia. Besides, there is a rapid and early fall-off in germ cell number after the first year of life. Studies [18,21] indicate that about 5% of cryptorchid testes are devoid of germ cells at that time, with about a quarter or a third aspermatogenic by age 2 years and further progression toward sterility by the completion of puberty. Because orchidopexy in trained hands can be done just as safely and effectively at 1 year of age as in older boys, orchidopexy at this age seems ideal. Detractors have argued otherwise: that testis location is far more important than age, with abdominally located testes having the poorest fertility prognosis [19]. Certainly orchidopexy should not be withheld in older prepubertal boys because of suspected infertility. WHO—World Health Organization. (Part B *adapted from* Hadziselimovic *et al.* [18]; part C *adapted from* Puri and O'Donnell [19].)



◗ **FIGURE 8-12.** Seminoma in a 31-year-old man who had undergone previous unilateral orchidopexy at 11 years of age. The risk of malignancy occurring in cryptorchidism is measured at about 50 per 100,000, which is 22 times that seen in the general population [22,23]. Various other reports indicate an increased risk of 10 to 30 times, although the *absolute* risk remains small. The risk is increased six times over testes located in other undescended positions when the testis is intra-abdominal, as well as in intersex patients having a Y chromosomal karyotype and in atrophic testes after failed orchidopexy. Traditional teaching indicates that orchidopexy (at any age) does not reduce the subsequent risk of germ cell testis tumor formation [24]; however, recent data indicate that testicular cancer risk in cryptorchid patients is related to the age that orchidopexy is done. In one large study, a progressive increase in testis tumor occurrence was noted as age of orchidopexy increased [25]. Conclusive data are inadequate at this time and answers will have to wait until the current generation of boys who have undergone early orchidopexy have matured.

Dosage Schedule for Human Gonadotropic Hormone Induction of Testicular Descent

Patient Age, y	*Dosage, IU*
≤1	250 IM
1–6	500 twice weekly for 5 weeks
≥6	1000 twice weekly for 5 weeks

◗ **FIGURE 8-13.** Hormonal treatment for testicular descent. Extreme variation in reported success using human chorionic gonadotropin (HCG) for induction of testicular descent has been noted, ranging between 5% and 50%. Multiple factors, including varied dosing schedules, differing age at treatment, inclusion of boys with retractile testes, and differing numbers of boys with "higher" testes explain the wide variation in success. Historically, Europeans have favored HCG over surgical primary treatment and have cited a greater frequency of success. Inclusion of a larger number of retractile and lower-positioned testes in these series are one probable reason because both would respond more favorably to HCG. Significantly, in some series, treatment at early ages—that is, precisely when successful descent is most important—was associated with a poorer success rate [26]. HCG is contraindicated for treating those with ectopic testes because these are mechanically impeded from descending into the scrotum, when a clinical hernia is also present, and in cases in which scar fixation of the testis is present after previous hernia repair or orchidopexy.

Introduction of gonadotropin-releasing factor (GNRH) analogues for testicular descent offered another potentially beneficial approach. Because GNRH is not available for this indication in the United States, all data were derived from overseas treatment studies. Just as with HCG, treatment results with GNRH have ranged from 17% to 38% in double-blind studies and 13% to 78% in open studies. A positive correlation was seen with increasing numbers of distally located testes and increasing age at treatment. Anatomic abnormalities precluding successful descent were discovered at subsequent orchidopexy in treatment failures in 80% [27]. GNRH has also been used in conjunction with subsequent HCG, with an 80% success rate [28]. The proven efficacy of orchidopexy must be weighed against these results. IM—intramuscularly.

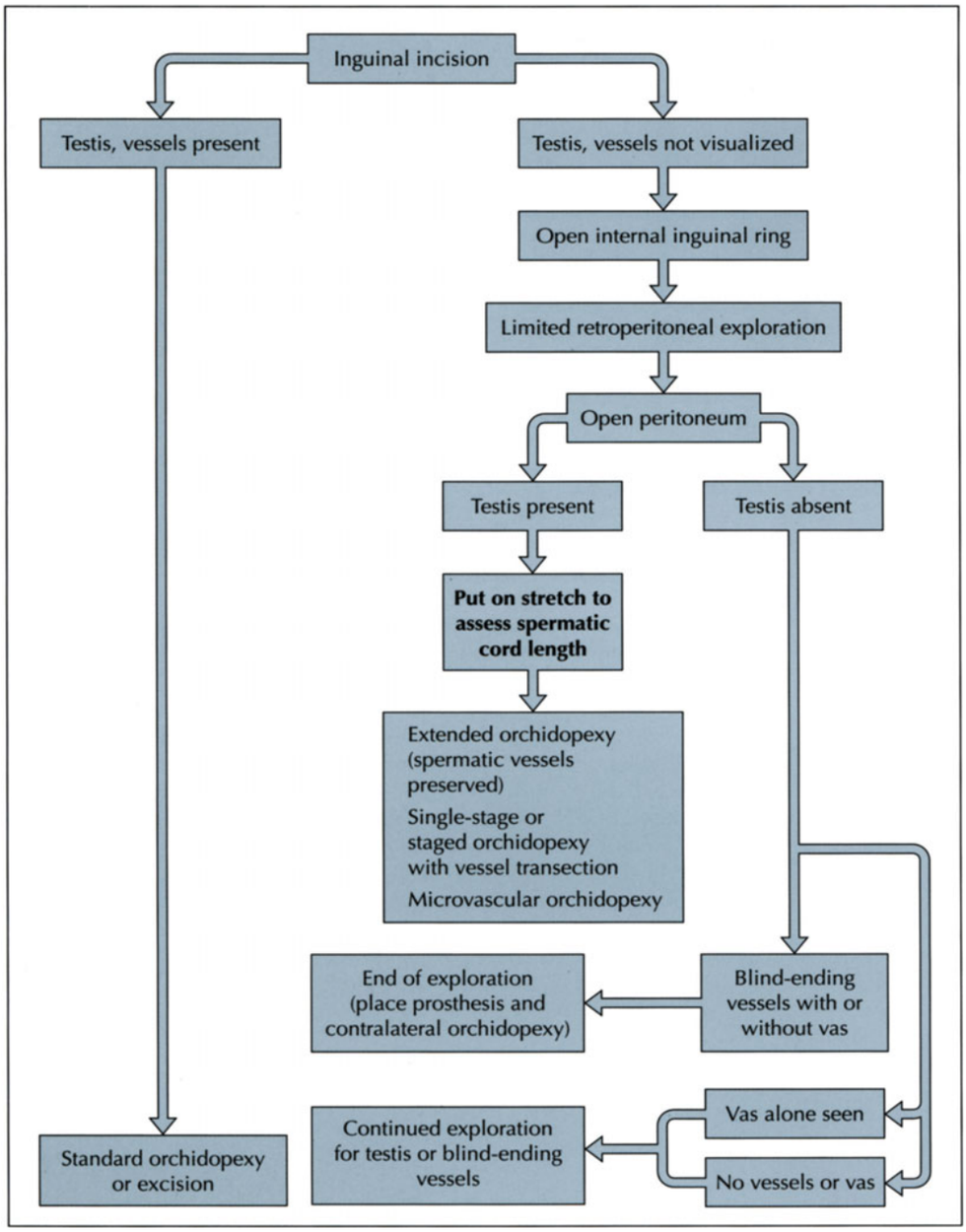
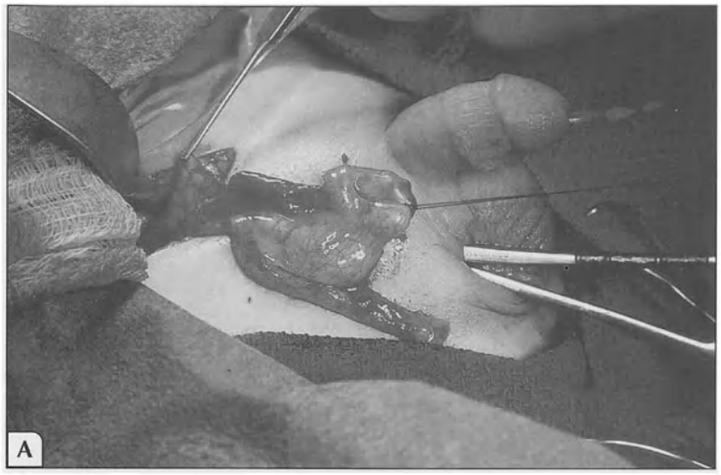
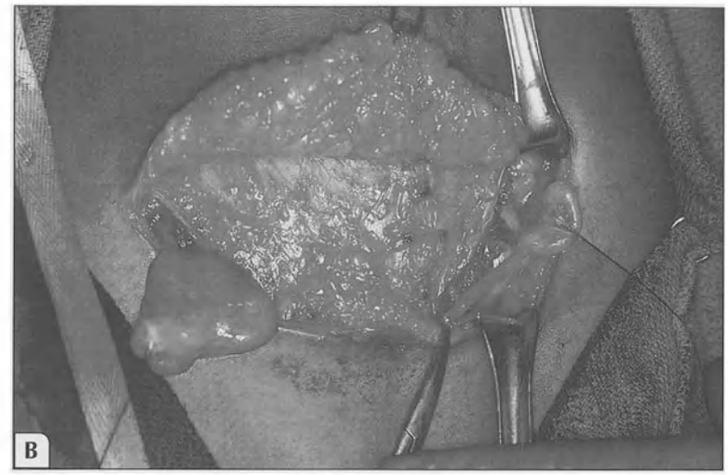
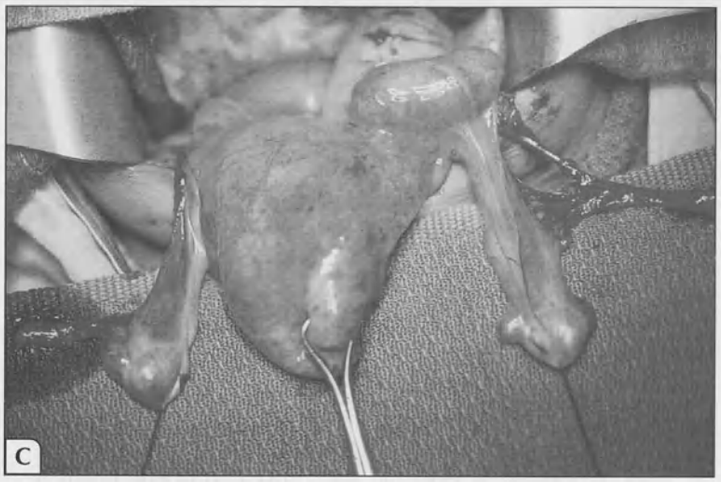


FIGURE 8-14. Diagnosis and surgical treatment of unilateral impalpable testis. Surgical treatment of higher impalpable testes is demanding and complex. Because approximately 20% to 40% of impalpable testes will ultimately prove to be absent, a properly planned exploration is the initial step. This may be done through an inguinal skin crease incision with intraperitoneal extension if necessary or by initial laparoscopy. If the testis is absent, the exploration may be terminated and a testicular prosthesis may be placed. The solitary contralateral descended testis should be "protected" by performing a scrotal orchidopexy to minimize the risk of potential subsequent testis torsion. If a testis is found to be present, a variety of open surgical techniques are available. The "testis stretch" maneuver done at the onset of the evaluation is critical in determining which technique of orchidopexy to use. Experience indicates that a "radical" high retroperitoneal dissection is often successful in descending testes, which seem initially to require more extensive procedures. If this is not feasible, a single-stage procedure sparing division of the spermatic vessels is preferred. If deliberate testis vessel transection is required, extensive previous high dissection must be avoided to prevent disruption of the collateral vessels accompanying the vas deferens. Considerable experience is necessary at this point in surgery because there are no guidelines described.



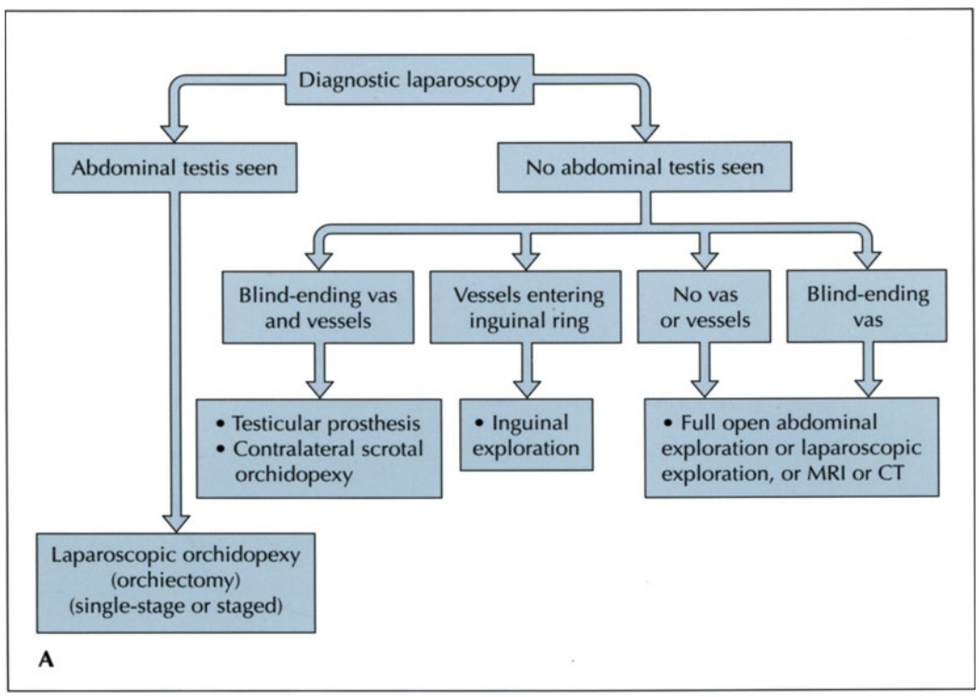




D. Open Surgical Techniques for Orchidopexy of High Undescended Testis

High retroperitoneal dissection
Intraperitoneal extended mobilization
Spermatic vessel transection
  Single stage
  Staged
  With microvascular anastomosis

◗ **FIGURE 8-15.** Choices of surgical procedures for patients with high undescended testes. After the testis is identified, the critical "testis stretch maneuver" is done by taking a traction suture through the testis capsule and putting the testis on stretch before any mobilization. This maneuver offers a subjective assessment of testis mobility and vessel length, enabling the surgeon to choose between a variety of open surgical techniques. These vary significantly from the standard inguinal orchidopexy used for those with palpable undescended testes and include high retroperitoneal dissection, intraperitoneal extended mobilization, and spermatic vessel transection (single stage or staged) with or without microvascular anastomosis. **A** to **C**, Three different examples of the "testis stretch" maneuver as the initial determinant of choice of procedure. **D**, Surgical techniques for orchidopexy of high undescended testis.



◗ **FIGURE 8-16.** Diagnostic laparoscopy for impalpable undescended testes. **A**, Laparoscopic diagnosis and treatment of impalpable undescended testes. **B**, Laparoscopic findings in 432 impalpable testes. A recent collation of five published series (432 impalpable testes) indicates the frequency of laparoscopic findings in this situation. Testes were present about one half of the time (n=241 [55%]) and absent one half of the time (n=191 [45%]). When present, 27% (n=118) were intra-abdominal and 28% (n=123) were inguinal. When absent, 9% (n=38) were intra-abdominal "vanishing" (*ie*, represented by a scar or blind-ending intra-abdominal spermatic vessels with or without a vas deferens), 34% (n=148) were inguinal "vanishing," and 1% (n=5) demonstrated no vas deferens or vessels at all [8].

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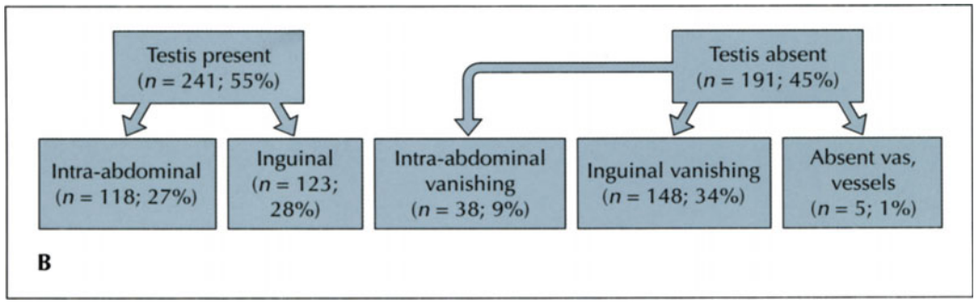
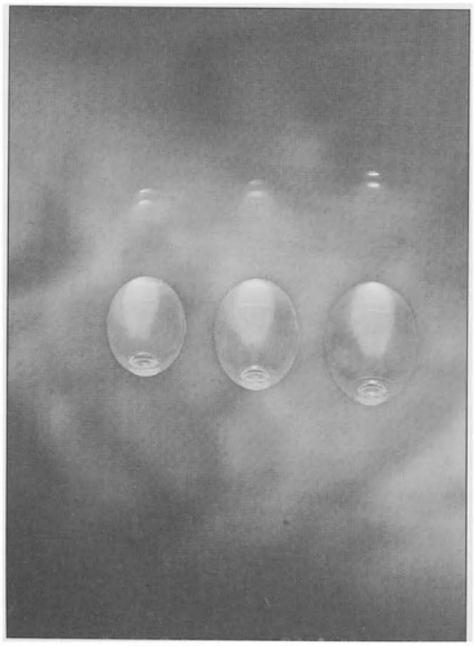


◗ **FIGURE 8-16.** (*Continued*) Laparoscopy immediately indicates whether an abdominal testis is present or not. If present, a single-stage or staged laparoscopic orchidopexy may be accomplished. For the former, two additional trocars are introduced, the peritoneum is incised, and the testis is mobilized. The optical magnification present complements the precise vessel dissection needed in managing these high abdominal testes. If the vessels are short, single-stage clipping and vessel transection can be done, providing that the collateral blood supply is adequate along the vas deferens. If any doubt exists, the vessels may be clipped before mobilization and a staged laparoscopic return may be done several months later, allowing adequate time for collateral vasal vesssel hypertrophy. Presently, the overall laparoscopic experience has been favorable, but there are indications that an overperformance of staged procedures and orchiectomy has occurred in the initial laparoscopic orchidopexy experience [29].



◗ **FIGURE 8-17.** Testis prostheses for absent testes. Testicular prostheses provide a cosmetic and psychologic benefit for boys with absent testes. Prosthesis placement in adolescent boys is essential and usually highly desired in this age group. Preadolescent placement in boys with absent testes is more controversial, but I personally recommend this approach. Early placement provides a sense of "normality" for the parents and, later, for the child. Scrotal growth and appearance are normal. In adolescence, the prosthesis is changed for an adult size.

In the past, testicular prostheses have been made with a silicone interior and an outer silicone shell, but more recent models are available with a saline-filled interior and a silicone envelope exterior. Health concerns regarding the safety of silicone testicular implants have not stood the test of scientific scrutiny. Additional risks of implantation, such as infection, hematoma, and extrusion, are uncommon. Testicular prostheses should not be implanted through a scrotal incision in prepubertal boys because the thin skin allows extrusion to occur more easily. (*Courtesy of* Mentor Corporation, Santa Barbara, CA.)

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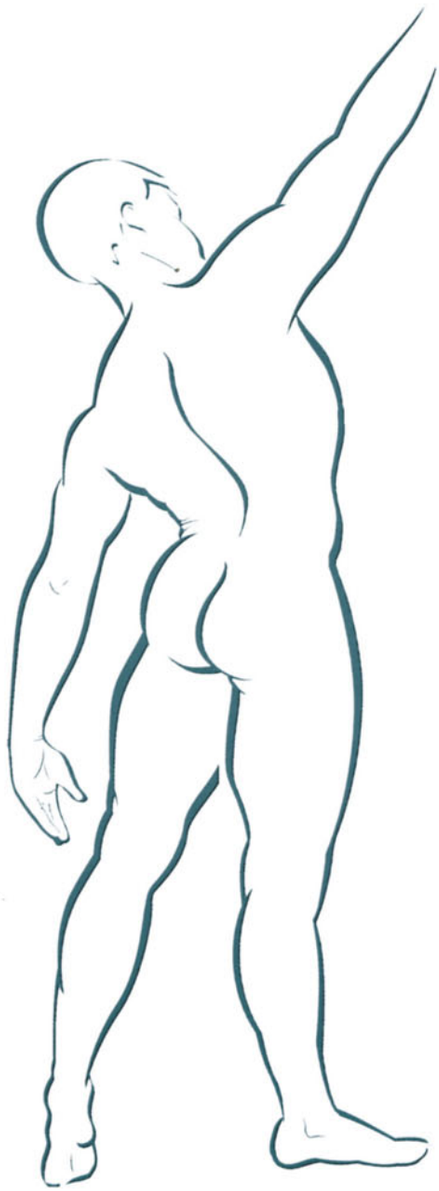
9

Urinary Tract Infections

William A. Kennedy II and Linda M. Dairiki Shortliffe



During the past 15 years, new imaging techniques and biologic probes have given further insight into the natural history and pathogenesis of urinary tract infections (UTIs) in children. UTIs are one of the common causes of fever in infants and young children. These infections are probably the most common cause for renal parenchymal loss in children. Thus, the goal of managing UTIs in children is based on the early identification of factors that may increase the risk of renal parenchymal and functional loss.

This chapter focuses on the host and bacterial mechanisms by which bacteria gain access to the bladder and kidney, examines the short- and long-term complications of renal infection, and discusses means of preventing renal damage. A detailed discussion is provided of the host and bacterial factors affecting the risk of bacteriuria and renal damage from UTIs in children. P-fimbriae and cell wall O antigens frequently characterize the bacteria responsible for bacteriuria and renal scarring. Whereas such bacterial virulence characteristics may increase the likelihood of any periurethral bacterial strain entering the urinary tract, there are also specific host characteristics that alter the risk of bacteriuria and subsequent renal damage. These factors include gender, periurethral colonization, uroepithelial adherence factors, age, preputial skin, and genitourinary tract anomalies.

Good urinary specimens with which to make the diagnosis of UTI may be difficult to obtain in children. Accurate methods of urinary specimen procurement are reviewed. Microscopic and chemstick urinary analysis findings are an adjunct to a definitive urinary culture in the diagnosis of a UTI in children. Guidelines for the interpretation of urine culture results are also discussed.

An algorithm for the effective use of radiologic imaging in the diagnosis and evaluation of UTIs is presented. The therapeutic strategy in managing children with UTIs is to first minimize renal damage at the time of the acute infection; the second is to minimize the risk of future renal damage from subsequent infections. This chapter also reviews current parenteral and oral antibiotics for acute treatment and outlines antibiotic prophylaxis for UTI prevention.

INCIDENCE AND EPIDEMIOLOGY

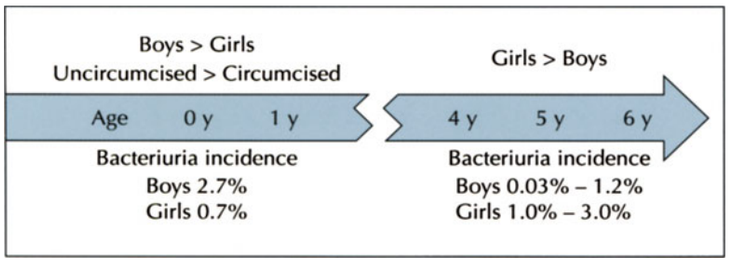


FIGURE 9-1. Incidence and epidemiology of pediatric urinary tract infections (UTIs). Boys are more likely than girls to get UTIs during the first year of life [1,2]; during this period, uncircumcised boys have as high as 10 times the risk as circumcised boys of having a UTI [3,4]. Approximately 2.7% of boys and 0.7% of girls have had bacteriuria by age 1 year [5]. This incidence decreases to less than 1% in school-age boys (ranging between 0.03% and 1.2% during the school year) but increases to 1% to 3% in school-age girls [6–8].

CLASSIFICATION

Characterization of Bacteria

Most common	Gram-negative Enterobacteriaceae (usually *E. coli*)
Serotypes	Cell wall O antigen serotyping:
	E. coli serotypes 01, 02, 04, 06, 07, and 075
Virulence factors	MRHA
	Presence of P-fimbriae

FIGURE 9-2. Characterization of bacteria infecting the urinary tract. The most common of these bacteria are the gram-negative Enterobacteriaceae, usually *Escherichia coli* [2,10,11]. Specific cell wall O antigens that can be identified by serotyping have shown that specific *E. coli* serotypes are associated with pediatric urinary tract infections (UTIs) [2,11].

Another bacterial trait that may increase its virulence for the urinary tract are surface structures called pili or fimbriae. The bacterial fimbriae mediate bacterial adherence to uroepithelial cells and red blood cell agglutination. Red blood cell agglutinating characteristics of *E. coli*, called hemagglutination, can be blocked by different sugars [12,13]. Using this characteristic, Källenius *et al.* [14] discovered that pyelonephritogenic *E. coli* cause mannose-resistant hemagglutination (MRHA) of human red blood cells. Characterization of this reaction showed that the terminal glycolipid of the human red cell P blood group antigen is a receptor that binds P-fimbriae on these *E. coli*. Therefore, two important markers for *E. coli* virulence are MRHA characteristics and P blood group–specific adhesins (P-fimbriae or P-pili) [14,15]. The importance of these two virulence markers has been supported by research examining their association with clinically diagnosed pyelonephritis and cystitis in the pediatric population [14,15].

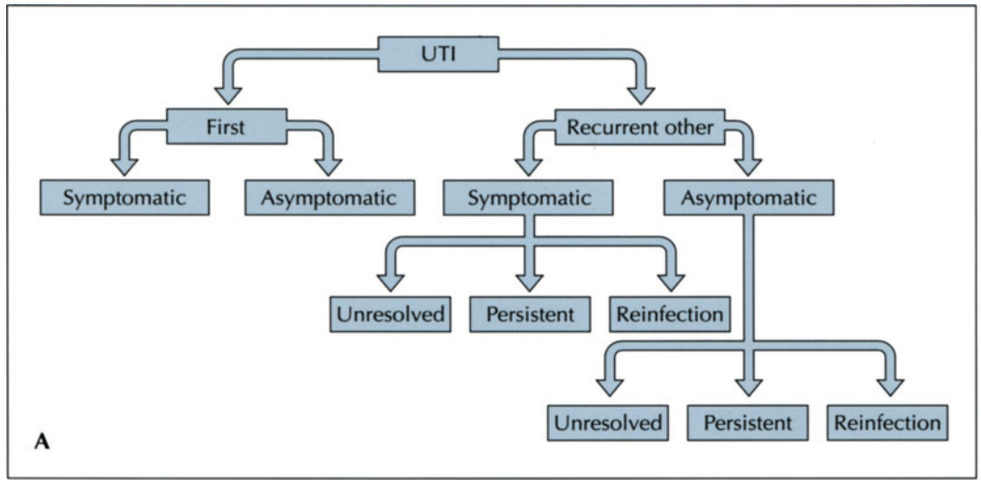


FIGURE 9-3. Classification of pediatric urinary tract infections (UTIs). **A,** For practical purposes, pediatric UTIs may be classified according to their evaluation and management: first infections and other (or recurrent) infections.

(*Continued on next page*)

B. Classification of Pediatric Urinary Tract Infections

First Infection	*Recurrent Bacteriuria*		
	Unresolved During Therapy	***Bacterial Persistence***	***Reinfection***
Complicated	Inadequate therapy Bacterial resistance Insufficient concentration of antimicrobial agent Proper culture and sensitivity required	GU anomaly harbors bacteria Infected kidney stones Infected nonfunctioning kidneys Infected ureteral stumps Vesicointestinal fistula Vesicovaginal fistula Infected necrotic papillae Unilateral medullary sponge kidney Infected urachal cyst Infected urethral diverticulum or periurethral gland	Majority of pediatric UTIs Same or different organism Reinfection rates Boys Age <1 y 18% Age >1 y 32% Girls Age <1 y 26% Age >1 y 40%

FIGURE 9-3. (*Continued*) **B,** Recurrent infections may be subclassified into three types [9]: 1) bacteriuria that remains unresolved during therapy, 2) bacterial persistence at an anatomic site, and 3) reinfections. Compared with adult UTIs, first urinary infections in infants and children should be considered complicated because of the management and treatment implications surrounding these infections.

Urinary tract infections may be unresolved because of inadequate therapy related to bacterial resistance to the selected therapeutic agent, inadequate antimicrobial urinary concentration caused by poor renal concentration or gastrointestinal malabsorption, or a multiple organism infection. Unresolved infections can usually be treated successfully after proper culture and antimicrobial sensitivity patterns are obtained. In infants and children, sources of urinary tract bacterial persistence are usually found as a result of prompt radiologic evaluation. The discovery of urinary tract sources of bacterial persistence that are surgically correctable are obviously important. Most UTIs are, however, reinfections with the same or a different organism. Girls are more likely to have recurrent infections than are boys [2].

Infections that are asymptomatic or covert as designated by Savage [8] and found only on screening urinary culture when a child is being examined for reasons unrelated to UTI can still be classified within these four types. GU—genitourinary.

FACTORS

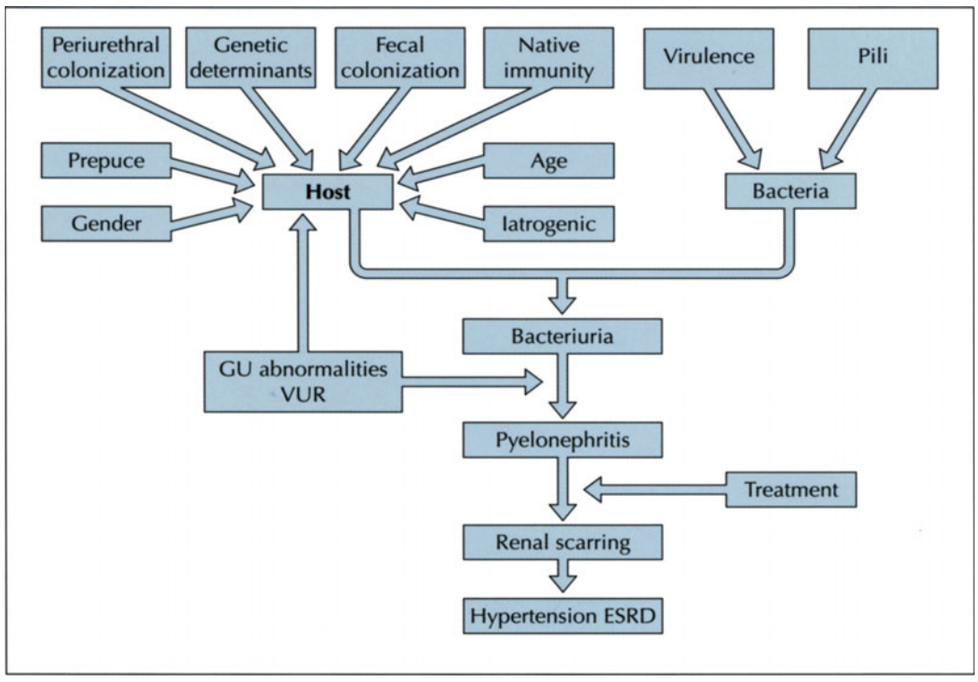


FIGURE 9-4. Factors affecting the natural history of urinary tract infections (UTIs). Host factors such as genetics, native immunity, gender, circumcision status, diet, and gut and periurethral colonization alter the course of UTIs in children. A child's risk factors and the bacterial virulence may predict the course of a UTI; however, these factors alone have not been useful in predicting which individuals will develop pyelonephritis, renal scarring, or parenchymal and functional loss from a single or recurrent urinary infection. About 3% of girls and 1% of boys will get a prepubertal UTI [2]; of these children, 17% or more will get infection-related renal scarring. Of those with scarring, 10% to 20% will become hypertensive, and a rare child will develop progressive renal dysfunction culminating in end-stage renal disease (ESRD). GU—genitourinary; VUR—vesicoureteral reflux.

Symptoms of Urinary Tract Infection

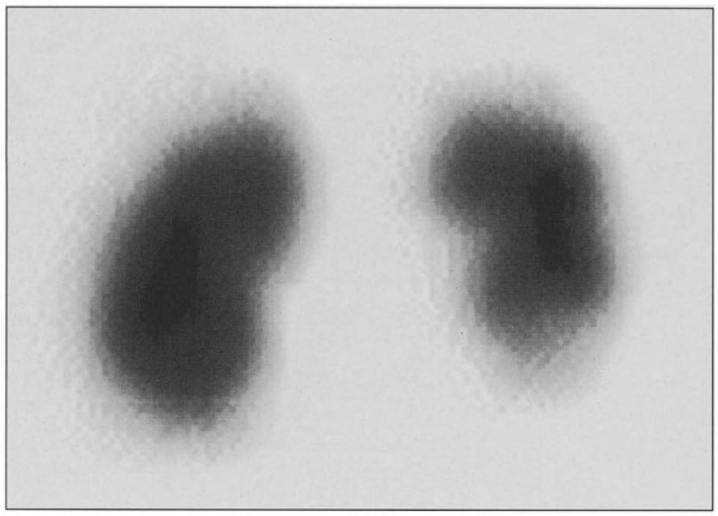
Symptom	*Patients, %*
Fever	67
≥38	100
≥39	57
Irritable	55
Poor feeding	38
Vomiting	36
Diarrhea	31
Abdominal distention	8
Jaundice	7

◗ **FIGURE 9-5.** Symptoms of urinary tract infection (UTI). UTIs are common causes of pediatric bacterial infections [16–18]. Febrile episodes account for about 20% of pediatric office visits [19], and UTIs are the cause in about 4.1% to 7.5% of these cases. In children younger than age 2 years, symptoms of UTI are vague and generalized: fever, irritability, poor feeding, vomiting, diarrhea, and ill-appearance [20]. Specifically, in febrile infants from birth to 8 to 10 weeks of age, neither clinical symptoms nor laboratory tests can be used to predict a presumptive UTI nor eliminate likelihood of a UTI even if other sites of infection are suggested clinically [17]. Older toilet-trained, talking children may indicate signs that better localize to the urinary tract, such as dysuria, suprapubic pain, voiding dysfunction, or incontinence, but many of these children still do not describe urinary tract symptoms.

Diagnosis of Pyelonephritis

Test	*Ability to Diagnose*
Clinical symptoms	+/-
Fairley test	+
Stamey test	++
DMSA scan	+++

◗ **FIGURE 9-6.** Diagnosis of pyelonephritis. The progression from cystitis to pyelonephritis and the relationship between these entities is difficult to determine because simple techniques with which to localize the level and extent of urinary tract bacteria are lacking. Although ureteral catheterization has been the gold standard for localizing upper and lower tract bacteriuria, this requires invasive cystoscopy and is an impractical way of following the course of infection [21]. The Fairley bladder washout localization technique requires urethral catheterization during acute infection and washing the bladder with sterile water to determine whether the source of bacteria is from the bladder or supravesical. In localization studies using the Fairley or ureteral catheterization techniques, however, clinical symptoms correlate poorly with location of bacteria. In one such study [22], fewer than half (47%) the patients with fever and flank pain had upper tract bacteria and almost 20% who were asymptomatic had upper tract bacteria. DMSA—dimercaptosuccinic acid.

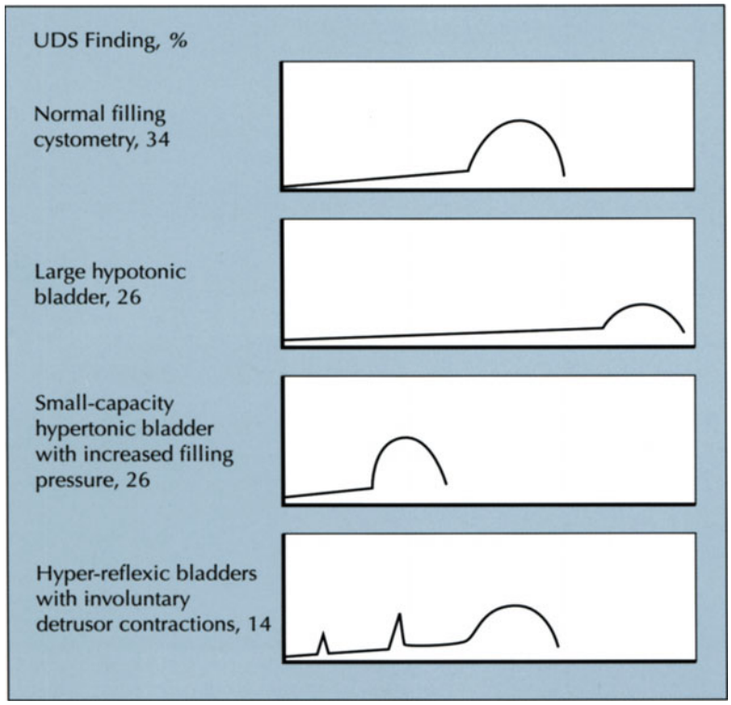


◗ **FIGURE 9-7.** Diagnosis of pyelonephritis using dimercaptosuccinic acid (DMSA) nuclear scan. Early renal cortical lesions from pyelonephritis can be detected by ^{99m}Tc DMSA nuclear scan. These lesions correlate with histopathologic areas of acute renal inflammation in animals; these models have advanced our knowledge of the natural history of urinary tract bacteriuria [23–26]. When DMSA lesions are used as the standard for diagnosing acute pyelonephritis, about 50% to 86% of children (about 60% of kidneys) with febrile urinary tract infections (UTIs) and other clinical signs have pyelonephritis [27–30]. About half (40% to 75%) of these lesions persist on DMSA scans performed 2 months to 2 years later [27,29], suggesting that as many as 40% to 50% of children with febrile UTIs develop renal scars.

Urinary Tract Anomalies Associated with Infection

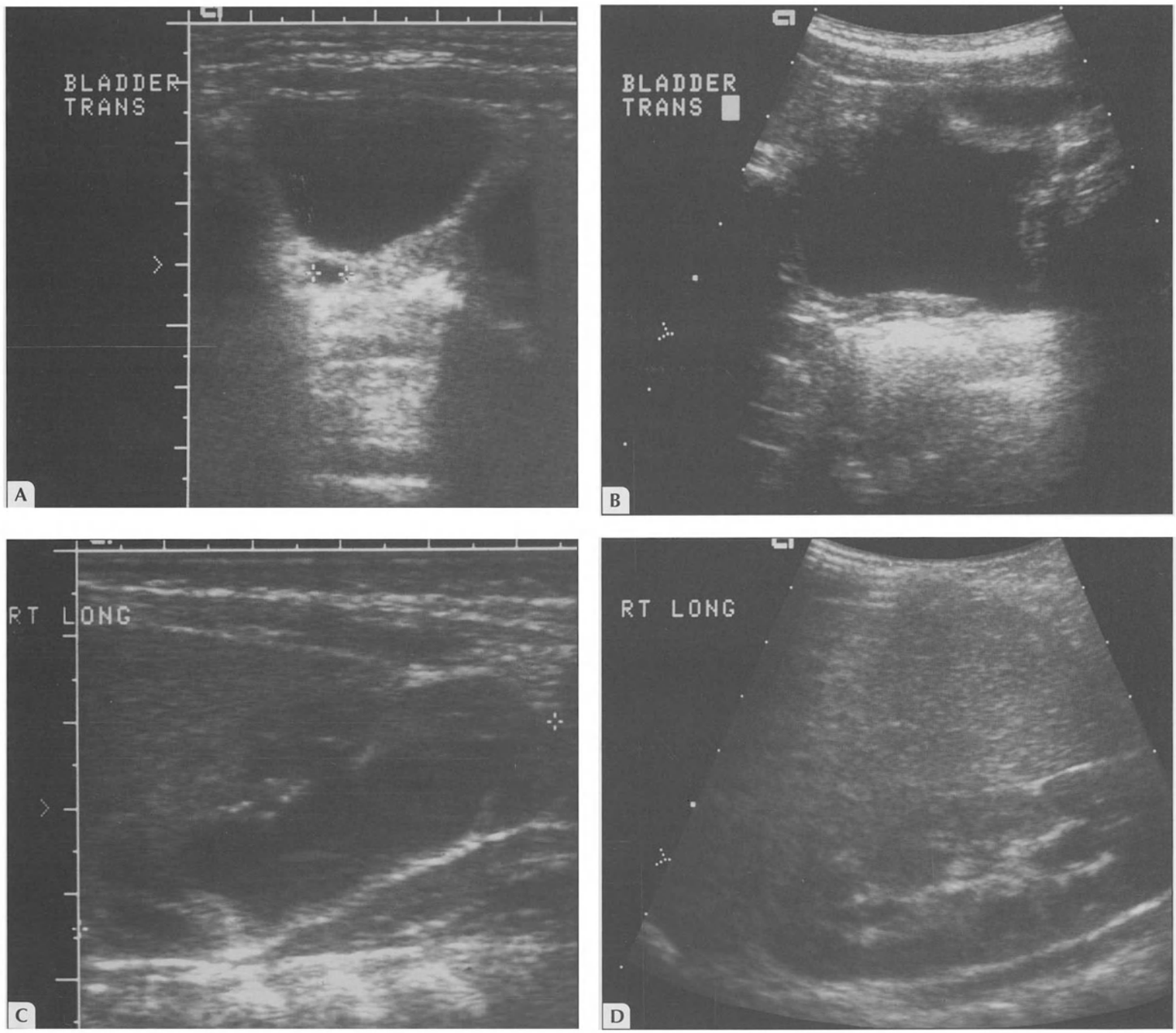
Anomaly	*Simple UTI, %*	*DMSA + Pyelonephritis, %*
VUR	21–57	25–83
Obstructive lesions	5–10	—

◗ **FIGURE 9-8.** Urinary tract anomalies associated with infection. Children with urinary tract infections (UTIs) have an increased incidence of both obstructive urinary tract lesions and vesicoureteral reflux (VUR) [1,2,11,31,32]. Children with febrile UTIs and reflux have a high incidence of acute dimercaptosuccinic acid (DMSA) defects. Whether these acute defects result in scars is still debatable, but the risk of scarring increases with grade of reflux [33]. Older investigations have documented scars in 5% to 20% of kidneys with grade 1 reflux and in 50% or more of kidneys with grade 5 reflux [34–36]. Conversely, when renal scarring is used as the index and children with renal scarring are examined, about 60% have VUR [1,8,32,37]. In 25% of children with renal scarring, the urinary tract is normal [37]. These data confirm that VUR is only one factor involved in the ascent of bacteria into the kidney and the subsequent risk of renal scarring.



◗ **FIGURE 9-9.** Urodynamic test (UDS) results in normal children with recurrent urinary tract infections (UTIs). Symptoms of nocturnal and diurnal incontinence are common in children with recurrent UTIs. Epidemiologic studies have shown that nocturnal enuresis alone is unassociated with UTIs but that diurnal enuresis or a combination of diurnal and nocturnal enuresis is associated with pediatric UTIs [38]. Girls who were 3 years of age or older when they had their first UTI were more likely to have symptoms associated with voiding dysfunction than those who had UTIs when younger than age 3 years [38]. Approximately 20% of children who experienced recurrent UTIs developed new diurnal enuresis with the onset of theses recurrent infections [39].

Urodynamic testing in neurologically normal children with recurrent UTIs and incontinence has shown abnormal cystometry and voiding patterns [38,40–46]. Bauer *et al.* [40] found that 34% had normal filling cystometry, 26% had large hypotonic bladders, 26% had small capacity hypertonic bladders with increased intravesical filling pressure and sustained uncontrolled detrusor contraction at a low volume, and 14% had hyperreflexic bladders showing uninhibited detrusor contractions during filling. Voiding dysfunction has also been described with staccato (*ie*, interrupted) urinary flows during voiding, showing increased pelvic floor activity during voiding with resulting incomplete bladder emptying [38,40,45,47,48]. Many of these children also have bowel dysfunction with constipation [49]. These findings do not establish causality between UTIs and voiding dysfunction; however, UTIs may initiate symptoms of bladder dysfunction with variable persistence. In some situations, treatment of constipation or voiding abnormalities (or both) has resulted in a decreased frequency of UTIs [40–43,47–50]. (*Adapted from* Bauer *et al.* [40].)



◗ **FIGURE 9-10.** The effect of bacterial infection on urinary tract urodynamics. Although acute renal infection can be caused by hematogenous dissemination, it is generally accepted that the vast majority of human urinary tract infections (UTIs) are caused by periurethral bacteria ascending into the urinary tract [51]. The bacteria then infect the bladder, ureter, renal pelvis, and kidney. Research has emphasized the importance of pyelonephritis because of the potential renal damage; however, bacterial infection of the collecting system also causes bladder and ureteral inflammation and changes that alter urinary tract urodynamics [52,53]. The mechanism of ureteral dilatation observed during acute infection is unclear; animal studies show that UTIs can cause abnormally elevated renal pelvic pressures even if (or especially if) vesicoureteral reflux is absent [54]. This supports the clinical observation that infection with certain pyelonephritogenic *Escherichia coli* may cause the temporary ureteral dilatation seen in children with acute pyelonephritis and otherwise normal upper collecting systems [55]. **A,** Acute UTI in the bladder. **B,** The bladder after infection. **C,** Acute UTI in the kidney. **D,** The kidney after infection.

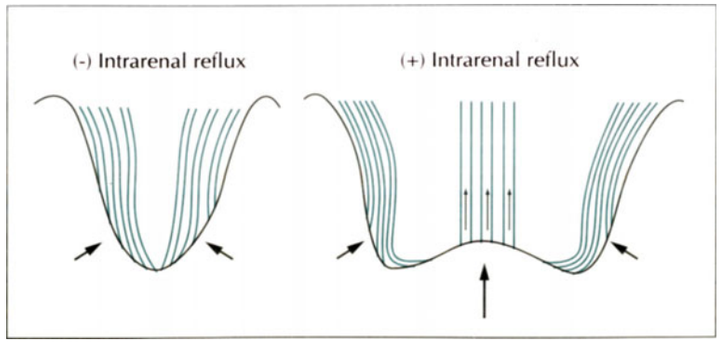


FIGURE 9-11. Pathogenesis of bacteriuria and renal scarring. Children's kidneys scar more frequently than adults' kidneys. Renal scarring appears to be affected by at least five factors: 1) intrarenal reflux, 2) urinary tract pressure, 3) host immunity, 4) age, and 5) treatment. In 1974, Rolleston *et al.* [56] found that areas of renal scarring were associated with foci of intrarenal reflux (*ie*, pyelotubular backflow) observed on voiding cystourethrography in children younger than age 4 years who had vesicoureteral reflux. Calyces allowing reflux contained papillae fused with adjacent papillae that caused the papillary ducts to open at right angles rather than at oblique angles more resistant to reflux [57]. These compound papillae were found most commonly at the renal poles, the areas in which clinical renal scarring is most commonly observed clinically [58]. (*Adapted from* Ransley [133].)

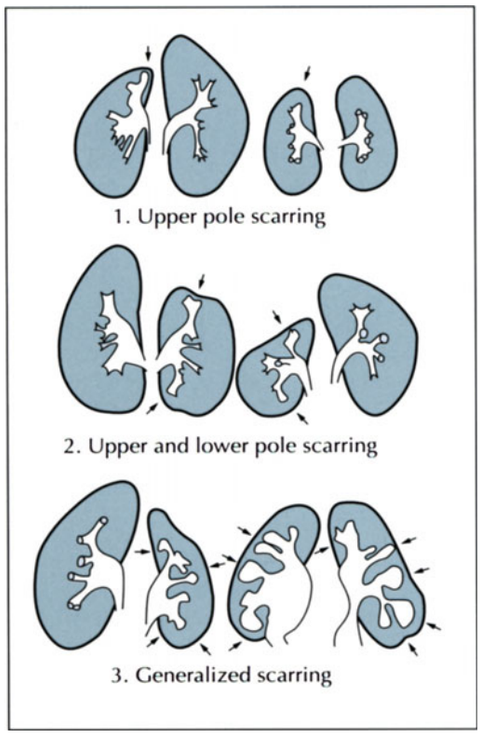


FIGURE 9-12. Patterns of renal scarring. Renal scarring occurs only when both vesicoureteral reflux (VUR) and bacteriuria are present [57]. Reflux alone without bacteriuria resulted in renal scarring only if the urethra was partially obstructed, causing abnormally high voiding [59,60]. Experimentally, therefore, the water hammer effect of VUR and intrarenal reflux caused renal scarring only if reflux occurred with abnormally high bladder and renal pressures.

Renal scarring is characterized by parenchymal thinning over a deformed calyx as examined from intravenous pyelograms. The extent of scarring may be related to single polar scars; multiple areas of upper, lower, and medial scars; or generalized scarring, as depicted. (*Adapted from* Hodson [134].)

Risk Factors for Renal Scarring in Young Children

Factor 1	Neonatal kidneys are more susceptible to the water hammer effect
Factor 2	Incompletely developed immune system
Factor 3	Vague symptoms = delay in treatment

FIGURE 9-13. Risk factors for renal scarring in young children. Several factors suggest that the kidneys in young children are at greatest risk of renal scarring from bacterial pyelonephritis. First, the neonatal kidney may respond in different ways than the adult kidney to urinary backpressure and the water hammer effect and at different thresholds. Studies on normal neonates (children younger than age 1 month) reveal that whereas intrarenal reflux into compound calyces may be created at low pressures of 2 mm Hg, the same reflux in a child 1 year old occurs at 20 mm Hg. Furthermore, in autopsy studies of children younger than age 12 years, intrarenal reflux occurs in all calyces, even simple ones, at 50 mm Hg [74]. This suggests that physiologically normal urinary intrapelvic pressures in adults or older children may be abnormally high in neonates. This effect may be augmented by increased renal pelvic pressures that may result from ureteral and pelvic smooth muscle dysfunction [54]. Second, very young children have incompletely developed immune and neurologic systems, which may allow bacteria to more easily colonize the bladder and kidney. Neurologic immaturity of the bladder may allow frequent uninhibited bladder contractions to transmit their pressures to the upper tracts in even apparently normal children [75]. Bacteriuria combined with reflux in these children may result in greater susceptibility to renal damage. Third, neonatal symptoms of urinary tract infection and pyelonephritis are often vague and nonspecific, resulting in delayed or inadequate treatment.

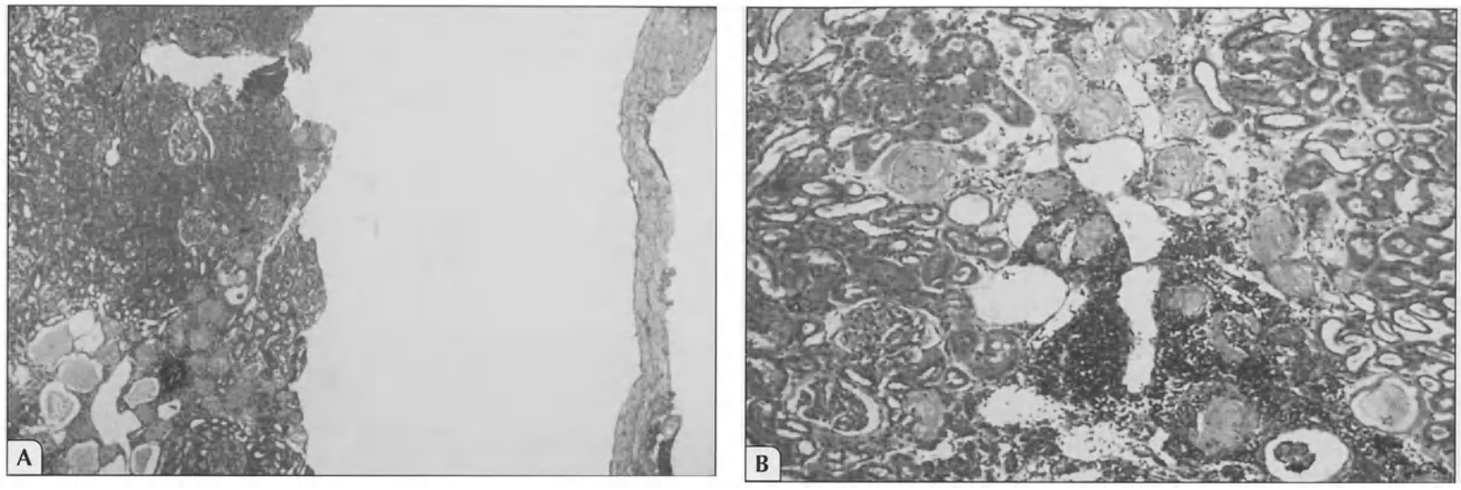


FIGURE 9-14. (*See Color Plate*) Microscopic changes associated with urinary tract infections (UTIs). Renal infection stimulates both humoral and cellular immune responses. In experimental rat models of pyelonephritis, maximal renal suppuration and exudation with inflammatory infiltration occurs 3 to 5 days after the infection starts [61–66]. During the acute inflammatory infiltration, granulocytic aggregation may cause vascular occlusion and ischemia with elevation in renin [67,68]. In addition, bactericidal activity of the neutrophils and the release of enzymes, superoxide, and oxygen radicals may cause the renal tubular damage observed in those with pyelonephritis [69]. Proximal and distal tubular dysfunction results, causing reduced urinary concentrating ability [70], with increased fractional sodium excretion, decreased phosphate reabsorption, and increased low molecular weight protein excretion [71]. Clinical studies [72] have correlated decreased renal concentrating capacity with severity of renal scarring. Increased urinary retinol-binding protein (RBP, a tubular protein giving evidence of tubular dysfunction) excretion has been correlated with the severity of renal scarring. Increased excretion of *N*-acetyl-B,D-glucosaminidase (NAG, an excretory protein indicating tubular damage) and albumin correlates mainly with bilateral renal scarring in children. These data suggest that tubular dysfunction occurs before glomerular dysfunction and commonly occurs in children with bilateral renal scarring [73].

A, Low-power microscopic examination of a renal biopsy with the renal capsule separated from underlying tissue secondary to fixation and underlying hyalinized glomeruli, atrophic tubules, thickened arterioles, and diffuse chronic inflammatory cell infiltration (magnification reduced from 40 ×). **B,** High-power microscopic view of the area below the capsule in **A** with hyalinized glomeruli and diffuse chronic inflammatory infiltrate (magnification reduced from 400 ×).

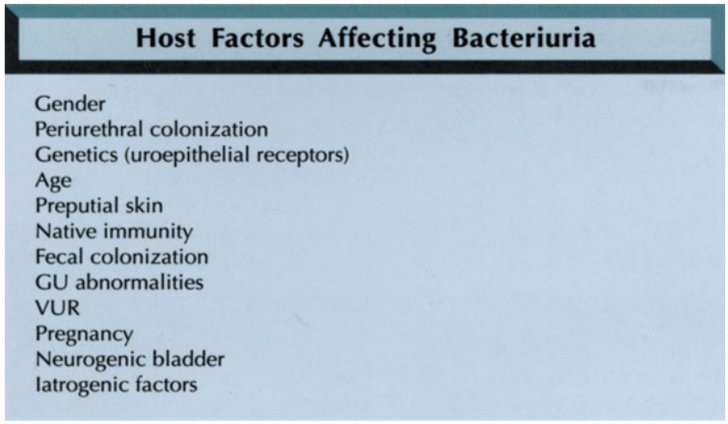
Signs of Pyelonephritogenic Nephropathy

Elevated plasma renin levels
Significant proteinuria
Glomerular sclerosis
Interstitial deposits of Tamm-Horsfall protein

FIGURE 9-15. Signs of pyelonephritogenic nephropathy. There are several biochemical and histologic correlates of pyelonephritogenic nephropathy. The renin–angiotensin system is probably involved. Plasma renin activity has been followed in children with reflux nephropathy who have been surgically corrected. A single elevated plasma renin activity level at the time of surgery did not predict hypertension 5 years later [76]. However, the normal tendency for the plasma renin activity to decrease with increasing age was not seen; instead, the opposite was observed: plasma renin activity increased with age and the standard deviation increased [77].

For more than a decade, glomerular lesions and progressive proteinuria have been observed in patients who have renal scarring [78,79]. Significant proteinuria (>1 g/24h) has been a routine finding in patients with vesicoureteral reflux (VUR) and progressive deterioration in renal function [79]. Moreover, certain investigators [78,80,81] have found glomerular sclerosis in nonscarred, radiologically normal kidneys in cases of unilateral reflux nephropathy. Two theories—one involving progressive renal damage from hyperfiltration of remaining nephrons and the other involving progressive immunologic damage to the kidney—have been postulated as causes.

Another explanation for the progressive renal dysfunction involves a chronic inflammatory response that develops as an autoimmune phenomenon. Although Tamm-Horsfall protein normally is found only in the urine and on the luminal side of the tubules, both clinically and experimentally the protein has been detected in interstitial deposits in kidneys that have been subject to infection or reflux and has been associated with mononuclear cell infiltrates and renal scarring [82]. This protein may account for findings of renal dysfunction or scarring associated with urinary VUR without known infections, and the autoimmune response related to it may also provide a reason why chronic or progressive renal damage occurs long after cessation of reflux or active infections [82].



◗ **FIGURE 9-16.** Host factors affecting bacteriuria. Although bacterial virulence characteristics may increase the likelihood that any periurethral bacterial strain will enter the urinary tract, there are specific host characteristics that alter risk of bacteriuria and subsequent renal damage.

As discussed previously, the ratio of urinary tract infections (UTIs) by gender shows a preponderance of infections in boys during the first year of life. Thereafter, more girls than boys have UTIs. It is known epidemiologically that the incidence of UTIs for all babies is higher during the first few weeks to months than at any subsequent time in the next few years. During this time, the periurethral area of healthy girls and boys is massively colonized with aerobic bacteria (especially *Escherichia coli*, enterococci, and staphylococci) [83]. Increased periurethral colonization is associated with increased risk of UTIs.

Glycolipids characterizing the P blood group system [84] may facilitate the adherence of bacterial P-fimbriae and cause increased bacterial colonization of the uroepithelium. Other blood group antigens on the urothelial surface (ABO, Lewis and secretor phenotypes) appear to also influence susceptibility to UTIs [85].

Age also affects the incidence of bacteriuria. Bacteriuria appears to be more common at the extremes of life (*ie*, in newborns and the elderly). The incidence of bacteriuria for both males and females younger than age 1 is higher than at other times during childhood.

The preputial skin may also affect the incidence of bacteriuria. During the first few months of life, there seems to be a connection between UTIs and the foreskin, periurethral, and preputial colonization. Although the reasons for this neonatal bacterial colonization of the foreskin may be related to interactive factors, including early immune status, unusual nosocomial colonization, breastfeeding [86], and other characteristics mediating bacterial adherence [87], this higher colonization is associated with a greater number of neonatal UTIs. In a series of retrospective reviews at US Army Hospitals, Wiswell and Roscelli [88] found that the incidence of infections in circumcised male infants was 0.11%; the incidence was 1.12% in uncircumcised infants and was 0.57% in female infants. The majority of infections occurred during the first 3 months of life. When the incidence of infections during the first and the final years of the study were compared, the total number of UTIs increased as the circumcision rate decreased [88,89], and Wiswell and Roscelli [88] concluded that UTIs were more frequent in uncircumcised boys. Although there may be difficulties with these data related to retrospective analysis and selection bias, periurethral colonization has been associated with increased risks of UTIs in girls and women as well. There is no evidence that prophylactic circumcision after a neonatal UTI will prevent future infections in boys.

Another factor is native immunity. The influence of the host's native cellular and humoral immunity on risk of UTI is unknown, but UTIs are common in infants and young children during a time that their immune system is incompletely developed. For example, serum IgG is lowest between age 1 and 3 months [90], when periurethral colonization is high in normal children. Secretory IgA, moreover, is an important human immunoglobulin at the secretory and mucosal surface and may be transferred to newborns in colostrum if the child is breastfed. Serum IgA is found in diminished concentrations for the first several months of life and is either absent or almost absent at the secretory surfaces of the nasopharynx, gut, and urothelium during this time [91–93]. The benefits of breast milk in preventing infection in infants have been expounded for some time, but it is unclear whether its effect is related to colostrol IgA or other factors. Children with specific immune deficiency syndromes have altered immunity and often have increased risk of bacteriuria and progression of infection. About 20% of HIV-infected children develop bacterial UTIs with both common and opportunistic organisms [94].

Another factor is fecal colonization. The human fecal flora depends on surrounding microbial ecology, native immunity, and microbial-altering drugs and foods. The importance of abnormal fecal colonization in neonates is emphasized by studies [95] showing that fecal colonization with specific pyelonephritogenic bacteria may occur in a neonatal nursery or hospital with subsequent bacteriuria or pyelonephritis occurring several months later.

Genitourinary (GU) anatomic abnormalities also affect the incidence of bacteriuria. Historically, UTIs have been markers for GU tract anatomic abnormalities in children. Specific GU abnormalities, especially nonfunctioning segments, may serve as a nidus of bacterial infection and cause bacterial persistence because of the difficulty in achieving urinary antimicrobial concentrations adequate to treat UTIs in a poorly concentrating renal segment. Similarly, conditions of GU partial obstruction or renal functional impairment may create increased risk of renal damage because of poor or inadequate treatment. Several special conditions that may alter a child's risk for UTIs include vesicoureteral reflux (VUR), pregnancy, and neurogenic bladder.

VUR is common in children with UTIs, but no correlation between reflux and susceptibility to UTIs has been found [2]. Epidemiologic surveys have shown that 21% to 57% of children who have had bacteriuria are subsequently found to have VUR [1,11,31,32].

Primary VUR that persists as a girl approaches puberty becomes statistically less likely each year to spontaneously resolve. For this reason, some have recommended that girls approaching puberty undergo surgical correction of VUR to avoid the risks of pyelonephritis during future pregnancies. Whether these girls are actually at increased risk of morbidity and should undergo routine correction of VUR is unclear. Although the prevalence of bacteriuria in pregnant women is the same as that in nonpregnant women [96], the likelihood that the bacteriuria may progress to pyelonephritis is greatly increased. Between 13.5% and 65% of pregnant women who are bacteriuric on a screening urinary culture will develop pyelonephritis during pregnancy if left untreated [97]; uncomplicated cystitis in nonpregnant women rarely progresses to pyelonephritis. The reason for this increased risk of pyelonephritis may be related to the hydronephrosis of pregnancy that occurs from hormonal and mechanical changes. Increased compliance of the bladder and collecting system, bladder enlargement, and an enlarging uterus may cause some anatomic displacement of the bladder and ureters [98].

Children who have neurogenic bladders with abnormally elevated bladder pressures risk increased renal damage from UTIs from the elevated urinary tract pressures and the increased use of instruments common with the condition. A neurogenic bladder with chronically or intermittently elevated bladder pressures may cause secondary VUR from decompensation of the ureterovesical junction from the elevated pressure [99]. If this does not occur, the elevated bladder pressures associated with a neurogenic bladder may also cause effective ureterovesical obstruction. This obstruction increases the risk of renal damage associated with UTIs. Intermittent elevations in bladder pressure associated with physiologic bladder dynamics in the immature bladder may exacerbate VUR and the risks associated with it.

(*Continued on next page*)

FIGURE 9-16. (*Continued*) Iatrogenic factors may also affect the incidence of bacteriuria. Although there are no good data regarding risk of catheter-induced infections in children, the incidence of catheter-induced UTI in adult women ranges from 1% to 20%, depending on the circumstances of catheterization [21]. It has been documented [100,101] that nosocomial UTIs frequently complicate hospitalization in children, especially when urethral catheterizaton has taken place. Children who develop hospital-acquired UTIs, have urinary tract abnormalities, have recently been instrumented, or have had recent antimicrobial treatment are more likely to have infections caused by unusual and more antibiotic-resistant organisms [102].

URINALYSIS

Urinary Specimen Procurement

Plastic bag
Midstream void
Urethral catheter aspirate
Suprapubic bladder aspirate

FIGURE 9-17. Urinary specimen procurement. With children, it may be difficult to obtain good urinary specimens with which to make the diagnosis of UTIs. The reliability of the diagnosis is related to the quality of the specimen. There are four routine ways to obtain urinary specimens in children. They are listed in order of least to most reliable for UTI diagnosis [103]: 1) plastic bag attached to the perineum (*ie*, a bagged specimen, 2) midstream void, 3) catheterized, or 4) suprapubic bladder aspirate.

Even after extensive skin cleansing, a plastic bag specimen usually reflects the perineal and rectal flora and often leads to indeterminate results. Although a midstream-voided specimen in a circumcised boy, older girl, or older uncircumcised boy who can retract his foreskin may reliably reflect bacteriuria, such specimens obtained in young girls and uncircumcised boys usually reflect periurethral and preputial organisms and cells. A catheterized specimen is reliable if the first portion of urine that may contain urethral organisms is discarded and the specimen is taken from later flow through the catheter; however, this has the disadvantages of being traumatic and potentially introducing urethral organisms into a sterile bladder [100,101]. The most reliable urinary specimen for culture is obtained by suprapubic bladder aspiration. This can be performed safely in children and even premature infants with a full bladder by cleansing the skin and percutaneously introducing a 21- or 22-gauge needle 1 to 2 cm above the pubic symphysis until urine is obtained by aspirating into a sterile syringe [104]. Organisms present in a suprapubic aspirate are pathognomonic of bacteriuria.

A. Determinations from Urinalysis Supporting the Diagnosis of Urinary Tract Infections

Pyuria	Microscopic analysis
Bacteriuria	Microscopic analysis
Urine leukocyte esterase	Chemical dip analysis
Urinary nitrate	Chemical dip analysis

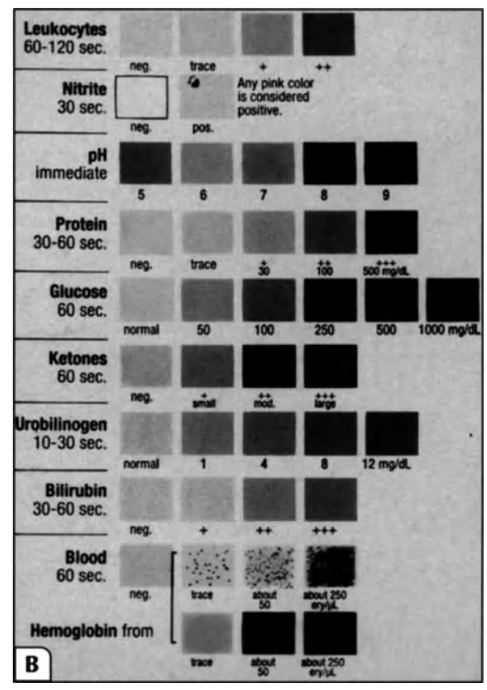


FIGURE 9-18. (***See Color Plate***) Urinalysis. **A,** Determinations from urinalysis supporting the diagnosis of urinary tract infections (UTIs). Quantitative urinary culture is the gold standard for the diagnosis of UTIs. Because it may take 24 or more hours before bacterial colony-forming units (CFUs) grow and the culture is complete, indirect urinary tests may be performed with routine urinalysis to detect the presence of bacteria or byproducts. Four determinations from the urinalysis have been advocated as useful for supporting a diagnosis of UTIs: 1) microscopic urinary examination for white blood cells (pyuria), 2) microscopic urinary examination for bacteria, 3) urinary leukocyte esterase, and 4) urinary nitrite.

B, Identification of components in urine. Although there are many confounding factors, the microscopic identification of bacteria in the urine is generally more sensitive and specific for diagnosing UTIs than for identifying pyuria [105,106]. Urinary leukocyte esterase detects urinary esterases produced by the breakdown of white cells in the urine, so it depends on the presence of white cells that may or may not be present with the infection. The test may be less reliable in infants [107]. Dietary nitrates that are reduced to nitrite by many gram-negative urinary bacteria may be measured by the urinary nitrite test. Serious drawbacks of this test are that bacterial reduction to nitrates may take several hours, making the test most useful only on first morning voided specimens. Most gram-positive bacteria do not perform this reduction. These tests are more unreliable when the bacterial count is below 100,000 CFU/mL. (Part B courtesy of Boehringer Ingelheim Gmbh, Germany.)

Culture Criteria for Urinary Tract Infection Diagnosis

Method of Collection	*Colony Count (Pure Culture)*	*Probability of Infection*
Cleanly voided (male)	$>10^4$	Infection likely
Cleanly voided (female)	Three specimens: $>10^5$	95%
	Two specimens: $>10^5$	90%
	One specimen: $>10^5$	80%
	5×10^4–10^5	Suspicious; repeat
	$1–5 \times 10^4$	Symptomatic
	$1–5 \times 10^4$	Suspicious; repeat
	$<10^4$	Asymptomatic
		Infection unlikely
		Infection unlikely
Catheterization	$>10^5$	95%
	10^4–10^5	Infection likely
	10^3–10^4	Suspicious; repeat
	$<10^3$	Infection unlikely
Suprapubic aspirate	Gram-negative bacilli: any number	>99%
	Gram-positive cocci: >few thousand	>99%

◗ **FIGURE 9-19.** Culture criteria for urinary tract infection (UTI) diagnosis. The technique by which the urinary specimen is collected is related to its reliability for UTI diagnosis [108]. Although ^{3}100,000 colony-forming units/mL (CFU/mL) of voided urine is the traditional definition for a clinically significant UTI [109], other studies [110,111] have shown that ^{2}10,000 CFU/mL or fewer organisms on a voided specimen may indicate a significant UTI. In febrile children younger than age 2 years, Hoberman *et al.* [107] showed that ^{3}50,000 CFU/mL in catheterized specimens constitutes a significant UTI.

PROPHYLAXIS

Antimicrobial Drugs Useful for Treating Pediatric Urinary Tract Infections

Parenteral

- Aminoglycosides
  - Gentamicin
- Penicillins
  - Ampicillin
  - Piperacillin
- Cephalosporins
  - Cefazolin
  - Cefotaxime
  - Ceftriaxone
  - Ceftazidime
- Other
  - Vancomycin

Oral

- Penicillins
  - Amipicillin
  - Amoxicillin
  - Augmentin
- Sulfonamides
  - Sulfisoxazole
  - Trimethoprim-sulfamethoxazole
- Cephalosporins
  - Cephalexin
  - Cefaclor
  - Cefixime
  - Cefadroxil
  - Cefprozil
- Other
  - Nitrofurantoin

◗ **FIGURE 9-20.** Antimicrobial agents useful for treating pediatric urinary tract infections (UTIs). The therapeutic strategy in managing pediatric UTIs is to first minimize renal damage during acutely diagnosed UTIs and then to minimize the risk of future renal damage from subsequent infections. Rapid recognition of a UTI and rapid, appropriate antimicrobial treatment are keys to preventing renal damage.

Treatment depends on the child's age and severity of illness. Parenteral broad-spectrum antimicrobial agents should be used to treat children younger than age 2 to 3 months with a presumptive UTI who look severely systemically ill or have a fever or flank or abdominal pain and are unable to take fluids. Immune-compromised children should also be treated with parenteral broad-spectrum antimicrobial agents. They should be considered for hospitalization or outpatient parenteral treatment depending on the child's clinical status. In appropriate infants and young children with presumptive UTIs who are taking fluids and have cooperative and reliable parents, some of the newer third-generation cephalosporins allow once-daily outpatient parenteral therapy. Parenteral treatment is generally continued for 2 to 4 days until the fever is gone and bacterial sensitivities are available and the child is clinically improved (afebrile and able to take fluids with sterile urine) to allow treatment with a drug with narrower spectrum. They may then be switched to an appropriate oral antimicrobial agent that attains adequate serum levels. Although the duration of treatment is debatable, the total duration of therapy has extended from 7 to 10 days in most studies involving treatment of young children with febrile UTIs.

Less ill older infants and young children who have presumptive UTIs and are capable of taking fluids and oral medicines may be treated with an antimicrobial agent that has a broad spectrum for genitourinary pathogens. Quinolones are useful because of their broader antimicrobial spectrum and special activity against *Pseudomonas aeruginosa*, but usage of this drug is limited in children because of studies showing quinolone-induced cartilage toxicity in young animals. With careful monitoring, limited quinolone usage has shown no cartilage-related toxicities, and an abnormal urinary tract with upper UTI with *P. aeruginosa* may be a potential indication for usage [112].

In school-age children who do not appear systemically ill and have a clinically uncomplicated bladder infection, many oral broad-spectrum antimicrobial agents that are well tolerated will cure the uncomplicated UTI in 3 to 5 days; there are no advantages to longer therapy [113–116]. In some of these children, single-dose treatment, particularly with intramuscular aminoglycoside, may be curative and cause less fecal antimicrobial resistance [117,118]; however, single doses may not be quite as effective as 3 to 5 days of treatment in unselected children [118,119].

Reasons for Urinary Tract Prophylaxis

VUR
Unstable urinary tract abnormality (*eg*, partial urinary tract obstruction)
Normal urinary tract but frequent reinfections
Awaiting radiologic evaluation after UTI
Urethral instrumentation
Clean intermittent catheterization
Immunosuppressed or immunocompromised
Infants with first UTI before age 8 to 12 weeks of life

◗ **FIGURE 9-21.** Reasons for urinary tract prophylaxis. Urinary prophylactic antimicrobial agents are effective in varying degrees in preventing bacteriuria under certain circumstances. In children, these agents are most commonly used to prevent urinary tract infections (UTIs) in the situations listed. VUR—vesicoureteral reflux.

Oral Antimicrobial Agents Useful for Pediatric Urinary Tract Prophylaxis

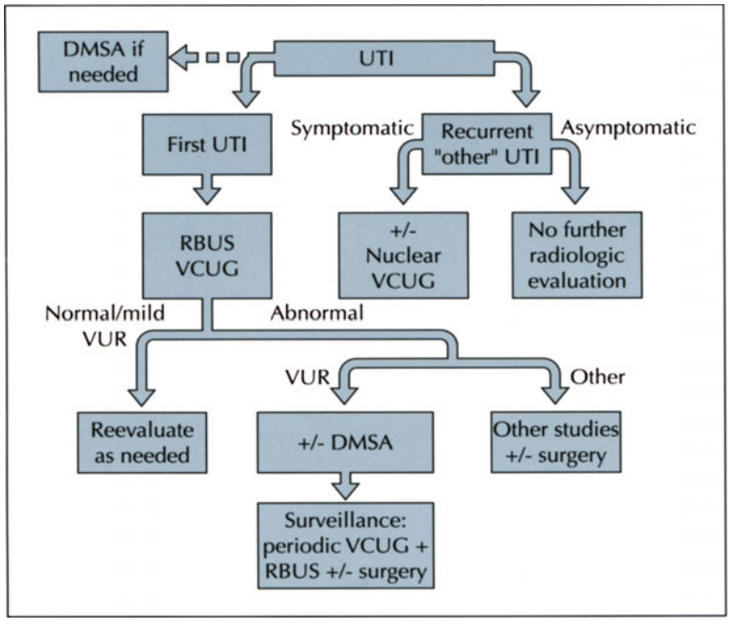
Drug	*Daily Dosage, mg/kg/d*	*Age Limitations, mo*
Useful and tested		
Nitrofurantoin	1–2	>1
Trimethoprim-sulfamethoxazole	2–3(trimethoprim) 2–3	>2
Cephalexin		
Possibly useful	5	
Amoxacillin	25–50	>2
Sulfisoxazole Trimethoprim	2	>2*

**Indicates few data.*

◗ **FIGURE 9-22.** Oral antimicrobial agents useful for pediatric urinary tract prophylaxis. The ideal prophylactic agent should have low serum levels, high urinary levels, and minimal effect on the normal fecal flora and be well tolerated and inexpensive. Because these agents are generally concentrated in the urine, the urinary drug levels should be much higher than the drug levels found simultaneously in serum, gut, or tissue, and if sufficiently low, antimicrobial resistance patterns should not develop in the gut. This characteristic of the prophylactic antimicrobial agents is most likely dose related, so inappropriately high dosing for prophylaxis is less effective because bacterial resistance will be created [120].

Doubling or tripling the dose of prophylactic antimicrobial agent each time a child develops the slightest symptom or cold may be, moreover, destroying the prophylactic value of the agent.

Because urinary prophylaxis is usually initiated after treatment of an infection for which long-term (10 days), high-dose treatment was given, the fecal flora may already be resistant to the treating drug and many of the prophylactic agents. Children who are very susceptible to urinary tract infections may then become reinfected with a bacteria resistant to the prophylactic agent before the gut is repopulated with more normal flora. This accounts for frustrating breakthrough infections that occur soon after a child is placed on prophylactic antimicrobial agents or after treatment of other frequent infections such as otitis media. For this reason, the treating antimicrobial agent should not necessarily be the prophylactic agent. In continent children, urinary tract prophylactic antimicrobial drugs should be given once nightly when they will be excreted into and remain in the urine overnight.



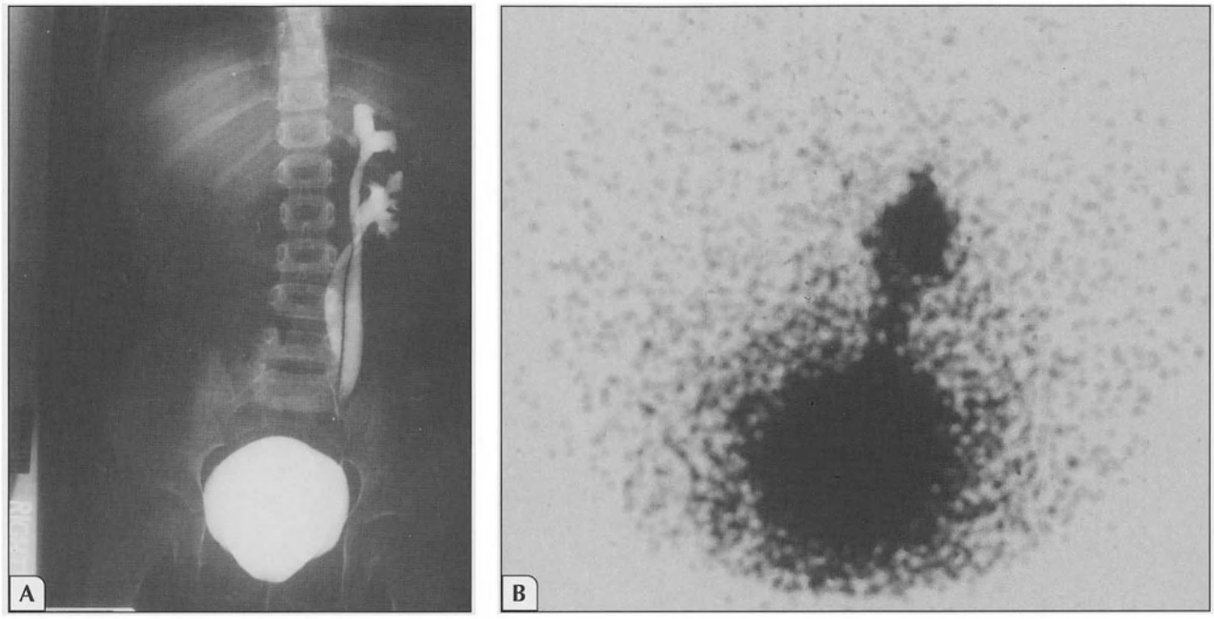
◗ **FIGURE 9-23.** Radiologic evaluation of patients with urinary tract infections (UTIs). Imaging studies are basic to urinary tract evaluation for infection. The goal of management of patients with UTIs is to minimize renal damage from the acute infection and minimize the future risk of renal damage. With the multiple imaging modalities available, however, the most efficient and rational order and selection of studies must be made with this goal in mind. Radiologic imaging can be used to 1) evaluate and localize the acute URI, 2) detect renal damage from the acute infection, 3) identify genitourinary anatomy that increases the risk of future renal damage from infection, and 4) evaluate change in the urinary tract over time. Deciding which studies are necessary in a child with a presumptive or diagnosed UTI should depend on whether potential radiologic findings would change the child's clinical management.

Early urinary tract imaging is important in seriously ill and febrile children in whom the site of infection is unclear and in those who have unusual circumstances. Circumstances that may warrant acute or early urinary tract imaging include newly diagnosed azotemia; a poor response to appropriate antimicrobial drugs after 3 to 4 days; an unusual infecting organism (*eg*, tuberculosis or urea-splitting organism such as *Proteus* spp.); known partial obstruction (*eg*, ureterocele, ureteropelvic junction obstruction, megaureters, nonfunctioning or poorly functioning renal units); a history of diabetes or papillary necrosis; and neuropathic bladder.

If treatment depends on localizing the infection to the kidney, an acute imaging study should be performed. This is particularly important in severely ill, hospitalized children who improve on initial parenteral treatment, but urinary cultures are inadequate or indeterminate for bacterial infection. An acute dimercaptosuccinic acid (DMSA) scan may show if acute renal inflammation is present and justify treatment or not. If, on the other hand, a UTI appears highly likely and antimicrobial treatment will be started regardless of radiologic findings, early DMSA scintigraphy is probably unnecessary.

Because UTIs in infants and young children may serve as markers for anatomic abnormalities, the child should be maintained on antimicrobial prophylaxis after the initial UTI has been adequately treated and radiologic studies performed to delineate the urinary tract. Although there is controversy on whether studies should be performed after the first or recurrent episode, if obstructive lesions are found in 5% to 10% of children and reflux occurs in 21% to 57% [1,11,31,32], early detection of these abnormalities merits full radiologic urinary tract evaluation after the first infection in young children. This usually consists of some form of renal and upper collecting system evaluation and a voiding cystourethrogram (VCUG). As previously emphasized, children's kidneys are prone to renal scarring, so evaluation of the renal morphology and documentation of any anomalies or scarring may be important to a child's management. Acute studies of the kidney, however, may cause overestimation of the renal size resulting from initial edema or lack of appreciation of renal scarring because mature renal scars may take up to 2 years to be seen by certain imaging techniques [121–125]. As a result, later studies may show smaller or scarred kidneys that may be misinterpreted and cause inappropriate changes in patient management. Obviously, obstruction and other anatomic abnormalities demonstrated by radiologic evaluation may require other evaluation specific to their diagnosis before definitive management is made. Patients in these situations need to be evaluated and treated individually.

Follow-up evaluation is important. When a child who has a UTI has no abnormality found after urinary tract radiologic evaluation, no further studies are routinely prescribed. If the collecting systems were normal but one or both kidneys showed massive generalized or focal edema with areas of possible hypoperfusion during the acute infection, a subsequent study should be performed to examine the kidney for signs of renal scarring or shrinkage. In this way, children who need to be reexamined for later renal dysfunction may be identified. If a child has recurrent symptomatic pyelonephritis and no reflux found on previous fluoroscopic VCUG, a nuclear VCUG may be more sensitive at revealing reflux although less likely to define it [126,127]. RBUS—renal/bladder ultrasounds; VUR—vesicoureteral reflux.



◗ **FIGURE 9-24.** Voiding cystourethrography (VCUG). VCUG is the most important examination in assessing vesicoureteral reflux (VUR) in children, and as such, is important for assessing urinary tract infections (UTIs). VCUGs may be performed either with fluoroscopy and iodinated contrast or with nuclear imaging agents (usually ^{99m}technetium-pertechnetate) using similar techniques. Traditional fluoroscopic VCUGs (**A**) can show urethral and bladder abnormalities and VUR. Radionuclide VCUGs (**B**) may be more sensitive for reflux detection, but it offers poorer spatial resolution so that urethral lesions, degree of reflux, and details of the collecting system may not be visualized. The main advantage of radionuclide VCUG has been the lower radiation exposure of 1 to 5 mrad (ovarian dose) compared with 27 to 1000 mrad (previously reported ovarian exposure depending on equipment) [128,129]. With modern imaging technology and a tailored examination, however, fluoroscopic VCUG has been done with 1.7 to 5.2 mrad [130]. In general, radionuclide VCUG may be most useful for VUR screening, for evaluating UTIs in older children who have lower risk of VUR, or for periodic reflux reevaluation [129]. Radionuclide VCUG should not be used to evaluate infections in infants or young boys in whom risk of genitourinary abnormality is high and urethral visualization important, nor in any child in whom imaging resolution of the lower urinary tract is important.

The VCUG may be performed as soon as the urine is sterile. Studies have shown that UTIs do not cause VUR, and even if reflux were associated with inflammation, this would be important to know and could alter management [131]. Whether a VCUG is done during treatment, immediately after, or a few weeks afterwards is not important as long as the child has normal renal function, responds rapidly to antimicrobial treatment, and is maintained on prophylactic antimicrobial treatment to keep urine sterile in the interval between the herald infection and the radiologic evaluation.

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10

Ambiguous Genitalia

Mark F. Bellinger and Francis X. Schneck

The clinical evaluation and assignment of gender of rearing in a neonate with genital ambiguity has been described as a medical emergency. Although expeditious investigation should be undertaken, it is also important to recognize that the worst injustice that can be committed during the initial evaluation is assignment of an inappropriate gender of rearing that subsequently must be altered. When the infant is first evaluated, the family should be reassured that the child's genitalia are in an incompletely developed state and, after the appropriate evaluation is complete, reconstruction can be completed.

Evaluation should begin with a complete family and gestational history, searching for evidence of consanguineous, infertile, or sexually ambiguous family members; for early neonatal deaths (salt wasting); and for maternal drug (*ie*, hormone, steroid) ingestion during pregnancy. Examination of the infant should include an assessment of phallic length, corporal diameter, and meatal position; a general assessment of the degree of masculinization; and an estimation of whether reconstruction in the male gender of rearing seems feasible. A most crucial aspect of the examination may be the presence or absence of at least one palpable gonad because this is most likely to be a testis and thus place the child in the category of male pseudohermaphroditism. Rectal examination may allow palpation of the uterus as a prominent midline structure, especially in a neonate when maternal estrogen stimulation results in some uterine enlargement.

Laboratory evaluation should begin with assessment of karyotype, which may take 3 days to complete. Serum electrolytes should be monitored to identify salt wasting, which may be manifest at 7 to 14 days of age. Plasma levels of 17-hydroxyprogesterone and urinary levels of 17-ketosteroids and pregnanetriol should be measured, all of which may be elevated in those with congenital adrenal hyperplasia [1]. Additional biochemical evaluation may be warranted to measure plasma precursor steroids in rarer forms of male and female pseudohermaphroditism. Pelvic ultrasound examination may be used to assess uterine development, and a genitogram (or retrograde urethrovaginogram) may be helpful in delineating the presence of a vagina, cervix, and uterine canal.

When female pseudohermaphroditism has been diagnosed, most pediatric urologic surgeons consider endoscopy and surgical correction at an early age (*ie*, 3 to 6 months) if the child's size and general medical condition permit, although some opt for neonatal correction [2]. The advantage of waiting several months is primarily the ability to avoid general anesthesia in the neonatal period, but it also allows enough time to ensure that medical replacement therapy has been well established and that the infant is stable

on an effective medical regimen. Frequently, clitoromegaly will diminish to a degree with the institution of steroid replacement therapy. Feminizing genitoplasty may include clitoroplasty and labioplasty, with perineal flap vaginoplasty performed as a simultaneous procedure unless the urethrovaginal confluence is high (above the sphincter mechanism), in which case delayed pull-through vaginoplasty may be appropriate [3]. If vaginal development is very rudimentary, bowel vaginoplasty may be required as a delayed procedure.

PATIENT EVALUATION

Classification of Ambiguous Genitalia in the Newborn

- Female pseudohermaphroditism (46,XX)
  - Congenital adrenal hyperplasia (CAH)
    - 21-Hydroxylase deficiency (virilism only)
    - 21-Hydroxylase deficiency (virilism with salt-losing syndrome)
    - 11-Hydroxylase deficiency (virilism with hypertension)
    - 3β-Hydroxysteroid dehydrogenase deficiency (virilism with adrenal insufficiency)
  - P-450 aromatase (placental) deficiency
  - Maternal source
    - Progestational agents
    - Virilizing tumor
    - Virilizing luteoma of pregnancy
    - Congenital virilizing adrenal hyperplasia (mother)
  - Non-androgen–induced female pseudohermaphroditism
- Male pseudohermaphroditism (46,XY)
  - Abnormal androgen biosynthesis
    - Deficiency of androgen and adrenal steroid synthesis (CAH)
      - P-450scc deficiency
      - 3β-hydroxysteroid dehydrogenase deficiency
      - $P\text{-}450_{c17}$ (17α-hydroxylase) deficiency
    - Deficiency of androgen synthesis
      - $P\text{-}450_{c17}$ hydroxylase/17,20-lyase deficiency
      - 17β-hydroxysteroid oxidoreductase deficiency
  - Abnormal androgen receptor
    - Complete androgen insensitivity*
    - Incomplete androgen insensitivity (*eg*, Reifenstein syndrome)
  - Abnormal androgen action
    - 5α-reductase deficiency
  - Abnormal müllerian regression
    - Persistent müllerian duct syndrome (hernia uteri inguinale)†
  - Leydig cell agenesis or hypoplasia
  - Dysgenetic male pseudohermaphroditism
    - Incomplete form of gonadal dysgenesis
    - Vanishing testes syndrome
- Gonadal disorders
  - Pure gonadal dysgenesis: complete form (46,XX or 46,XY)*
  - Gonadal dysgenesis (Turner's syndrome) (45,X)*
  - Mixed gonadal dysgenesis (45,X/46,XY)
  - Klinefelter's syndrome (47,XXY; 48,XXXY, and so on)†
  - XX male syndrome (46,XX)†
  - True hermaphroditism (46,XX; 46,XY; mosaic)
- Unclassified disorders
  - Abnormal müllerian development
    - Rokitansky sequence*
  - Microphallus (nonsyndromic)
  - Hypospadias with or without cryptorchidism

*Nonambiguous female genitalia in the neonatal period.
†Nonambiguous male genitalia in the neonatal period.

A. Evaluation of Ambiguous Genitalia in Newborns

- History
  - Maternal virilization
  - Medications (especially progesterone)
  - Family members with ambiguous genitalia, neonatal deaths, developmental abnormalities, consanguinity, sterility, amenorrhea, hirsutism
  - Prenatal history
    - Ultrasound
    - Amniocentesis
- Physical examination
  - Presence or absence of palpable gonads
  - Phallic stretch length
  - Location of the urethral meatus
  - Corporal body development
  - Labioscrotal fusion
  - Labioscrotal hyperpigmentation
  - Rectal examination (cervix and uterus)
  - Dehydration, failure to thrive
- Laboratory studies
  - Serum electrolytes
  - Serum 17-hydroxyprogesterone
  - Urinary 17-ketosteroids, pregnanetriol
  - Chromosomal analysis
  - If male pseudohermaphroditism suspected:
    - Serum FSH, LH, and testosterone
    - hCG stimulation test
    - Androgen precursor steroid analysis
    - Genital skin biopsy: fibroblast culture*
      - Androgen receptor analysis
      - Testosterone to DHT conversion
- Ultrasound
- Genitogram (retrograde urethrovaginogram)
- Endoscopy
- Laparotomy or laparoscopy with or without gonadal biopsy

*If available.

◗ **FIGURE 10-2.** Evaluation of ambiguous genitalia in newborns shown in table form (**A**) and as an algorithm (**B**) (*on the next page*). The *asterisk* in **B** indicates the following: anatomy is dependent on the timing of fetal testes deficiency. Before the 8th week, normal female internal and external genitalia; 8 to 10 weeks, ambiguous genitalia and variable development of müllerian and wolffian ducts; after 12 to 14 weeks, normal male internal and external genitalia with anorchia. The dagger in **B** indicates normal female phenotype in neonatal period. CAH—congenital adrenal hyperplasia; DHT—dihydrotestosterone; hCG—human chorionic gonadotropin; FSH—follicle-stimulating hormone; LH—luteinizing hormone.

◗ **FIGURE 10-1.** Classification of ambiguous genitalia in newborns.

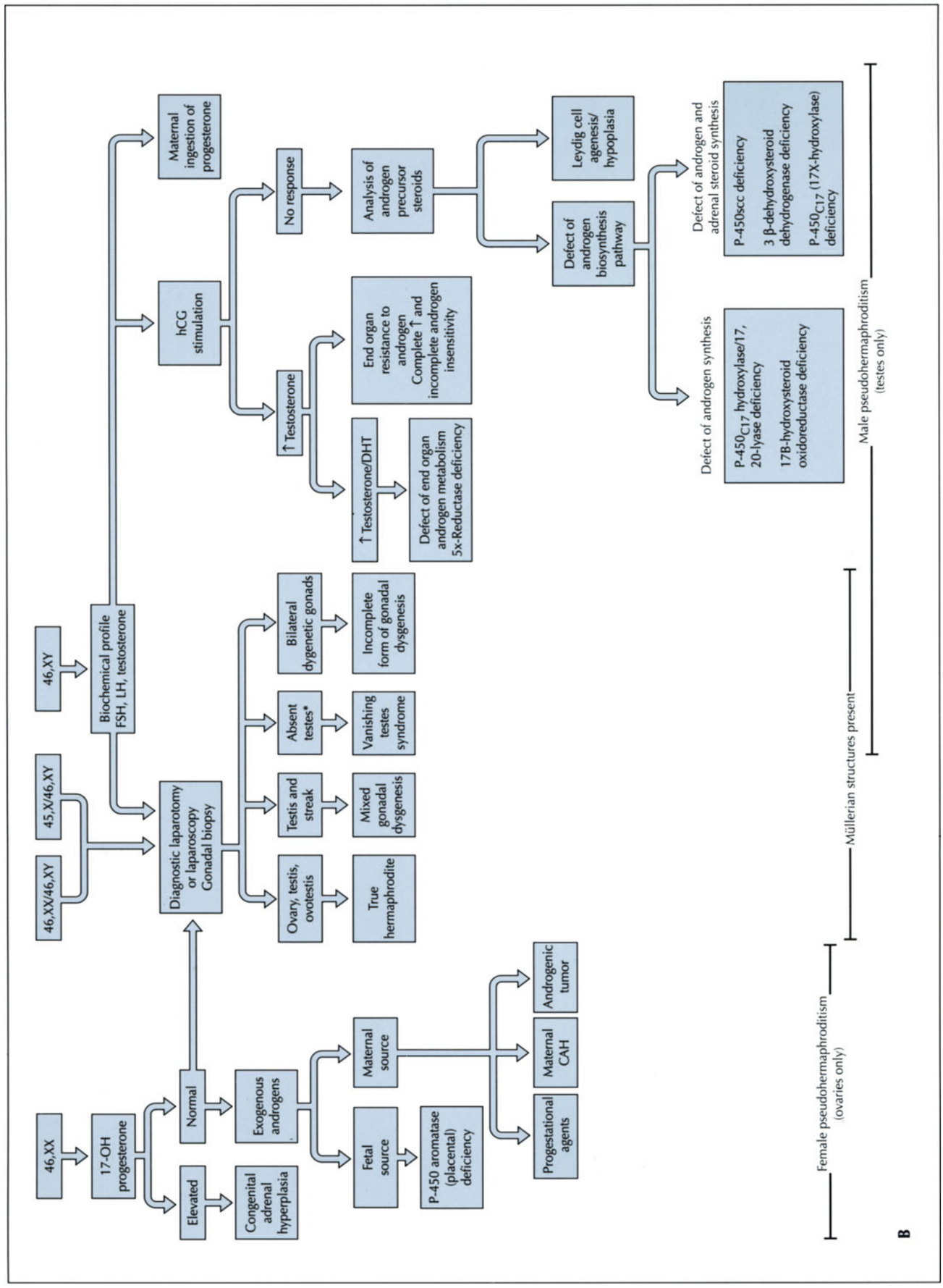
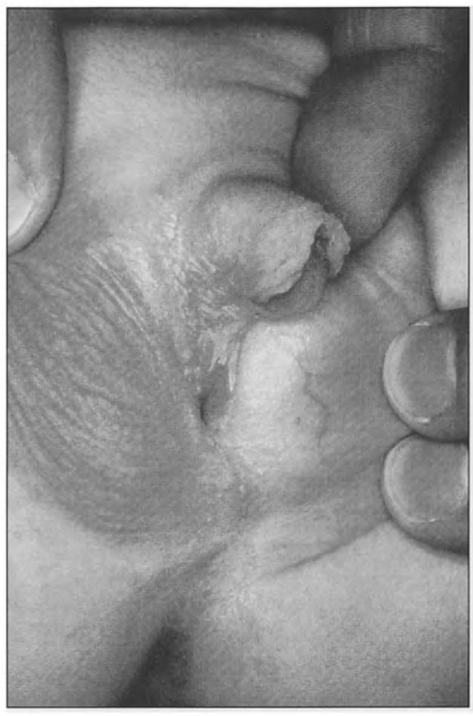
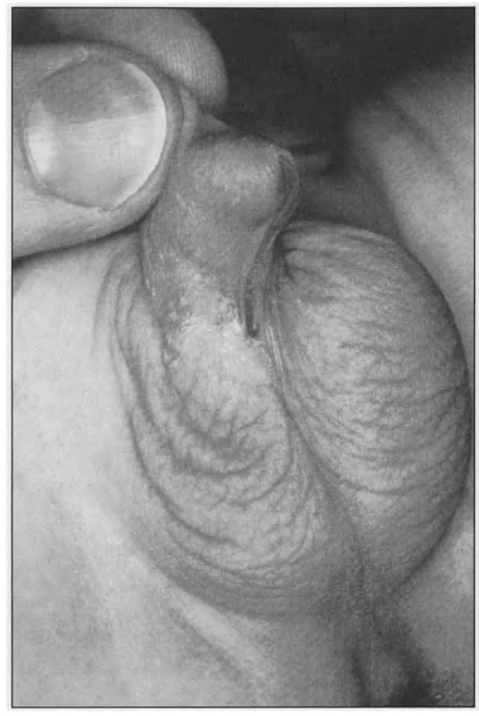


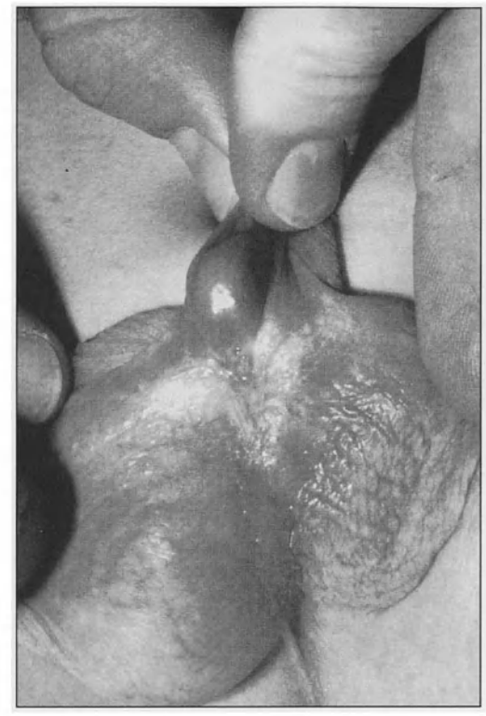
FIGURE 10-2. (*Continued*)



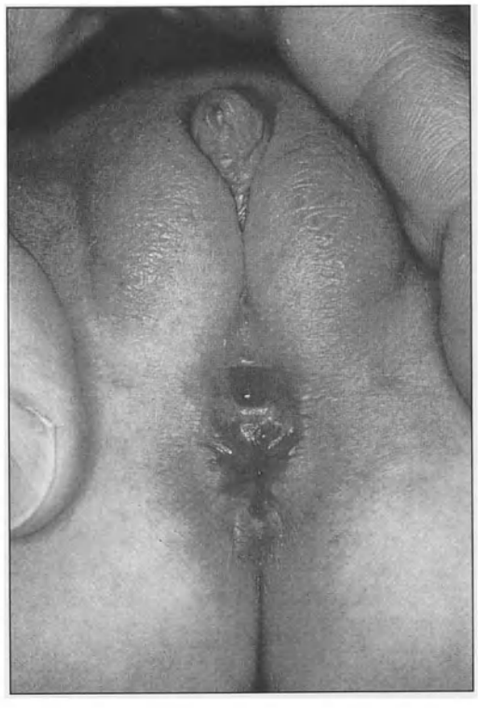
◗ **FIGURE 10-3.** The genital configuration of a neonate with congenital adrenal hyperplasia. Note the enlarged phallus (clitoris) with severe chordee and a dorsal hood prepuce. The urogenital meatus is located between rugated labioscrotal folds. No gonads are palpable.



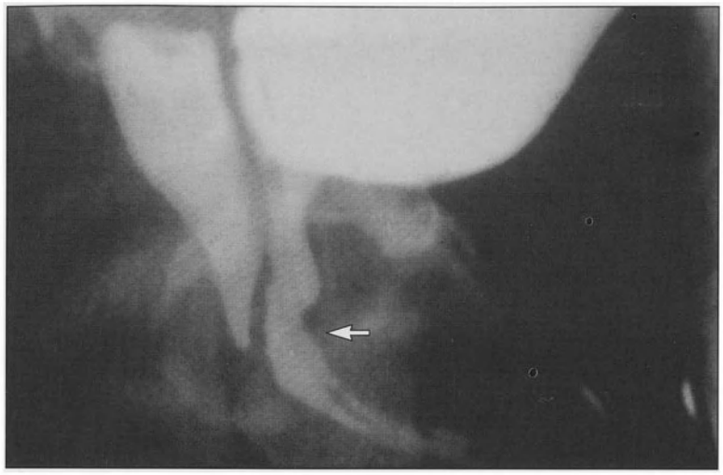
◗ **FIGURE 10-4.** Genitalia of a neonate with mixed gonadal dysgenesis. Note the similarity to that of Figure 10-3. The immediate difference noted is the presence of a visible and palpable testis in the left labioscrotal fold. The phallus is more prominent, the urethral meatus is located at the penoscrotal junction, and severe chordee appears to be present [4].



◗ **FIGURE 10-5.** A neonate with penoscrotal hypospadias and unilateral cryptorchidism. Note the small phallus with severe chordee and a very deficient dorsal hood prepuce. The scrotum is bifid and the left testis is nonpalpable. All children with hypospadias and a cryptorchid testis should have karyotype assessment [5].

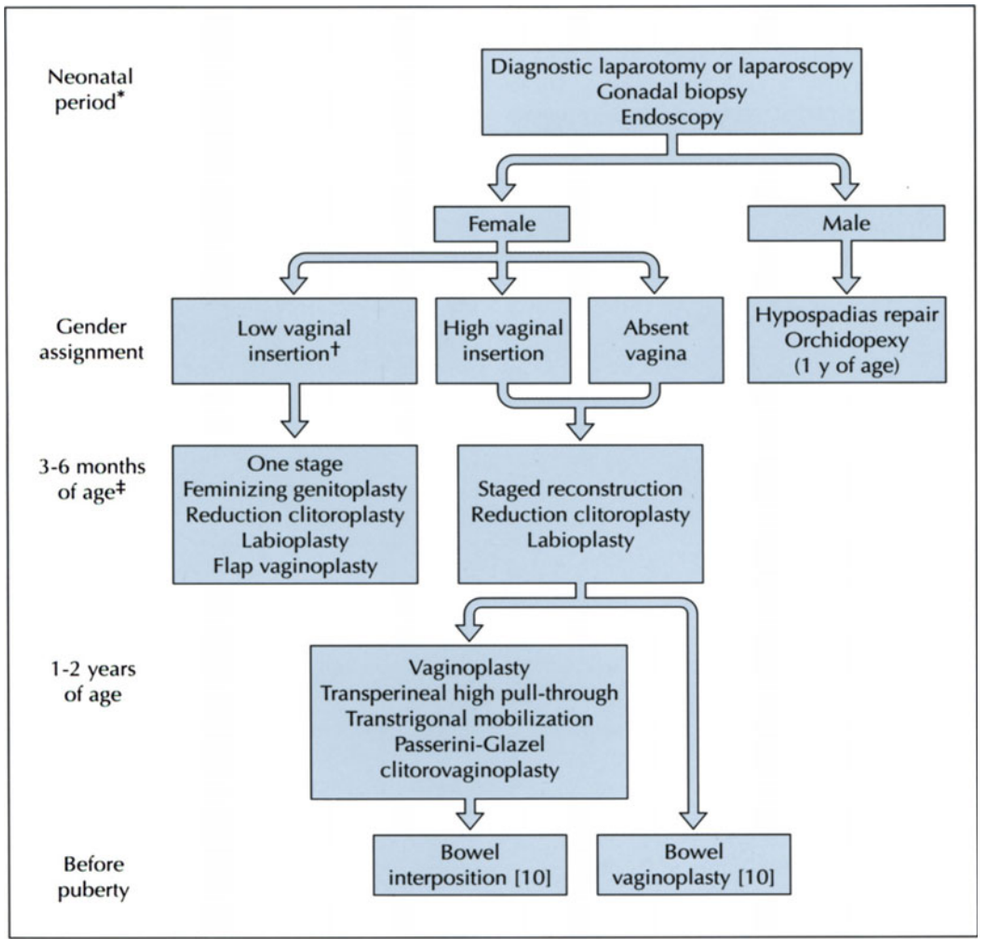


◗ **FIGURE 10-6.** A female neonate with accessory phallic urethra and posterior displacement of the urogenital sinus [6]. This unusual anomaly is associated with neither genetic nor gonadal abnormalities but is an apparent embryologic deformation. The perineum is flattened and lacks labia minora, and the opening of the urogenital sinus is displaced posteriorly with a resultant deficiency of the perineal body. These children have a duplicate urethra that exits on the glans clitoris.



◗ **FIGURE 10-7.** Genitogram of a child with congenital adrenal hyperplasia and a low urethrovaginal confluence. The *arrow* marks the location of the urethral sphincter, well above the junction of urethra and vagina. This child is thus a good candidate for a perineal flap vaginoplasty.

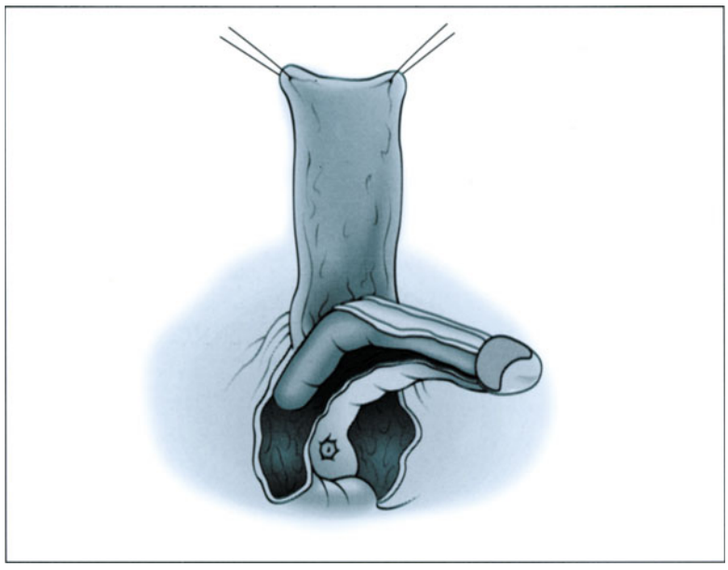
SURGICAL RECONSTRUCTION



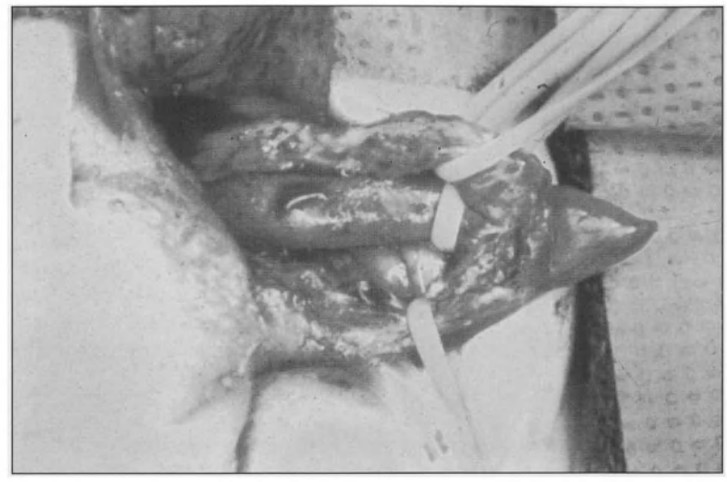
◗ **FIGURE 10-8.** Algorithm of the surgical approach to a child with ambiguous genitalia. The *footnotes* in this figure are defined as follows: *Indicated in patients with mixed gonadal dysgenesis, male pseudohermaphroditism, and true hermaphroditism to assess wolffian and müllerian structures and biopsy gonadal tissue. A genital skin biopsy is indicated in suspected cases of 5α-reductase deficiency, to measure testosterone to dihydrotestosterone conversion, and incomplete androgen insensitivity for androgen receptor analysis; however, these laboratory studies may not be readily available.

†Gonadectomy and excision of wolffian and müllerian derivative structures incompatible to gender assignment should be considered at this time. Gonadectomy is also indicated in cases of potential malignant transformation. This includes streak gonads and dysgenic testis in children with an XY karyotype or mosiacism, which includes a Y chromosome.

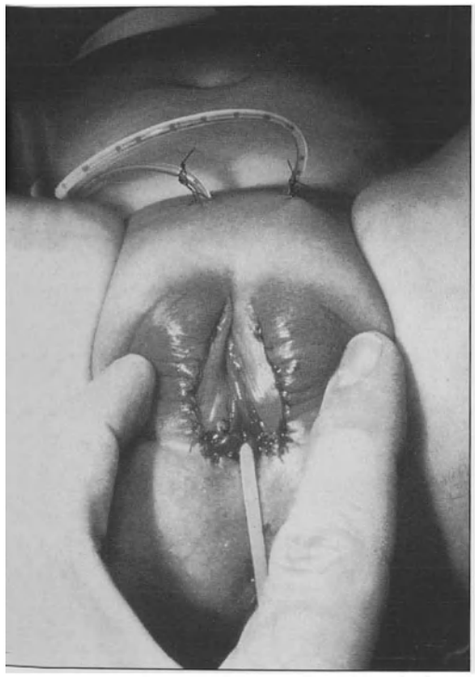
‡Low vaginal insertion, confluence of the urogenital sinus distal to the external sphincter, and high vaginal insertion, confluence of the urogenital sinus proximal to the external sphincter, are assessed by genitogram and endoscopy.



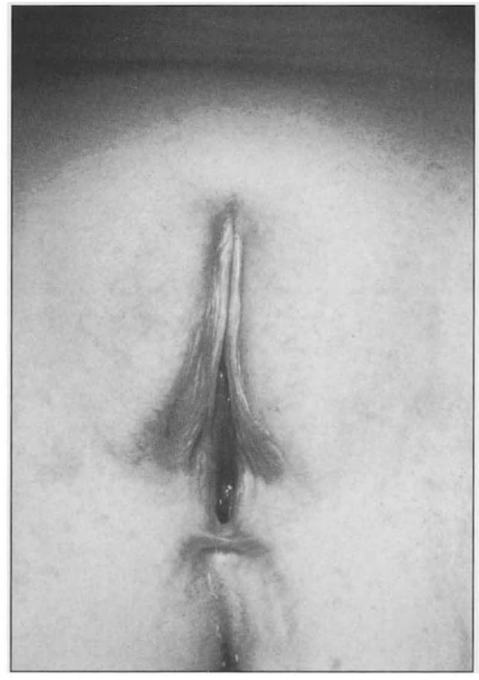
◗ **FIGURE 10-9.** Initiation of clitoroplasty. The phallus has been degloved by a circumcising incision carried around the dorsal coronal margin and toward the urethral meatus along each side of the urethral plate, which is preserved between the introitus and glans [7].



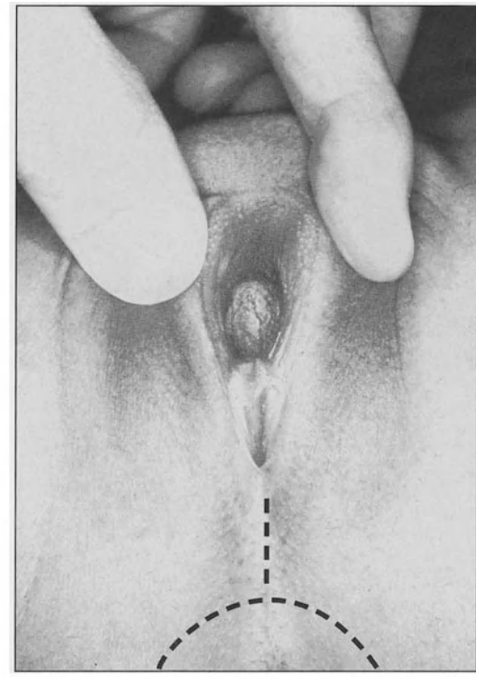
◗ **FIGURE 10-10.** Dissection carried a bit further than that shown in Figure 10-9. Vessel loops are around the dorsal neurovascular bundle (which has been preserved and separated from the corporal bodies, which are retracted by the middle vessel loop) and the ventral urethral plate.



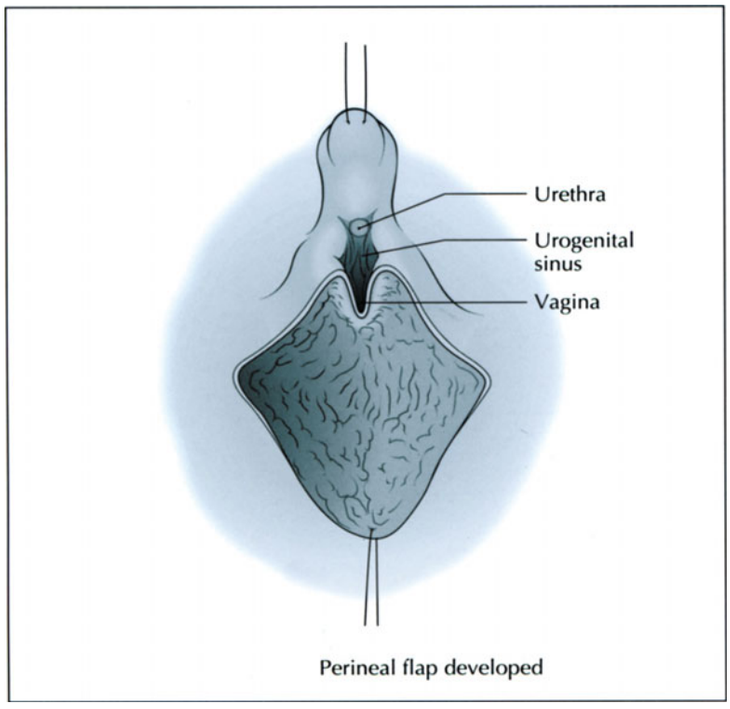
◗ **FIGURE 10-11.** Immediate postoperative result of clitoroplasty. Note the small, partially concealed glans clitoris, and the symmetrical labia minora and labia majora. Suprapubic suction drains and a urethral catheter will remain in place until the morning after surgery.



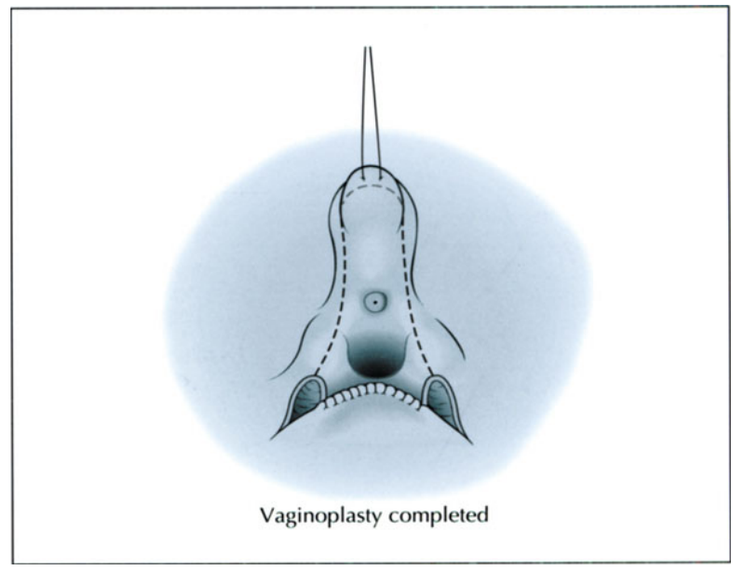
◗ **FIGURE 10-12.** Delayed postoperative result of feminizing genitoplasty. The labia minora and majora are symmetrical. The vaginal introitus is adequate in caliber and well placed.



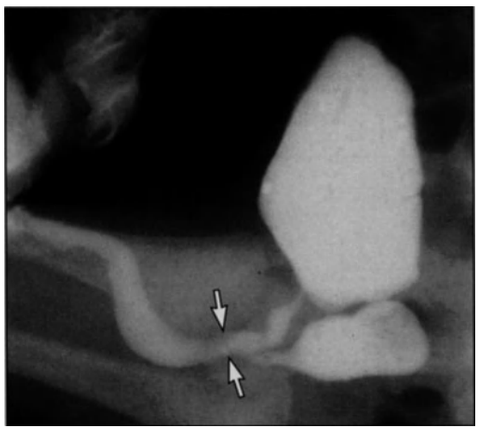
◗ **FIGURE 10-13.** Prevaginoplasty appearance of child with congenital adrenal hyperplasia and low urethrovaginal confluence. The *dashed line* identifies the incision that will be made for perineal flap vaginoplasty. The posterior wall of the urogenital sinus will be incised and the flap sewn in to bring the vaginal introitus to the perineum [8].



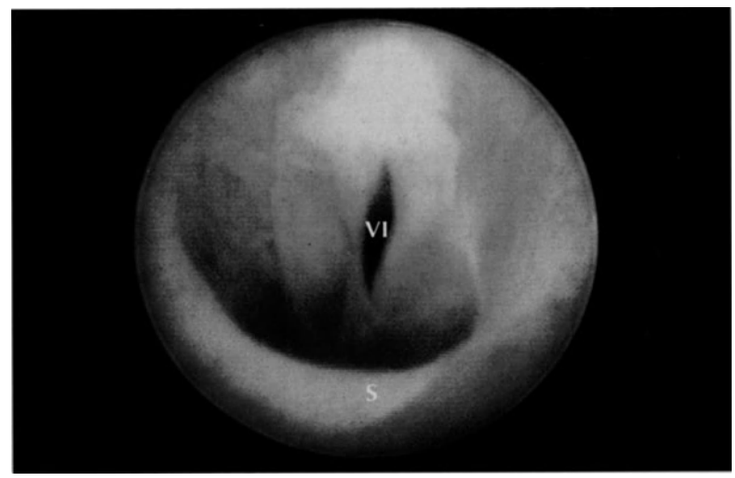
◗ **FIGURE 10-14.** Perineal flap vaginoplasty. The flap has been developed and the perineal cutback carried out [8].



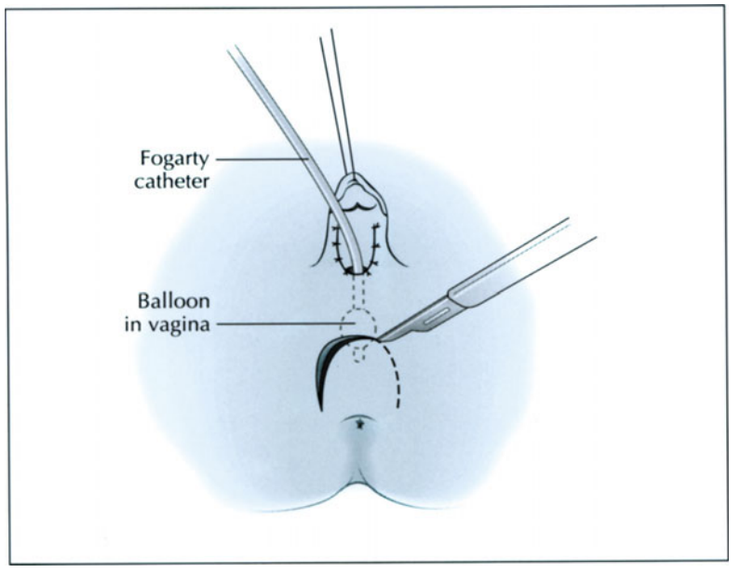
◗ **FIGURE 10-15.** Completed perineal flap vaginoplasty.



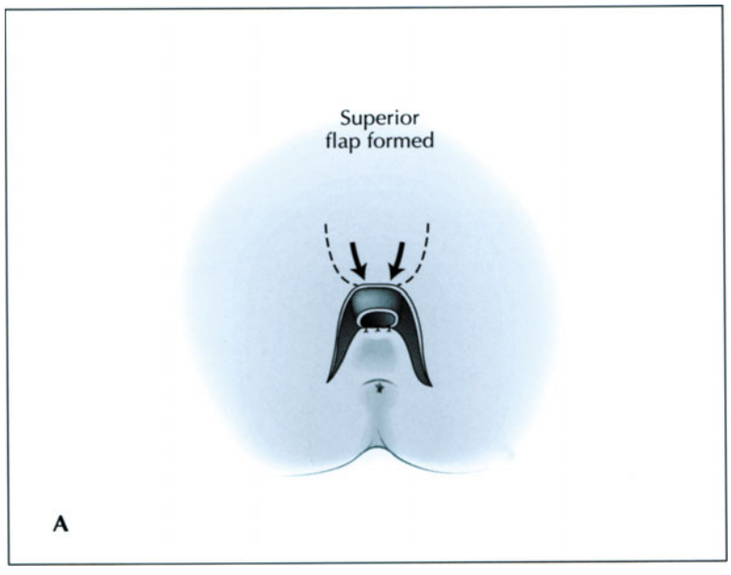
◗ **FIGURE 10-16.** Flush vaginogram of infant with congenital adrenal hyperplasia and high urethrovaginal confluence near the urethral sphincter (*arrows*). This child is not a candidate for a perineal flap vaginoplasty and will require a perineal pull-through procedure to bring the vagina to the perineum [9].

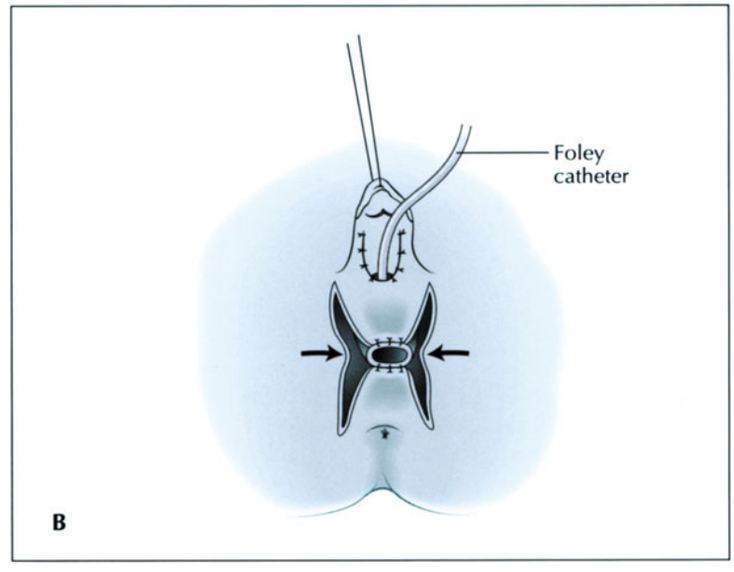


◗ **FIGURE 10-17.** Endoscopic appearance of the proximal urethra in the same child as in Figure 10-16. The vaginal opening is above the urethral sphincter. Perineal cutback would injure the urethral sphincter mechanism. S–sphincter; VI–vaginal introitus.



◗ **FIGURE 10-18.** Perineal incision for a patient with high urethrovaginal confluence. Note that a perineal cutback incision is not performed so that injury to the urethral sphincter mechanism is avoided. A small Fogarty catheter placed into the vagina endoscopically will help in identifying the vagina and its insertion into the urethra [9].





◗ **FIGURE 10-19.** Perineal pull-through vaginoplasty. **A,** The perineal flap has been developed and dissection has been carried along the urethra, isolating the vagina and dividing it sharply from the urethra. The urethra is then carefully closed to prevent stricture formation. **B,** The vagina has been separated from the urethra. Posterior- and anterior-based perineal skin flaps are developed and brought to the vagina, which will be spatulated to enlarge the introitus [10].

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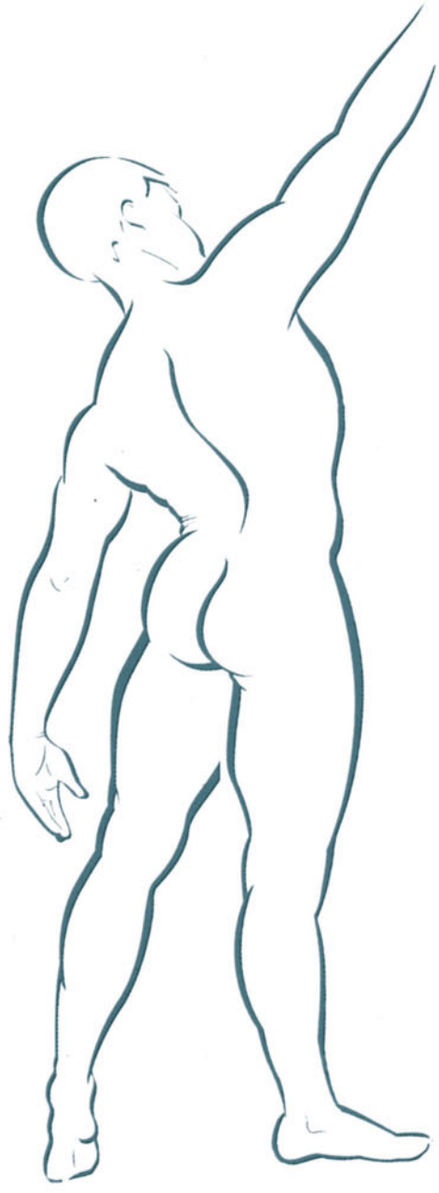
11

Neurogenic Vesical Dysfunction

Richard C. Rink and Anthony J. Casale



Many tremendous advances in the management of neurovesical dysfunction have taken place over the past two decades. Gone are the days of severe hydronephrosis, renal failure, and even death from neurogenic urinary dysfunction. Only rarely do we now see children who present with significant urinary tract changes. The social debilitation from life-long incontinence or incontinent abdominal wall urinary stomas should also only be a memory. Combining these advances with newer surgical approaches to fecal incontinence should now allow these children to be free of diapers. The advances made in medical and surgical approaches to neurogenic bladders have greatly changed overall pediatric urologic care, allowing reconstruction of even the most significant anatomic congenital anomalies.

There is a long list of potential etiologies of neurogenic vesical dysfunction (*see* Fig. 11-1). The overwhelming majority of children with these disorders have some form of spinal dysraphism; myelomeningocele is the most common disorder in these children. The progress made in the management of children with neuropathic bladders has dealt not so much with the actual diagnosis, but rather with exactly how the bladder and sphincter behave physiologically and their relationship to one another. This allows a treatment plan to be formulated. The goals of management have not changed over the years; the upper urinary tract must be protected and urinary infection avoided, and ultimately urinary continence must be achieved. In children with myelomeningocele, the spinal cord abnormality is obvious at birth and a management plan is started on day 1. Usually the urinary tract is normal in these children at birth. It is incumbent on the urologist to maintain it as such. Early neonatal evaluation has been extremely helpful in the management of these children to prevent deterioration of their urinary tracts. Unfortunately, after changes have taken place, they may be permanent. Urodynamic evaluation is the mainstay of preventive management and should provide information to assist in a long-term treatment plan, thus preventing anatomic changes from occurring. Bauer *et al.* [1] and van Gool [2] have shown that these studies may help determine which children are at significant risk for deterioration of their urinary tract. A grading system to determine the risk of upper tract changes was provided by McLorie *et al.* [3], who looked at bladder capacity, contractility, and dyssynergia. In children with occult spinal dysraphism in whom the anatomic anomalies are frequently missed or diagnosis is delayed, changes may have occurred before patient presentation to the urologist. Urodynamic studies are also critical in their evaluation.

In each child with a neurogenic bladder, assessment of his or her overall physical and mental status is mandatory. Is the patient capable of self-care?

Is the patient ambulatory, and will he or she be so in the future? Is the patient's upper extremity function normal? It is equally important to know the status of the urinary tract. Is it normal? Is there hydronephrosis or scarring, a concentrating defect, vesicoureteral reflux, or other abnormality? How does the bladder behave? At a minimum, a renal ultrasound, serum chemistries, voiding cystourethrogram, and urodynamics are necessary to begin treatment. With these factors in mind, we can begin our approach to the child with neurovesical dysfunction.

ETIOLOGY

A. Etiology of Neurogenic Dysfunction in Children

Spinal dysraphism
- Myelomeningocele
- Lipomeningocele

Occult spinal dysraphism
- Lipomeningocele
- Diastematomyelia
- Anterior meningocele
- Dermoid cysts
- Intradermal lipoma
- Tethered filum

Sacral agenesis
Traumatic spinal cord or head injury
Cerebral palsy

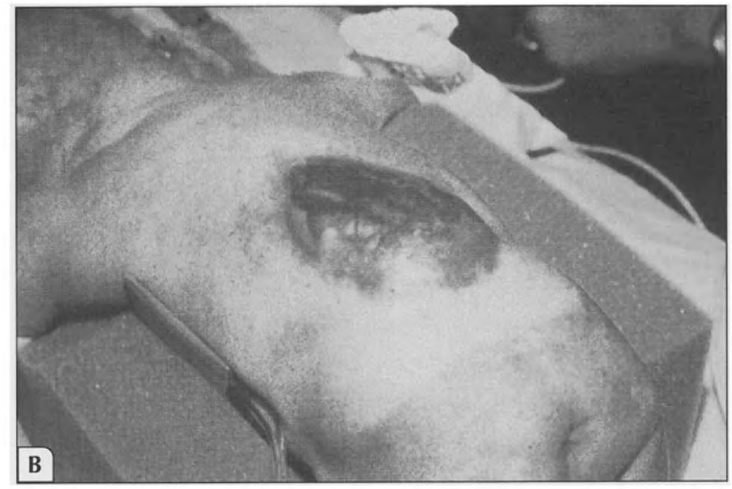
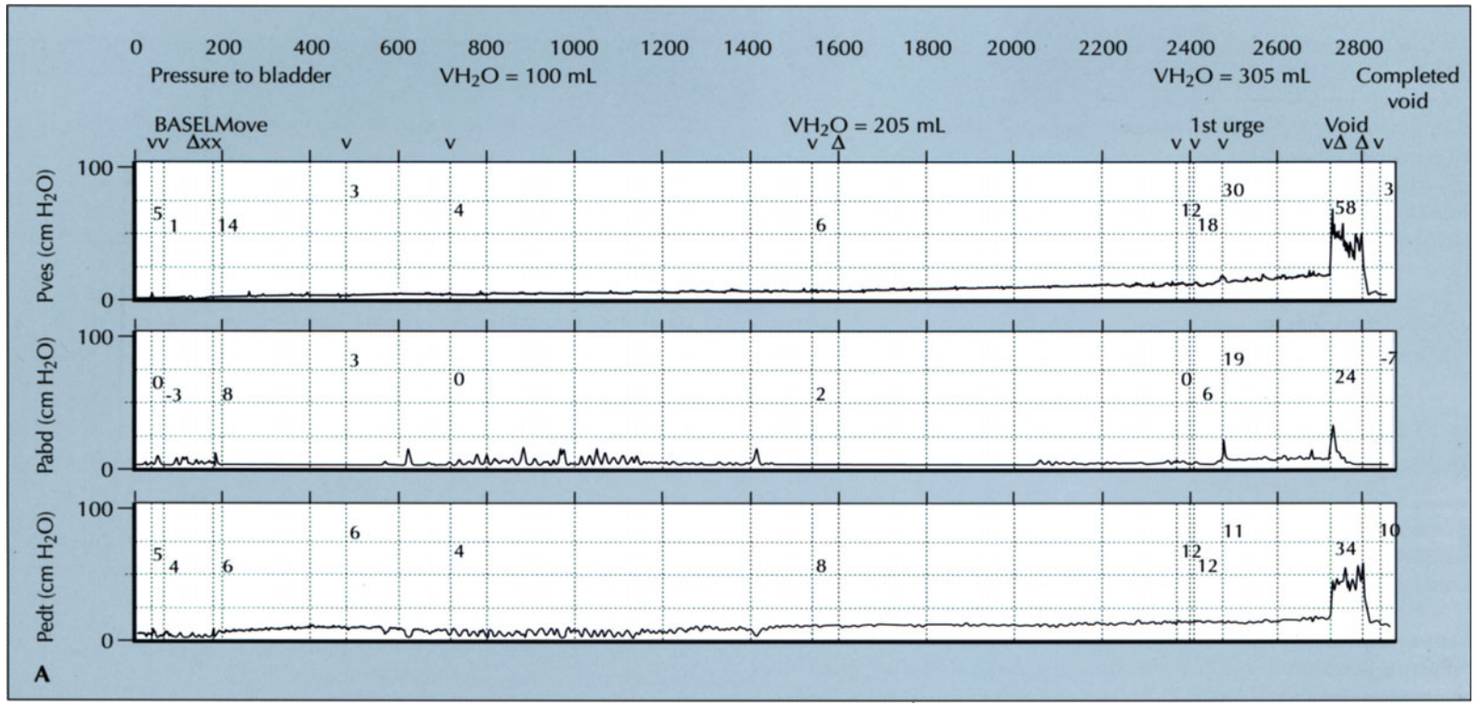
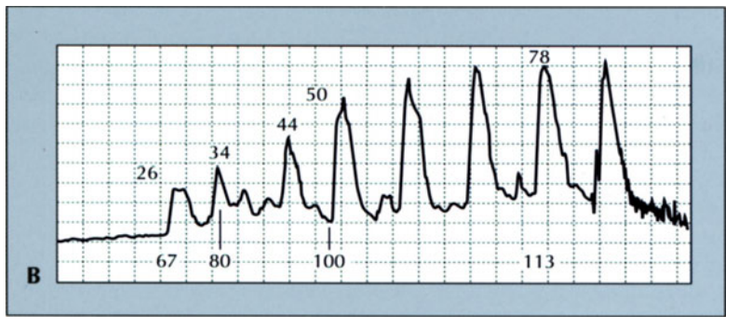
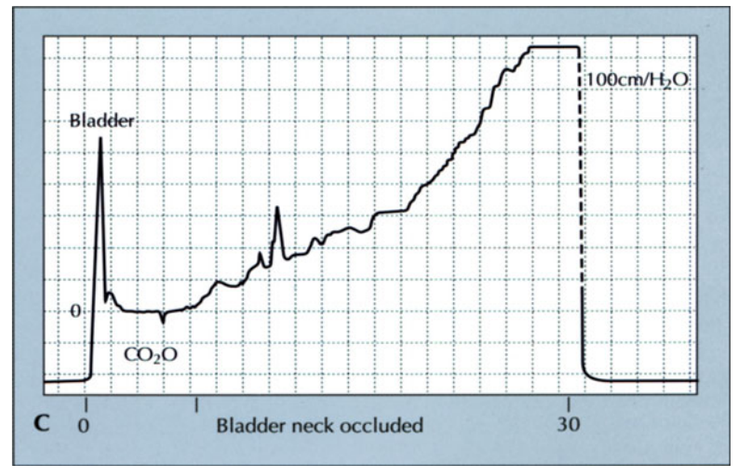


FIGURE 11-1. The causes of neurogenic dysfunction. **A**, Etiology of neurogenic dysfunction in children. **B**, Myelomeningocele. This lesion is by far the leading cause of neurogenic bladder in children, with the spinal lesion most often involving the lumbosacral area [4]. It makes up 90% of all open spinal dysraphism [5]. It is important to realize that the neurologic findings in these dysraphic states are variable and may not correlate with the bony lesion. The findings may even differ from side to side. Therefore, each child must be fully evaluated urodynamically.

Furthermore, the neurologic lesion often changes with time, requiring life-long follow-up evaluation. Forty percent of these patients have a change during the first 3 to 5 years of life [6]. Occult spinal dysraphisms are much less obvious and often missed; however, 90% have a cutaneous lesion in the lumbosacral area [7]. This may take the form of a dimple, hair patch, or area of increased pigmentation. Mandell *et al.* [8] have noted that 40% of these patients with occult dysraphism have a malfunction of the lower urinary tract. The neurologic changes in these children vary but tend to be progressive [9]. Fortunately, some are reversible with surgery; however, the older the patient, the less likely normal function will be restored [10]. Sacral agenesis is noted in 1% of offspring of mothers with insulin-dependent diabetes mellitus. This frequently results in neurogenic dysfunction [11]. Fortunately, traumatic spinal cord injuries in children, as opposed to those in adults, are uncommon and make up only a small percentage of lower urinary tract neurologic abnormalities. The resultant neurologic deficit usually corresponds to the level of the bony injury. A few other conditions may give rise to neurogenic bladder; these conditions include cerebral palsy, imperforate anus, and sacrococcygeal teratomas.







◗ **FIGURE 11-2.** Cystometrogram (CMG) of normal (**A**), hypercontractile (**B**), and poorly compliant (**C**) bladders. Urodynamic evaluation forms the basis for all therapy in children with neurogenic dysfunction. The cystometrogram defines the "three Cs" (capacity, compliance, and contractility) of the bladder that one must understand to formulate a treatment plan. Compliance is particularly important to determine future outcome. The rate of bladder filling influences detrusor pressures and therefore should be carefully controlled in children [12]. Bauer [13] recommends never to exceed 10% of predicted bladder volume per minute. Two formulas have been used to estimate bladder capacity. Berger *et al.* [14] reported that bladder capacity equals the patient's age in years plus 2 [14]. Houle *et al.* [15] later reported that 16 (age in years) plus 70 mL more accurately defined bladder capacity. Recently, Palmer *et al.* [16] noted that bladder capacity in children with myelomeningocele grew at a rate approximately 25% less than normal and that the bladder volume increased approximately 24 mL per year. They calculated that bladder capacity equals 24.5 (age in years) plus 62 in the myelomeningocele group for the first 9 years of life. These urodynamic studies should be done as soon as a neurologic abnormality is suspected.

Not only must the behavior of the bladder be defined, but the pressure at which the child leaks urine around the catheter (leak point pressure [LPP]) must be documented. McGuire *et al.*'s [17] classic description of upper urinary tract deterioration in the presence of sustained intravesical pressures of more than 40/cm H_2O has been confirmed by a number of groups. The LPP has also been used to determine the potential for continence. Although there is no exact LPP number above which the patient will be continent, if it is significantly lower than 40/cm H_2O, surgical techniques to increase urethral resistance are usually necessary to achieve dryness.

External sphincter electromyography can be performed most accurately with a fine needle electrode, but for the purposes of predicting the behavior of the sphincter, most pediatric urologists have used surface electrodes satisfactorily [18]. Persistent sphincter electromyographic activity during bladder contractions (*ie*, dyssynergia) is often quite detrimental to the urinary tract.

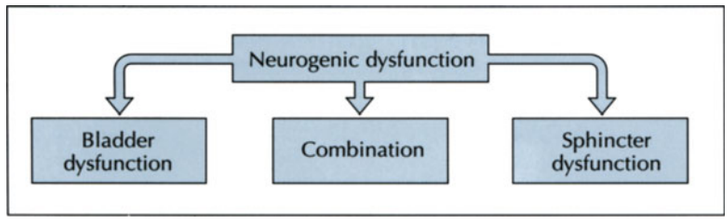


FIGURE 11-3. Spectrum of vesical and sphincteric dysfunction. Although much work has been done to understand the various etiologies of neurogenic dysfunction and how exactly each lesion affects the lower urinary tract even on a molecular basis, the treatment is based on two factors: how the bladder behaves and how the sphincter behaves. We use urodynamics to classify these patients on a spectrum of bladder dysfunction to sphincter dysfunction or a combination of the two [19]. If the child is old enough to cooperate during evaluation, we would first have them void or perform the Valsalva maneuver and then we would measure the voided volume. A 7-F urodynamic catheter is placed and the residual volume is measured. Slow-fill urodynamics are performed. Both sphincter electromyogram and rectal pressures are simultaneously measured. After defining how the bladder and sphincter behave and interact, a treatment plan is outlined. Again, the goal remains to protect the kidneys and prevent infection. At the appropriate age, the achievement of continence becomes important, but it should never come at the expense of the first two goals.

During infancy, if the sphincter activity is coordinated or outflow resistance is very low, no interventional therapy may be necessary. Clearly, children with detrusor-sphincter dyssynergia and those with significant hypercontractility are at risk for upper urinary tract deterioration. Bauer [20] showed that 71% of newborns with dyssynergia have deterioration of the urinary tract over the first 3 years of life. Those with synergy who later deteriorated were found to have converted to the dyssynergic state. Again, this shows the need for early evaluation and reevaluation during childhood.

MEDICAL MANAGEMENT

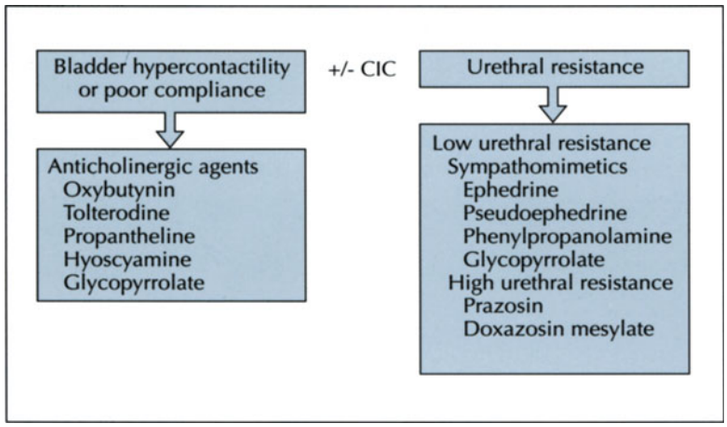


FIGURE 11-4. Medical management of patients with neurogenic dysfunction. The mainstay of therapy of these patients is clean intermittent catheterization (CIC). Its introduction in 1972 by Lapides *et al.* [21] has had profound impact on the care of these children. No longer does one need to provide a means for bladder emptying; therefore, treatment can be based on creating a storage reservoir. This can be started as early as the newborn period. The basis of initial therapy is CIC combined with pharmocologic measures. In all patients, efforts at medical management are exhausted before any surgical intervention is considered. When using medical management, only 10% of patients have deterioration of their urinary tracts [22]. In our experience, continence is achieved in approximately 5% with spontaneous voiding alone.

Approximately two thirds of patients can be dry with CIC with or without medication; the remaining 25% of patients require some operative procedure [23]. Medical efforts to lower intravesical pressures are based on anticholinergic medication. Oral oxybutinin is the most commonly used medication, but its side effects can be significant in some children. In these children, intravesical oxybutinin has been successful. α-Sympathomimetic agents are used in an effort to increase urethral resistance. Although this can be successful, in our experience, this is more difficult to achieve than lowering intravesical pressures. It is important to remember that any time urethral resistance is increased to achieve continence, bladder dynamics may change adversely.

Occasionally it is helpful to lower urethral resistance; this can be done by prescribing α-sympatholytic agents such as doxazosin. If this is unsuccessful, urethral dilatation as popularized by Bloom *et al.* [24] can be performed; they demonstrated a decrease in leak point pressure, which subsequently improved bladder compliance.

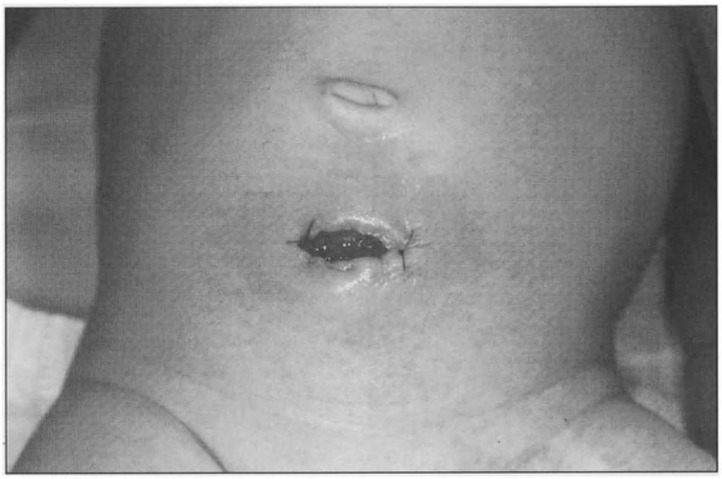


FIGURE 11-5. Cutaneous vesicostomy. Occasionally clean intermittent catheterization (CIC) and medication does not stabilize the bladder and upper urinary tract. At other times, the family cannot or will not permit CIC to be performed. In these situations, the urinary system can be decompressed with a temporary cutaneous vesicostomy. With CIC now used in newborns, vesicostomies are performed less often but they still provide reliable free drainage of urine into the diaper at low intravesical pressures. The Blocksom technique as popularized by Duckett [25] is most commonly used. These vesicostomies are easily closed at a later date. Complications are uncommon, but stenosis and prolapse are the most frequently noted risks.

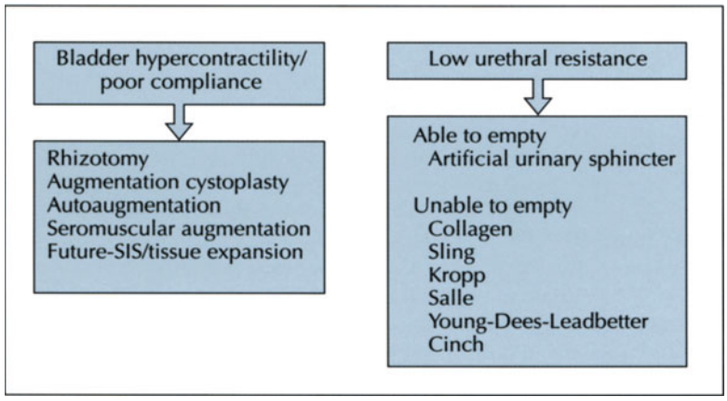


FIGURE 11-6. Surgical management of patients with neurovesical dysfunction. If medical management fails to protect the kidneys or achieve urinary continence (which in our hands occurs in 25% of those with myelodysplasia), surgical options must be considered. If the primary problem lies with the bladder, one must first consider the possible use of bladder stimulation. Kaplan *et al.* [26] believe that bladder stimulation may improve bladder compliance and in some high-risk patients may help to avoid enterocystoplasty [27,28]. Although this therapy has not improved voiding, it may have a role in increasing sensation, increasing bladder capacity, and lowering intravesical pressures in some patients [28]. It is, however, very time consuming; Decter *et al.* [29], who noted the lack of significant improvement with this therapy, no longer offer it.

The surgical approach to the treatment of patients with neurogenic lower urinary tract dysfunction is again directed at either the bladder, the sphincter, or both with the goal of providing a low-pressure, large-capacity bladder with adequate urethral resistance to provide continence. The determination of bladder compliance in patients with low urethral resistance can be quite difficult. Serious upper tract consequences can result if the surgeon fails to identify poor compliance and proceeds with an operation to increase urethral resistance. Furthermore, the bladder dynamics may change when urethral resistance is increased [29–31]. We have recently tried to predict from urodynamic data which bladders would require augmentation after artificial sphincter placement but were unable to do so [32].

Bladder compliance and capacity have been improved by bladder augmentation using virtually every segment of the gastrointestinal (GI) tract. In children, the native bladder is bivalved to allow anastomosis of a detubularized, reconfigured GI segment. Although augmentation with bowel has reliably improved compliance and capacity, other risks have led urologists to seek different options to augment the bladder, such as using ureter or even bladder mucosa.

The surgical options to increase urethral resistance are based on whether the patient can perform the Valsalva maneuver and empty the bladder to completion. The artificial urinary sphincter is the only option that allows for spontaneous emptying; therefore, it is attractive for patients who can void. However, if clean intermittent catheterization is required, then an artificial device is less advantageous. The number of options available to increase urethral resistance indicates that no procedure works well in all situations. SIS—small intestine submucosa.

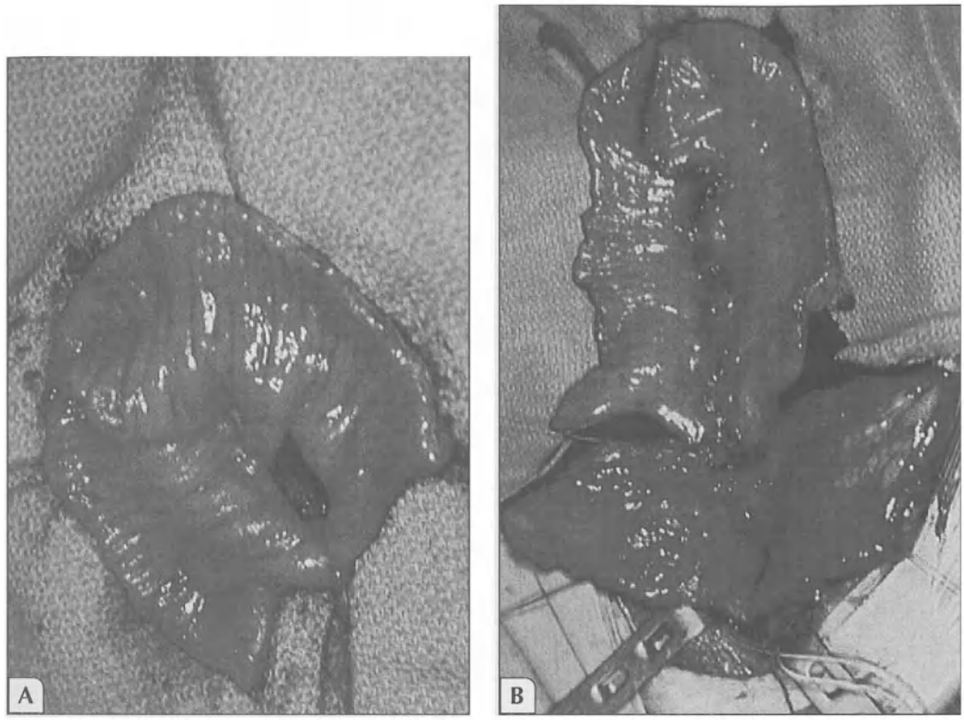


FIGURE 11-7. Technique of ileocystoplasty. **A,** Segment of ileum opened on its antimesenteric border and folded in a "U" shape. **B,** Reconfigured ileum sewn on to bivalved bladder. The least contractile bowel segment is ileum, making it an excellent choice to improve bladder compliance and capacity [19,33,34]. A segment of ileum approximately 15 cm proximal to the ileocecal valve is selected (**A**). After ileoileostomy, the selected segment, which is 20 to 40 cm in length, is detubularized and reconfigured as demonstrated in **B**. Opening any bowel segment and reconfiguring it to a more spherical shape has been shown to provide a number of advantages [35,36]. This maximizes the ultimate capacity, blunts bowel contractions, and improves overall compliance. The bowel segment is then anastomased to the bivalved bladder. If only compliance and capacity are an issue and no implantation of ureter or appendix is necessary, ileum is our segment of choice.

In a similar fashion, sigmoid colon can be used to augment the bladder. In the past, we recommended simple closure of the two ends of the sigmoid segment and opening its antimesenteric border [37]. We have seen increased contractility and rupture of the augmentation segment with sigmoid more often than noted in other series [19,34,38], and therefore would now recommend reconfiguration of the segment as demonstrated for the ileum.

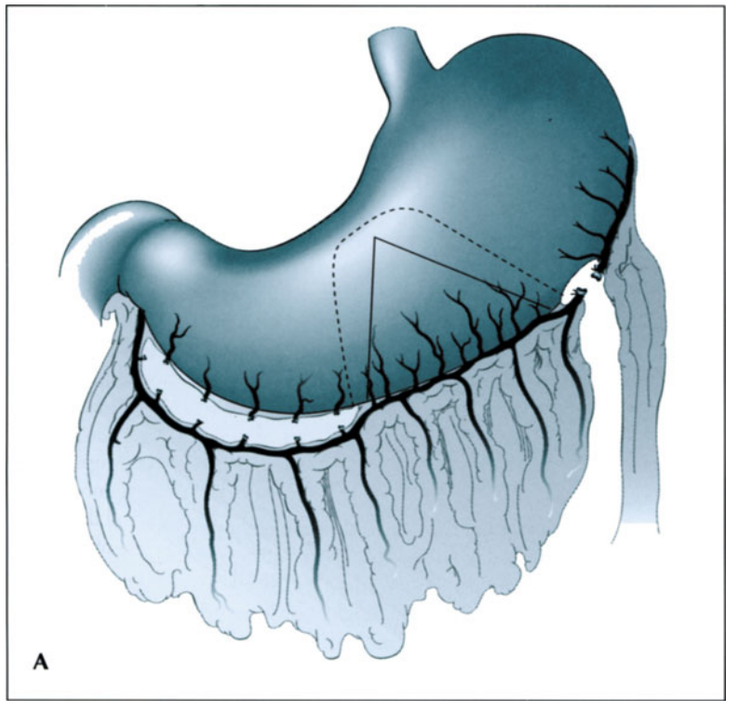
The ileocecal segment has been successfully used for both bladder augmentation and complete bladder replacement and has some advantages. However, in the neurogenic population, removal of the ileocecal valve from the gastrointestinal tract can result in intractable diarrhea; therefore, its use should be discouraged if other options are available [39,40].

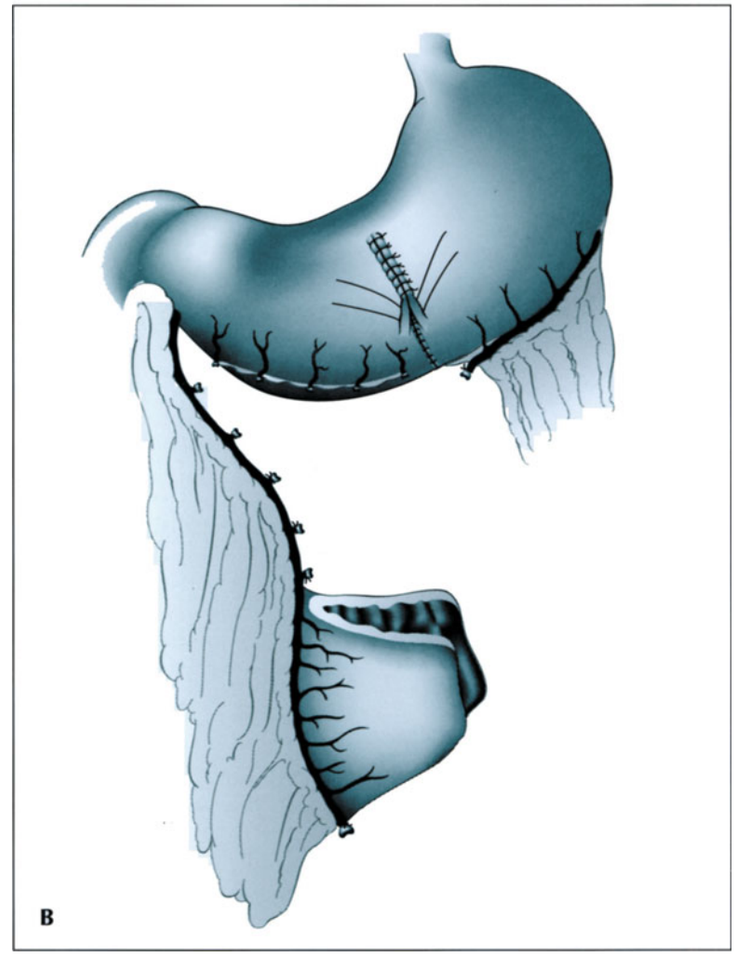
Comparison of Gastrointestinal Segments in Pediatric Augmentation

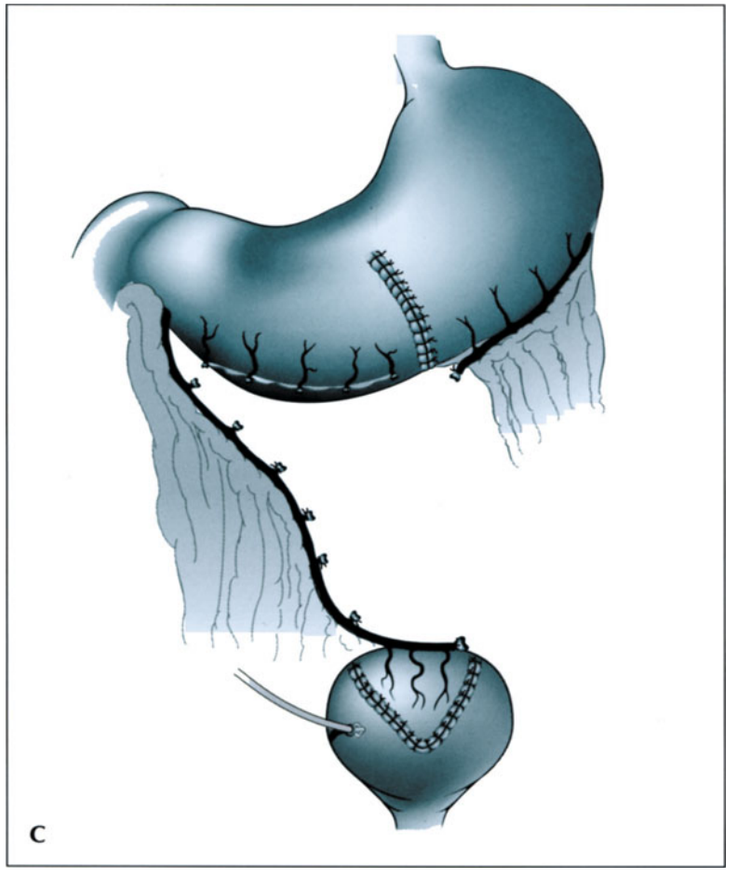
GI Segment	*Advantages*	*Disadvantages*
Ileum	Most compliant	Diarrhea
	Less mucus	Vitamin B_{12} deficiency
	Tail for short ureters	Short mesentery
		Hyperchloremic acidosis
		Difficult implantation
Sigmoid	Readily mobilized	Unit contractions
	Ease of implantation	Lower compliance
	Good muscle backing	Mucus
		Hyperchloremic acidosis
		? Perforation risk
Ileocecal	Valve as antireflux and continence mechanism	Hyperchloremic acidosis
	Good capacity reservoir	? Perforation risk
	Constant blood supply	Hyperchloremic acidosis
	Good muscle backing	Diarrhea in neurogenics
	Ease of implantation	Not always available
		Contractile
Stomach	Short gut and radiation	Hyperchloremic alkalosis
	Chloride pump	Rhythmic contractions
	Minimal mucus	Hematuria and dysuria
	Fewer infections	
	Ease of implantation	
	Good muscle backing	

FIGURE 11-8. Comparison of gastrointestinal (GI) segments in pediatric augmentation. Each bowel segment used for augmentation has its own inherent advantages and disadvantages. Ileum is the most compliant segment and has less mucus production than the large intestine. Ureteral implantation into ileum, however, is much more difficult. At least 15 cm of terminal ileum should be left intact to prevent diarrhea and vitamin B_{12} deficiency. Sigmoid is usually redundant in the neurogenic bladder population, allowing ease of mobilization. It has excellent muscle backing for implantation but produces the most mucus; in our hands, it has demonstrated significant contractility and a statistically significant increase in risk of perforation [34]. As noted previously, we seldom use the ileocecal segment in children with neurovesical dysfunction because of the potential for diarrhea.

Each of these segments may result in hyperchloremic metabolic acidosis. The postoperative serum chloride level was greater than the preoperative level in virtually all patients who have undergone intestinocystoplasty, but those with normal renal function generally had chloride levels that remained within normal limits [41]. Hall *et al.* [42] noted that the exact mechanism of the acidosis is unknown but ammonium reabsorption may be the key factor. Patients with renal insufficiency may require bicarbonate replacement therapy. The body's response is to excrete the increased acid using bony buffers, which may result in bone demineralization and has led to concern regarding overall growth in children. (*Adapted from* Rink [38].)







◗ **FIGURE 11-9.** Technique of wedge gastrocystoplasty. **A,** Larger wedge from greater curvature now used, based on the right gastroepiploic artery. **B,** Wedge excised and stomach closed. **C,** Gastric wedge anastomosed to bivalved bladder.

Because of the previously discussed risks of incorporating intestine into the urinary tract, we began using stomach as the augmentation segment. Sinaiko [43] first reported its use in dogs in 1956. Leong and Ong [44] later used gastric antrum. We noted in the laboratory decreased mucus production, a net chloride excretion, and less tendency toward acidosis [45–47]. We reported our experience at Riley Hospital for Children in 1988 using a gastric wedge from the body of the stomach [48].

A 10-cm rhomboid-shaped segment of the body of the stomach (usually based on the right gastroepiploic artery as its vascular supply) is removed and placed on the bivalved bladder as the augmentation segment. The vascular pedicle should be secured to the retroperitoneum.

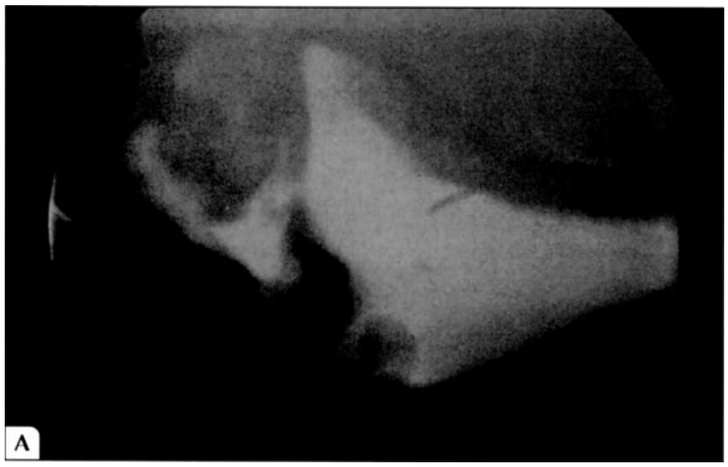
We have seen good bladder compliance, with only two of 46 patients not having a flat tonus limb [49]. However, we and others have noted frequent rhythmic contractions. Atala *et al.* [50] found these contractions in 10 of 43 patients, and Gosalbez *et al.* [51] noted these in 15 of 24.

We have had fewer infections using stomach [34], and stomach produces the least amount of mucus [45]. Bladder calculi, common in intestinal segments, has been reported rarely with gastric augmentation [52,53]. Submucosal tunneling of the ureter or appendix is also easy to perform into the stomach. Although these advantages seem to favor the use of stomach, particularly in those with renal insufficiency, there are significant disadvantages of rare but profound hypochloremic hypokalemic, alkalosis, and the frequent hematuria dysuria syndrome. This latter characteristic has been noted to necessitate medication in approximately one third of children after gastrocystoplasty and can be extremely bothersome if there is normal sensation [49,54]. A recent publication [55] has suggested that the stomach may contract over time, a particularly worrisome finding.

◗ **FIGURE 11-10.** Large bladder calculus comparable in size with a golf ball. One of the concerning problems after augmentation cystoplasty has been the increasing incidence of bladder calculi. Early reviews of intestinocystoplasty did not mention stone formation. In 1990, Hendren and Hendren [56] and, in 1991, Hirst [57] reported an 18% incidence. However, Blyth *et al.* [58] later reported a 30% incidence; if catheterizing through an abdominal wall stoma, the incidence was even higher. Palmer *et al.* [59] reported the highest incidence (52%). We found only an 11% incidence in 287 patients and attributed the low incidence partially to daily bladder irrigation to clear mucus and crystals [52]. We have noted only one stone after gastrocystoplasty, and this patient had a staple as a nidus. Bladder calculi are generally struvite, with their etiology being multifactorial (*ie*, urea-splitting organisms, stasis of urine, and mucus from poor emptying by clean intermittent catheterization). Hypocitraturia may be another factor in these patients [60].

◗ **FIGURE 11-11.** Urine specimens from a normal subject (*left*) and from a patient with augmentation cystoplasty (*right*). Note the presence of mucus in the specimen on the *right*. Gastrointestinal (GI) segments continue to produce mucus after their incorporation into the urinary tract. In children who empty using a small diameter catheter, mucus plugging can be a significant problem that can lead to poor emptying, slow drainage, and the need for frequent irrigations. Kulb *et al.* [45] have shown that colon produces the most mucus, followed by ileum; stomach produces the least [45]. Furthermore, villous atrophy in the ileum is thought to result in decreasing mucus production with time, a finding not seen in the colon [61].

Mucus from those who form bladder calculi has been shown to have a high calcium-to-phosphate ratio [60]. We insist on bladder irrigation with saline three times a day starting in the immediate postoperative period. This is decreased to two times per day in weeks 2 and 3. Daily irrigation until the patient is clear of mucus, regardless of the GI segment used, continues for life.



◗ **FIGURE 11-12.** Bladder perforation. **A,** Cystogram demonstrating contrast extravasation from perforation of augmented bladder.

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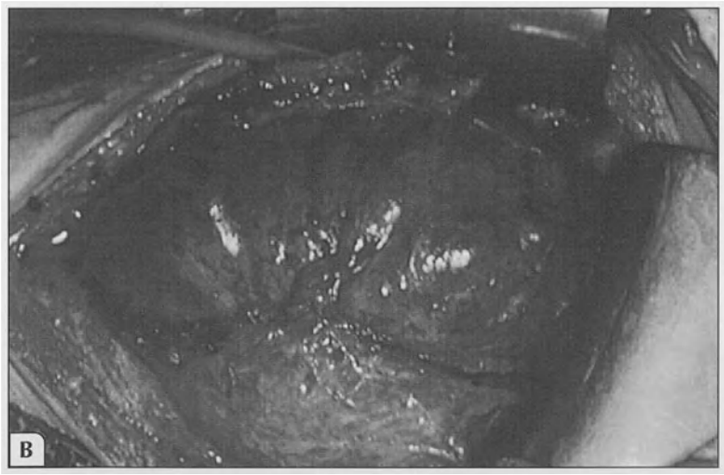
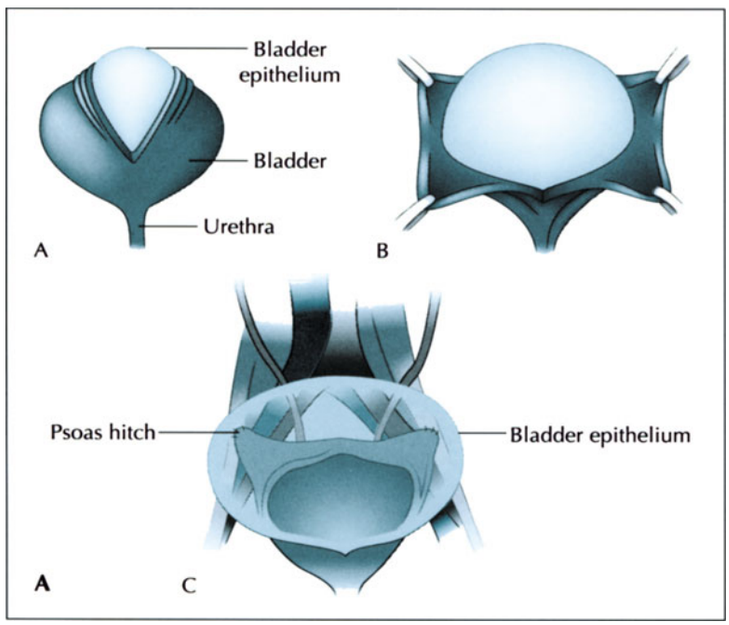


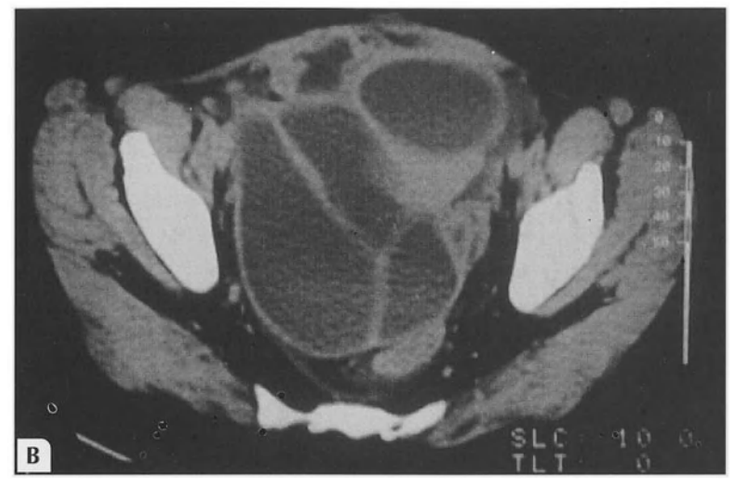
◗ **FIGURE 11-12.** (*Continued*) **B,** Large urinoma demonstrated on CT scan from bladder perforation. The most disturbing and potentially lethal complication of augmentation enterocystoplasty has been rupture of the augmented bladder. Unfortunately, these children with neurogenic dysfunction have impaired abdominal sensation, which often delays symptoms and diagnosis. In our experience, presentation has occurred in three distinct patterns: frank septic shock, abdominal pain but clinically stable, and an incidental finding of a urinoma [62]. Most patients present with abdominal pain and distention, fever, and decreased urine output [63,64]. To further complicate the diagnostic dilemma, radiographic confirmation can be difficult. Cystography has often yielded false-negative results. Braverman and Lebowitz [65] showed improved accuracy by studying fluoroscopy until bladder filling stops. We and others have found CT cystography to be the most reliable.

The incidence of perforation in our group of patients is 7%, with 32% of these suffering a second perforation. One child in this group perforated four times [62].

Various causes of perforation have been proposed, but most likely the cause is multifactorial. It occurs most often in those with neurogenic dysfunction and poor sensation with high urethral resistance. These children have overdistention secondary to poor emptying, which results in high intravesical pressures. These factors combine to result in ischemic areas, which may rupture. In our experience, perforations have been statistically significant and more likely to occur in those with sigmoidcystoplasty [34]. Although conservative management has been suggested, we would recommend this only for completely stable patients with sterile urine. All others appear best managed by exploration, drainage, and closure of the perforation.

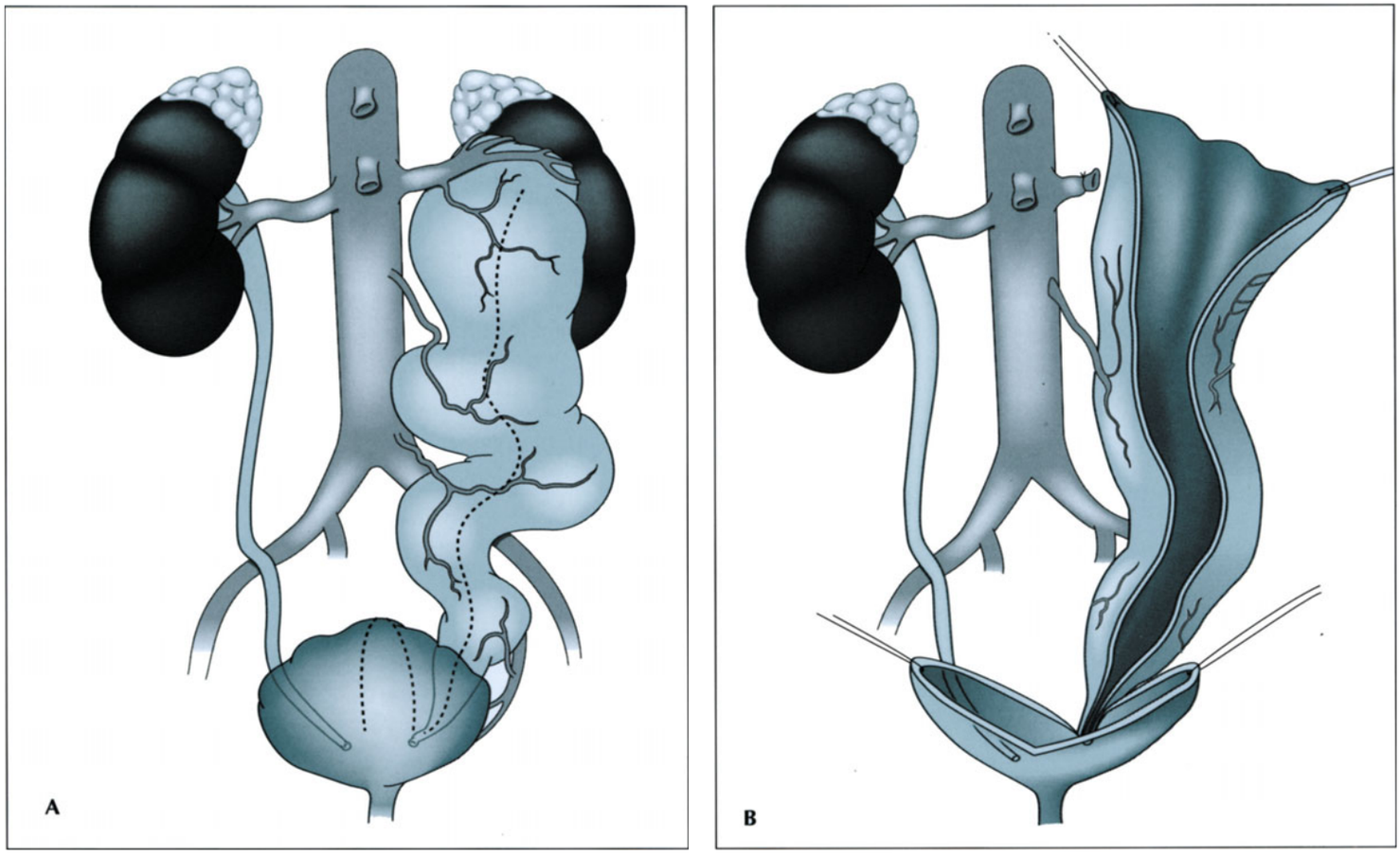


◗ **FIGURE 11-13.** Autouagmentation. **A,** Technique. **B,** Operative view. Intestinocystoplasty has been a great advance in the care of children with neurologic impairment; however, the risks noted previously have caused urologists to seek other alternatives. Cartwright and Snow [67] proposed an ingenious way to increase capacity and compliance without incorporating tissue from outside of the urinary tract. The use of native urothelial tissue avoids the metabolic changes, mucus production, and the need for intraperitoneal surgery. In their procedure known as autoaugmentation, the muscle overlying the dome of the bladder is excised, allowing the intact mucosa to bulge as a wide-mouthed diverticulum. This procedure is now well accepted as a means to improve compliance, but unfortunately it has provided "modest at best" increases in capacity [68]. In a combined series, 25 patients underwent autoaugmentation: in 52% the results were good, 28% acceptable, with 20% poor [69].



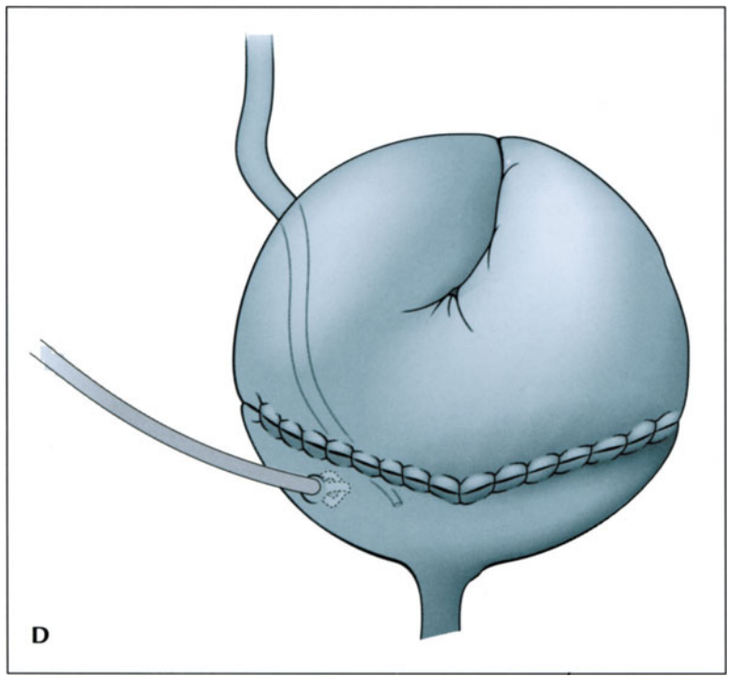
Ehrlich and Gershman [70] performed a similar procedure laparoscopically (detrusor incision) that was clinically successful. It allowed a shortened hospitalization but was an intraperitoneal procedure.

In response to the occurrence of fibrosis of the mucosa in autoaugmentation, two groups have been interested in combining this procedure with a demucosalized segment of sigmoid [71] or stomach [72]. This allows not only native urothelial lining but also provides muscle backing. Gonzalez *et al.* [73] reported their experience with the sigmoid seromuscular cystoplasty with urothelial lining (SCLU) in 16 patients. They found a 2.4-fold increase in capacity in 14 of 16 patients. End-filling pressures also improved, decreasing from 51.6 to 27.7 cm H_2O. The procedure failed in two patients; they later required ileocystoplasty. Failures are thought to be secondary to inadequate bladder distention in the early postoperative period [74]. (*Courtesy of* Dr. Brent Snow.)



◗ **FIGURE 11-14.** Ureteral augmentation technique. **A,** Proposed incisions. **B,** Nephrectomy completed; ureter and bladder opened. **C,** Ureter folded to create more spherical shape.

(*Continued on next page*)



◗ **FIGURE 11-14.** (*Continued*) **D,** Ureteral augmentation completed. In patients with a massively dilated ureter with reflux, the ureter already "augments" the bladder capacity. It is a natural extension to use this urothelial tissue to enlarge the bladder. This was originally done in patients with a nonfunctioning kidney after nephrectomy [75,76]. The ureter is opened longitudinally away from its blood supply, to the level of the bladder (**A**). The bladder is bivalved and the ureter is reconfigured (**B**) to maximize capacity and is anastomosed to the bladder (**C**). This has generally been done through a midline transperitoneal approach but has been done extraperitoneally through flank and suprapubic incisions [77,78]. We have also noted that it may not be necessary to open the ureter completely to the bladder [79]. The advantages are similar to those for autoaugmentation. More than 50 patients have now been reported with the upper urinary tracts remaining stable or improved in all with only rare complications [80]. Landau *et al.* [81] compared ureterocystoplasty with ileocystoplasty and showed that the two provided very similar capacity and compliance. It is our procedure of choice when this tissue is available. The obvious disadvantage is that it is our hope that no patient with modern management would have massive reflux with a nonfunctioning kidney. Therefore, the patient population is limited. (*Adapted from* Rink and Adams [82].)

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12

The Role of Laparoscopy in Pediatric Urology

Steven G. Docimo

Laparoscopy (and minimally invasive surgery in general) has been slower to gain acceptance among pediatric urologists than among many other specialists. This is largely because of the reconstructive rather than extirpative focus of pediatric urology, as well as the small size of our patients. Recent advances in technology, as well as innovative thinking regarding applications for laparoscopy, have begun to change the situation. For example, laparoscopy has been used for more than 20 years as a diagnostic adjunct in the management of the nonpalpable testicle [1]. With the introduction of cord clipping for a first-stage Fowler-Stephens operation [2] and then laparoscopic orchidopexy [3], the era of therapeutic laparoscopy in pediatric urology was born. Today, laparoscopic orchidopexy is a well-accepted part of the urologist's repertoire for dealing with high testicles [4–8].

Experience with laparoscopic techniques and collaboration with adult urologic laparoscopic pioneers led to the now common laparoscopic nephrectomy [9], as well as laparoscopic partial nephrectomy [10]. Attempts to treat patients with vesicoureteral reflux in a minimally invasive fashion have included laparoscopic extravesical ureteral reimplantation [11], as well as the development and refinement of endoscopic techniques of ureteral manipulation within the bladder [12–14].

The reconstructive era of pediatric laparoscopic surgery is just beginning. The first major reconstructive effort was a laparoscopic gastrocystoplasty performed in 1994 [15]. Autoaugmentation of the bladder has also been applied laparoscopically [16]. Perhaps the future of these techniques is represented by the laparoscopic-assisted bladder reconstruction, combining the morbidity and cosmetic advantages of laparoscopy with the ability to perform complex tissue assembly through a low abdominal incision [17,18].

Future applications of laparoscopy await improvements in technology as well as our imaginations. Already, 2-mm laparoscopic instruments, automatic suturing apparatus, telerobotic laparoscopic mentoring [19], and the application of techniques such as laser welding [20] give some hint as to the potential for minimally invasive surgery in the future.

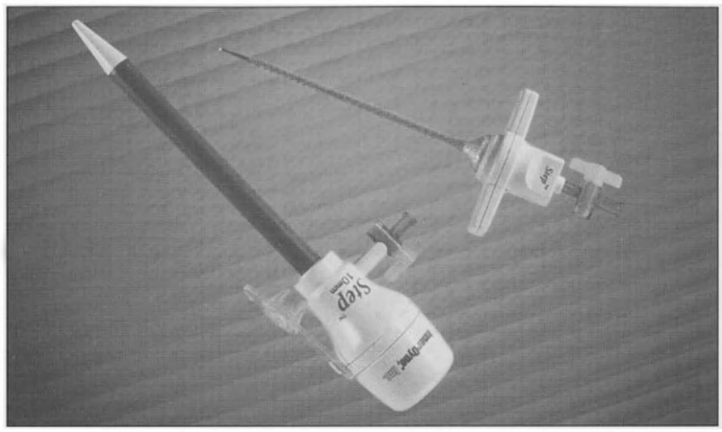


FIGURE 12-1. Trocar used for the open technique for pneumoperitoneum. In small children and infants, pneumoperitoneum can be obtained using the Veress needle or, preferably, open access [21]. A new technique for open access that I adapted using a radially expandable trocar (STEP; Innerdyne, Inc., Sunnyvale, CA) enhances the safety of this procedure even further. The small (2-mm) expandable sleeve is placed through an umbilical incision directly into the peritoneal cavity. It is then dilated using either the 5- or 10-mm insert, after which insufflation is commenced and the laparoscope is introduced. No fixating suture is needed because the dilating trocar is naturally held in place by friction. Upon removal of the trocar, the skin and fascial incisions are significantly smaller than those that would have been required for a standard 5- or 10-mm trocar. All 5-mm or greater trocar sites in children should be closed [22], which can be accomplished by tying the fascial stay sutures together at the end of the procedure.

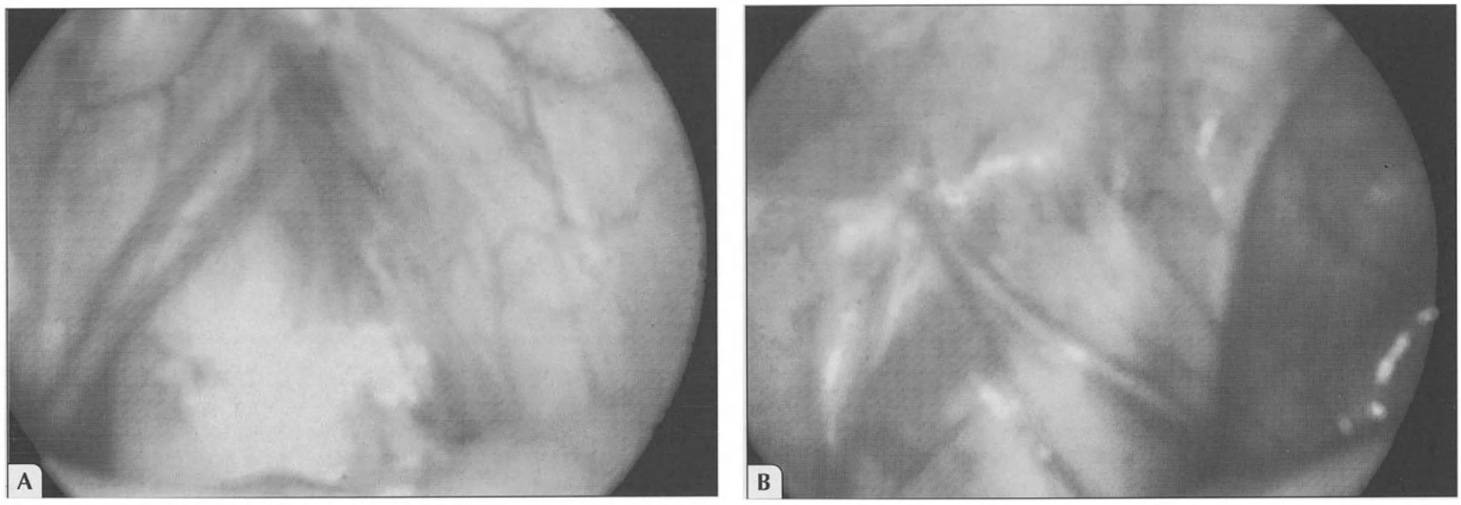


FIGURE 12-2. Vas deferens and spermatic vessels exiting the internal ring. Diagnostic laparoscopy for the nonpalpable testis results in one of three main findings [23–24]. The most common finding (45%) is the presence of a vas deferens and spermatic vessels that exit the internal inguinal ring. This signifies that there is definitely no ipsilateral testicular tissue within the abdomen and that the groin or scrotum should be explored for a testicle or testicular nubbin. Often, as in the case pictured, the vessels on the affected side appear attenuated [25], further suggesting that the testicle is not normal. Here, the right sided vas and vessels (**A**) appear normal but the affected left side (**B**) demonstrates vessels that are not as well defined. Some controversy exists concerning exploring the groin or scrotum in this situation [25,26], but most authors continue to recommend exploration [27–29].

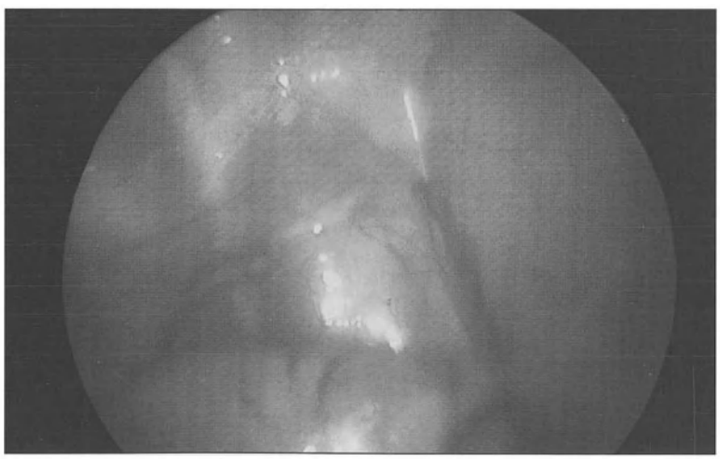
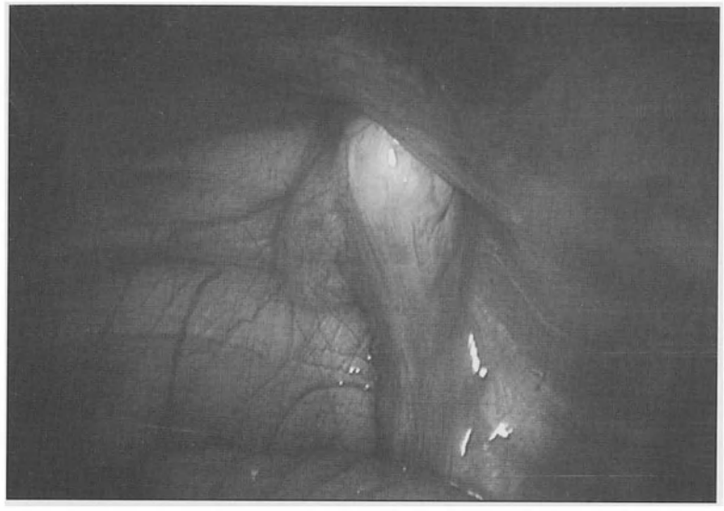
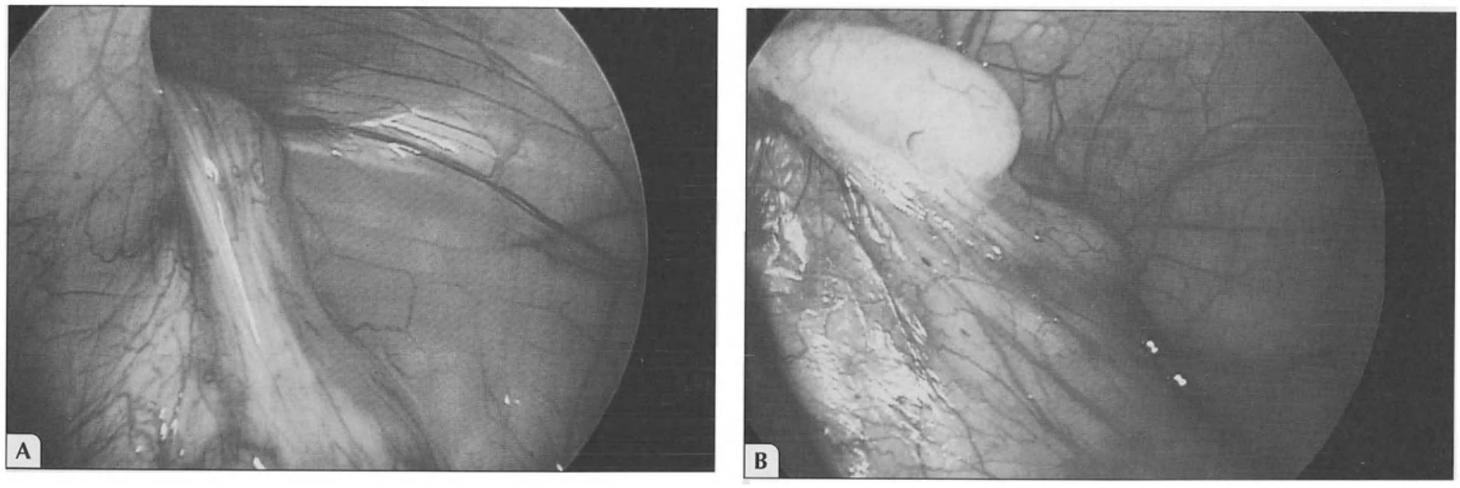


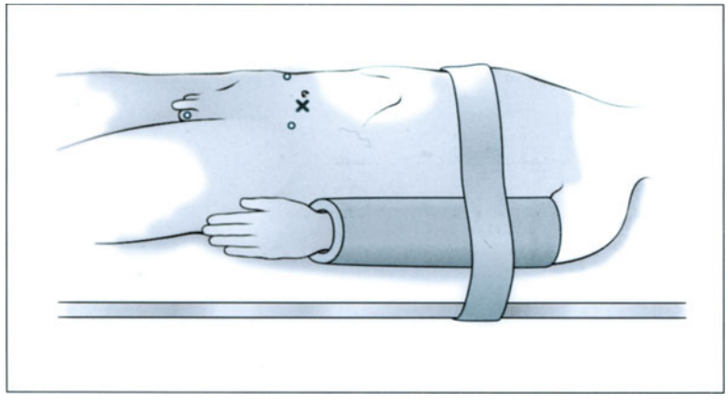
FIGURE 12-3. Blind-ending spermatic vessels. Laparoscopic exploration in the face of a "vanishing testis" will reveal blind-ending spermatic vessels. Blind-ending vessels must be seen in order to make the diagnosis of a vanishing testis because the absence of spermatic vessels and true testicular agenesis are extremely rare [30]. There can be disjunction between the wolffian system and the testis, so the presence of a blind-ending vas deferens without blind-ending vessels is not necessarily diagnostic [31]. In contrast to Figure 12-2, in which the vas deferens and vessels are seen to meet at the internal ring, here there is clearly a space between these structures. This is the typical appearance of blind-ending spermatic vessels and vas deferens.



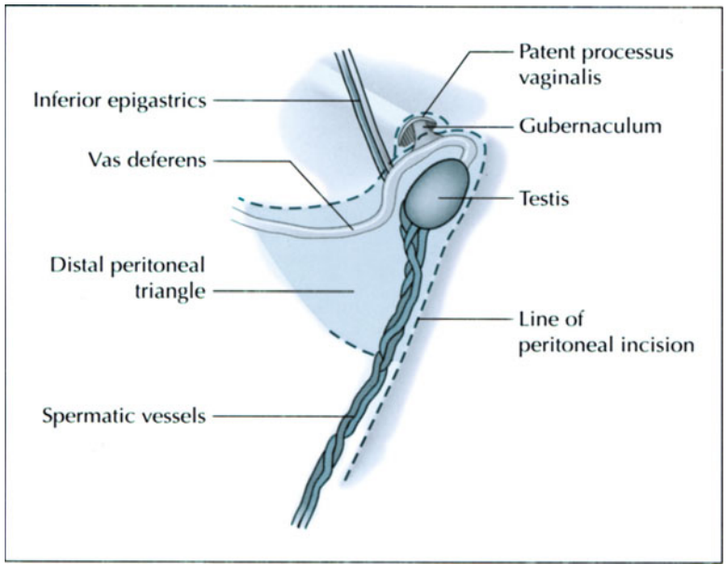
◗ **FIGURE 12-4.** Low intra-abdominal (or "peeping") testis. This is the typical appearance of an intra-abdominal testis. In this case, one can see some redundancy of the spermatic vessels and a testicular position at the internal ring, suggesting that this testis can be brought surgically to the scrotum without division of the spermatic vessels (Fowler-Stephens approach [32]). The main advantage of laparoscopic orchidopexy lies in the ability to preserve the spermatic vessels in the majority of cases, thereby hopefully improving the surgical outcome [33].



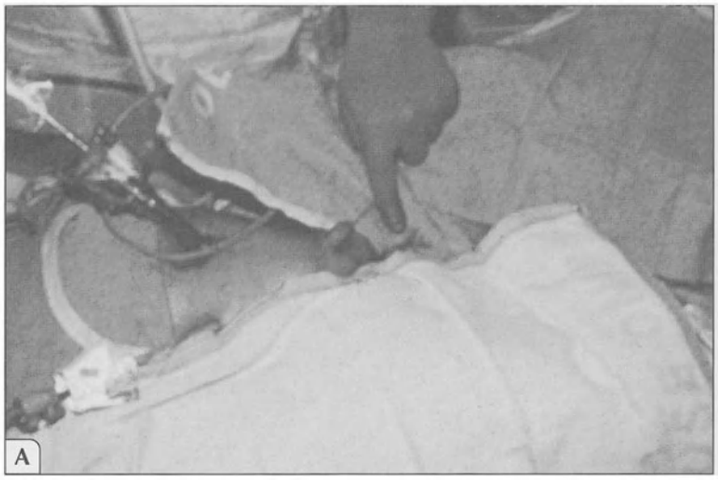
◗ **FIGURE 12-5.** High intra-abdominal testis. The alternative to single-stage laparoscopic orchidopexy is to perform a two-stage Fowler-Stephens procedure [34] by clipping the spermatic vessels at the time of diagnostic laparoscopy [2] and returning 6 to 12 months later to bring the testis into the scrotum based on the vasculature of the vas deferens. This second stage can also be performed laparoscopically [5]. **A,** The testis is 4 cm above the internal ring with very short spermatic vessels, as demonstrated by the long gubernaculum leading into the patent processus vaginalis. **B,** Laparoscopic clips can be seen on the spermatic vessels.

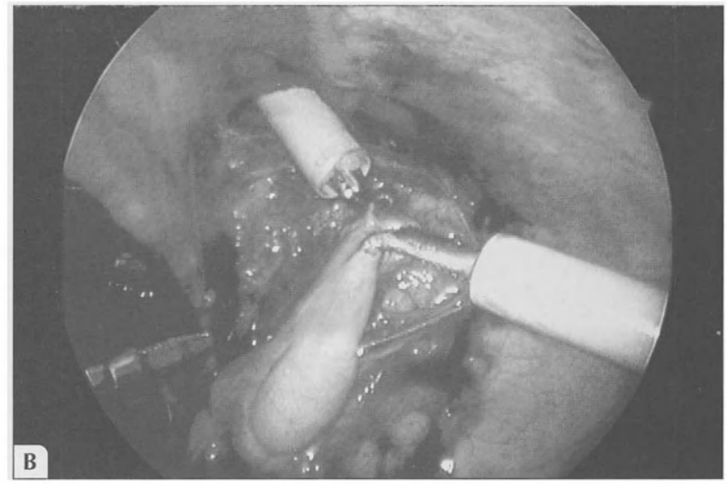


◗ **FIGURE 12-6.** Cannula placement for laparoscopic orchidopexy. Laparoscopic orchidopexy [3] is generally performed through three abdominal trocar sites and one trocar site in the scrotum [21]. According to my practice, there is a 5-mm umbilical trocar for the laparoscope (X) and a 2-mm port on either side of the abdomen for instruments (O). The patient is supine, with loose tape over the chest to secure the patient in the deep Trendelenburg position. The arms are tucked to allow maximum mobility for the surgeons.



◗ **FIGURE 12-7.** Intraperitoneal dissection for laparoscopic orchidopexy. To free the testis for placement in the scrotum, an incision is made in the peritoneum lateral to the spermatic vessels and distal to the vas deferens. This incision is carried over the anterior aspect of the inguinal ring and care is taken to avoid injury to the inferior epigastric vessels. The gubernaculum is then divided, and the surgeon watches for a long-looped vas deferens. The distal triangle of peritoneum between the spermatic vessels and the vas deferens is carefully preserved, both to allow conversion to a Fowler-Stephens approach, if necessary, and to enhance vascularity to the testis. Proximal to the distal peritoneal triangle, the peritoneum can be peeled off the spermatic vessels to increase length. Care must be exercised in order to avoid avulsion of the spermatic vessels during delivery of the testis into the scrotum, especially if the peritoneum has been stripped.





◗ **FIGURE 12-8.** Delivering the testis into the scrotum. The ipsilateral laparoscopic instrument is passed either medially or laterally to the inferior epigastric vessels and out through an anterior scrotal incision. Although 5-mm instruments are shown here (**A**), currently a 2-mm instrument would be passed through the scrotum and a radially dilating trocar (STEP; Innerdyne, Inc. Sunnyvale, CA) would be introduced over the instrument and then dilated to 5 mm. A 5-mm grasper is then introduced through the scrotal trocar (**B**) and used to advance the testis into the scrotum. If the spermatic vessel length is abundant, the natural course of the inguinal ring lateral to the epigastric vessels is used. The surgeon can theoretically achieve an extra 1 to 2 cm of length by bringing the testis medial to the inferior epigastric vessels [36]. The testis is then secured in the scrotum using whichever method seems most appropriate.

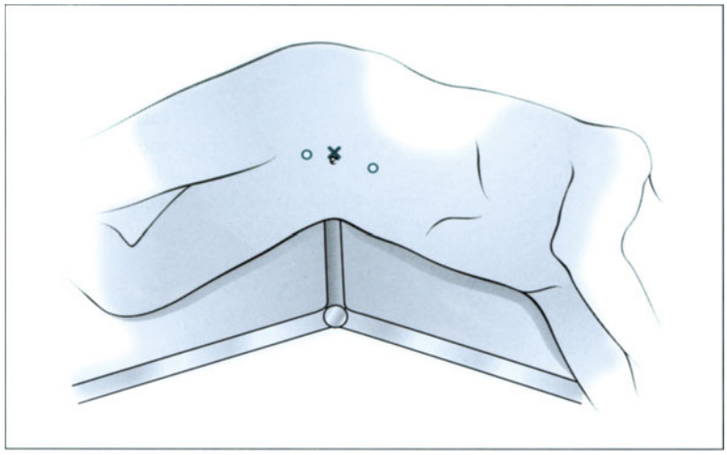


FIGURE 12-9. Cannula placement for nephrectomy. Transperitoneal laparoscopic nephrectomy [9] is performed with the patient in the flank position. Twelve-mm (X) and 5-mm (O) trocars have generally been used, but nephrectomy has recently been performed using 2-mm instrumentation (Peters C, Personal communication). A 5-mm trocar is still required in at least one position: for the use of clip appliers on the renal vessels. Nephrectomy in adults or adolescents may require the use of vascular staplers or a morcellator, which must be introduced through 12-mm trocars.

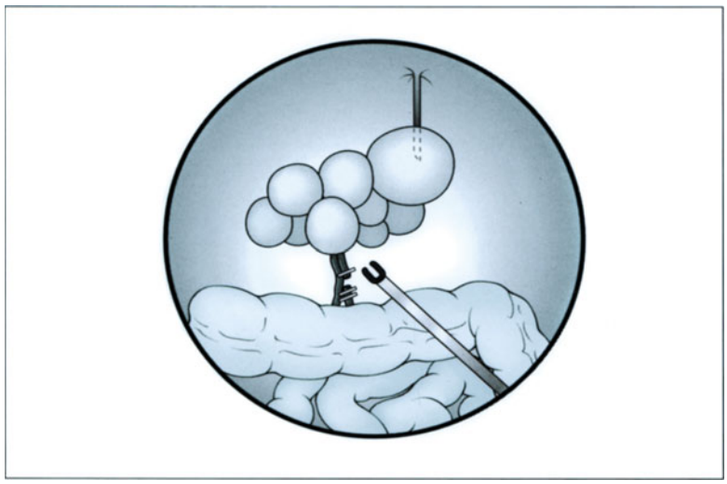


FIGURE 12-10. Removal of multicystic, dysplastic kidney. The dissection for transperitoneal nephrectomy is no different than for that of the open operation. The colon on the affected side is reflected, revealing Gerota's fascia. Gerota's fascia is then entered and the kidney is mobilized appropriately. For multicystic kidneys, the cysts can be percutaneously decompressed using a spinal needle under direct vision from within, making mobilization of the kidney easier. Endoscopic clips are used on the vessels, and the kidney is either removed in its entirety through the largest trocar site or it is fragmented or morcellated within a laparoscopic surgical tissue pouch [9]. Laparoscopic nephrectomy is especially useful when ureterectomy is also required [37,38]. The ureter can be dissected to a point just behind the bladder, where it can be divided using clips or a stapling device, thus obviating the need for two incisions. In addition, partial nephroureterectomy, as in the case of a patient with ectopic ureterocele, is readily accomplished laparoscopically [10,38].

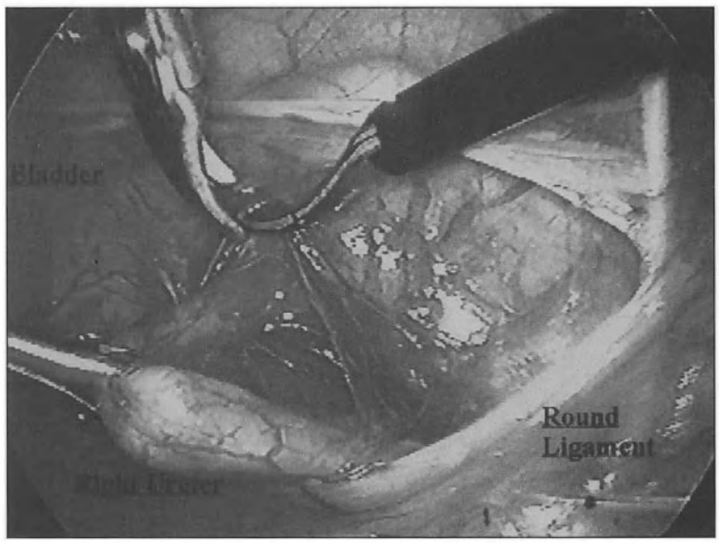
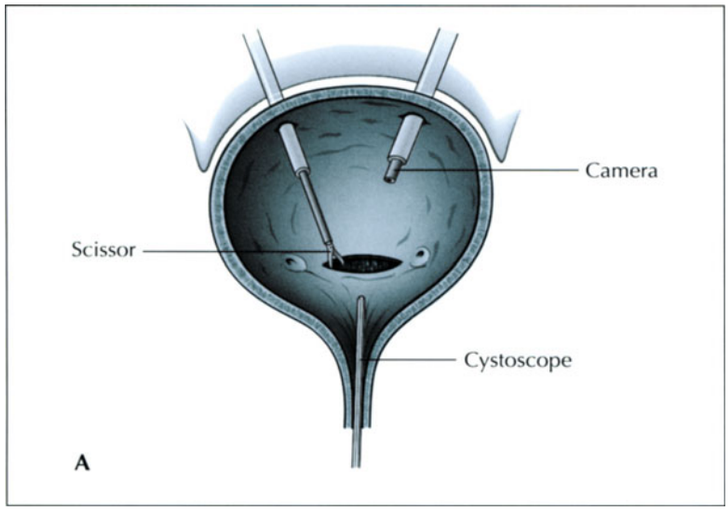
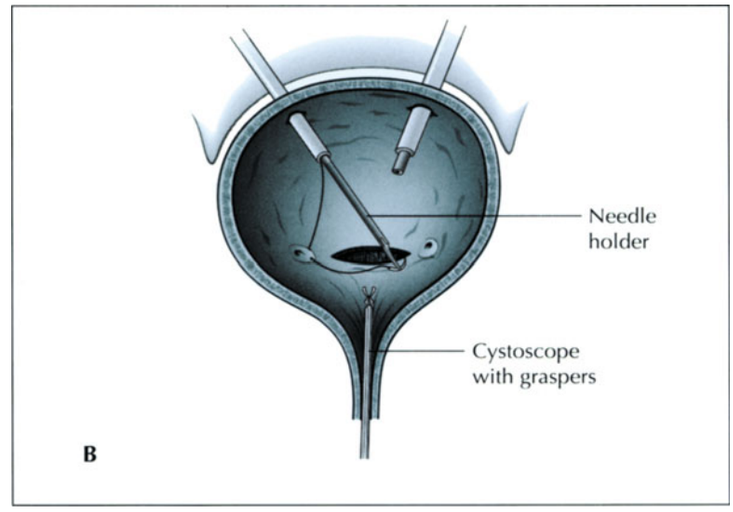
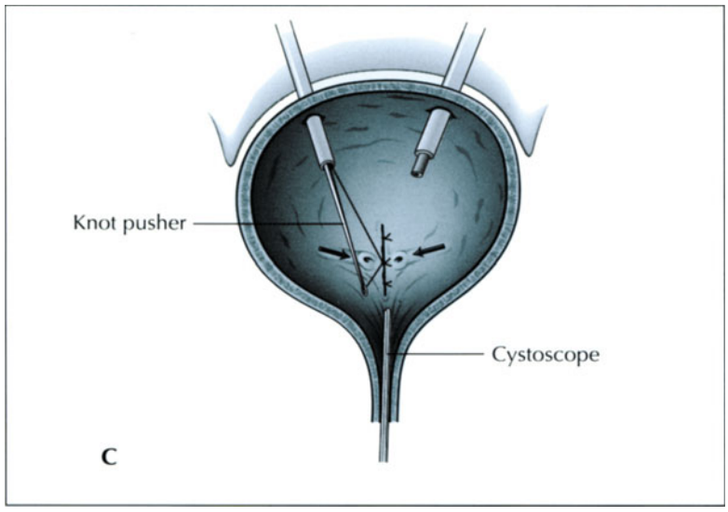


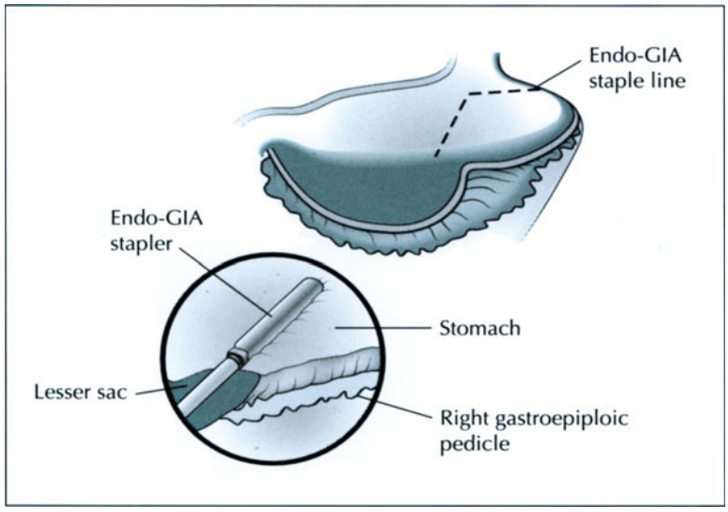
FIGURE 12-11. Extravesical laparoscopic ureteral reimplant. Vesicoureteral reflux (VUR) is surgically managed by open ureteral reimplantation, an operation that can be performed through a small Pfannenstiel incision and generally requires only 2 to 3 days of hospitalization [39]. Against this baseline, it has been difficult to come up with a minimally invasive procedure that significantly decreases morbidity while maintaining the nearly 100% success rate of the standard open operation. Although the subtrigonal injection of materials is a minimally invasive approach to VUR, there is no long-lasting material in the United States that has proven highly successful. The most widely applied laparoscopic approach to VUR has been the laparoscopic extravesical reimplant [11]. This is performed in the manner of Lich-Gregoire [40]. The ureterovesical junction is exposed transperitoneally by incision between the round ligament and the bladder [41]. As shown here, an incision is made in the bladder muscle adjacent to the ureter and extended cephalad, staying outside of the bladder mucosa. A trough is created with mucosa as its base. The bladder muscle is then closed over the ureter using interrupted laparoscopic suture and tying techniques to effectively create a submucosal tunnel. (*Courtesy of* Y. Lakshmanan and LCT Fung, University of Massachusetts.)



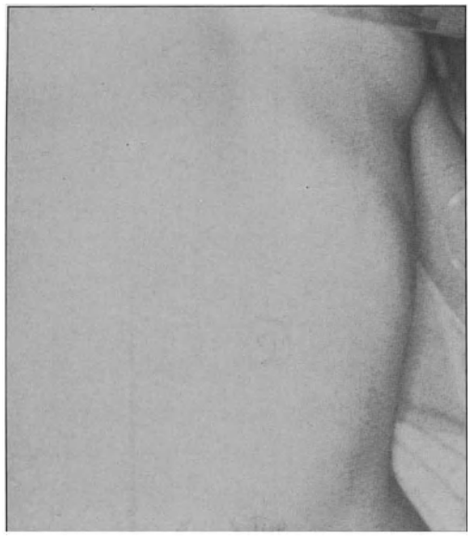




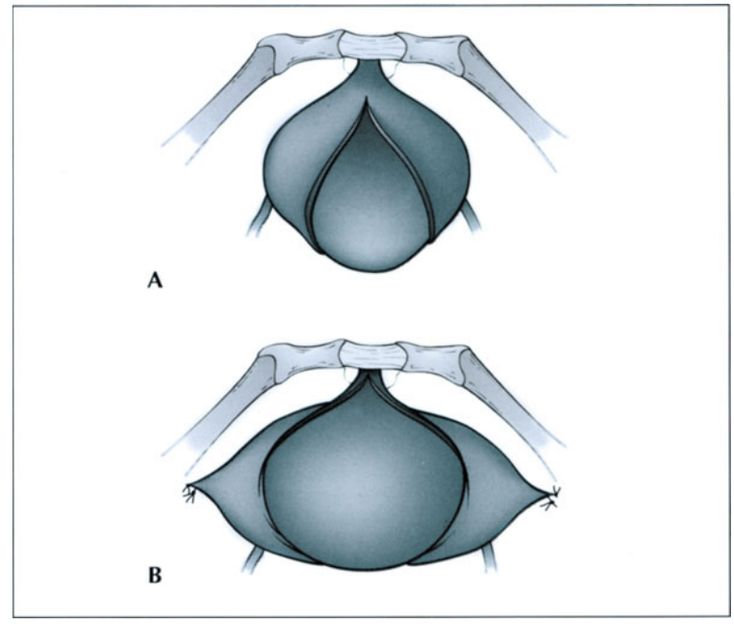
◗ **FIGURE 12-12.** Percutaneous endoscopic trigonoplasty. Smaller instrumentation has allowed experimentation and clinical experience in intravesical endoscopic surgery. The most well-established operation through this route is percutaneous endoscopic trigonoplasty, a modification of the Gil-Vernet procedure [13,14]. In this operation, a horizontal incision (**A**) from ureteral orifice to ureteral orifice is closed vertically (**B**), pulling the orifices toward the midline and enhancing the fixation of the ureteral tunnel (**C**). Unfortunately, the initial promise of trigonoplasty has not been realized with long-term follow-up [42]. Going one step further, it has been shown both experimentally [12] and clinically (Snow BW, Cartwright P, Personal communication) that the ureters can be dissected free of the bladder muscle and reimplanted using an endoscopic technique. (*Adapted from* Cartwright *et al.* [14].)



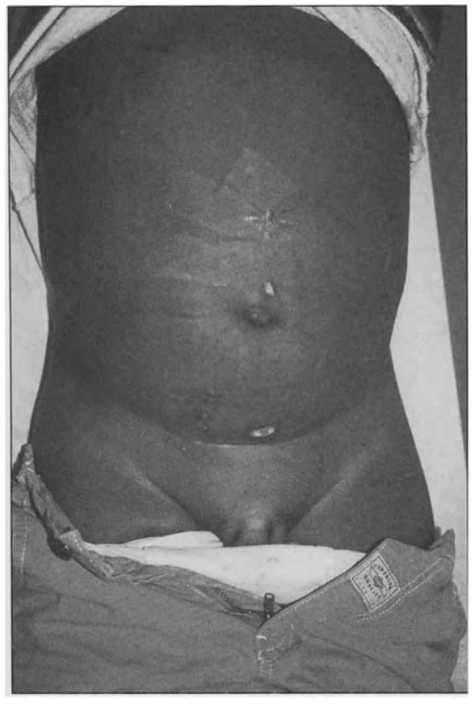
◗ **FIGURE 12-13.** Laparoscopic gastrocystoplasty. The era of major urologic laparoscopic reconstruction is in its infancy. In the first reported laparoscopic bladder augmentation [15], a wedge of stomach was harvested with multiple firings of an endogastrointestinal anastomosis (Endo-GIA) stapler. This was done after multiple laparoscopic clips had been used to divide vessels between the right gastroepiploic artery and vein and the greater curve of the stomach creating the gastroepiploic pedicle. This wedge of stomach was then sutured to the open bladder using the EndoStitch (AutoSuture Company, Norwalk, CT). A drain and suprapubic catheter were brought through laparoscopic ports at the end of the procedure. (*Adapted from* Docimo *et al.* [15].)



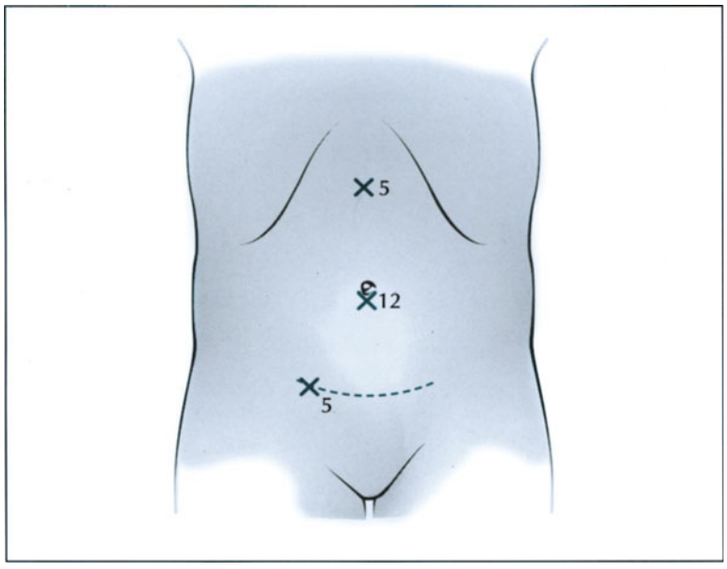
◗ **FIGURE 12-14.** Postoperative cosmetic appearance after laparoscopic gastrocystoplasty.

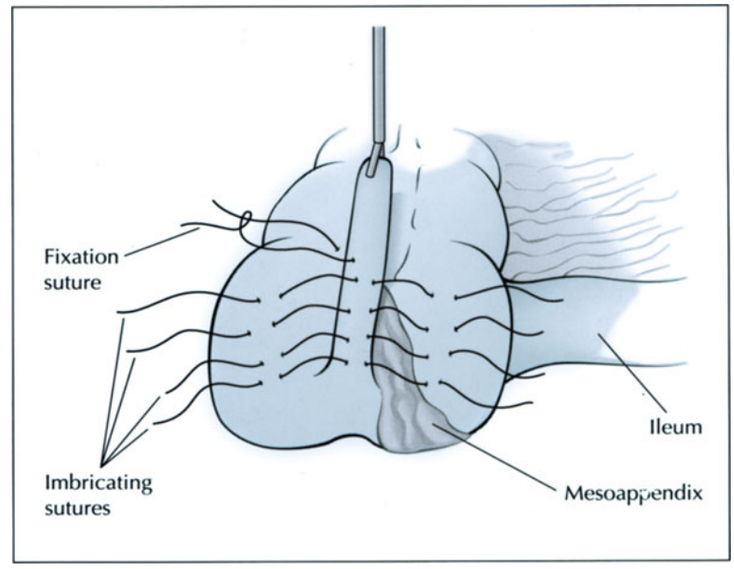


◗ **FIGURE 12-15.** Laparoscopic autoaugmentation. The concept of autoaugmentation is essentially the creation of a bladder mucosa diverticulum [43]. The application, longevity, and indications for autoaugmentation are all somewhat controversial; however, this operation can be performed laparoscopically or extraperitoneally using laparoscopic instrumentation [16,44]. **A,** The bladder muscle has been divided and carefully separated from the underlying mucosa. **B,** The bladder muscle is then sutured to Cooper's ligament on each side of the pelvis to avoid reclosure of the muscle. (*Adapted from* McDougall *et al.* [16].)



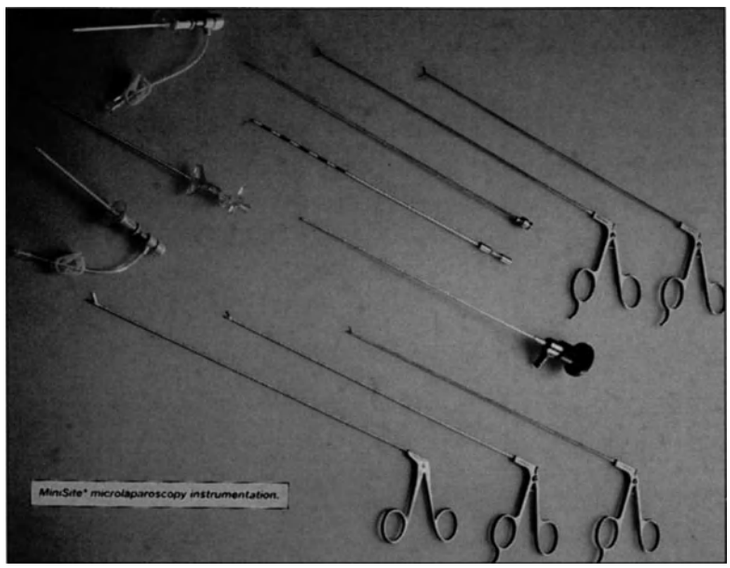
◗ **FIGURE 12-16.** Improved cosmesis with laparoscopic assistance. Although laparoscopic bladder augmentation using gastrointestinal segments is perhaps prohibitively technically difficult and requires long operating times, the combination of laparoscopic and open techniques represents the current state of the art for bladder augmentation. By using laparoscopic techniques to mobilize the right colon, harvest the appendix [18], or harvest stomach [15], there is no need for an upper abdominal incision. The more technically demanding assembly of these parts in the area of the bladder is then performed through a Pfannenstiel or low midline abdominal incision. This is not only cosmetically more acceptable but theoretically results in fewer intra-abdominal adhesions than the standard open reconstruction [45]. The boy shown had ileal bladder augmentation with creation of a continent appendiceal stoma 4 weeks earlier and has just had his suprapubic catheter removed. Similar cosmetic results have been obtained for patients with bladder exstrophy and spina bifida [17].





◗ **FIGURE 12-17.** Port placement for typical laparoscopically assisted urinary reconstruction. By placing the laparoscopic ports strategically, one port is hidden in the umbilicus and the other becomes part of the Pfannenstiel incision. The only laparoscopic site that creates a scar is the epigastric site, which is 5 mm in size and can be placed using a radially dilating system, which minimizes the scar even further.

◗ **FIGURE 12-18.** Laparoscopic Malone antegrade continence enema (ACE) procedure. The ACE procedure [46] can be performed using laparoscopically assisted techniques either using the appendix or, experimentally, a stapled cecal tube [47]. Clinically, a completely laparoscopic ACE procedure is performed by imbricating the colon around the base of the appendix, as demonstrated. Through experience, it has been found that this should be done using permanent sutures or staples because this imbrication can fail when absorbable sutures are used.



◗ **FIGURE 12-19.** Two-mm laparoscopic instruments. Miniaturization is one of the technical advances that will make laparoscopy more amenable to large reconstructive procedures. The 2-mm instruments and trocars pictured (AutoSuture, Norwalk, CT) can be introduced into the abdomen through a needle puncture, thereby allowing as many instruments as necessary to be brought into play with very little cosmetic impact or morbidity.

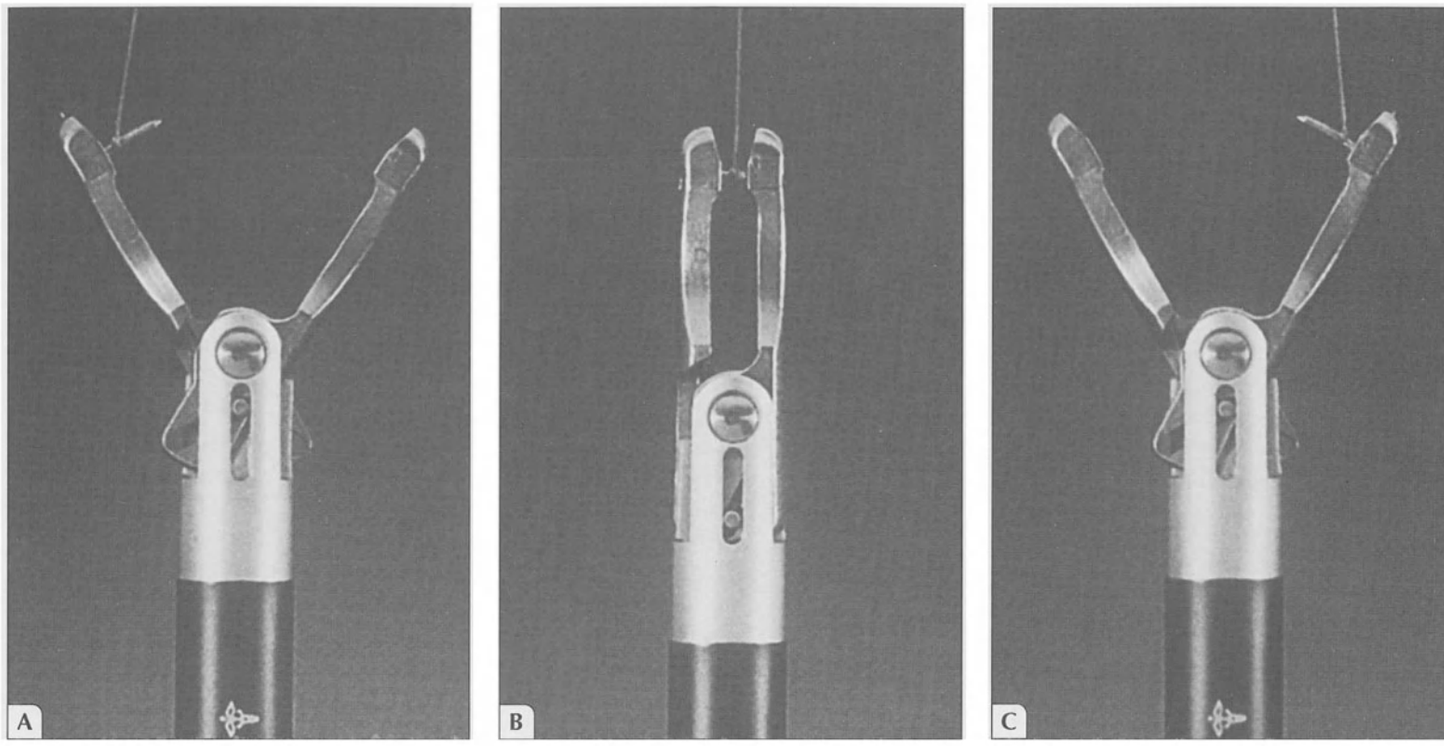


FIGURE 12-20. Automatic suturing device (**A–C**). The EndoStitch (AutoSuture, Norwalk, CT) has already allowed many procedures, such as the laparoscopic gastrocystoplasty, to be performed that would otherwise be too time consuming using traditional laparoscopic suturing methods. Further advances in automatic suturing technology are required before procedures such as infant pyeloplasty are widely accepted.

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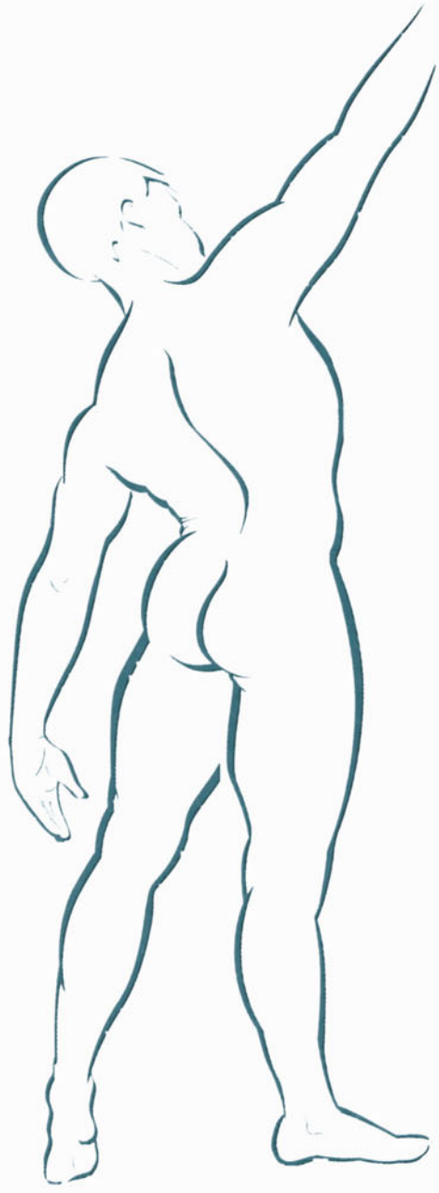
13

Renal Tumors in Childhood

Robert Kay and Jonathan H. Ross



Renal tumors in children range from the benign neonatal congenital mesoblastic nephroma to the highly malignant anaplastic Wilms' tumor. Despite the intense interest in renal tumors in children because of their genetic implications and understanding of oncogenesis, these tumors are relatively rare. Wilms' tumors are the most common genitourinary solid tumor in children, yet they only occur in one in every 10,000 children [1]. The treatment, however, of Wilms' tumor as well as the other tumors in children is one of the great modern miracles of medicine. Before the combination of chemotherapy, radiation therapy, and surgery, the survival rate of Wilms' tumor in the early 20th century was only 20% [2]. Currently, as a result of better understanding of the tumors themselves and the multimodal approach to therapy, survival has continued to improve to its current rate of more than 90% [3–5].

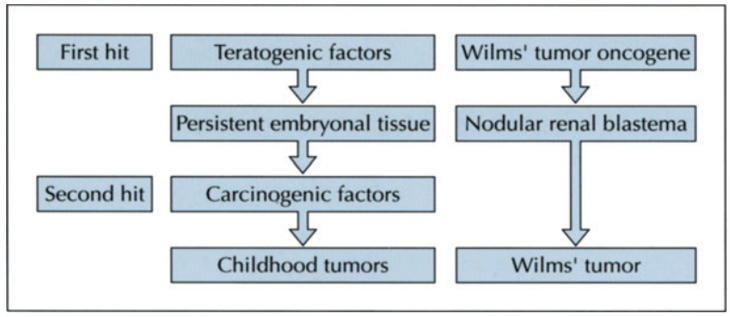
The diagnosis of renal tumors of childhood is based on clinical presentation, radiologic imaging, and histopathologic examination. Although many children present with only a solitary mass, other children's tumors may be detected on screening because of clinical syndromes that are known to be associated with malignancy. Radiographic imaging is quite straightforward with the use of ultrasound, computed tomography, and magnetic resonance imaging. Images today are clear, distinct, and informative regarding the size and location of tumors. Radiographic appearance is not unique to each tumor; therefore, histologic evaluation is needed to confirm the type of tumor. Because the treatment of these tumors is so different, ranging from chemosensitive Wilms' tumors to nonchemosensitive renal cell carcinoma, it is essential that pediatric urologists work closely with pathologists to define the histologic type and then the most appropriate adjuvant treatment.

Despite a significant increase in survival of patients with all types of kidney tumors, much is still to be learned about renal tumors in childhood. As further research has focused on the molecular and biologic behavior of these tumors, it is apparent that tumors in childhood in general probably have a genetic basis. As further refinement and our understanding of the Wilms' tumor oncogene and other locations throughout the human genome are delineated, better understanding of these tumors may lead to more novel treatments as well as preventive treatments in children who are at high risk for these tumors. In the past, Wilms' tumor has served as a model for the understanding of oncogenesis, and it is believed that a better understanding of Wilms' tumor and the other renal tumors in children will continue this fantastic voyage into the understanding of oncogenesis and tumor behavior.

Differential Diagnosis of Renal Tumors in Children

Wilms' tumor
Congenital mesoblastic nephroma
Renal cell carcinoma
Clear cell sarcoma
Multilocular cyst (cystic nephroma or cystic partially differentiated nephroblastoma)
Malignant rhabdoid tumor of the kidney
Angiomyolipoma
Lymphoma
Other (fibroma, leiomyoma, leiomyosarcoma)

◗ **FIGURE 13-1.** Differential diagnosis of renal tumors in children. Renal masses in children must first be differentiated between cystic and solid. After it is clear that a solid mass is present, even with cystic components, the differential diagnosis can be narrowed. The most common pediatric renal mass is Wilms' tumor, but the most common mass in neonates is congenital mesoblastic nephroma. It is important to recognize that renal cell carcinoma may occur in any age group, particularly in adolescents. The diagnosis of infiltrative diseases such as lymphoma must also be considered, particularly when there are bilateral tumors. Other benign tumors such as multilocular cysts, angiomyolipomas, fibroma, and leiomyomas must also enter the differential diagnosis but, in general, are less common.



◗ **FIGURE 13-2.** The two-hit theory of oncogenesis. In 1972, Knudson and Strong [6] proposed their two-hit theory of oncogenesis based on the childhood tumor of retinoblastoma. This theory has persisted over the ensuing years and is thought to apply to Wilms' tumor. There clearly seems to be a genetic basis for Wilms' tumor. Three Wilms' tumor oncogenes have been identified: *WT1* at 11p13; *WT2* on 11p15; and the *WT3* oncogene, which has been postulated in several different locations [7,8]. It is also well recognized that the premalignant tissue postulated by Knudson and Strong [6] is present as nodular blastema, in 25% to 40% of unilateral Wilms' tumors, and up to 100% of bilateral Wilms' tumors [9].

Clinical Syndromes Related to Wilms' Tumor

Aniridia
Hemihypertrophy
Beckwith-Wiedemann syndrome
Denys-Drash syndrome
WAGR syndrome
Perlman syndrome

◗ **FIGURE 13-3.** Clinical syndromes related to Wilms' tumor. One of the more fascinating aspects of Wilms' tumor is its relationship to other clinical syndromes. This clearly supports the genetic basis of Wilms' tumor because it is known to occur in patients with specific diseases and clinical syndromes. Although slightly less than 1% of patients with Wilms' tumors have aniridia, one third of patients with sporadic aniridia develop a Wilms' tumor [1]. Children with hemihypertrophy or Beckwith-Wiedemann syndrome consisting of macroglossia, visceromegaly, and omphalocele are also at increased risk for the development of Wilms' tumors [10]. The Denys-Drash syndrome is the association of Wilms' tumor, ambiguous genitalia, and glomerular disease usually presenting with renal failure [11]. The WAGR syndrome consists of Wilms' tumor, aniridia, and mental retardation; the Perlman syndrome is a familial syndrome consisting of visceromegaly, macrosomia, polyhydramnios, abnormal facies, and an increased risk of nephroblastomatosis and Wilms' tumor [12].

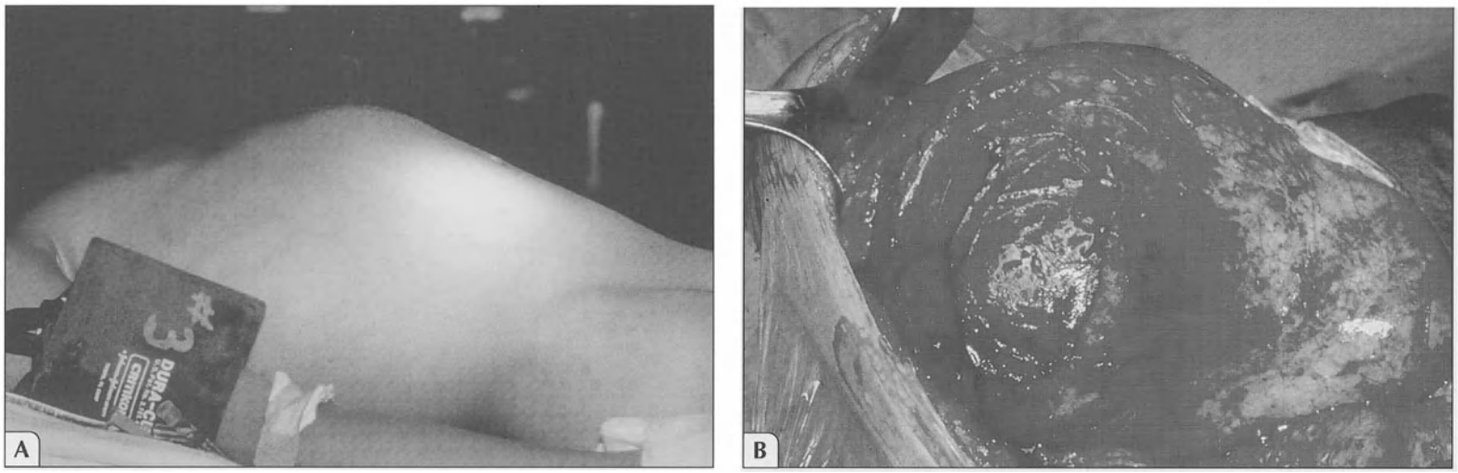
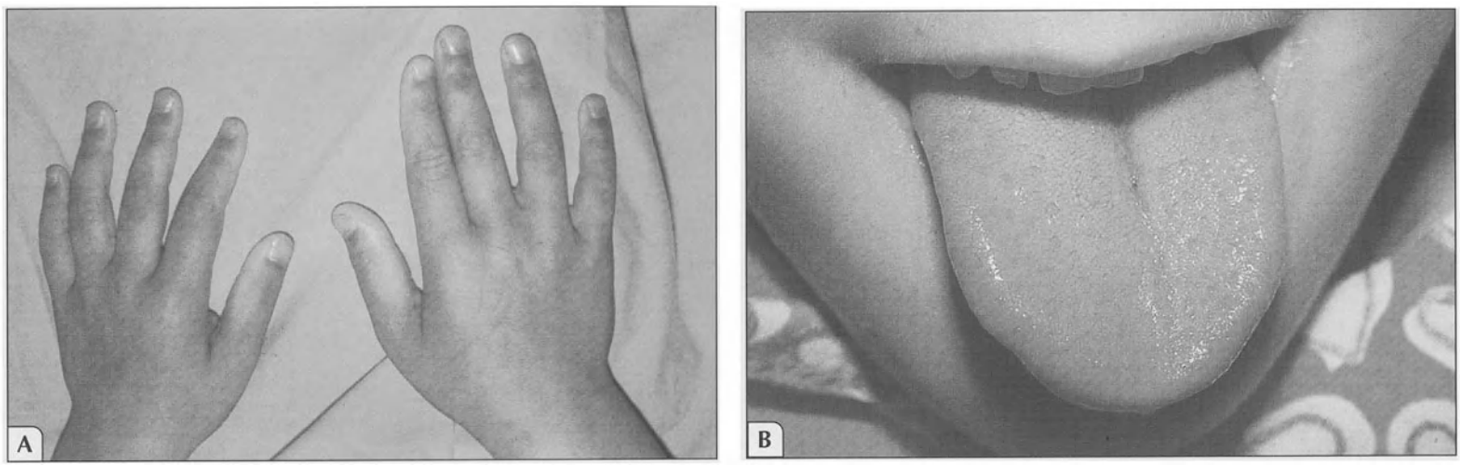


FIGURE 13-4. Presentation of patient with Wilms' tumor. A palpable mass (**A**) is the most common presentation of Wilms' tumor. A total of 95% of patients present with a palpable abdominal mass [13]. Other signs, including pain, vomiting, fever, hypertension, and hematuria, may be seen to a lesser degree. Complications of the tumor, such as trauma leading to hemorrhage (**B**), may also occur. Patients with renal cell carcinoma, however, usually present with vague systemic symptoms such as fever, malaise, and weight loss, as opposed to a mass as seen in those with Wilms' tumor, leading to a somewhat delayed diagnosis [14,15].



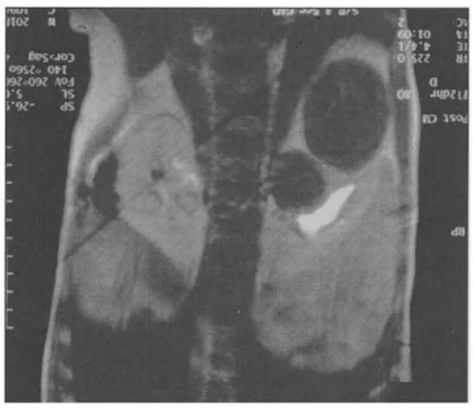


FIGURE 13-5. Five-year-old girl with Beckwith-Wiedemann syndrome. She had hemihypertrophy involving her hands (**A**) and tongue (**B**). Two Wilms' tumors in her right kidney were detected on a surveillance program (**C**). Patients who are at high risk, such as those with sporadic aniridia, Beckwith-Wiedemann syndrome, or hemihypertrophy should be screened and followed. The risk for these patients seems to be limited to approximately 7 years of age, so it is suggested that patients have a physical examination and ultrasound every 3 months until that age [16]. This allows for early detection of a tumor and perhaps early surgery and limited adjuvant therapy.

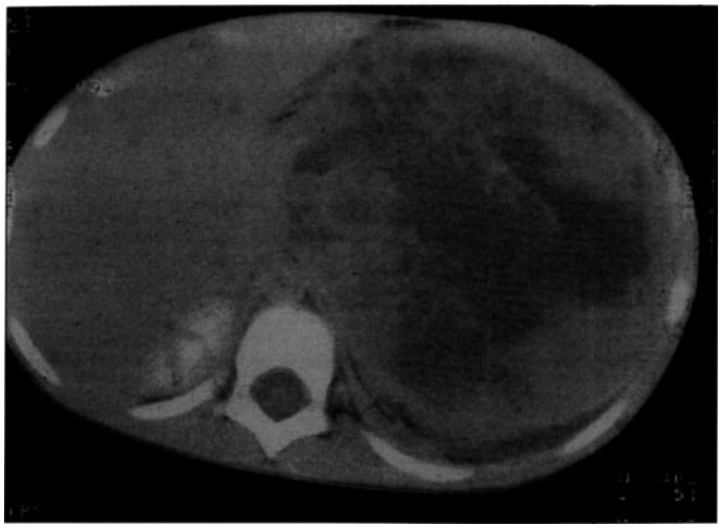


FIGURE 13-6. Computed tomographic (CT) scan of an abdominal mass. Pediatric renal tumors usually present with an abdominal mass. An ultrasound should be obtained initially to differentiate a cystic mass from a solid one. If a solid mass is seen, the vena cava may be screened initially by ultrasound for its patency. CT scanning and magnetic resonance imaging (MRI) are the modalities of choice for further evaluation. MRI offers better visualization of the vena cava and is more sensitive for nephroblastomatosis. However, CT scans are more easily obtained and simplify the evaluation because it may be combined with CT of the chest to rule out lung metastases. A routine urinalysis, creatinine level, and complete blood count should be obtained. If the vena cava is noted to have a tumor thrombus by either ultrasound or MRI, the distal extent of it must be delineated. Approximately 20% of patients with caval thrombus have an intra-atrial extension, and superior vena cavography or echocardiography may be required [17]. Angiography is rarely used in the evaluation of patients with Wilms' tumor.

Staging of Wilms' Tumor

Stage	*Description*
I	Limited to kidney: completely excised
II	Extrarenal extension (completely excised), biopsied tumor, local tumor spillage
III	Residual nonhematogeneous intra-abdominal disease, lymph nodes positive for tumor, or gross tumor spillage
IV	Hematogenous metastases
V	Bilateral tumors

FIGURE 13-7. Staging of Wilms' tumor. This staging is based on surgical findings and histopathologic confirmation. The use of adjuvant chemotherapy, radiotherapy, or both depends completely on the staging of the tumor; therefore, accurate staging must be performed. Staging is straightforward, with stage I being limited to the kidney and completely excised. Stage II tumors are completely excised but may extend beyond the renal capsule or into the renal sinus on a histopathologic basis. Local tumor spillage or the presence of a tumor thrombus also mandates a stage II classification. Any tumor that is incompletely excised, including the presence of lymph nodes positive for the tumor, is stage III if limited to the abdomen. Stage IV tumors are those with distant metastases that usually involve the lung, liver, and, less often, bone and brain. Finally, stage V represents bilateral Wilms' tumors, which occur in 5% to 10% of cases. Stage V does not necessarily portend a worse prognosis than the other stages.

HISTOPATHOLOGY

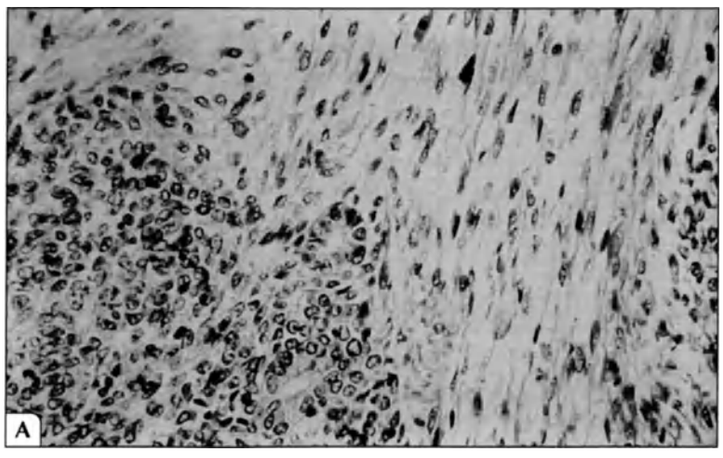


FIGURE 13-8. (*See Color Plates*) Histopathology of renal tumors in children. **A,** A classic Wilms' tumor consists of epithelial cells, blastema cells, and stromal cells. In the National Wilms' Tumor Studies [3–5], the histopathologic appearance of the tumor clearly was the most important prognostic factor for Wilms' tumor. Favorable-histology tumors, which have the classic Wilms' tumor appearance without any anaplastic elements, have survival rates of more than 90% regardless of the stage at presentation [5].

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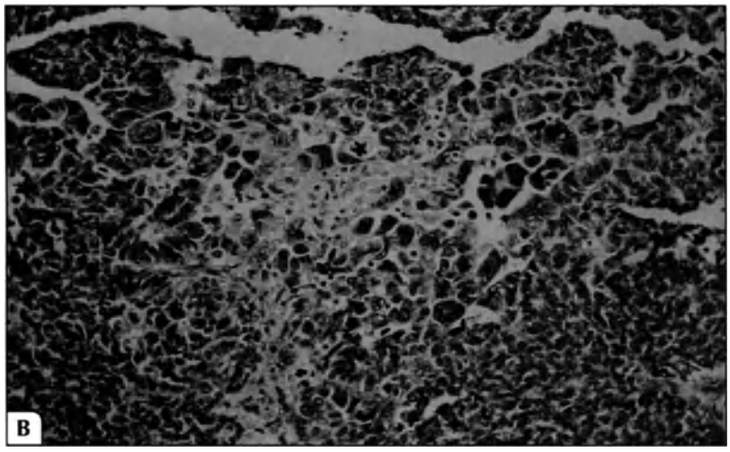
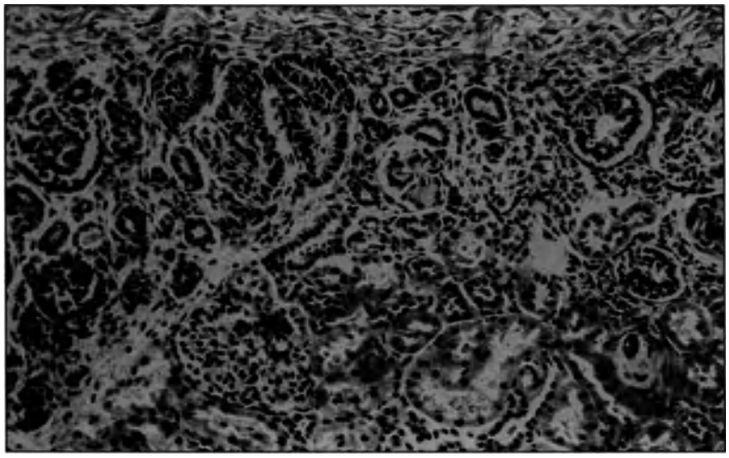


◗ **FIGURE 13-8.** (*Continued*) **B,** Unfavorable-histology tumors contain either focal or diffuse anaplasia, and the survival rates are significantly less than that for favorable-histology tumors. Unfavorable histology, which occurs in only 5% of patients with Wilms' tumors, may account for as many as 40% of the deaths [3]. It is essential that the tumors be carefully examined for anaplasia because different and more intense treatment is required to improve survival rates.



◗ **FIGURE 13-9.** (***See Color Plate***) Subcortical nephrogenic rests or nodular renal blastema. This is fetal tissue that normally regresses in late fetal life. This tissue has been demonstrated, however, in 1% to 2% of perinatal autopsies. It is seen in 25% to 40% of neonates with Wilms' tumors and as many as 100% of patients with bilateral Wilms' tumors [9]. This persistent fetal tissue may represent Knudson and Strong's [6] premalignant lesion and, if it does not regress, may lead to a Wilms' tumor.

Survival and Treatment for Patients with Wilms' Tumor from NWTS-3

Stage	*Histology*	*Survival, %*	*Relapse-free Survival, %*
I	Favorable histology	96	90
II	Favorable histology	92	88
III	Favorable histology	87	79
IV	Favorable histology	82	75
I–III	Unfavorable histology	62	65
IV	Unfavorable histology	55	55

◗ **FIGURE 13-10.** Survival for patients with Wilms' tumor from NWTS-3 (National Wilms' Tumor Study 3). There have been four such Wilms' tumor studies, with more than 4046 patients entered. Although NWTS-4 has concluded, results have not yet been published. The last published results of survival are from the NWTS-3, as shown here [5]. These results clearly show the superior results that are achieved if the patient presents with a low-stage, favorable-histology tumor.

Adjuvant Treatment of Patients with Wilms' Tumor in NWTS-5

Stage	Histology	Treatment
I	Favorable or unfavorable histology	Actinomycin D + vincristine
II	Favorable histology	Actinomycin D + vincristine (+ doxorubicin for focal anaplasia)
III and IV	Favorable histology	Actinomycin D + vincristine + doxorubicin + radiation
II–IV	Unfavorable histology	Vincristine + doxorubicin + etoposide + cyclophosphamide + radiation

FIGURE 13-11. Adjuvant treatment of patients with Wilms' tumor in NWTS-5 (National Wilms' Tumor Study 5). Surgery is indicated in patients in stages I to IV as the initial form of treatment, if feasible. The operation is accomplished transperitoneally. After abdominal exploration, a radical nephrectomy is performed and regional lymph nodes are sampled. According to the NWTS protocol, a thorough contralateral renal exploration is undertaken before nephrectomy, to rule out bilateral disease. Although preoperative chemotherapy is widely used in Europe, it is reserved in the United States for patients with bilateral tumors, suprahepatic caval thrombus, or unresectable tumors (an intraoperative decision). Postoperative treatment for NWTS-5 is depicted here. Those with stage I favorable and unfavorable histology tumors are treated with surgery and then actinomycin D and vincristine for 18 weeks. This is also true for those with stage II favorable histology tumors. Those with stage III or IV favorable histology tumors are treated with surgery and radiation therapy plus actinomycin D, vincristine, and adriamycin for 24 weeks. Patients with stage II, III, and IV unfavorable-histology tumors are treated with surgery, radiation therapy, and then an aggressive combination of chemotherapy.

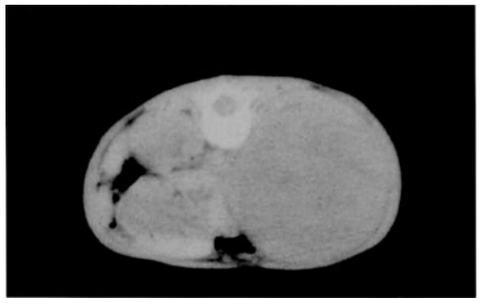


FIGURE 13-12. Computed tomography scan in a 7-month-old child who presented with hematuria. The scan demonstrates a large tumor in the left kidney that was palpable on a physical examination. Note the unsuspected right central tumor, confirming bilateral disease. Stage V tumors require a biopsy of each kidney and then chemotherapy, based on the higher stage tumor.

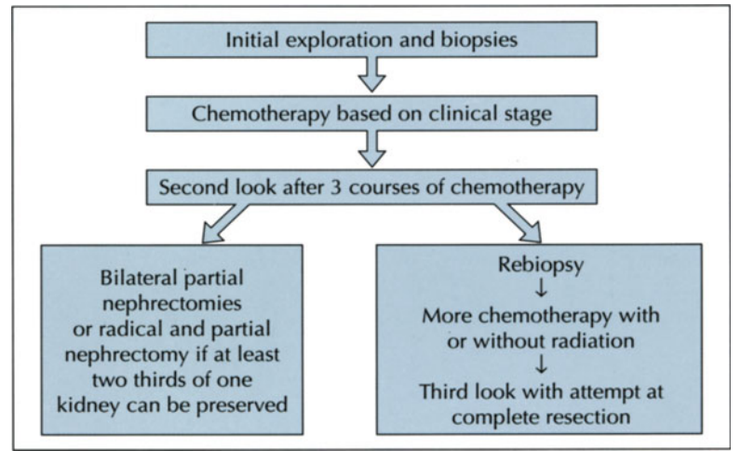
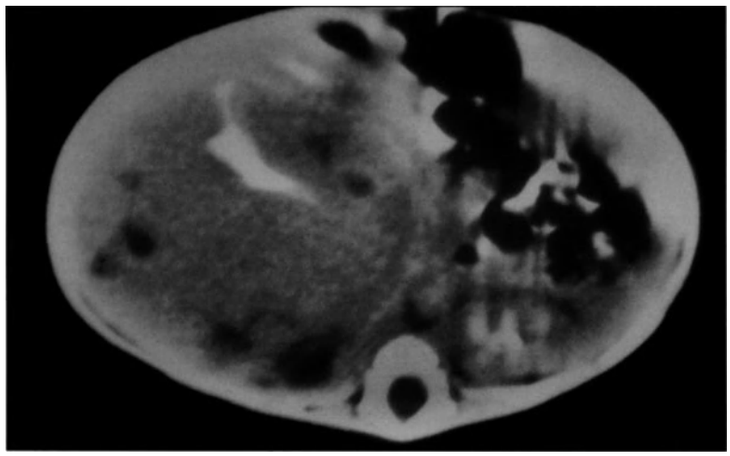
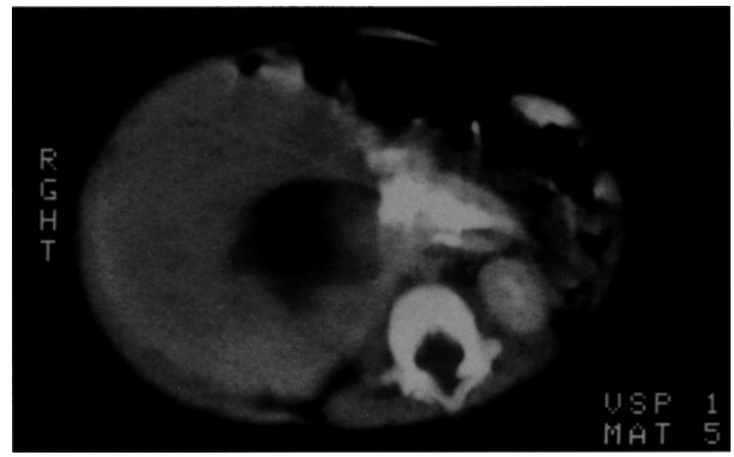


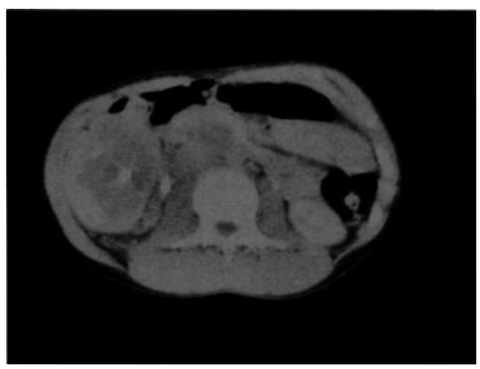
FIGURE 13-13. Management of bilateral Wilms' tumors. Bilateral Wilms' tumors represent a unique disease when compared with unilateral ones, and they are a true challenge to pediatric urologists. A conservative treatment has clearly been shown to be efficacious in the treatment of children with bilateral Wilms' tumors [18,19]. Because the majority of these patients do have favorable histology and are chemosensitive, chemotherapy is the mainstay of treatment. In addition, because many children do very poorly after bilateral nephrectomy, it is important to try to preserve as much renal tissue as possible. This is best accomplished by preoperative chemotherapy, with the shrinkage of the tumors and surgery playing a secondary role. If required, partial nephrectomies may be performed after chemotherapy rather than at the initial presentation. This approach to management relies on chemotherapy to reduce the tumors to a size that allows nephron-sparing surgery. Although not always possible, the need for bilateral nephrectomies or increased morbidity should be minimized.



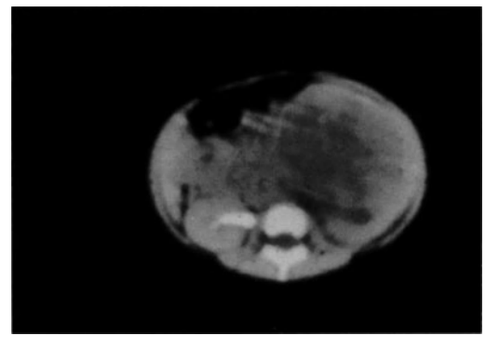
◗ **FIGURE 13-14.** Computed tomography scan of a neonate with a palpable abdominal mass demonstrating a congenital mesoblastic nephroma. This is the most common tumor in neonates. Often confused with Wilms' tumor, congenital mesoblastic nephroma is a clearly distinct tumor that represents more of a hamartoma. In almost all cases, it is a benign tumor cured by nephrectomy. A cellular variant of congenital mesoblastic nephroma has been reported with both local recurrence and metastasis to the brain [20–23]. This normally occurs in children older than 3 months of age. The surgeon and pathologist must be aware of this unique subset of patients with congenital mesoblastic nephroma. Many of these tumors are now being detected on prenatal ultrasonography.



◗ **FIGURE 13-15.** Computed tomography scan of an 18-month-old child with clear cell sarcoma. A large right renal mass can be seen. Preoperative biopsy for purposes of chemotherapy diagnosed a clear cell sarcoma. Clear cell sarcoma of the kidney or the bone metastasizing tumor of childhood was first described in 1970 and was initially believed to be a variant of Wilms' tumor [24,25]. However, it has clearly been shown to be a sarcoma that is not related to Wilms' tumor either on a molecular or a histologic basis [26]. Clear cell sarcoma is unique in that it responds very well to treatment with doxorubicin. Initial survival rates were very poor in the National Wilms' Tumor Study until this recognition had been made. After doxorubicin was added to the regimen, patients with clear cell sarcomas attained survival rates of approximately 85% [5].

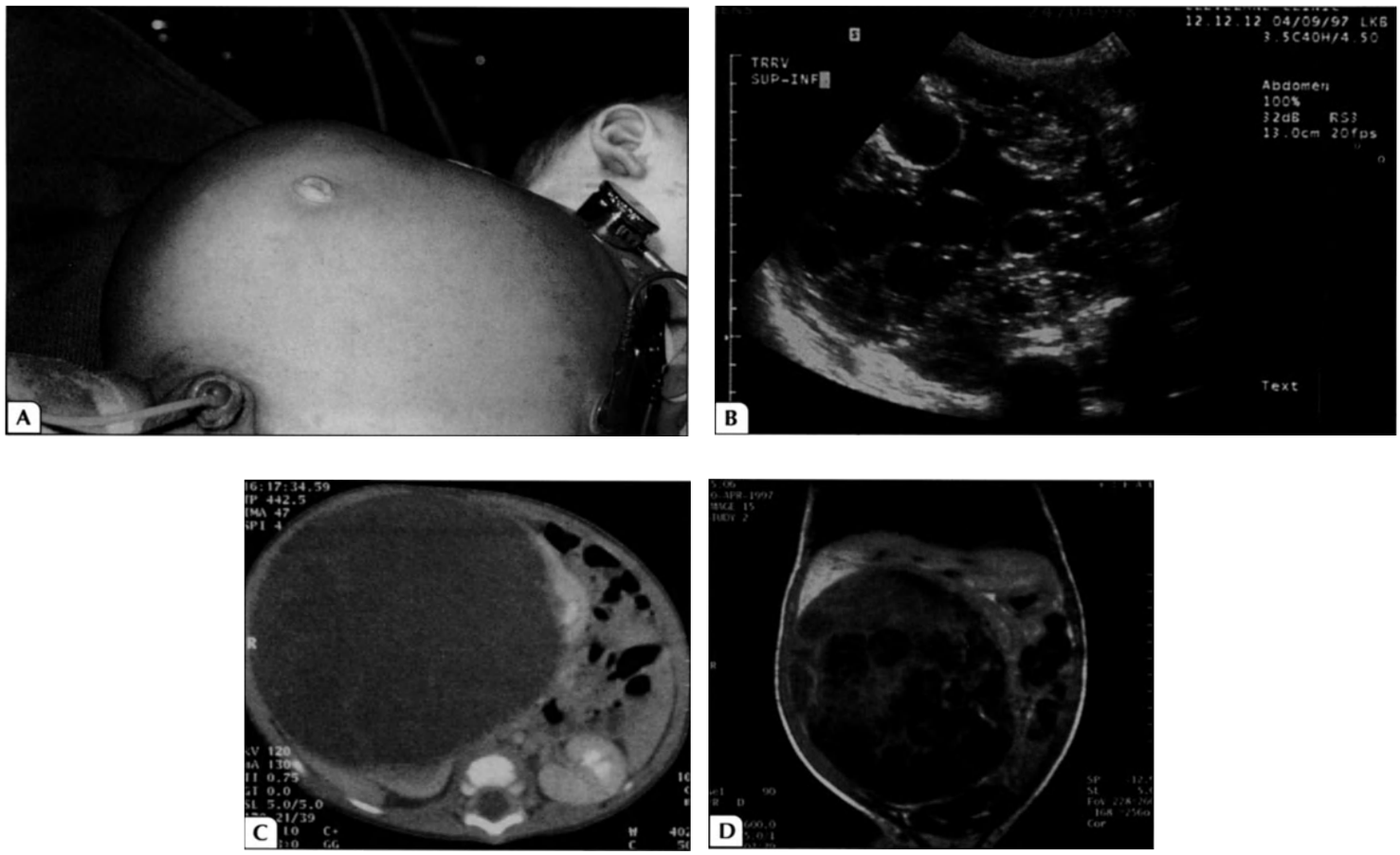


◗ **FIGURE 13-16.** Computed tomography scan depicting right renal cell carcinoma with a caval thrombus in a 14-year-old boy. It is important to recognize that renal cell carcinoma occurs in children [14,15]. Usually presenting with symptoms of advanced disease, as opposed to a mass, there is often a delay in diagnosis. Renal cell carcinoma may occur at any age, although it is more common in adolescents than in infants. As in adults, chemotherapy is not effective, so other forms of treatment continue to be sought for patients with metastatic disease. It is a rare tumor but needs to be recognized by surgeons so that it is not treated as a Wilms' tumor.



◗ **FIGURE 13-17.** Malignant rhabdoid tumor. Malignant rhabdoid tumor of the kidney was initially thought to be a variant of Wilms' tumor. After the National Wilms' Tumor Study 1, however, it was recognized as a distinct tumor. It has a very poor prognosis, and aggressive chemotherapy must be initiated immediately in the postoperative period [27,28]. There are no radiographic criteria to differentiate malignant rhabdoid tumors from Wilms' tumors, but the histologic diagnosis is clear.

This 3-year-old girl presented with an abdominal mass. Histologic examination of the nephrectomy specimen revealed a malignant rhabdoid tumor. She received aggressive adjuvant chemotherapy and survived.



◗ **FIGURE 13-18.** Cystic renal tumors. Shown is a 7-month-old child with a large abdominal mass (**A**). The ultrasound (**B**) shows a complex cystic mass confirmed on a computed tomography scan (**C**) and a magnetic resonance image (**D**). An intraoperative photograph (**E**) shows the size of the mass, confirmed on histologic examination as a cystic partially differentiated nephroblastoma.

Cystic renal tumors consist of two lesions: cystic nephroma and cystic partially differentiated nephroblastoma. Both are hamartomas and are completely benign in nature. They are cured by nephrectomy, and no adjuvant therapy is required. However, rare local recurrences have been reported for each if there is intraoperative tumor spillage.

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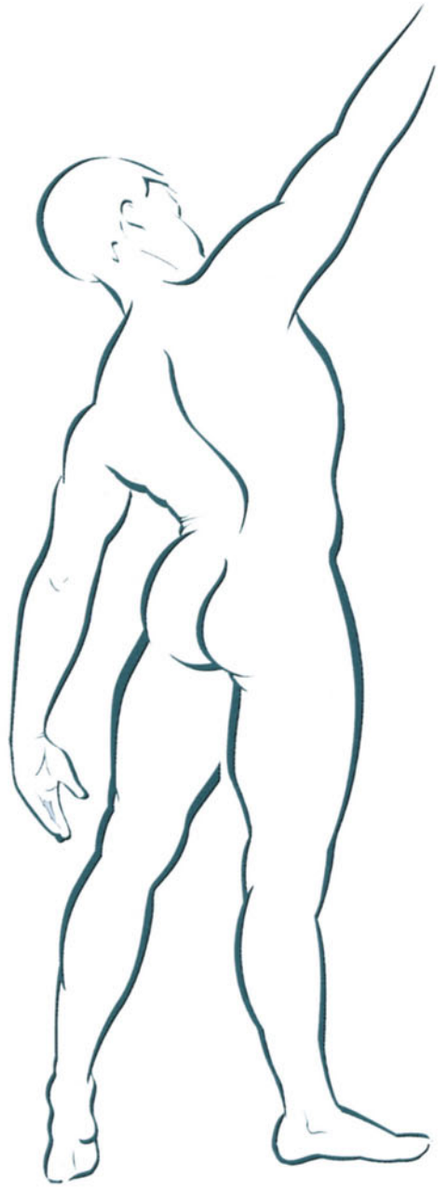
14

Cystic Diseases of the Kidney

Michael P. Solliday and Kenneth I. Glassberg



This chapter is divided between genetic and nongenetic entities, and each subtype is discussed individually. There is a brief description of etiology, clinical features, histopathology, radiologic characteristics, and management possibilities for each cystic disease.

In most cystic diseases of the kidney, whether congenital, sporadic, or acquired, the cysts arise from the nephron and collecting ducts after they have formed. Multicystic dysplasia is an exception representing a defect in embryologic development of the kidney, secondary either to a problem with the abnormal nephrogenic blastema, abnormal metanephric induction, or obstruction early in fetal life. Multilocular cysts are another exception and represent neoplastic growth. The exact nature of simple cysts is also not clear, and they may develop in kidneys that are structurally normal.

Several factors have been implicated in human and experimental cystic diseases:

1. Compliant basement membrane theory proposes that a defect in one or more basement membrane (BM) proteins alters the integrity of the tubule epithelium and results in faulty morphogensis. Winyard *et al.* [1] studied the BM of infant polycystic kidneys and found that the loss of the ubiquitous BM constituent collagen IV ("the backbone of the BM") leads to cystic tissue transformation. They hypothesize that in other cystic transformations, a similar BM "dysregulation" may occur, resulting in the formation of cysts.

2. The proliferative theory postulates that epithelial hyperplasia occurs in a disordered fashion, causing cystic dilatation. Nerlich [2] chemically induced cyst formation in rats with phenol II and found that a potent cohesive factor termed *clusterin* appeared in the epithelial cells of the induced cysts. The clusterin was found only in the rapidly proliferating cells of the newly formed cyst. When the inciting agent was removed, the cysts disappeared and the clusterin was no longer found in the epithelium. This study lends compelling evidence for the role of epithelial hyperplasia in cyst formation.

3. The obstructing-ballooning theory states that epithelial hyperplasia obstructs the lumen of the tubule, causing obstruction and subsequent cyst formation [3].

4. Sodium potassium adenosine triphosphate (Na/K-ATPase) is a transporting membrane protein found in the epithelial cell that may be involved in cystogenesis. It is believed that upregulation of the Na/K-ATPase pump causes abnormal net fluid transportation and the

progression of cystic dilatation. The exact mechanism behind this upregulation in humans is not yet known [4].

5. Epidermal growth factor has also been indicated experimentally in cyst formation.

Despite numerous animal models that have produced cysts by chemical injury to the tubules, the exact mode of cyst formation in humans remains unclear.

Classification of Cystic Diseases of the Kidney

- Nongenetic
  - Simple cyst
  - Caliceal diverticulum
  - Multicystic dysplastic kidney
  - Multilocular cystic disease
  - Medullary sponge kidney
  - Acquired renal cystic disease
  - Unilateral renal cystic disease
  - Sporadic glomerulocystic kidney disease
- Genetic
  - Autosomal dominant polycystic kidney disease
  - Autosomal recessive polycystic kidney disease
  - Juvenile nephronopthisis–medullary cystic disease complex
    - Juvenile nephronophthisis (autosomal recessive)
    - Medullary cystic disease (autosomal dominant)
  - Congenital nephrosis
  - Familial hypoplastic glomerulocystic kidney disease

◗ **FIGURE 14-1.**
Classification of cystic diseases of the kidney [5].

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Genetics of Autosomal Dominant Polycystic Kidney Disease

Variant	*Genomic Locus*	*Patients, %*
ADPKD 1	Short arm of chromosome 16	90
ADPKD 2	Long arm of chromosome 4	5–10
ADPKD 3	No genomic locus yet found	<5

◗ **FIGURE 14-2.**
Genetics of autosomal dominant polycystic kidney disease (ADPKD). ADPKD is one of the most frequently inherited disorders, with an incidence of one in 1000 [6]. ADPKD causes renal failure in approximately 10% of the patients receiving chronic hemodialysis in the United States and Europe [7,8]. About 85% of the affected individuals have a mutation at the *PKD-1* locus on chromosome 16 p13.3 [9]. Since the *PKD-1* gene was identified in 1994, few mutations have been found [10].

Although geneticists have gained much insight recently into the human genome, many questions concerning ADPKD remain unanswered. We do not know the function of the product of the *PKD1* gene or how a mutation leads to the disease. Approximately 5% to 10% of cases are caused by a mutation in the long arm of chromosome 4 (*ADPK-2* gene), and this causes a milder form of the disease [11]. The *ADPKD-3* gene genotype has been identified, but no genomic locus has been found to date [12]. Persons carrying the *ADPKD* gene manifest cysts in their kidney by age 30 and 50% of their offspring have the genetic trait because it is transmitted in an autosomal dominant fashion.

• Clinical Features of Autosomal Dominant Polycystic Disease-1 •

Presentation and Clinical Features of Autosomal Dominant Polycystic Kidney Disease

Age of presentation	*Clinical features*
Neonatal	Renomegaly
	Respiratory distress
	Stillbirth
>1 y	Hematuria
	Proteinuria
	Enlarged kidneys
	Hypertension
Adult presentation >30 y	Hypertension
	Flank pain
	Hematuria
	Renal colic
	Urinary tract infection
	Renal insufficiency

FIGURE 14-3.
Presentation and clinical features of autosomal dominant polycystic kidney disease (ADPKD). ADPKD presents differently in affected individuals and even within members of the same family. The disease can have a neonatal onset, and the most common feature in this age group is renomegaly. Respiratory distress and stillbirths are possible in severe cases. Because of the increased numbers of children undergoing renal screening and prenatal sonography, large numbers of children with renal cysts are being identified. The adult presentation of ADPKD has changed over the past decade. Previously, ADPKD diagnosed in adults was divided into groups. The first group presents in the fourth decade of life with flank pain, hematuria, urinary tract infection, gastrointestinal symptoms, and renal colic. The gastrointestinal symptoms are most likely secondary to mechanical compression on the bowels by the kidneys, and the colic is secondary to stone or blood clot passage. The second group presents a decade later with hypertension and renal insufficiency. Currently, with blood pressure monitoring of all persons at risk, hypertension has become the most common presentation in older patients [12]. Renal failure is rare before 40 years of age. ADPKD is associated with cysts in other organ systems including liver, spleen, and lung, as well as aneurysms of the circle of Willis. ADPKD can also be associated with cardiac valvular disorders, aneurysms of coronary arteries and aorta, inguinal and abdominal wall hernias, and colonic diverticuli.

• Risk Factors in Autosomal Polycystic Disease •

End-Stage Renal Risk Factors for Autosomal Dominant Polycystic Kidney Disease Patients

ADPKD-1
Age at time of diagnosis < 30 y
Development of hypertension before age 35 y
Episode of gross hematuria

FIGURE 14-4.
Risk factors for end-stage renal disease patients with autosomal dominant kidney disease (ADPKD). In one series of 1215 patients with ADPKD, Johnson and Gabow [12] identified those groups of patients with worse renal survival and those with the greatest risk of end-stage renal disease. They found that patients with ADPKD-2 had longer renal survival than patients with ADPKD-1 (median survival, 68 vs 52 years). Patients diagnosed before the age of 30 and those who develop hypertension before the age of 35 had worse renal survival than those diagnosed after age 30 and those who remain normotensive after age 35. Those patients who had an episode of gross hematuria had a worse renal outcome than those who did not (relative risk ratio, 2.6). Those individuals considered to be at high risk might require closer follow-up and consideration for therapeutic interventions when they become available [12].

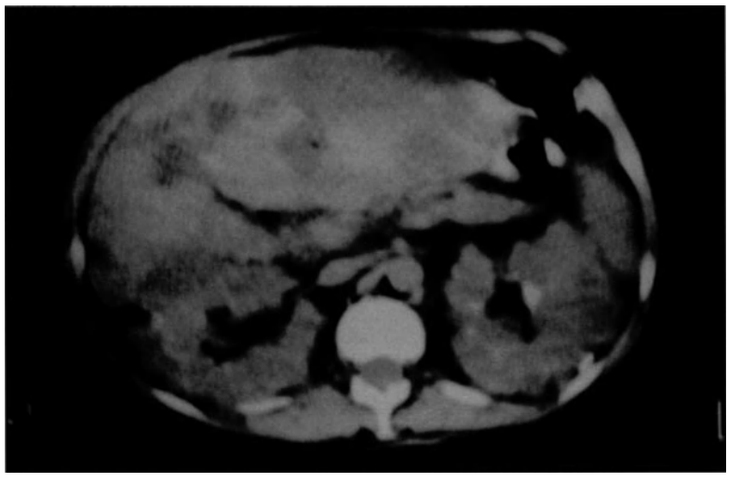


FIGURE 14-5.
Computed tomographic (CT) image of adult patient with autosomal dominant kidney disease (ADPKD). Bilateral renal cysts are seen, as well as large cysts in the liver. Histologically, the cysts may be a few millimeters to several centimeters in size and occur diffusely throughout the cortex and medulla. The basement membrane is often thickened, and the epithelial lining may be hyperplastic, leading to adenoma formation in the cyst. The incidence of renal cell carcinoma is no higher than that in the general population. This finding seems contradictory considering that renal cell carcinoma in the patient with ADPKD is more often multicentric (28% vs 6%), sarcomatoid in type (33% vs 1% to 5%), and often bilateral (12% vs 1% to 5%) [13]. At this time, CT scan is the most accurate radiologic imaging study to identify cysts in the kidney as well as associated organs. The best diagnostic study on the horizon, however, is cytogenetic screening. The treatment is geared toward the organ system affected and is supportive in nature. Hypertension is controlled, renal stones are dealt with, salt and protein intake is regulated; and in the end stages, dialysis and transplantation are performed [11]. These patients are now living longer owing to our improved ability to deal with infections, high blood pressure, renal calculi, and renal failure.

AUTOSOMAL RECESSIVE ("INFANTILE") POLYCYSTIC KIDNEY DISEASE

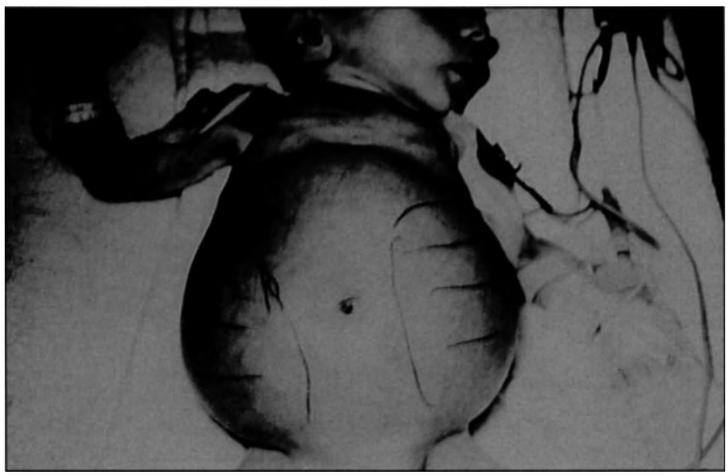
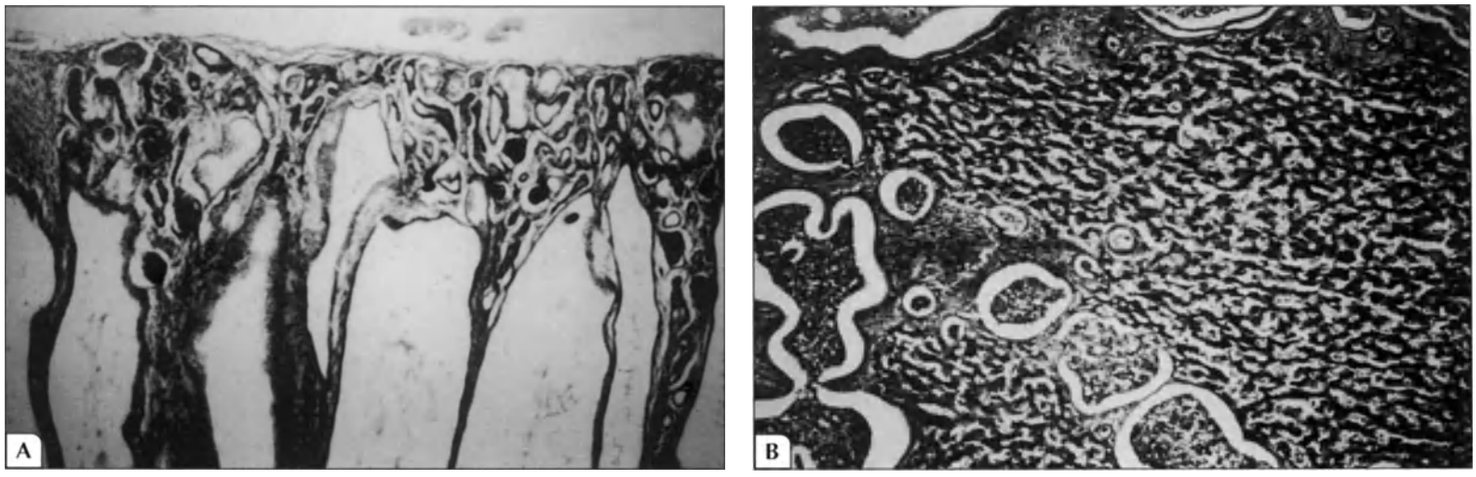
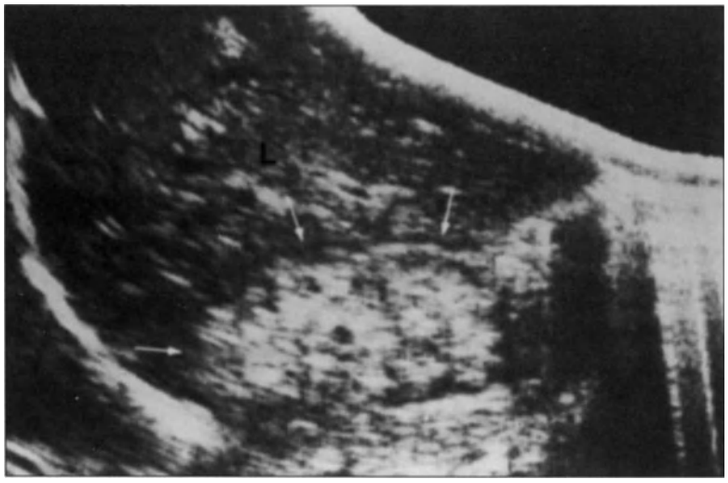


FIGURE 14-6.
Newborn with autosomal recessive polycystic kidney disease (ARPKD). This child has large grossly palpable kidneys occupying more than 50% of the abdominal cavity and a normal-sized liver. In the past, ARPKD has been referred to as the "infantile" form. This term is misleading because the disease can first manifest in adolescents and young adults, although this occurs rarely. The reported incidence of ARPKD varies from country to country, with a frequency of about one in 10,000 in Finland [14] to about one in 40,000 live births elsewhere. More than half of the affected newborn infants die soon after birth. ARPKD has a varied spectrum of presentation, with the most severe form presenting at birth. Some children present later in childhood (generally by age 13, rarely extending to the 20s), and most of these patients have congenital hepatic fibrosis. Geneticists have recently assigned the only known locus for this disorder, PKHD 1, to chromosome 6p21-P12 (chromosome 6 locus p21-p12). Research is currently under way to clone positionally the *PKHD-1* gene [15]. (*From* Glassberg [16]; with permission.)



◗ FIGURE 14-7.
Histology of autosomal recessive polycystic kidney disease (ARPKD). Histologically, the ARPKD kidney retains its fetal lobulation with the cortex crowded with minute cysts. The primary abnormality is in the collecting ducts, which are saccular and dilated, and arranged in a radial array extending from the calyx to the renal capsule. The renal pelvis and ureter are not affected. The liver demonstrates varying degrees of periportal fibrosis and ectatic biliary ducts in all affected [17].

A, The histologic appearance of kidney affected with ARPKD with dilated tubules radiating from the calyx out to the capsule. **B,** The histologic appearance of the liver illustrating ectatic ducts in the left half of the figure and extensive periportal fibrosis in the upper margin. (*From* Glassberg [18]; with permission.)



◗ FIGURE 14-8.
In utero ultrasound of an 18-week-gestation fetus demonstrating homogeneous hyperechogenic kidneys bilaterally. Lucency in the center of each kidney represents a full renal pelvis, proven postnatally. Two older siblings had previously been diagnosed with autosomal recessive polycystic kidney disease (ARPKD).

In utero ultrasonography often reveals oligohydramnios secondary to diminished fetal urine production. In both the fetus and newborn, ultrasonography of the kidneys reveals a large kidney with a homogeneous hyperechogenicity. This increase in echosignals is due to the tightly packed dilated collecting ducts that create multiple interfaces for the sound waves to bounce off. The liver is less echogenic. With the advent of high-resolution ultrasonography, ultrasound is better able to demonstrate the underlying pathologic state in the perinatal period, and CT is rarely required. Although most ADPKD kidneys in neonates have large cysts, on rare occasion, a neonate with ADPKD may also have large hyperechoic kidneys resembling ARPKD. As the child with dominant disease ages, the kidneys become enlarged with many cysts. In the child with recessive disease, the kidneys will develop large cysts with time, but eventually the kidneys decrease in size with advancing age [19].

This sonogram of the left kidney in an infant with ARPKD illustrates the homogeneously hyperechoic kidneys in marked contrast to the less echogenic liver. The increased echogenecity is due to the multiple interfaces created by the dilated medullary ducts. (*From* Grossman *et al.* [20]; with permission.)

Differential Diagnosis of the Infant with Hyperchoic, Enlarged Kidneys

ARPKD
Autosomal dominant polycystic kidney disease
Renal vein thrombosis
Contrast nephropathy
Sporadic glomerulocystic kidney disease

FIGURE 14-9.
The differential diagnosis of the infant with hyperechoic, enlarged kidneys. To date, no cure has been found for autosomal recessive polycystic kidney disease (ARPKD). The future lies in genetic engineering and alteration of the human genome. Currently, care is primarily supportive. The neonatologist can offer respiratory support, hypertension can be controlled with medication, and congestive heart failure and renal and hepatic failure can be managed temporarily medically. Patients who develop portal hypertension may require left renal vein–to–splenic vein bypass. Ultimately, hemodialysis and renal transplantation may be required.

JUVENILE NEPHRONOPHTHISIS AND MEDULLARY CYSTIC DISEASE COMPLEX

Comparison of Medullary Cystic Disease and Juvenile Nephronophthisis

	Medullary Cystic Disease	*Juvenile Nephronophthisis*
Incidence	Autosomal dominant	Autosomal recessive Chromosome 2
Inheritance	1: 100,000	1: 50,000
End-stage renal disease	30–40 y old	By age 12–13
Medullary cysts	May develop before renal failure	Develop after renal failure
Incidence of renal cysts	85%	40%
Tubular basement membrane	Not always thickened	Thickened
Symptoms	Polydipsia, polyuria, anemia, hematuria, proteinuria	Polydipsia, polyuria, growth retardation after age 2

FIGURE 14-10.
Comparison of medullary cystic disease and juvenile nephronophthisis. Juvenile nephronophthisis (JN) and medullary cystic disease (MCD) are similar clinically and anatomically, but they have a different genetic transmission and clinical onset. Both entities have been known by other names in the literature, such as salt-losing enteropathy, uremic sponge kidney, and uremic medullary cystic disease. Both can occur sporadically, but JN is usually inherited as an autosomal recessive trait and manifests between the age of 6 and 20 years. Linkage analysis has assigned a locus on chromosome 2, and further characterization using polymerase chain reaction has led to a precise noninvasive method for diagnosis in the majority of patients suspected of having JN [21]. MCD is inherited in an autosomal dominant fashion and presents in the patient's 30s.

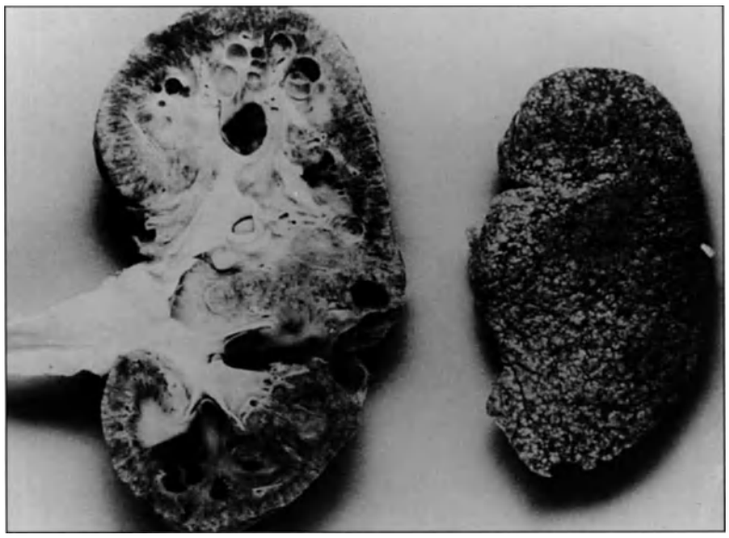


FIGURE 14-11.
Clinical features of juvenile nephronophthisis (JN) and medullary cystic disease complex (MCD). Gross appearance of a sectioned and subcapsular surface of a kidney from a patient with MCD. Cysts are found at the corticomedullary junction.

Juvenile nephronophthisis and MCD represent an interstitial nephritis that leads to terminal renal failure. Polydipsia and polyuria are seen in more than 80% of the cases. These children are unable to concentrate urine, have sodium wasting, and are frequently anemic. The child's growth is slowed and he or she often presents with malaise, anemia, excessive nocturnal enuresis, and polyuria [22]. JN can be associated with a variety of extrarenal symptoms, including retinal disorders, hepatic fibrosis, skeletal abnormalities, and mental retardation. The kidneys are initially normal in size, but over time, the kidney atrophies and develops a granular surface, and cysts appear at the corticomedullary junction. Histopathology reveals an increase in glomerular mesangial cellularity and matrix, mild focal tubular atrophy, and alternating thickening and thinning of renal tubule basement membrane [23]. Sonography reveals renal hyperechogenicity, poor corticomedullary differentiation, corticomedullary cysts, and small kidney size. Renal cysts and renal atrophy usually appear later when the disease has progressed [24]. Thin-section CT has shown promise in the imaging of small medullary cysts [25]. The treatment involves sodium replacement early in the disease course and ultimately dialysis and renal transplantation. The allograft is not susceptible to the same disease process [26]. (*From* Kissane [27]; with permission.)

Comparison of Finnish-Type Congenital Nephrosis and Diffuse Mesangial Sclerosis

	Finnish Type	*Diffuse Mesangial Sclerosis*
Incidence	1: 8200 Births in Finland Autosomal recessive	Usually consanguineous marriages; approximately 30 cases reported
Prenatal features	Enlarged edematous placenta	Placenta usually not enlarged
Age at presentation	Symptomatic by 3 months	Onset variable but diagnosed by 1 y
Clinical features	Massive proteinuria Edematous neonate Die before 6 months without dialysis	Proteinuria usually present Terminal renal failure by 3 y
Histology	Initially normal-sized kidneys with proximal tubule dilatation Fusion of glomerular podocytes Interstitial fibrosis In advanced disease, glomeruli contracted and sclerotic	Initially normal-sized kidneys with proximal tubule dilatation Fusion of glomerular podocytes More extensive interstitial fibrosis Glomeruli accumulate mesangial fibrils that are periodic acid–Schiff positive In advanced disease, glomeruli contracted and sclerotic
Diagnosis	Amniocentesis by 6th week of gestation with high α-fetoprotein	Use of α-fetoprotein not reported
Treatment	Adequate nutrition Treat infections Once kidneys fail, transplantation may be curative	Too few cases reported, but transplantation most likely curative

FIGURE 14-12.
Comparison of Finnish-type congenital nephrosis and diffuse mesangial sclerosis.

Congenital nephrosis predominately occurs in two forms. The more common Finnish type is an autosomal recessive disorder characterized by massive proteinuria in utero and nephrosis at birth. The reported incidence is 1 in 8200 in Finland [28]. The other type, diffuse mesangial sclerosis (DMS), is rare, usually the result of a consanguineous marriage [29]. The Finnish type is usually discovered at birth when a grossly enlarged placenta is delivered. The neonate has massive proteinuria and develops edema within the first few days of life. The large amount of protein lost in the urine essentially starves the baby and makes the baby susceptible to infections. Without dialysis, half of the patients die before 6 months; the rest are dead by their fourth birthday [30]. In DMS, the placenta is not affected and the onset of symptoms varies. The diagnosis is usually made by 1 year of age and the child will have end-stage renal disease by 3 years of age. Both types of congenital nephrosis have normal-sized kidneys and proximal tubule dilatation. In both conditions, the glomeruli podocytes fuse and there is interstitial fibrosis. Later in the disease process, the glomeruli become sclerotic and contracted. The nephropathy of Denys-Drash syndrome (DDS; nephrotic syndrome associated with pseudohermaphroditism or Wilms' tumor) is DMS. A mutation in the *WT 1* gene, which is a transcription factor involved in renal and gonadal development, has been implicated in DDS [31]. The Finnish type can be diagnosed in utero by the sixth week of pregnancy due to the elevated levels of α-fetoprotein. These children are susceptible to septic infections associated with invasive neonatal monitoring. Antibiotics that have good staphylococcus coverage should be instituted in the nephrotic child who is not doing well [32]. Once the kidneys have failed, transplantation can be curative.

MULTIPLE MALFORMATION SYNDROMES ASSOCIATED WITH RENAL CYSTS

A. Autosomal Dominant Malformation Syndromes Associated with Renal Cysts

Autosomal Dominant	*Prevalence*	*Clinical Presentation*	*Features*	*Renal Findings*	*Radiographic Findings*	*Renal Sequelae*	*Management*
Tuberous sclerosis	1:9000 to 1:170,000 infants	Bilateral flank masses in infant Hematuria Hypertension Renal failure in 30s	Epilepsy: 80% Mental retardation: 60% Adenoma sebaceum: 75% Retinal phakomas: 50% Cerebral hamartomas Periventricular subependymal nodule Cardiac rhabdomyomas Distal phalangeal tuft erosion by ungual angiofibromas Liver angiomyolipomas Pancreatic cysts	Renal angiomyolipomas: 40%–80% Cysts from microscopic to 3–4 cm in size Cysts throughout kidney Can be associated with renal cell cancer	Ultrasound Angiomyolipoma hyperechoic Cysts anechoic CT scan of renal cysts that may be associated with hamartomas often containing fat	Cystic disease may obstruct or compress kidney Rarely leads to renal failure	Control hypertension Renal-sparing surgery Emobilization of angiomyolipomas that bleed Multidisciplinary approach
von Hippel–Lindau syndrome	Autosomal dominant with 100% penetrance so 50% siblings affected	Renal cysts usually asymptomatic Abdominal pain, flank mass Hematuria Metastatic renal cell carcinoma in older patient	Renal cysts ≈ 60% Retinal angiomatosis Cerebellar hemangioblastomas Pheochromocytoma ≈ 10% Cysts of pancreas, kidney, epididymis Renal cell carcinoma	Multiple small bilateral cysts (0.5–3.0 cm) in 60%–70% Clear cell renal carcinoma arises in cyst wall ≈ 30%	CT more useful because can image adrenal better MIBG scan can be useful to localize pheochromocytomas	Cystic disease may compress or obstruct Rarely leads to renal failure Primary concern renal cell carcinoma	Annual CT scan for those affected Screen family members with eye exam, CT head and abdomen at ≈ age 18 Renal-sparing surgery Multidisciplinary approach

◗ FIGURE 14-13.
Malformation syndromes associated with renal cysts. Many multiple malformation syndromes are associated with renal cysts. **A**, Tuberous sclerosis (TS) and von Hippel–Lindau disease are the most significant. TS has a prevalence of between 1:9000 to 1:170,000 infants [33]. It is characterized by hamartomas in the brain, eye, kidney, and skin. TS is often associated with epilepsy (80% of cases), mental retardation (60% of cases), adenoma sebaceum (75% of cases), and retinal phakomas (50% of cases) [33,34]. Renal lesions associated with TS include simple cysts, angiomyolipomas, and renal cell cancer. About half of the TS patients have an identifiable renal lesion, with 75% of the lesions being angiomyolipomas. The second most common lesion is a simple renal cyst, which is seen in 17% of patients [34]. Angiomyolipomas are more likely to grow than remain stable, and periodic imaging is suggested in children with TS [34]. Because the neurologic sequelae are managed more effectively, the urologist can anticipate seeing more of these patients with renal masses.

(*Continued on next page*)

B. Autosomal Recessive Malformation Syndromes Associated with Renal Cysts

Autosomal Recessive	Prevalence	Clinical Presentation	Features	Renal Findings	Radiographic Findings	Renal Sequelae	Management
Jeune's asphyxiating dystrophy	Rare	Restrictive breathing, often ventilator dependent from birth	Small chest Short limbs Varied renal findings	Various findings: Diffuse cystic dysplasia Cortical microcysts Tubular interstitial disease with dilated medullary collecting ducts	Renal findings varied, short ribs and limbs on routine x-ray studies Prenatal sonogram may reveal diminished thoracic circumference	Chronic nephrosis or renal failure	Respiratory support Kidneys will need sonographic follow-up if child survives Surgery has been performed to expand thorax
Meckel's syndrome	Rare	Polydactyly Kidneys may be grossly palpable May be mentally retarded	Polydactyly Posterior encephalocele Cystic kidneys	Deficiency of glomeruli Poor corticomedullary development Large cysts that originate from collecting ducts	Kidney may be hypoplastic or markedly enlarged with multiple cysts	Renal failure	Children do poorly
Zellweger's cerebrohepatorenal syndrome	Rare	Hypotonic newborn with high forehead Enlarged liver and spleen Mentally retarded	Peroxisome deficiency Cerebral cortical anomalies Renal problems usually minor	Microscopic glomerular cysts to cysts up to ≈ 1 cm that form glomerulus or tubules	MRI helpful to image brain and brainstem Sonography good to image cysts	Rarely have mild azotemia, usually no manifestations	Children usually die in 1st year of life, not renal-related

C. X-linked Dominant Malformation Syndrome Associated with Renal Cysts

X-Linked Dominant	Prevalence	Clinical Presentation	Features	Renal Findings	Radiographic Findings	Renal Sequelae	Management
Orofaciodigital syndrome I	Rare	Alopecia Syndactyly Bradydactyly Cleft lip, palate, and/or tongue Hypertrophic buccal frenulum Hypoplastic alinasal cartilage	Lethal in boys Affected girls may survive May develop hypertension and grossly palpable kidneys later in life	Polycystic kidneys Often confused with ADPKD	May have no cysts at birth but may resemble ADPKD later in life	Delayed development of cysts Renal failure may follow appearance of cysts	Girls that survive may develop renal failure

D. Chromosomal Disorders Associated with Renal Cysts

Trisomy 13 (Patau's syndrome) Trisomy 19 (Edwards' syndrome) Trisomy 21 (Down syndrome)	Renal cystic changes usually not significant Cysts are microscopic (subcortical, glomerular or dysplastic cysts)

FIGURE 14-13. (*Continued*)
von Hippel–Lindau disease (VHL) is an autosomal dominant syndrome characterized by cysts of the pancreas, kidney, and epididymis. It is also associated with cerebellar hemangioblastomas, retinal angiomata, renal cell, and pheochromocytomas [35,36]. About 60% of patients with VHL have renal cysts [37]. Renal cell carcinoma is found in 25% to 45% of patients, and it is commonly multifocal and bilateral [38]. Screening for renal cancer is essential for these patients because it is the most common cause of death in patients with VHL [39]. **B–D,** Some of the more common malformation syndromes associated with cysts are categorized according to mode of transmission.

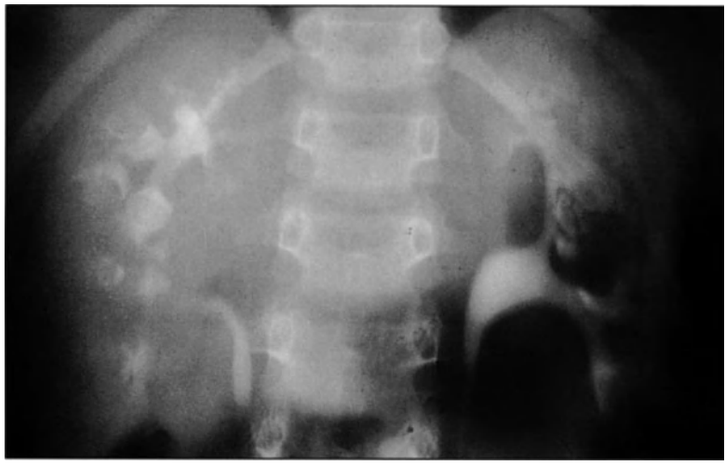


FIGURE 14-14
Medullary sponge kidney (MSK). MSK is a developmental disorder characterized by cystic and ectatic malformation of the collecting ducts and tubules [40]. The prevalence of MSK in renal stone formers is significantly higher than that in the non–stone-forming population (8.5% vs 1.5%). However, the prevalence in the general population is unknown because a significant number of people with MSK are not symptomatic [41]. MSK is not inherited and is often associated with developmental disorders, including congenital hemihypertrophy [40], anodontia, Caroli's disease, and Ehlers-Danlos syndrome [42]. The patient with MSK is usually not symptomatic before 20 years of age, and most initially present with renal colic. The patients can also present with urinary tract infections and hematuria [43]. MSK histologically is characterized by small medullary cysts and dilated intrapapillary collecting ducts. The cysts may communicate with each other, and with the proximal collecting tubule and calyx. The intracystic milieu of cellular debris, defect in renal acidification, and high urine pH leads to the formation of calcified intraluminal concretions composed of calcium oxalate or apatite [44]. These concretions can erode through the cyst wall and papillary wall, and pass into the renal pelvis as a stone. The best test to diagnose MSK remains intravenous urogram. The classic urographic findings are renal enlargement, papillary calcification, and elongated linear papillary contrast blush. Hypercalciuria is seen in 40% to 50% of patients, and MSK can be associated with hyperparathyroidism.

Shown is an intravenous urogram in a 9-year-old girl presenting with hematuria and found to have MSKs. Note the characteristic papillary blush and puddling adjacent to each calyx. (*From* Glassberg *et al.* [45]; with permission.)

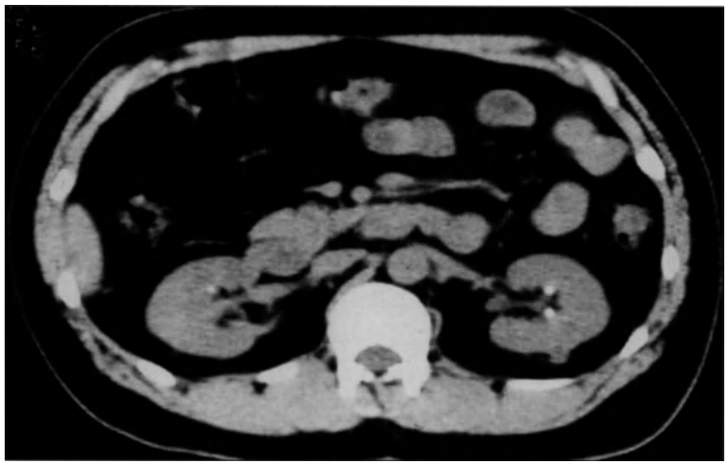


FIGURE 14-15.
Spiral CT demonstrating renal papillary calcifications in both kidneys. CT scan can be used when a patient has poor renal function or the intravenous urogram is compromised by overlaying stool or bowel gas.

The management of medullary sponge kidney (MSK) deals mainly with calculus formation and infection. In those patients diagnosed with renal stones, the management is the same as that used for the patient without MSK. The stone clearance rate using extracorporeal shock-wave lithotripsy is similar to that of patients without MSK [46]. Thiazides may be administered to reduce hypercalciuria and limit stone formation. Alkalinization and the use of inorganic phosphates may be appropriate in certain cases. The long-term prognosis is good as long as stones and urinary tract infections are treated effectively.

SPORADIC GLOMERULOCYSTIC KIDNEY DISEASE

Conditions Associated with Glomerular Cysts

- Multiple malformation syndromes
  - Meckel's syndrome
  - Trisomy 13
  - Tuberous sclerosis
  - Zellweger's syndrome
  - Orofaciodigital syndrome type I
  - Short rib polydactyly
  - Renal-hepatic-pancreatic dysplasia
  - Brachymesomelia renal syndrome
- Autosomal dominant polycystic kidney disease
- Juvenile nephronophthisis in association with hepatic fibrosis
- Familial hypoplastic glomerulocystic disease
- Sporadic glomerulocystic kidney disease

FIGURE 14-16.
Conditions associated with glomerular cysts. The term *glomerulocystic* designates that cysts of Bowman's space or glomeruli are present diffusely and in both kidneys. The presence of glomerular cysts does not prove that the patient has glomerulocystic disease. Cysts of the glomeruli are seen in many conditions. Classically, glomerulocystic disease is defined as a noninheritable condition, producing bilaterally enlarged kidneys, which contain cysts in Bowman's space [46]. Recently, a large, three-generation black family with glomerulocystic kidney disease seen in all generations was studied. Linkage studies demonstrated a locus distinct from autosomal dominant polycystic kidney disease loci (*PKD1* and *PKD2*) that was transmitted from a father to his sons, suggesting autosomal dominant transmission. This study suggests that dominantly transmitted glomerulocystic kidney disease is a distinct genetic entity, not a new mutation of autosomal dominant polycystic kidney disease [47]. This finding further confuses the classification of glomerulocystic kidney disease. Nevertheless, as more of the human genome is studied, these areas may be elucidated.

ACQUIRED RENAL CYSTIC DISEASE

FIGURE 14-17.
Acquired renal cystic disease (ARCD). ARCD was initially thought to occur only in patients on hemodialysis, but it appears to be a feature of end-stage kidney disease, even before the initiation of hemodialysis and in patients receiving peritoneal dialysis [48]. The lack of uniform criteria to define ARCD has led to a wide range of reported incidences. ARCD may be seen in as many as 8% to 13% of azotemic patients not treated with dialysis [49,50]. The condition is seen more frequently in patients on hemodialysis because hemodialysis extends the time that cysts can develop. The prevalence of ARCD is 10% to 20% at 3 years of hemodialysis, 40% to 60% at 3 to 5 years of hemodialysis, and greater than 90% after 5 to 10 years of hemodialysis [49]. Serial radiologic imaging has demonstrated an increase in renal volume and cyst number with time [51]. The exact mechanism underlying cyst formation is not known. It is postulated that interstitial scarring and progressive loss of renal tissue leads to tubular obstruction. In turn, there is an accumulation of cystogenic substances causing the hyperplasia and hypertrophy of surviving nephrons with accumulation of fluid in the hyperplastic renal tubule [52]. ARCD affects both sexes, but the severity of cystic transformation appears to be greater in men than in women [53].

This renal sonogram of a 10-year-old patient on hemodialysis for 3 years shows increased renal echogenicity, loss of corticomedullary differentiation, and multiple sonolucent areas that represent cysts.

The majority of patients with ARCD are asymptomatic, but they can present with retroperitoneal hemorrhage and metastatic renal carcinoma [54]. There appears to be a three- to six-fold increased incidence of clinically significant renal cancer in dialysis patients [55,56].

This renal sonogram of a 10-year-old patient on hemodialysis for 3 years shows increased renal echogenicity, loss of corticomedullary differentiation, and multiple sonolucent areas that represent cysts.

Many questions are raised regarding the management and radiologic imaging of patients with acquired cystic disease. Cardiac disease, infection, cerebrovascular accidents, and withdrawal from dialysis account for most deaths of patients on dialysis, not malignancies [57]. It has been suggested that because the frequency of ARCD increases significantly after 3 years of dialysis, screening should be instituted after completion of the third year of dialysis [49]. An effective screening program would require annual ultrasound or CT scans. Sarasin *et al.* [50] concluded that the average gain in life expectancy was not large enough to justify routine screening in older dialysis patients. They found that the mortality rate associated with radical nephrectomy for the discovery of small asymptomatic renal tumors in the older dialysis patient with severe cardiovascular disease may actually decrease the survival time for these patients [50]. Several authors have suggested a selective screening program of patients with known risk factors for carcinoma, including prolonged dialysis [58], male gender [59], and large kidneys [60]. The literature on the influence of renal transplantation on ARCD and renal neoplasms after transplantation is contradictory. In a longitudinal study of transplant recipients, Ishikawa *et al.* [61] showed variable responses of renal cysts in the native kidneys of patients with successful renal transplantation. Some patients showed an increase in the number of cysts, whereas some showed a decrease [61]. It has been postulated that ARCD patients who have undergone successful renal transplantation are at an increased risk for developing renal cancer in their native kidneys due in part to immunosuppressive therapy [62]. Several authors reject this theory, and some have found that the prevalence of renal cell carcinomas is the same in patients with ARCD on hemodialysis or post-transplantation [63,64]. The prospective transplant recipient should have a renal ultrasound preoperatively. Also, because most of these patients have routine ultrasound studies of the transplanted kidney, the native kidney should be imaged at the same time. (Courtesy of RH Barth, MD.)

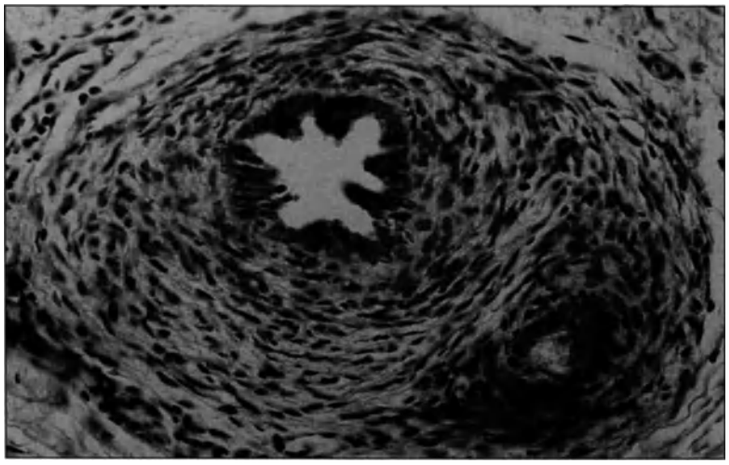


FIGURE 14-18.
Multicystic dysplastic kidney (MCDK). A primitive duct is seen with the concentric arrangement of connective tissue and smooth muscle encircling the duct. This is a typical finding in the dysplastic kidney.

MCDK is a nonhereditary, developmental anomaly associated with multiple cysts of variable size and number in one or both kidneys. Unilateral MCDK is one of the most common abdominal masses in the newborn and is the most common form of renal cystic disease in children [65]. Both sexes are affected equally [66]. Most children have no symptoms, but there is a relatively high incidence of contralateral anomalies, including ureteropelvic junction obstruction and other ureteral anomalies [67,68]. The left kidney is more commonly involved, just as it is in primary congenital megaureter and ureteropelvic junction obstruction [69,70]. There have been isolated reports of the association of MCDK with hypertension, malignancy, and infection, but the true incidence may be no higher than for normal kidneys. When a child is born with bilateral multicystic kidneys, they are often stillborn or die soon after birth [67]. These children usually have Potter facies and severe pulmonary hypoplasia due to oligohydramnios [71]. The most common presentation in adults is abdominal pain that resolves after nephrectomy in half of the patients [72]. The role of nephrectomy may be justified to treat symptoms. No study has clearly shown an increased incidence of malignancy or hypertension in the patients with MCDK [73]. (*From* Glassberg [74]; with permission.)

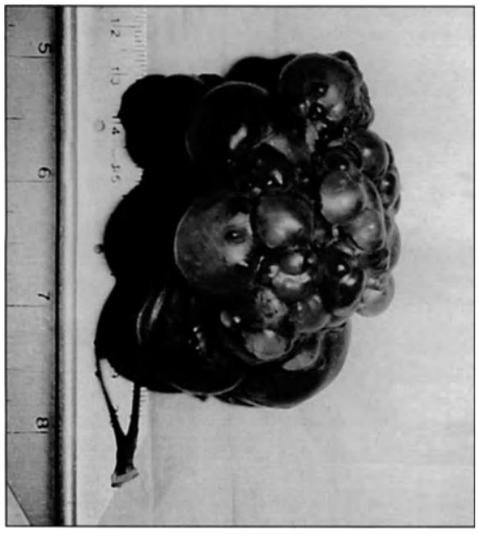
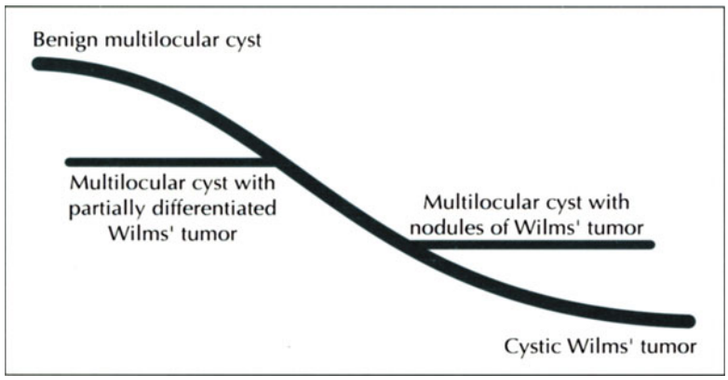
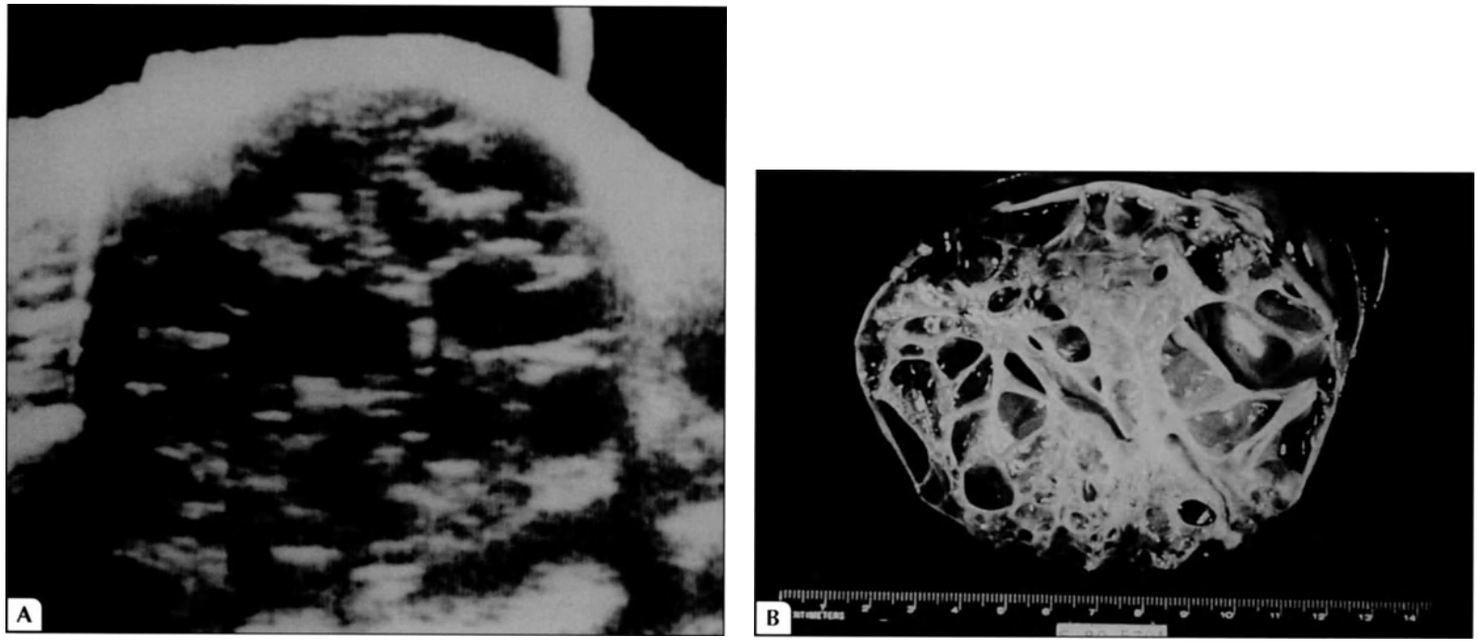


FIGURE 14-19.
Multicystic dysplastic kidney with multiple cysts and minimal renal parenchyma. This is typically called a "bunch of grapes" and represents a Potter type II A form. Grossly, multicystic dysplastic kidney (MCDK) is composed of multiple cysts with little or no normal renal parenchyma. MCDK is associated with an atretic or absent ureter, atresia or hypoplasia of renal pelvis, and small or absent renal artery [71]. Microscopically, there are primitive glomeruli, primitive ducts lined by tall columnar epithelial cells surrounded by concentric rings of connective tissue, cartilage, and an occasional mature glomerulus [75]. Two forms of dysplasia are described: multicystic dysplasia and diffuse cystic dysplasia. In multicystic dysplasia, the cysts tend to be larger with minimal stroma present. In diffuse cystic dysplasia, the cysts tend to be smaller with more stroma. Potter referred to the large cystic variety as type IIA and the smaller cystic variety as IIB disease [76]. Cysts in MCDK are classically described as noncommunicating. However, recently, Glassberg *et al.* [77] studied seven multicystic dysplastic kidneys with ex vivo intracystic contrast injection and found communication between cysts in all.



◗ FIGURE 14-20.
The spectrum of neoplastic lesions ranging from multilocular cyst to cystic Wilms' tumor. Currently, most pregnant mothers have antenatal sonograms and the urologist is called on to evaluate more newborns with antenatally diagnosed hydronephrosis. The most important distinction to make is between hydronephrosis and multicystic kidney. In the patient with multicystic dysplastic kidney (MCDK), ultrasound reveals a lateral location of larger cysts, visible interfaces between cysts, and absence of a distinct renal sinus [78]. The cysts tend to be haphazardly distributed, with minimal renal parenchyma identifiable [78]. The patient with ureteropelvic junction obstruction has a dilated renal pelvis with communications to the dilated renal calyces. If the diagnosis is unclear, a ^{99m}Tc-mecaptoacetyltriglycine or ^{99m}Tc-dimercaptosuccinic acid renal scan may be used. The obstructed kidney usually demonstrates function with collection of contrast in the dilated renal pelvis, whereas the MCDK concentrates only enough agent to be faintly visible. The study also allows the physician to evaluate the function of the contralateral kidney [79]. Voiding cystourethrography should also be used in the initial work-up to rule out contralateral vesicoureteral reflux that can be seen in 20% to 28% of the patients with MCDK [67,80]. Early management of these patients deals with the contralateral kidney. The MCDK is usually only removed in the neonate if it is so large that it causes feeding or respiratory problems. The dysplastic kidney decreases in size in 60% to 65%, disappears in 20%, increases in size in 15% to 19%, and remains unchanged in 3% to 16% [81,82]. The majority of multicystic dysplastic kidneys that decrease in size or undergo complete involution do so over the first 2 years of life [83]. The debate over operative and nonoperative management of neonatal dysplastic kidneys continues. The child with unilateral MCDK is at minimal risk for infection, pain, or hypertension. The primary concern is always malignancy, but with a maximum risk of 0.1% for the development of the Wilms' tumor, controversy exists as to the benefit of any screening regimen [84]. Most urologists would advocate nephrectomy if the diagnosis is uncertain, if adequate follow-up is not possible owing to social issues, or if the patient is symptomatic [85].

Multilocular cystic nephroma (MCN). The definition of a multilocular cyst is somewhat unclear. It is not a renal segment affected by multicystic disease, and it is not clear if it is a harmartomatous malformation, a neoplasm, or a segmental form of dysplasia. The multilocular mass in a kidney can be a benign multilocular cyst, a multilocular cyst with partially differentiated Wilms' tumor, multilocular cysts with nodules of Wilms' tumor, or a cystic Wilms' tumor. Beckwith and Kiviat [86] believe that the multilocular cyst lies at one end of a spectrum and cystic Wilms' tumor at the other. It is not proposed that one lesion transforms into the other, but all of these lesions may derive from similar tissue. Hemihypertrophy and aniridia, which are often associated with Wilms' tumor, have not been seen in a patient with a multilocular cyst [87]. MCN in men has two peak ages: less than 4 years old and again in the 50s or 60s. In women, two peaks are seen: 4 years old to the age of 20 and again between the ages of 40 and 60. Children usually present with an asymptomatic flank mass, whereas adults present with hematuria or abdominal pain [88]. The hematuria in adults is secondary to herniation of the cyst through the calyx into the collecting system [89]. MCNs are almost always unilateral, but there have been a few reported instances of bilateral multilocular cysts [90,91].

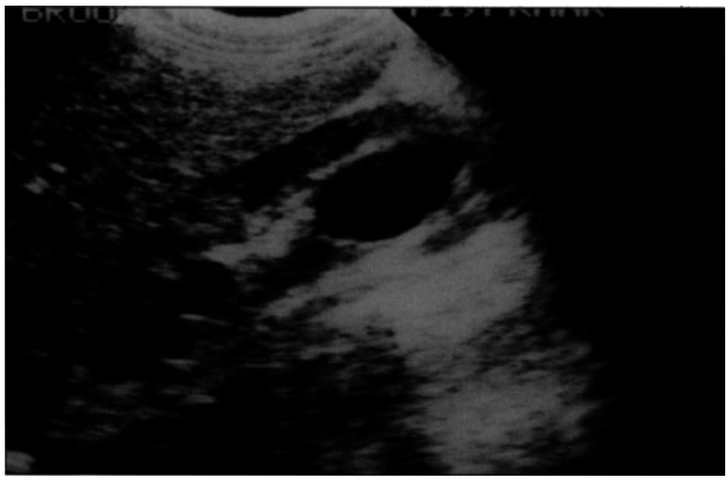


◗ FIGURE 14-21.
Benign multilocular cyst. **A,** Renal ultrasound of a kidney with a large mass having sonolucent cystlike areas. Note the bright white areas representing the posterior cyst walls that are acoustically enhanced by the cyst fluid. **B,** Sagittal section through the kidney demonstrates a multinodular cyst and a crescent of preserved renal parenchyma in the lower right corner.

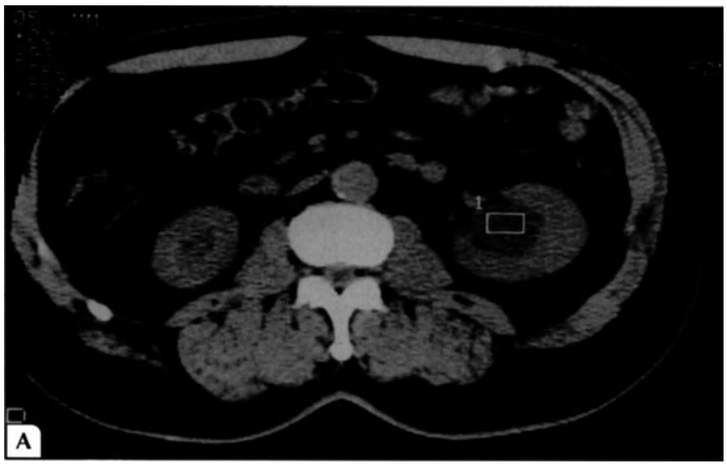
Grossly, a multilocular cystic nephroma is a bulky, sharply demarcated lesion with a thick capsule. The cysts are distinct from the adjacent normal renal parenchyma. As the lesion grows, it may encroach on the renal pelvis, compress adjacent renal parenchyma, or extend beyond the renal capsule into surrounding perinephric fat. The loculi may range in size from several millimeters to several centimeters. The loculi are lined by low columnar or cuboidal epithelium and filled with a straw-colored fluid. There is no communication between loculi [92]. The septa contain collagenous tissue and spindle cells but no nephrons. When the septa contain embryonic mesenchyme or primitive tubules, the exact nature of the lesions comes into question, which may lend credence to the lesion being part of a neoplastic spectrum [93,94].

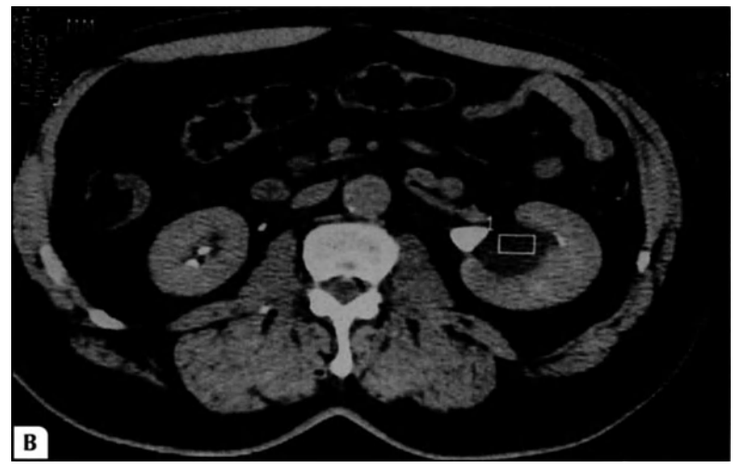
A benign multilocular cyst probably represents a neoplastic lesion; therefore, the term *multilocular cystic nephroma* is preferred by some. This term should only be used when the lesion is composed entirely of differentiated tissues, with no embryonal or blastemal elements. The designation of "multilocular cysts with partially differentiated Wilms' tumor" should be applied to those cystic lesions lacking nodular regions, with blastemal or embryonal cells present in the septa of the cysts [95]. The term *multilocular cyst with nodules of Wilms' tumor* is used when there are distinct nodules of Wilms' tumor. The lesion at the end of the spectrum, cystic Wilms' tumor, is a Wilms' tumor with cysts lined by epithelial cells. Some Wilms' tumors can contain areas of cystic hemorrhage or necrosis, but these regions are not lined by epithelium and should not be referred to as a cystic Wilms' tumor.

Sonography, magnetic resonance imaging, or CT can differentiate multicystic kidney and multilocular cyst. None of these studies, however, can distinguish multilocular cyst, multilocular cyst with foci of adenocarcinoma or Wilms' tumor, clear cell sarcoma, congenital mesoblastic nephroma, or cystic Wilms' tumor. Spiral CT has improved the quality of images but has done little to differentiate these entities radiographically [96]. Sonographically, the loculi are sonolucent, the septa highly echogenic, and a distinct capsule is visualized. On CT, the normal renal parenchyma is more dense than the septa of the loculi. The loculi can contain debris and almost appear solid on CT. Angiography is rarely helpful in the diagnosis but can localize arterial supply for preoperative embolization [96]. The treatment of a multilocular cyst is nephrectomy. If a cystic Wilms' tumor is found, then the patient should be treated in accordance with the National Wilms' Tumor study recommendations. These patients with cystic Wilms' tumor usually present before the age of 1 year, and the tumor usually is not as aggressive as the classic Wilms' tumor [97]. The nonaggressive nature of the tumor questions whether therapy beyond a nephrectomy is really necessary. Nephrectomy is, as a rule, curative, but cystic Wilms' tumor have recurred locally and metastasized [98]. If a patient has a favorable histology and adequate renal parenchyma, a partial nephrectomy can be performed. These patients need close CT follow-up [99]. (*From* Glassberg [100]; with permission.)



◗ **FIGURE 14-22.**
Large lower pole simple cyst and smaller more central cyst in a 9-year-old boy. Note the white area behind the large cyst representing acoustic enhancement, a characteristic finding of simple cysts.





◗ **FIGURE 14-23.**
CT of a simple cyst adjacent to the renal pelvis (*ie*, a parapelvic cyst).
A, CT without contrast reveals fluid with 3 Hounsfield units (H).
B, Following contrast, there is no enhancement, which is a characteristic of simple cysts.

Simple renal cyst. The simple renal cyst constitutes the majority of renal masses discovered by radiologic methods. A simple renal cyst is lined by a single layer of flat or cuboidal epithelium, with the cyst wall containing no renal elements. Renal sonography performed on 686 healthy volunteers revealed that prevalence of simple renal cysts was 5.2%, ranging from 0% at age 30 to 9.7% at age 70 [101] Despite these data, simple renal cysts are known to occur on rare occasions in children. Their data suggest that an average renal cyst needs about 10 years to reach 2 cm in size [101]. Simple renal cysts vary greatly in size, ranging from several millimeters to greater than 10 cm. The majority are usually less than 2 cm in diameter [102]. Most studies have shown no gender predilection. Kissane and Smith [17] found that more than half of the adults over 50 years old had simple renal cysts at autopsy. The most common presentation of a simple cyst is as an "incidentaloma" discovered on CT scan, urography, or sonography for other abdominal complaints. They can present as an abdominal mass, or with abdominal pain, but this is uncommon. Patients have presented with hematuria when a cyst ruptures into the caliceal system, but this is rare [103]. Intraparenchymal renal cysts are able to increase internal hydrostatic pressure, causing segmental ischemia and subsequent hypertension [101].

Magnetic resonance imaging (MRI) of simple renal cyst. The classic benign cyst sonographically has a sharply marginated smooth wall, allows thoroush transmission of sound waves with subsequent acoustic enhancement behind the lesion, produces no internal echoes, and is spherical or ovoid in shape [104]. The CT scan definition of a simple cyst is a well-marginated, nonenhancing, homogeneously low attentuation lesion (0 to 20 H) with thin, smooth walls [105]. These CT criteria are sufficient to exclude malignancy and do not require further evaluation [106]. The simple cyst has no vascular supply and does not communicate with the nephron; therefore, it does not enhance. A lesion is considered to enhance if "any portion of the mass demonstrates a rise in CT attenuation or at least 10 to 20 H following the intravenous injection of contrast media"[107]. The fluid in a benign cyst may, however, have a delayed enhancement several days after contrast injection [108]. Cyst puncture with contrast injection or aspiration, which was popular in the 1970s, is rarely performed today. MRI has a limited role in the classification of a simple cyst. The most common indication for a MRI of the kidney remains the detection of inferior vena cava extension in renal cell carcinoma [109]. Although T_1-weighted images are useful in identifying intracystic fluid, T_2 images are useful for identifying bloody intracystic fluid, *ie*, as an extremely bright image. MRI would also have a diagnostic role in the patient with renal insufficiency or dye allergy.

Bosniak Classification of Cystic Renal Lesions Based on CT Features

Category	CT Features	Treatment
I. Simple or benign cysts	Anechoic lesion with sharply marginated smooth wall Nonenhancing	Monitor
II. Complicated cyst	Thin border-forming calcification with no nodularity or soft tissue mass Thin septa in cyst	Monitor
III. Indeterminant cyst	Contain some features of malignancy Thick calcified wall Many septations Thickened cyst wall	Individualized approach
IV. Malignant cystic lesions	Definite solid features Irregular or thick margins Large or non–border-forming calcifications Unequivocal enhancement	Radical nephrectomy; partial nephrectomy in selected cases.

FIGURE 14-24.
Bosniak classification of cystic renal lesions based on CT features. The Bosniak classification classifies cystic lesions based on certain imaging features [110]. Bosniak defines four categories of renal cysts: I, benign simple cyst; II, complicated cyst; III, indeterminant cyst; and IV, malignant lesion. A category I lesion is a simple cyst and meets all the criteria for a simple cyst. The work-up can end with a renal sonogram if the lesion is sharply marginated, anechoic, and smooth walled. No CT confirmation is needed [111]. If the lesion is septated, is nodular, contains calcifications, or is poorly visualized on ultrasound, then a CT is warranted. Category I lesions are benign. Category II lesions are complex cysts. They are cysts that contain small amounts of border-forming calcification, thin septa, and no soft tissue mass or nodularity. Bosniak also includes the "hyperdense cyst" in category II. A hyperdense cyst is a well-defined lesion with smooth walls that on nonenhanced CT is homogeneously hyperdense (40 to 90 H). The lesion does not enhance with the administration of contrast. Category II lesions are almost certainly benign, but the risk of malignancy is higher than for category I. Category III lesions are indeterminant and present us with our toughest diagnostic dilemma. An example of category III lesion is a cyst with numerous thin septa or a thick calcified wall. These lesions include hemorrhagic cysts, multiloculated cysts, complex septated cysts, cystic renal cell carcinoma, and multilocular cystic nephroma. Category III lesions almost uniformly require exploration. Weyman *et al.* [112] found 50% of these lesions to be malignant on removal. Category IV lesions are cystic lesions with definite solid features, such as irregularly thickened margins, thickened septa, large or non–border-forming calcifications, or unequivocal enhancement. Curry *et al.* [113] found that lesions meeting three or more of these criteria had a 96% chance of malignancy. These lesions are to be considered cancer until proven otherwise. Radical nephrectomy and possibly (in selected cases) partial nephrectomy are indicated.

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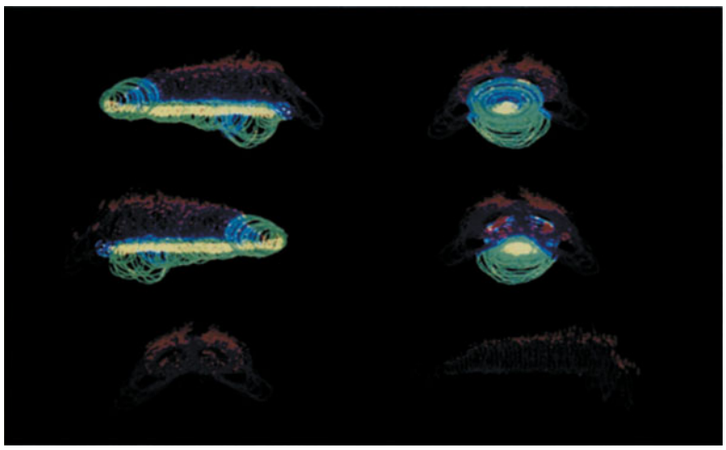
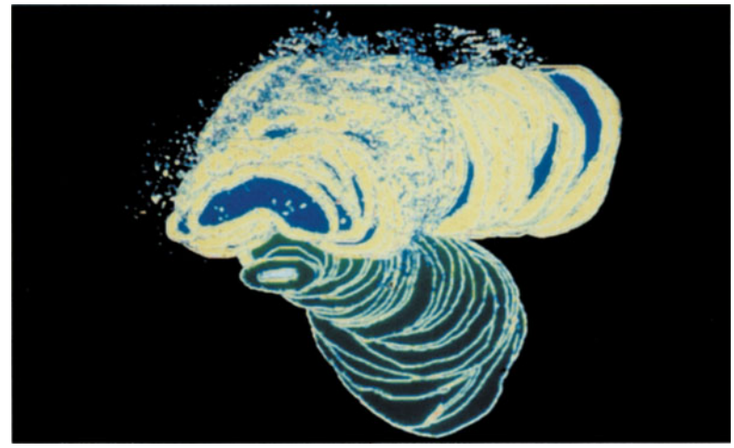
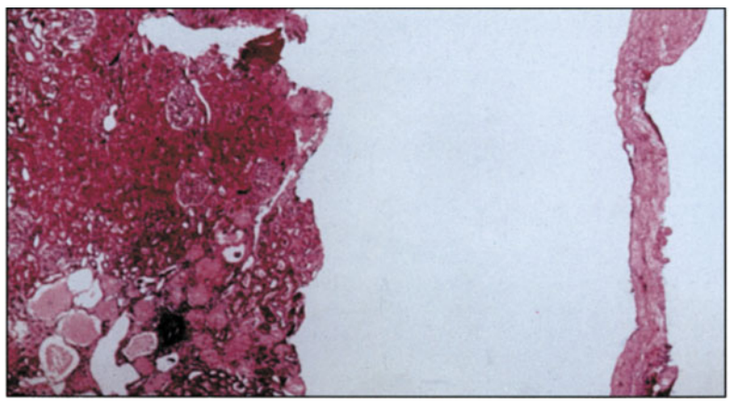
INDEX



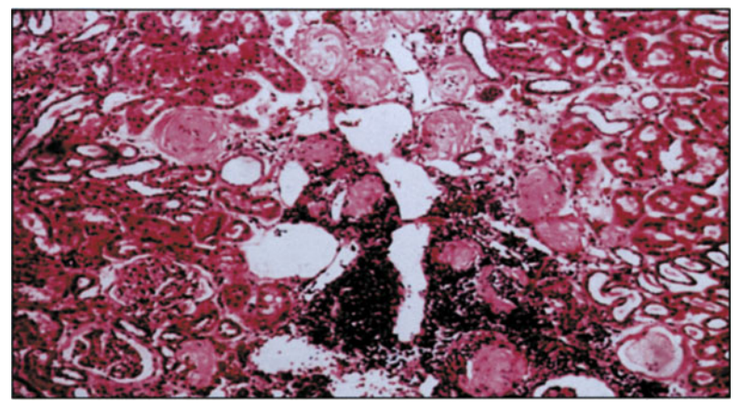
◗ FIGURE 6-4.



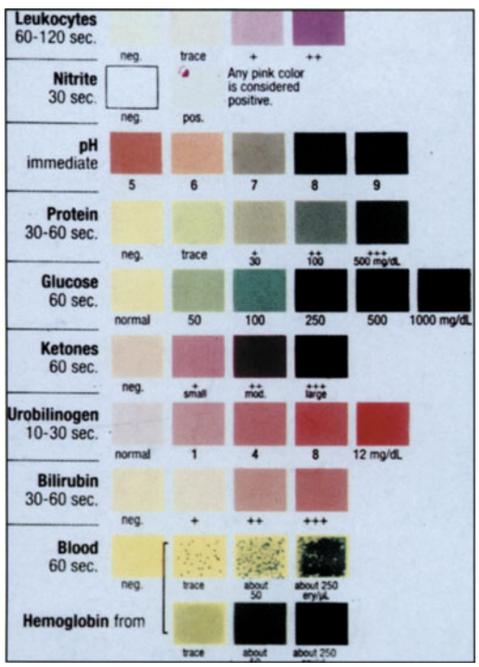
◗ FIGURE 6-6.



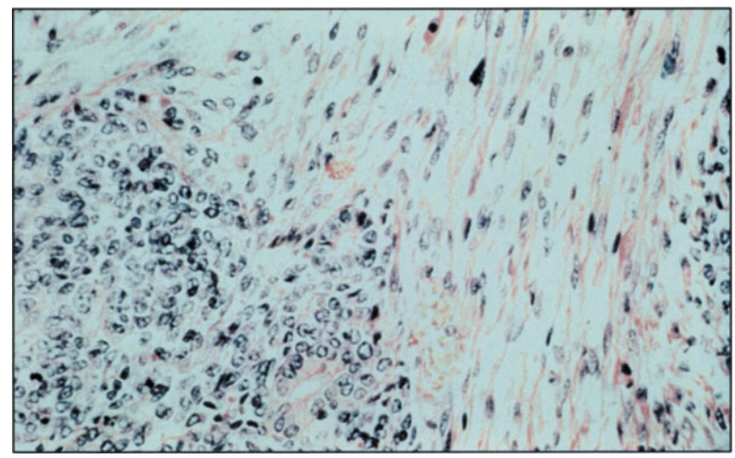
◗ FIGURE 9-14A.



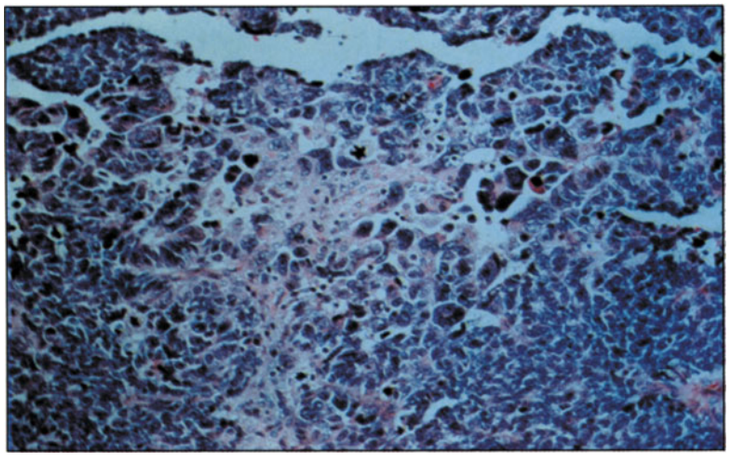
◗ FIGURE 9-14B.



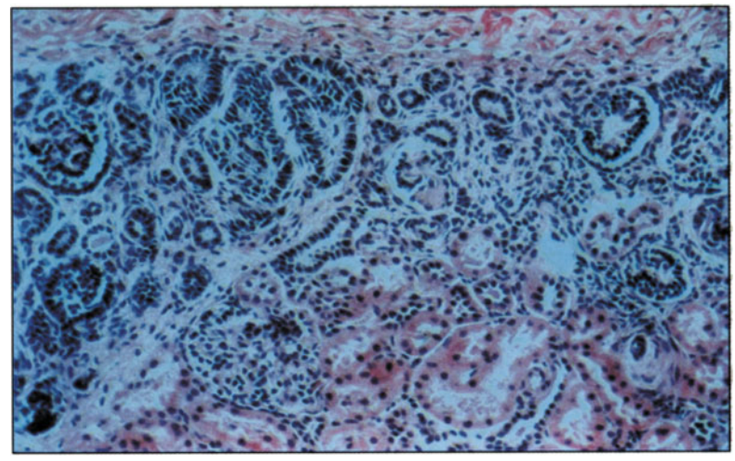
◗ FIGURE 9-18B.



◗ FIGURE 13-8A.



◗ FIGURE 13-8B.



◗ FIGURE 13-9.